Giorgi Javakhishvili

CXCR4, UB, SDF1 and TnI protein analysis in non-damaged myocardium and in myocardial infarction

Under the Supervision of Professor Rusudan Sujashvili

New Vision University
Tbilisi
2022

Giorgi Javakhishvili

CXCR4, UB, SDF1 and TnI protein analysis in non-damaged myocardium and in myocardial infarction

New Vision University

Tbilisi, 2022

Under the Supervision of Professor Rusudan Sujashvili

Abbreviations

ACS – Acute coronary syndrome
ADP – Adenosine diphosphate
ATP – Adenosine triphosphate
AVP – Arginine vasopressin
CABG – Coronary artery bypass graft
CAD – Coronary artery disease
cAMP – Cyclic adenosine monophosphate
CDC – Center of disease control
CHD – Coronary heart disease
CHF – Congestive heart failure
CKD – Chronic kidney disease
CKF – Chronic kidney failure
CK-MB – Creatinine kinase muscle brain isozyme
CMR – Cardiac magnetic resonance
CP – Catalytic part
CRP – C-reactive protein
CSF – Cerebrospinal fluid
CVD – Cardiovascular disease
CXCL12 - C-X-C motif chemokine 12 (Also known as SDF1)
CXCR4 - C-X-C Motif Chemokine Receptor 4
DAMP – Damage associated molecular pattern molecule
DAPT – Dual antiplatelet therapy
DUB - Deubiquitinating enzyme
ECG – Electrocardiogram
ELISA – Enzyme linked immunosorbent assay
ESR – Erythrocyte sedimentation rate
ER – Emergency
HBD3 - Beta-defensin-3
HIV- Human immunodeficiency virus
Hs-cTt – High sensitivity cardiac troponin test
HMGB1 - High mobility group box 1 protein
IVUS – Intravascular ultrasound

kDa – Kilodalton

Kt/V – K-dialyzer clearance of urea, t-dialysis time, V-volume of distribution of urea, measurement of adequacy of dialysis

MI – Myocardial infarction

MIF - Migration inhibitory factor

MINOCA – Myocardial infarction without occlusion of the coronary arteries

PCI – Percutaneous coronary intervention

PE – Pulmonary embolism

RF – Rheumatoid factor

RP – Regulatory part

SDF1 – Stromal derived factor 1 (Also known as CXCL12)

SPECT – Single photon emission tomography

STEMI – ST segment myocardial infarction

SOB – shortens of breath

TEC – Transthoracic echocardiography

TnC – Troponin C

TnI – Troponin I

TnT – Troponin T

TRF - time-resolved fluorometry

UA – Unstable angina

UB – Ubiquitin

UPS – Ubiquitin proteasome system

US – Ultrasound

Acknowledgements:

I would like to thank my friend and colleague Irina Ioramashvili for all the help and support with my thesis and Miss Ia Avaliani MD, PhD far helping with patient finding and selection.

Tasks and porpoise of our research

Despite the high diagnostic value of cTn in MI, increased cTn levels are known in patients with Myocarditis and Chronic CKF. Patients with CKF have increased levels of creatine kinase-myoglobin binding protein (CKMB) and cTn. ECG can be normal or inconclusive in ischemia and MI partially due to electrolyte abnormalities in CKF. Time of diagnosis and treatment determines the outcome of MI. Therefore, it's the porpoise of our research to help decrease morbidity and mortality in undiagnosed/silent cases of myocardial infarction. To accomplish that, our tasks are to study UB, CXCR4 and SDF1 proteins as alternative markers in MI cases, where the standard markers are useless or inconclusive. For that porpoise we needed to compare the effectiveness of the before-mentioned proteins with classic gold-standard markers in controlled situations where the diagnosis (MI or No Damage), levels of troponin, cardiac artery occlusion levels, etc. were already known. 120 (60 healthy and 60 MI) patients were chosen to see how our proteins of interest would work as markers of disease/healthy states. Patients with UA were excluded from the experiment as troponin levels are normal in UA despite significant sichemia. Also, patients with CKD regardless of the diagnosis were excluded from the study as they might have had baseline elevations of troponins. UB, SDF1 and CXCR4 protein levels of proteins were measured by ELISA test and further statistical analyses conducted to determine effectiveness of proteins as alternative markers of MI. Patients were divided into MI and NoDamage groups and all three proteins showed statistically significant difference between groups and being higher concentration in MI groups. MI and NoDamage groups were divided by sex. The important differences between groups were shown in male patients, while no statistically significant difference for UB, CXCR4 and SDF1 was observed in female group, leading to a conclusion that

previous difference in MI/NoDamage groups without gender was due to male group. When MI patients were divided into STEMI and NSTEMI groups and compared to NoDamage group only UB was statistically different for STEMI/NoDamage and NSTEMI/NoDamage comparison while for CXCR4 and SDF1 difference was observed in STEMI/NoDamage group. ROC was constructed for the proteins of interest to test their usefulness as MI markers. The initial results were confirmed showing UB having high AUC for STEMI and NSTEMI, while CXCR4 and SDF1 had acceptable results for STEMI only having unacceptably high FP results in NSTEMI groups. Although the research was limited by the small number of test subjects and further studies are required to evaluate the value of these proteins as alternative MI markers, the data shows the high potential for UB as alternative troponin marker in complicated MI cases.

Introduction

MI is one of the most common causes of morbidity and mortality around the world. According to the CDC 2019 statistical report the heart disease is still number one cause among the top 10 death causes in United States (1). Introduction of coronary artery stenting and CABG has decreased the morbidity and mortality MI still causes millions of deaths. The most challenging step in treating MI is the time. Time is essential to prevent or minimize the necrosis of the myocardial cells that in turn will prevent mortality and morbidity (e.g. heart failure, mitral valve regurgitation, myocardial wall rupture etc.) As the diagnosis of MI may seem relatively easy considering the specific clinical symptoms associated with it, existence of portable ECG machines which allow for paramedics ECG taking on site, Troponin tests that can detect early myocyte damage, and the cardiac US that can show cardiac wall akinesia there are a lot of MI cases that don't follow the "Classic" presentation. Dull crushing sternal pain can often not be felt in patients with long lasting diabetes because of the damage to the sensory nerves, or pain can be felt as positional mimicking isolated pericarditis in patients with STEMI complicated with pericarditis. Not all MI can be seen on ECG for example posterior wall MI. And not always is myocardial damage or death associated with visible

akinesia of the ventricular wall on cardiac US. Finally the troponin which will be the main focus of our future study along with UB, CXCR4 and SDF1 can be elevated in conditions other than MI. Firstly the recurrent MI occurring several hours to several days after the first one renders troponin useless as the troponin levels stay elevated in blood for 7 to 14 day (2). Troponin can also become elevated during myocarditis, after cardiac defibrillation, CABG and coronary stenting, acute heart failure, PE further complicating the diagnosis of acute MI. Chronically elevated troponin levels occur in patients with severe renal dysfunction and can be especially confusing for cardiologists and ER doctors when a patient presents with chronically elevated troponin levels and mild MI symptoms as in diabetic patients (3). The "false" elevation of troponin can lead to late or non-diagnosis of MI in case of CKF or incorrect diagnosis of MI in case of PE. This leads to increased morbidity and mortality. In some instances CK-MB protein testing can be used. Nowadays CK-MB is replaced by Troponin as it showed superior results in detecting early MI and studies exposed that about 10% of the patients with acute MI were sent home from ER during the time when CK-MB was still widely used as a test marker. The use of CK-MB is especially effective in patients with recurrent MI that occurred hours to days after the first one. Because the plasma concentration of CK-MB peaks at 12 and begins to fall after 24 hours. However, CK-MB has its own limitations. It can be falsely elevated in severely ill patients with cancer or rhabdomyolysis, and like troponin is chronically elevated in patients with CKF (4, 5, 6). This small but just as important subset of patients especially CKF patients having MI with minor confusing symptoms Troponin and CK-MB are not very predictive. For this group clearly other markers for early detection of myocyte damage should be looked for to minimize the misdiagnosis, treatment time and of course mortality. Measuring the levels of UB CXCR4 and SDF1 in serum may prove helpful in detecting myocardial damage in situations when Troponin and CK-MB are not predictive and clinical symptoms are confusing.

UB is a small globular protein that plays a role in huge number of cellular and extra-cellular processes including protein degradation, repair of damaged DNA, cell movement and immunity (7). UB has also demonstrated a role in various cardiac diseases including ischemia and MI. For a long time, UPS was considered to play an essential role in cardiac remodeling and several experimental models showed cardio protection after inhibiting the UPS. But another experiment showed the exogenous UB to decrease heart damage in ischemia-reperfusion injury in MI after stenting or CABG (8,9). SDF1 and its membrane receptor CXCR4 have long been studied in human MI and laboratory MI models. SDF1 levels often rise after MI and it promotes the mobilization of bone marrow stem cells to the damaged myocardium (10). In addition, artificial upregulation of SDF1 levels in rats with MI showed better engraftment of bone marrow stem cell in the damaged myocardial tissue and hence better cardiac function (10, 11). SDF1 and UB both are the ligands for CXCR4 receptor. UB binding to the CXCR4 promotes similar effects as SDF1 (Chemotaxis, Ca^{+2} mobilization etc.). Although they appear to interact with different CXCR4 regions. SDF1 interacts with N-terminal region of CXCR4 and extracellular loops 2 and 3 while UB only interacts with loops (12). Considering all these factors these proteins could serve as a potential marker for detection of myocardial injury when testing is complicated by other traditional means.

We decided to measure the levels of UB CXCR4 and SDF1 in healthy and MI patients, compare their levels in this groups and compare their correlation with each other (since they are in a receptor ligand relationship) and troponin. In the conducted trial we had 60 patients with no ischemia (30 males and 30 females), 25 patients with NSTEMI (15 males and 10 females) and 35 patients with STEMI (20 males and 15 females). Patients who had UA demonstrated by cardiac specific pain or other symptoms, ECG, cardiac ultrasound, negative TnI and hemodynamically significant ischemia on coronarography that required stenting were not included in this experiment as we wanted to compare the diagnostic effectiveness of the before-mentioned proteins compared

to Troponin for future diagnostic use where Troponin is constantly elevated (Specifically CKF patients with MI) and Troponin is not elevated in UA. Also, patients with CKD regardless of the diagnosis were excluded from the study as they might have had baseline elevations of troponins. All the patients were admitted to the same hospital with chest pain suggestive of ACS. The age, gender and the associated diseases of all patients are known. All of them had ECG done during the pain episodes, cardiac ultrasound was performed and serum TnI was measured with AQT90 method described below. The Elisa test of the UB, SDF1 and CXCR4 proteins was performed on the same serum samples used to measure TnI. Finally, coronarography for all the patients serving as a gold standard to diagnose coronary artery ischemia helped us exclude patients that had increased levels of TnI because of reasons other than MI (for example myocarditis). STEMI and NSTEMI are both diseases caused by coronary artery occlusion, subsequent ischemia, damage and necrosis of the heart muscle. These distinct diagnoses have slightly different treatment protocols in clinical medicine (especially time for allowable delay from diagnosis to coronarography table). Troponin increase above the 99th percentile is considered MI both for troponin T and Troponin I and the numbers above mostly do not play a role for MI diagnosis in medicine. TnI, UB, SDF1 and CXCR4 concentrations were compared to define any significant numerical correlation or regression. In addition, being in a receptor ligand relationship the correlation of UB, CXCR4 and SDF1 was checked to determine positive/negative interdependency in healthy and diseased states. Last but not least we did the ROC test and constructed the AUC curve for UB, CXCR4, SDF1 and Troponin to understand the effectiveness of all three proteins as MI marker test in comparison to the gold standard Troponin.

The statistically significant differences were shown for all studied proteins in STEMI group and concentrations were higher in MI group compared to NoDamage group.

When we divided the MI and NoDamage patients according to sex. UB and SDF1 were statistically different in male MI and NoDamage groups,

while CXCR4 was on the level of statistical significance. For females no difference was observed far all three proteins.

When the patient groups were divided into STEMI, NSTEMI and NoDamage groups UB proved and excellent marker for MI showing the statistically important difference between NoDamage/STEMI and NoDamage/NSTEMI groups. As for CXCR4 and SDF1 the difference was shown for NoDamage/STEMI groups only.

ROC curves showed sensitivity of test for UB 89% (STEMI) and 90% (NSTEMI), while for CXCR4 and SDF1 about 80% (STEMI) and about 50% (NSTEMI).

As our research was limited due to relatively low number of patients further studies are required to understand the effectiveness of UB, CXCR4 and SDF1 as alternative markers for MI.

Literature Survey

Acute coronary syndrome, Myocardial infarction, Unstable angina

ACS is a broad compilation of symptoms that can range from mild pain in the chest to the cardiogenic shock or hemodynamic instability or the pain can be totally gone by the time patient arrives to the clinic. The starting symptom of the ACS is usually tight crushing pain in the left chest or retrosternal area or it can be a symptom equivalent to chest pain like SOB or left shoulder pain. On ECG ACS can be divided into two types: Persistent (>20 minute) ST segment elevation ACS which almost always transforms into STEMI as persistent ischemia damages the myocytes. And non-persistent ST segment ACS, where there can be a short-time (<20 minutes) elevation of segment, depression of the ST segment or the ECG can be normal. This can in turn progress to the NSTEMI if the damage to myocytes occurs or become the UA if the ischemia is present but not enough to damage the myocytes. Although all three STEMI, NSTEMI and UA require revascularization the separate diagnosis of all of them is still important for practicing clinicians. First STEMI always requires immediate revascularization and if it's not available than thrombolysis, while NSTEMI and UA should be revascularized immediately if available

but if not, thrombolysis therapy is not indicated and delayed revascularization considered (up to 72 hours depending on symptoms). Also, while UA has less mortality and morbidity compared to the STEMI and NSTEMI, patients with UA appear to get less benefit from antiplatelet and revascularization therapy (13,14,15,16).

Epidemiology of Myocardial Infarction

CVD is a group of diseases that involves both the heart and blood vessels. It includes CAD that itself includes the CHD and MI. MI being the most common end outcome of CAD and the most common cause of mortality as well. The incidence of MI varies vastly among the world as does the MI mortality. For example, 25-30% of deaths in US still occur because of MI while the numbers are 3 times lower in Japan and in south-east Asia the mortality is 80%. That being said MI is still number one cause of mortality worldwide. The decrease in morbidity and mortality of MI in different countries is attributable to the modifiable risk factors (Discussed below) that account for about 90% of all risk factors and of course better treatment options such as coronary artery stenting and CABG. Health promotion and healthy life-style awareness in Western Europe has decreases both the MI and mortality significantly while the MI cases still continued to increase in Eastern Europe even in early 2000s. Analysis of 2000 – 2017 in US have even found statistically significant difference in MI incidence and mortality after diagnosis in different states. And in china despite the development of medical facilities and focus of Chinese health system on education and prevention of MI risk factors the MI cases continue to increase. The regional difference of MI incidence is mostly attributed to the lifestyle change and modifiable risk factors but ethnicity, age and sex also play a partial role. The MI is about 3 times more prevalent in males than in females. This is being especially evident in young <45 y/o populations. The sex difference of MI and MI mortality begins to decrease at about age 60 and becomes almost the same at the age 75. Ethnicity apparently plays a role in MI as the prevalence of MI among black population is higher than white population in US, while the Latino population has the lowest MI incidence of the three groups. According to the different health organizations the CVD and MI is only going to increase in the future years and the best way to counter this phenomenon is to educate the population to change the modifiable risk factors leading to MI (17-21).

Risk factors leading to MI

There is not a single risk factor that can cause the MI/CAD, rather it's always a combination of factors that ultimately leads to MI. Some risk factors such as age, gender, family history and race are non-modifiable. But luckily a lot of others are partially or totally modifiable and that can account from 80 to 95% of all the risk factors in a given patient. The risk prevention can be primary when a patient without MI can change the lifestyle to prevent it in the future or secondary when a patient who already had the MI is advised to have a healthy lifestyle to minimize the MI complications and chances of future MI recurrence. One of the famous MI risk calculations is a Framingham risk calculation that determines the 10-year risk of MI in patients and allows the doctor to choose the appropriate treatment and lifestyle regiment. The study takes its name after a small town in US where the first CAD risk study was done after the death of president Roosevelt and now a third-generation study is done in the same town to further improve our understanding of the CVD risks. The major risk factors that can be partially or totally prevented with lifestyle or medications include but are not limited to: hypertension, diabetes, obesity, sedentary life, smoking. Modifying this risks can significantly reduce or even prevent MI risks in patients. The data from Nurses Health Study showed that weight, diet, exercise, smoking stopping and moderate drinking reduced the risk factors by 84%. Yet only 3% of women adhered to that regimen. That indicates that the health care system around the world needs to be rethought and modified to educate patients and raise the CAD risk awareness (22-27).

Diagnosis and clinical presentation of MI and ACS

Diagnosis of ACS may seem easy considering the typical symptoms and lots of diagnostic tools and cardiac markers at our disposal (Described below), but just as patients are different from each other by age, sex, weight, height, race, comorbidities, and even pain tolerance (the same intensity of pain can be described as 5 out of 10 by one and 9 out of 10 by another patient), just the same clinical presentation and diagnostic analysis data can vary from patient to patient. IN ACS typical crushing

sternal pain in one patient can be manifested as a fatigue only in another, or a patient with MI can have a "normal" ECG while another one without MI can have a typical ST segment elevation (So called "frozen" elevations present during left ventricular aneurism). Most often the typical symptoms and signs are present in males and younger patients while the atypical ones are often present in women, older patients and patients with diabetes or CKF. A physician should suspect ACS based on symptoms, diagnostic tools, cardiac markers and last but not least risk factors of the patient such as family history past medical history, CVD risk factors etc. No one tool or symptom can diagnose the MI as it is defined as increase of cardiac troponins above the 99th percentile and at least one of these: new changes on ECG indicative of ischemia, symptoms of ischemia, imaging loss of mobility of myocardial wall, or occlusion of the coronary artery detected by coronarography (13). As seen from the above only a skilled and experienced doctor can diagnose and consequently mange the MI especially in the atypical cases which constitute a significant percentage of patients going to the ER with ACS.

Clinical presentation of ACS/MI is quite variable. The most common and typical symptoms are crushing retrosternal pain, left jaw/arm or shoulder pain. However, the pain can be present in the right shoulder or between the scapula and is often accompanied by fear, sweating, nausea, vomiting. More isolated and thus atypical symptoms can be syncope, fatigue, dyspnea or they can be present together with the typical ones. Even the "classic" decrease or total alleviation of pain by nitroglycerin cannot be 100% diagnostic of ACS as nitrates can relief other chest pains (like esophageal spasm). Men and younger patients usually get the typical symptoms while women, older patients and patients with long lasting diabetes mellitus or CKD usually have the atypical ones. Family history, past history of MI, atherosclerosis, CAD, smoking etc. can vastly aid in the diagnosis of ACS. Such taking a little time to take a complete patient history can be important (28-32).

ECG

Although the ECG has been around for more than 150 years it is still an irreplaceable tool in modern medicine. The first ECG from the frog heart was recorded by C. Matteucci in 1842 and later in 1887 A.Waller recorded the first human heartbeat. However, it is W. Einthoven that is considered the father of modern ECG (The term he used first that we use nowadays) because he is the one who mathematically corrected the recorded waves for better comprehension, gave them their corresponding names (P, Q, R, S, T) and developed the concept of Einthoven's triangle. For those achievements he was awarded a noble prize in 1924 three years before his death (33,34).

ECG is used to help detect a wide range of cardiac anomalies: arrhythmias, hypertrophy of the heart chambers, heart blocks, conduction defects, pericarditis, and of course the ischemia and MI. Before we discuss the electrical changes on ECG during ischemia it should be mentioned that ECG is never used as a separate tool to diagnose any cardiac disease. Separate ECG finding for example even as obvious as ST segment elevation can indicate MI or a persistent aneurism of the ventricular wall and without further exam can be inconclusive. Rather the ECG is used by a skilled physician in combination with symptoms, risk factors, other diagnostic tests etc. to find the appropriate diagnosis.

The earliest sign of ischemia on ECG are Peaked T waves but they are usually not seen in clinical settings as they disappear in minutes after the start of ischemia. Most commonly detected changes during ACS are ST segment elevations or depressions which last from minutes to hours after the start of ischemia. ST segment depressions occur when ischemia occurs in the subendocardial part of the heart and does not spread through the whole thickness of the wall. This can be a UA when there is no necrosis of the myocytes (Troponin negative) or NSTEMI when the necrosis is present (Troponin positive). Persistent ST segment elevations occur when ischemia spreads through the whole thickness of the heart walls and if (usually is) accompanied by myocyte necrosis is termed STEMI. Later changes on ECG are loss of R wave that happens over hours to days and

persistent Q waves and inverted T waves that happen days after the MI. We will not focus on these changes as they occur late in the MI when necrosis of the cardiac cells already took place and treatment (Stenting, CABG) have very limited or no benefit to the patient. And last but not least the cheap, fast and noninvasive nature of ECG makes it invaluable tool in medicine for the foreseeable future (35-42).

Cardiac biomarkers

The most widely used and the most sensitive biomarkers available today are cardiac troponins but as they are the major part of our research, they will be discussed in detail in the separate section below. The other biomarkers that may have value in MI are CK-MB, myosin-binding protein C, and copeptin and all of them are usually used in combination with cTns (13).

Copeptin is the 39 amino acid glycopeptide that is part of the AVP precursor protein (specifically present on the C-terminal side of the protein). It is stable in the plasma and can function not only as a predictor of AVP release but also as a predictor in variety of diseases especially the acute ones like infections (lower respiratory tract disease), MI or stoke and many others. In case of MI, copeptin showed effectiveness when measured together with troponin in early admission patients if high-sensitivity cardiac troponin tests were not available. The use of high-sensitivity cardiac troponin tests continues to increase worldwide and a number of clinics already equipped with them are only going to increase. For these reasons copeptin is very rarely used in clinical settings for the diagnosis of MI (13, 43-54).

Myosin binding protein C is a protein that is associated with thick filaments in skeletal and cardiac muscle. Cardiac myosin binding protein C is an isoform of the protein that consists of eight immunoglobulin-like domains and three fibronectin-like-domains and is predominantly located in cardiac muscle. It is a substrate for the cAMP protein kinase and functions in thick filament structure maintenance and muscle contraction. Mutations of cardiac myosin binding protein C can lead to hypertrophic cardiomyopathy. As a marker for MI it is more abundant

inside the myocytes and can function as marker of cardiac damage. One study showed the efficacy of cardiac myosin binding protein C to be comparable to the high-sensitivity troponin T tests (especially patients presenting early after symptom onset) but for now the studies and data done on the subject is very limited and cardiac myosin binding troponin C is rarely used in hospitals (13, 55-59).

Creatine kinase is a dimeric enzyme that is about 80 000 kDa in weight consisting of two almost identical monomeric subunits. There are three major isoforms of Creatine kinase which differ in tissue to tissue localization and monomer composition. Brain form consists of two B (from brain) monomers hence the name creatine kinase BB, skeletal muscle contains the two M (from muscle) monomers creatine kinase MM and the heart muscle dimer consists of both M and B monomers CK-MB. This tissue specificity of isomers is the reason CK-MB is used in MI diagnosis about which we will talk below. Creatine kinase catalyzes formation of phosphocreatine a high-energy molecule that can quickly transfer the high-energy phosphate bond to the ADP creating the ATP. Since the number of ATP and ADP molecules in the cell is limited this allows additional storage of high energy molecules in the cell and quick replenishing of the ATP when needed (60-65).

CK-MB levels in plasma and creatine kinase index were used to detect cardiac damage. The mechanism behind those tests was that during cardiac ischemia and injury creatine kinase would leak out and increase in the plasma. CK-MB levels were measured separately and the 99th percentile increase could indicate MI along with other diagnostic or clinical criteria. In case of creatine kinase index the increased levels of CK-MB (above 2.5%) compared to total plasma creatine kinase levels were taken as a cut off values for diagnosis of MI. The new troponin testing proved more effective by many different clinical trials and made CK-MB testing almost absolute. It still can be used in periprocedural coronary artery stenting/CABG MI and some clinicians still use it in early recurrent MI detection as CK-MB levels rise 4-6 hours after MI, peak at

12-24 hours and get back to normal in about 2-3 days which is much faster than troponin levels (66-74).

Finally, like troponin, CK-MB levels are chronically elevated in patients with CKD and usually cannot be used as a diagnostic marker for MI. The mechanism behind elevation can be increased half-life of plasma CK-MB or increased release of creatine kinase from myocytes due to chronic damage of cardiac cells as patients with CKD are at increased risk for CVD (75-78).

Non-Invasive imaging

Coronary artery angiography can be used in diagnosis of MI (for example in MINOCA etc.) but is an invasive imaging and often continues with coronary artery stenting, thus it will be briefly discussed in the MI treatment section.

The TEC is an indispensable tool in cardiology and also should be available in emergency departments. It is noninvasive technique, usually does not require much time and shows the condition of the heart in real time. TEC can detect cardiac wall hypokinesia or akinesia suggestive of ischemia and if the cardiac wall motion abnormalities are not visible contrast echocardiography can identify heart perfusion abnormalities. Also, TEC can also help us identify other pathologies that cause chest pain and can be confused with MI (Dissection of the thoracic aorta, large pulmonary embolism, pericardial effusion, aortic valve stenosis etc.) Out of the all noninvasive imaging tools TEC is the most widely used and present in virtually every clinic with cardiology department (79-84).

CMR can detect cardiac wall motion abnormalities like TEC but can also assess perfusion problems. Additionally, CMR detects scar tissue and differentiates between recent and old MI. This allows CMR to be used to differentiate between MI, Takotsubo and myocarditis making it an excellent tool for MI diagnosis. Some studies also showed that using CMR decreased the need for the unnecessary coronary artery angiography in patients presenting with chest pain. Still TEC is far more widely used in clinical settings for now (85-91).

SPECT is the least commonly used of the non-invasive imagine methods mentioned there. The reason behind this is significant radiation in some of the SPECT machines and absence of wide availability of 24-hour service. SPECT can detect myocyte blood delivery defects in resting mode and rest-stress mode combination further improves the diagnostic value of SPECT especially in combination with cardiac markers ECG and clinical presentation (92-95).

Pharmacological and Invasive treatment of MI

Before we start discussion of the pharmacological treatment of MI it should be mentioned that dosing of the MI medications and special situations (e.g. prosthetic valve in a patient with MI) are not discussed here as they are beyond the topic of our research. For more information about these situations see the references bellow.

Not so long ago the only treatment for MI was pharmacological and no invasive procedures likes stenting or CABG were developed which resulted in a significantly higher morbidity and mortality for MI and increased risk for post-MI complications. Medications are mandatory in MI treatment and when used according to the guidelines significantly decrease ischemia and thrombotic complications.

Some treatment like oxygen can be administrated in the ambulance even before arriving to the hospital. Similarly, opioids such as morphine are often administered in the ambulance as they are a first choice for pain relief in both STEMI and NSTEMI. Sometimes benzodiazepines can be used to relieve the anxiety and calm the patients.

The most important medications for MI are anticoagulants and antiplatelet medications. But their ability to counter the ischemia can be complicated by hemorrhage and the role of the skilled doctor is to find the golden middle so the benefits outweigh the risks. This should include the detailed clinical history including history of hemorrhage, medications, comorbid conditions etc. Heparin is the anticoagulant of choice and should be started as soon as possible in hospital and enoxaparin should be considered in a patient with increased risk of

bleeding. Antiplatelet medications are a must even if there is no PCI is planned and a must if the PCI is planned as periprocedural treatment. Aspirin invented more than 100 years ago is still a widely used medication in cardiology and is usually used in combination with another antiplatelet medications (Prasugrel, Ticagrelor or Clopidogrel).

And the last but not least are the nitrates and beta-blockers. Nitrates intravenous or sublingual are effective in controlling the symptoms and sometimes resolving the ST depressions characteristic of ischemia on ECG. Beta-blockers decrease the oxygen use by the heart by decreasing the heart rate, contraction and blood pressure. However, beta-blockers can have side effects in the patients with ongoing comorbidities like asthma, COPD and early use of them during the hospital admission is not recommended.

The drugs listed above along with others are a cornerstone of MI treatment and are probably there to stay in the near future (13, 14, 96-105).

The coronary angiography which is an invasive diagnostic procedure can be used either to confirm the suspected artery lesion or not. To further increase the diagnostic value of coronary angiography it can be used with IVUS which have been shown to increase the effectiveness of angiography. If the suspected artery lesion is confirmed angiography can either continue as PCI or CABG can be scheduled depending on the patient's risk factors. If not other reasons for myocardial injury should be investigated. Being an excellent tool for diagnosis of MI coronary angiography is an invasive procedure and has a risk of complications (bleeding, coronary artery dissection etc.) and should not be performed indiscriminately in all patients.

PCI is a procedure where the closed metal stent is inserted into the coronary arteries and inflated with the balloon to open the closed artery and stop the ischemia. The stent will stay inside the coronary arteries and eventually be covered by new endothelium while the DAPT will reduce the risk of stent thrombosis. While used in both STEMI and NSTEMI the

treatment protocols for PCI still vary. In STEMI immediate invasive strategy (<2 hours) is always used while in NSTEMI depending on the clinical scenario immediate invasive, early invasive (<24 hours) or even selective invasive (>24 hours) strategies can be used.

CABG or coronary artery bypass graft is an open-heart surgery where the patient's own veins or arteries (or both) are attached to the aorta and the coronary arteries thus creating the alternative blood supply channel to the heart bypassing the occluded areas. While 80 to 90% of all invasive treatment in MIs is PCI the rest is still CABG. The method of treatment is chosen depending on clinical and anatomical characteristics of the patient, multi-vessel lesions, severely reduced (<40%) left ventricle ejection fraction, left coronary artery occlusion, diabetes and contraindications to DAPT being in favor of CABG.

In conclusion to treatment both pharmacological and invasive ones have drastically decreased mortality and improved the quality of life for millions of patients (106-118, 13, 14).

Mechanism of troponin release during myocardial injury

Troponin is a 46 to 52 kDa protein that is essential for striated muscle contraction regulation. Troponin is actually a complex of three different proteins present in the cytoplasm of both cardiac and skeletal muscles. The three subunits TnT, TnI and TnC. TnC is a 18kDa protein consisting of two globular subunits bound together by a hydrophobic peptide chain. TnC was named after Calcium as its role is to sense the calcium concentrations, bind Calcium ions when high and induce the conformational change in TnI. TnI is a 210 amino acid peptide approximately 24kDa consisting of four alpha helixes connected by short peptide loops. TnI is attached to actin contained in thin filaments of the muscle (discussed below) and holds tropomyosin-actin complex together in resting muscle. TnT is the largest of the three subunits and its molecular weight is 36 kDa. It attaches to the tropomyosin thus the troponin complex serves as a clamp keeping actin-tropomyosin complex together. Despite being present in both cardiac and skeletal muscle cardiac and skeletal troponins are not identical. While the TnC is

identical in both muscles there are separate cardiac and skeletal isoforms of TnT and TnI which can be differentiated by specific tests. This makes troponin an excellent marker for detection of cardiac injury (119-124).

Cardiac troponin levels are essential for the diagnosis of MI and other causes of myocardial injury, but understanding the mechanisms of troponin relocation from myocytes to plasma may be important in further advancing the diagnostic techniques. First it should be mentioned that abnormal increase in troponin levels is considered when the increase is above the 99th percentile of the normal troponin levels. (The 99th percentile number varies depending on the troponin type and the test used) This means that cardiac troponins are normally present in blood but in lower levels compared to cardiac injury. Two hypothesis state that low troponin levels are either a result of constant leaking of troponins from healthy cardiac cells or a result of normal apoptosis/renewal cycle of the heart. (Or both)

The mechanism of troponin release from myocytes in MI is simple. Ischemia of the heart causes decreased oxygen delivery to the heart and eventually damage of myocytes and necrosis. Necrotic cells disintegrate and release cytoplasmic proteins including troponin. The mechanism is supported by observation that the troponin release after MI is biphasic. The first peak occurs 10-20 hours after MI while the second on about 80 hours later. This occurs because about 2-6% of the troponins are in a free form in the cytosol of myocytes and are released immediately, while the rest are attached to the contractile fibrils and are released only after disintegration of the sarcomere. Because of this model mentioned above the increase of plasma troponins in blood was always thought to be associated with necrosis of cardiac cell. While still considered true for MI this model does not explain the troponin rise in many other cardiac conditions and several other models have been proposed.

First in the short-term ischemia (that can be induced experimentally or by strenuous exercise) there was an increase in plasma troponin levels but no cardiac necrosis was demonstrated, indicating the injury was reversible. It was proposed that the injured myocytes produced blebs in

the plasma membrane that contained various proteins including (free cytoplasmic) troponins. These blebs ruptured and released troponin into the blood leading to troponin increase without irreversible cardiac injury. This model is supported by the observations that during strenuous exercise or short-term ischemia the troponin increase has only one peak (10-20 hours) and probably no second peak occurs because there is no necrosis and disintegration of the sarcomere.

The increased release of troponins is also seen in patients with increased myocyte stretching in CHF. The mechanism of this is poorly understood but probably involves integrins, the transmembrane proteins connecting cytoplasm to the extracellular matrix. Integrins are shown to stimulate myocyte stretching in CHF and in one model where cardiac integrin levels were upregulated in vitro myocyte the levels of released troponins were much higher compared to the control myocytes with normal integrin levels.

Increased troponin levels in other diseases such as pulmonary emboli, sepsis, chemotherapy can be caused by one of the above models, their combination or some entirely different mechanisms (125-134).

Troponins as markers for MI

Troponins have been used as a marker for MI for more than 30 years. The first use of troponin as an MI marker was suggested in 1990 and European Society of Cardiology recommended it as the number one MI marker in 2000. Thus, a lot of cardiac troponin tests were developed. The tests are usually designed to show as positive when the concentration of Troponin is above the 99th percentile. American heart association and European society of cardiology together suggested the use of 99th percentile of troponin levels as a cut off for diagnosis of MI. It should be taken in consideration that the cut of value is established by individual test makers and should be the one described in the test instructions as absolute numbers of troponin (especially TnI) can vary from test to test. Hs-cTt being very helpful are but a tool in hands of a doctor and only help in establishing diagnosis. For example, negative test can suggest another reason for chest pain while a positive test can also occur in myocarditis or

CKD. This shows that even hs-cTt is an excellent tool, the human factor continues to play a dominant role in the foreseeable future (135-143).

Troponins in patients with CKD

CKD is divided into 5 stages 1 through 5 with decreasing level of glomerular filtration rate and severity respectively. There when we mention CKD, we mean stage 3 through 5. CKD is a serious medical condition on its own and can be caused by a variety of conditions. Patients with CKD have an increased risk of CAD and MI. This stems from decreased immunity, increased endothelial damage, accelerated atherosclerosis, inflammation, progressive coronary artery calcification probably occurring because of toxic effects of uremia. In fact, about 50% of patients with advanced CKD die of cardiovascular causes and this number only continues to increase.

To make matters worse MI clinical presentation can be atypical in CKD patients, often being totally clinically silent. Even other diagnostic tools such as ECG can be inconclusive because of altered electrolyte balance further complicating the diagnosis. Both STEMI and NSTEMI can have an atypical presentation in CKD but silent NSTEMI is more common.

cTns are also chronically increased in majority of patients with CKD and the increased levels do not directly correlate with the stage of CKD. There is no one factor for troponin increase in these patients, rather a combination of decreased renal clearance of troponin, cardiac injury, silent myocardial necrosis and microinfarctions associated with abnormal perfusion and endothelial dysfunction are thought to play a role in chronically increased troponin levels. In one study, a coronarography was performed in 100 patients with CKD, typical chest pain and abnormal troponin levels. Only approximately 50% had coronary artery occlusions while the rest were normal. More ever several different studies showed that patients with CKD and MI are less likely to receive coronary artery angiography than patients with only MI.

Obviously typically presenting MIs with classical symptoms, ECG changes, severely elevated troponin levels or distinctly visible akinesia on

cardiac ultrasound are easy to diagnose even in CKD patients. Unfortunately, this is often not the case and MIs can be overlooked, increasing the mortality in already ill patients.

Several options have been proposed. Increasing the cut off value for troponin has been suggested. Unfortunately, the cut off value for CKD patients is hard to establish as elevated troponin levels vary from patient to patient, not directly correlate with the severity of the disease, can fluctuate if the patient is on dialysis and no guidelines have been released in spite of the problem being recognized for many years. Same difficulties can occur if baseline elevated troponin levels checked in CKD patients to know their "normal" elevated troponin levels and detect increase in MI. Additionally, taking blood samples regularly will cause the compliance problem with the patients. Another option is to measure the increase of troponins after admission (first check after admission and then after 3 hours). If the levels increase with time this means the MI is more likely. Unfortunately, the stable level of increased troponin does not rule out the MI and delay of treatment for several hours leads to the increased damage and necrosis of the myocardium. The simple solution would be to do coronary artery angiography in all patients with high suspicion of MI. Unfortunately, angiography is an invasive procedure and carries the risk of complications plus the contrast injected is nephrotoxic. CKD patients are more vulnerable to angiography complications like bleeding or infection and contrast-induced nephropathy damage can make a CKD patient from dialysis free to dialysis dependent (13, 14, 136, 144-153).

The situation in the CKD group of patients led us to a conclusion that a new marker is necessary for the diagnosis of MI. The UB, CXCR4 and SDF1 proteins could be the answer to the dilemma. The properties and the reason we chose these proteins for research are described in the appropriate sections bellow.

Ubiquitin

The UB is a small 76 amino acid (8.5 kDa) protein. The UB mediated protein degradation is targeted and selective. It is ATP dependent process and requires 3 enzymes: E1, E2 and E3. The ubiquitination of the protein is subject to variation as only single UB molecule can be attached to the substrate (mono-ubiquitination), several UB molecules can be attached on different sites of the same protein (multi-mono-ubiquitination) or many UB proteins can be attached to the first UB molecule creating a UB tail (poly-ubiquitination).

To make matters more complicated not all ubiquitinated proteins are degraded, for example mono-ubiquitinated histones functions in transcription while poly-ubiquitinated ones can be a target for degradation. Both these facts and the existence of multiple E2 and E3 families makes the job of putting down the exact detailed map of UB protein degradation extremely difficult.

UB function is by no means limited to the protein degradation, the term being everywhere an also be applied to the functions of UB in eukaryotic cells. UB functions in a vast amount of physiologic and pathologic processes (some described below) including but not limited to: immune response, DNA repair, transcription, apoptosis, ischemia, cell proliferation, variety of tumors and cancers, cell signaling (154-158).

Extracellular UB

While UB was initially discovered as an extracellular protein the discovery of the UB mediated intracellular protein degradation has shifted the most of the research to examine the intracellular work of UB. Only relatively recently has focus come back to the actions of extracellular UB as possible diagnostic marker or a target molecule for treatment. Both mono- and polyubiquitin have been found in blood, urine, CSF and seminal fluid of healthy individuals. The normal apoptosis mediated cell turn-over release and release of UB in healthy cells through blebs have been proposed as the mechanism of extracellular UB. Moreover, increased levels of UB were shown in CSF (in case of central nervous diseases) and blood (during burns, tumors etc.) in many

pathologic conditions. Obviously, the increased levels of UB in diseased patients can be explained by increased number of damaged/dead cells. But many independent studies showed that extracellular UB is not just a passive product of damaged cells but can mediate a number of important functions. In mice intraperitoneal injection of UB normalized leucopoiesis after it was inhibited by cyclophosphamide compared to the control group of mice where only cyclophosphamide was injected. UB coated defective sperm cells were seen in epididymal fluid and extracellular UB has been suggested as a controller or correct spermatogenesis. Also, E1, E2 and proteasome complexes were also found in the epidydimal fluid that led the authors to suggest that if E3 is also present the UB-proteasome complex can have a role in sperm maturation regulation. Extracellular UB has also shown to participate in immunomodulation, inhibition or induction of apoptosis and probably many more physiological and pathological mechanisms, opening many opportunities to research it as a target molecule for treatment and diagnosis of various conditions (159-163).

UB and CKD

UB concentration can be increased in some patients with CKD, just like CK-MB and cTn. Elevated UB levels were demonstrated with stage 5 CKD, the latest stage that requires the dialysis. The vast majority of patients having CKD are in stage 1 through 4 (1 in 7 American adults) and elevated troponin levels are already present in earlier stages of CKD (especially stages 3-4). Only mono-ubiquitin levels were significantly elevated in patients with stage 5 CKD while UB chains were not. It was shown that patients with adequate hemodialysis treatment (Kt/V >1) had lower UB levels than patients with inadequate dialysis regime (Kt/V <1). More ever patients whose Kt/V changed from <1 to >1 showed decrease in serum UB levels demonstrating a negative correlation between adequate dialysis and UB levels. Thus patients receiving adequate hemodialysis 1 or 2 times a week will have normal UB levels and if MI (with atypical, confusing symptoms) occurs in these patients increased

UB levels can be accurately used to diagnose acute myocyte damage and necrosis (162, 164-171).

Extracellular UB as a ligand for CXCR4 and a potential biomarker for MI

As mentioned before extracellular UB has many physiologic and pathologic actions. Some of them can be accomplished through its action on CXCR4. CXCR4 is a chemokine receptor discussed in details later. SDF1 has long been known to be the CXCR4 ligand but later has been discovered UB/CXCR4 ligand-receptor relationship. In case of ischemia, myocardial injury and MI, UB/CXCR4 was shown to increase, stimulate angiogenesis, inhibit myocyte apoptosis, decrease cardiac remodeling after ischemia-reperfusion injury, and decrease cardiac inflammatory response further decreasing the damage. Furthermore, artificially increased UB levels (either by UB injection or increased UB expression) showed increased cardioprotective properties compared to controls. All of this contribute to the decreased area of necrosis in MI, improved heart function and lesser chance of developing heart failure. All of these data indicate that UB can serve not only diagnostic tool in MI but as a therapeutic target in the future (172-181).

The role of both intracellular and extracellular UB in MI is intensively being studied to understand the role of UB in pathogenesis and possible therapeutic implications. But the focus of our research is to find out if UB can be a valid diagnostic marker in MI (along with CXCR4 and SDF1). As mentioned above extracellular UB levels (blood, CSF) have shown to be increased in many pathologic conditions, including tumors, burns, stroke and ACS. Vannucci S. and colleagues demonstrated that after ischemia was induced only to one side of the brain, the ischemic side demonstrated significantly increased levels of UB compared to the normal. While the increase of UB in MI can be partially explained by cell damage and necrosis Chen and colleagues showed that peripheral inflammatory cells (monocytes and lymphocytes) of patients with ACS also expressed increased levels of UB that correlated with the severity of the disease (MI more than UA). Thus, other mechanisms of extracellular increase of UB

during MI can be present. Another study showed that extracellular UB levels were increased in patients with CAD compared to the control group and the levels of UB positively correlated with the severity of the CAD (However, the aim of the research was not to investigate the role of UB as an MI diagnostic marker). We believe that measuring and analyzing the UB (CXCR4, SDF1) levels in the serum of STEMI, NSTEMI and healthy groups can greatly aid in diagnosing MI in patients CKD patients with "falsely" elevated troponin levels (182-184, 160).

CXCR4 and SDF1

SDF1 also known as CXCL12 is a small protein (like all chemokines 7-14kDa) that is a member of the chemokine family. Chemokines or chemotactic cytokines promote cell migration and attraction and have many functions.

SDF1 is unique compared to other chemokines, that it has surprisingly low number of receptors. Namely CXCR4 and CXCR7. We are going to discuss the CXCR4/SDF1 interaction, as it is vastly more studied than CXCR7 and is the topic of interest in our research. CXCR7/SDF1 interaction appears to activate MAP kinases and promote melanocyte migration. While the CXCR4/SDF1 axis plays a role in regulation of stem cell trafficking, embryogenesis, tissue and organ regeneration, vasculogenesis and angiogenesis in hypoxia/ischemia, movement and retention of hematopoietic cells, cancer progression and possibly in many more (185-189).

CXCR4 is a classical "serpentine" G-protein coupled receptor. It consists of 352 amino acids, coded on the second chromosome in humans, has extracellular N-terminal part, transmembrane, intracellular, extracellular loop and C-terminal part inside the cell. It is widely expressed in many different types of cells and larger numbers of CXCR4 are found in embryonic and cancer cells compared to others. Its canonical ligand is considered to be SDF1 and another ligand UB we already discussed. CXCR4 binds to many ligands and we are going to briefly discuss them. HBD3 appears to promote CXCR4 internalization after binding without triggering the calcium influx or chemotaxis. CXCR4 can also serve as a

receptor for external proteins like GP120 of HIV which is important for internalization of the virus (190-195).

As can be seen CXCR4 has many functions but we will focus on the CXCR4/SDF1 axis as it is the most studied, have been shown to be important in MI and coronary artery ischemia that is the focus of our research.

Serum CXCR4 concentration as a marker for the disease

As the role of CXCR4 in ischemia and MI will be discussed later it is important to remember that the focus of our research is to test serum concentrations of CXCR4 for diagnosis of MI. As such we were interested in the research done before us. To our knowledge while research was done to measure CXCR4 expression in cardiac myocytes during ischemic states no research was done to measure serum CXCR4 levels in MI. However, serum levels of CXCR4 were measured in other pathologic conditions. For example, CXCR4 was found to be a valuable tumor marker for pancreatic cancer, both CXCR4 and SDF1 levels were elevated in blood and synovial fluid of patients with rheumatoid arthritis compared to healthy controls and they positively correlated with other classical markers (CRP, RF, ESR). Similarly, both CXCR4 and SDF1 were elevated in patients with adult-onset Still's disease compared to healthy controls and they also positively correlated with disease's markers. In addition, their levels decreased after resolution of the disease. Two separate studies found elevated levels of CXCR4 in women with breast cancer. Another interesting finding occurred in patients with esophageal cancer where while the SDF1 was elevated in cancer patients compared to controls, CXCR4 levels were significantly lower in cancer patients compared to controls. All of these data give us hope that CXCR4 serum concentrations and its correlation with its ligands can be a valuable prognostic marker in patients with MI (196-201).

SDF1/CXCR4 role in MI

Heart muscle is considered as a tissue without regenerative potential. If part of the cardiac tissue dies it is replaced by scar tissue and heart contraction ability decreases. The treatment of MI follows these rules; it is a medical emergency and treatment is aimed to open the occluded artery as soon as possible to prevent or decrease the necrosis of ischemic heart cells. However, this can all change in the future. The activation of the SDF1/CXCR4 axis was shown to decrease the death rate of ischemic cells, reperfusion injury, cardiac remodeling. It was also shown to increase angiogenesis, migration of stem cells from the bone marrow to the injured heart muscle, repair and regeneration. It was shown that myocytes, endothelial cells and fibroblasts secreted increased amounts of SDF1 in ischemia and SDF1 levels increased minutes to1 hour after MI peaked at 3 days and returned to baseline in 7 days. The SDF1 positive effect on cardiac muscle is thought to be mediated trough action on CXCR4 receptor in damaged cardiac and bone marrow stem cells. It was shown that after increase in SDF1 stem cells showed increase in CXCR4 expression and actively migrated to the damaged myocardium. Use of AMD3100 a potent CXCR4 agonist or inhibiting the MAP kinase pathway (a secondary messenger pathway activated by the CXCR4, SDF1 binding) diminished the effect. In cases where SDF1 was injected or its expression artificially enhanced the negative effects of MI were significantly diminished compared to controls. Considering this data why does not human heart regenerate in after MI? The answer is time. It is considered that CXCR4 expression in cells in considerable amounts starts much later than SDF1, in 1 day and remains elevated for more than two weeks. It is considered that the time overlap of SDF1 and CXCR4 concentrations in amounts necessary for regeneration is not long enough. Studies by M.Penn and colleagues showed that stem cells did not migrate to the damaged heart in response to SDF1 when harvested after 1 hour but showed significant increase in migration if harvesting was delayed for 6 hours even though both of them already had CXCR4 on their membranes. The SDF1 responsiveness and CXCR4 expression of stem cells continued to increase even after 4 to 7 days of MI, time when SDF1 levels are

already drastically decreased. This shows that bone marrow stem cells need longer time to activate and to migrate and adhere to the damaged site in myocardium, which is limited by short half-life of SDF1. One of the solutions for this problem is inhibition of a protein called DDP4. DDP4 is a transmembrane protease of the S9B protease family that is involved in proteolysis of many different proteins including SDF1. In vitro pretreatment of donor cells in mice or in vivo inhibition of DDP4 has shown to increase engraftment of CD34+ graft cells. Similar results were shown in lung transplant models. All of these research gives us a careful hope that in the near future MI morbidity and mortality will be further decreased (202-208).

We also would like to focus the attention on the fact that SDF1 plasma concentrations begin to increase minutes after ischemia. Measuring SDF1 levels in patients with MI could provide us with the excellent new marker for STEMI, NSTEMI in cases where troponin levels are chronically elevated.

Medical histories of the selected patients

1 Patient Birthyear - 1952

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension grade III (ESH/ESC) I 67.4 – Hypertensive encepalophaty I 83.9 – Varicose disease of the lower limbs without ulcers and complications.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis.

Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Ischemic stroke in 2018.

ECG – Sinus rhythm, QRS axis of the heart normal, no acute ischemic changes are visible.

LVEDv - 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV – 58 ml	EF – 55 %	LA – 40 mm	RV -37 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Mild dilatation of the left atrium. Systolic function normal EF – 55 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP normal. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I 0.021

2 Patient Birthyear - 1948

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension grade III (ESH/ESC)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. First Obtuse Marginal branch has a 40% stenosis, others without stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections.

ECG – Sinus rhythm, QRS axis of the heart normal. Negative Twave in lead III. Incomplete R wave progression in V1 – V3 leads.

LVEDv - 52 mm	LVESd - 36 mm	FS – 27 %	IVS – 16 mm	PW – 11 mm
LVEDV - 129 ml	LVESV – 55 ml	EF – 57 %	LA – 42 - 45 mm	RV -37 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Mild – moderate dilatation of the left atrium. Systolic function normal EF – 57 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta mild dilation and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I 0.019

3 Patient Birthyear - 1941

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA III)

ICD 10 Comorbidities

I 10 – Primary hypertension grade III (ESH/ESC) I 34.0 – Mistral valve regurgitation, I 48 – Atrial fibrillation and flatter, I 36.1 – Tricuspid valve insufficiency, I 50 – Congestive heart failure.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – 40% stenosis medial and 30% proximal parts. Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. First Obtuse Marginal branches without stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Gastric bleeding three years ago, that was required endoscopic coagulation.

ECG – Rhythm atrial fibrillation. I, aVL – R (+T), II aVF – R (-/+T), III -rS (-/+T), V2 - V6 - Rs, HR - 119, QRS - 90, QT - 342

LVEDv - 52 mm	LVESd - 41 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV – 74 ml	EF – 44 %	LA – 45 mm	RV - 40 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Moderate dilatation of the left atrium. Systolic function moderately decreased EF – 44 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta mild dilation and aortic arch normal. Aortic valve tricuspid, calcified. Mild mitral and tricuspid valve regurgitation +2/+4. Pulmonary artery pressure PASP 30 elevated. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I < 0.019 ng/ml

4 Patient Birthyear - 1951

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 44.4 – Left anterior bundle of Hiss hemiblock.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) J 44.9 – Chronic obstructive lung disease.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Right inguinal hernia and repair surgery in 2007, gastroduodenal bleeding in 2012, esophageal hernia reconstitution surgery in 2017.

ECG – Sinsu rhythm, Left anterior hemiblock of the left bundle of Hiss.

LVEDd - 54 mm	LVESd - 38 mm	FS – 27 %	IVS – 12 mm	PW - 11mm
LVEDV - 141 ml	LVESV - 62ml	EF - 56 %	LA - 43 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic

valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

5 Patient. Birthyear – 1950

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 25.8 – Chronic cardiac ischemic desease

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 48 – Atrial fibrillation and flatter I 34.0 – Mitral valve regurgitation I36.1 – Tricuspid valve regurgitation I27.2 – Pulmonary hypertension B 18.2 – Chronic hep. C, not treated E 66.0 – Obesity because of high caloric intake (BMI – 27).

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

ECG – Atrial fibrialtion, tachysistoly (110), frequent premature ventricular contraction.

LVEDd - 63 mm	LVESd - 48 mm	FS – 23 %	IVS – 15 mm	PW - 11 mm
LVEDV - 202 ml	LVESV – 107 ml	EF - 47 %	LA - 53 mm	RV - 46 mm

IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function moderately decreased EF - 47 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

6 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Kidney stones treated with lithotripsy

ECG – Sinus rhythm, pulse 75, rS (+T) V2 - V3 Rs (+T) V4 - V6. No acute ischemic changes are present.

LVEDd – 52 mm	LVESd - 37 mm	FS – 26 %	IVS – 13 mm	PW - 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF - 55 %	LA – 41 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			RA – 37 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

7 Patient Birthyear - 1961

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) J 44.9 – Chronic obstructive lung disease, R 73.0 – Positive glucose tolerance test.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques.

Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS axis normal, No acute ischemic changes are present.

LVEDd - 54 mm	LVESd – 39 mm	FS – 26 %	IVS – 12	PW - 11 mm
LVEDV -141 ml	LVESV - 66 ml	EF - 53 %	LA – 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

8 Patient Birthyear - 1981

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) J 45.9 – Asthma, N 20.2 – Kidney and urethral stones, K 76.0 – Fatty liver.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior

descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Cholecystitis, Acute pneumonia in 2018.

ECG – Sinus rhythm, - T wave in aVR, aVL waves, R wave incomplete progression in V1 – V4 waves.

LVEDd - 57 mm	LVESd - 42 mm	FS – 25 %	IVS – 14 mm	PW - 11mm
LVEDV - 100 ml	LVESV - 40 ml	EF- 50 %	LA - 45 mm	RV- 38 mm
IVC - 13 mm	> 50 % collapses			RA – 38 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

9 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS heart axis left deviation. No acute ischemic changes are visible.

LVEDd - 50 mm	LVESd - 34 mm	FS – 27 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV – 47 ml	EF – 60 %	LA - 42 mm	RV - 38 mm
IVC -13 ∂∂	>50% kolab.			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

10 Patient Birthyear - 1960

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Tuberculosis of the lung in 1998, did a 1 year treatment course, 2014 diagnosed with uterine multiple fibromas.

ECG – Sinus rhythm, QRS heart axis normal, no ischemic changes are visible.

LVEDd - 50 mm	LVESd - 34 mm	FS – 28 %	IVS – 12 mm	PW - 10 mm
LVEDV -118 ml	LVESV - 47ml	EF – 56 - 57 %	LA - 38 mm	RV - 37 mm
IVC - ∂∂	>50% kolab.			RA-38∂∂

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

11 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 27.2 – Secondary pulmonary hypertension.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) J 44.9 – Chronic obstructive pulmonary disease, F 45.3 – Autonomic (vegetative) disfunction.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

J44.9 – Chronic obstructive pulmonary disease, F45.3 – Somatotrophic autonomic (vegetative) disfunction.

ECG – Sinus rhythm, QRS heart axis normal, negative T wave in aVR, aVL, R wave incomplete progression in V1 – V2 leads.

LVEDd – 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 12 mm	PW - 11 mm
LVEDV - 129 ml	LVESV – 58 ml	EF – 55 %	LA-42 mm	RV-38 mm
IVC - 13 mm	> 50 % collapse			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation

+1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

12 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) B 18.2 – Chronic viral hepatitis C

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS heart axis normal, negative T wave III lead, R wave incomplete progression in V1- V2 leads.

LVEDd - 53 mm	LVESd - 38 mm	FS – 27 %	IVS – 11 mm	PW - 10 mm
LVEDV - 136 ml	LVESV- 58 ml	EF – 56 %	LA - 40 mm	RV – 34 mm
IVC - 13 mm	> 50 % collapses			RA - 34 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

13 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 05.1 – Rheumatic mitral regurgitation, moderate

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS heart axis normal, - T wave and R wave incomplete progression in leads V1 – V5.

LVEDd - 50 mm	LVESd – 38 mm	FS – 26 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV - 62 ml	EF – 47 %	LA - 41 mm	RV - 35 mm
IVC - 13 mm	> 50 % collapses			RA - 35 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

14 Patient Birthyear - 1952

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 45.0 – Complete block of right bundle of Hiss

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) E 03.9 – Hypothyroidism

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Appendectomy in childhood, hypothyroidism takes 50mg of Euthyroxine

ECG – Sinus rhythm, QRS electrical axis left deviation, complete right bundle bunch block, signs of left ventricular hypertrophy.

LVEDd - 50 mm	LVESd - 35 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 118 ml	LVESV- 51 ml	EF – 56 %	LA - 39 mm	RV - 36 mm
IVC - 13 mm	> 50 % kolab.			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

15 Patient Birthyear - 1957

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 25.8 Chronic ischemic heart disease

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) HFpEF

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) E 66.0 Obesity caused by excess caloric intake (BMI 32), E 78.8 – Hypercholesteremia, I 89.0 Lymphedema,

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible

stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Appendectomy in childhood, tonsillectomy in 1995, several medical abortions, hepatitis A in 1962, hypercholesteremia, goutier.

ECG – Sinus rhythm, QRS electrical axis normal, pulse 71, PQ - 0.13 QRS - 0.09 QT - 0.44 rS (-T)I II, rs (-T) V1, Rsr (-T) V2 RS (-T) V3

LVEDd - 49 mm	LVESd - 33 mm	FS – 27 %	IVS – 11 mm	PW – 10 mm
LVEDV - 112 mm	LVESV - 40 ml	EF - 60 %	LA - 40 mm	RV – 35 mm
IVC - 13 mm	> 50 % collapses			RA - 35 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

16 Patient Birthyear - 1968

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I, I 34.0 – Mitral valve regurgitation, I 44.7 – Complete left bundle bunch block.

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II) I 27.2 – Secondary pulmonary hypertension

ICD 10 Comorbidities

I10 – Primary hypertension I (ESC/ESH) E 11.8 – Insulin dependent Diabetes Meletus type 2

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Appendectomy in childhood

ECG – Sinsur rhythm, heart rate 105, Complete left bundle bunch block.

LVEDd - 64 mm	LVESd - 52 mm	FS – 19 %	IVS – 13 mm	PW – 11 mm
LVEDV - 209 ml	LVESV – 129 ml	EF – 38 %	LA - 47 mm	RV-38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

17 Patient Birthyear - 1959

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, sinus arrythmia, heart rate 55, left anterior fascicular block, several premature ventricular contractions, no acute ischemic changes are present.

LVEDd - 54 mm	LVESd - 39 mm	FS – 26 %	IVS – 13 mm	PW – 11 mm
LVEDV - 141 ml	LVESV – 66 ml	EF - 53 %	LA - 40 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

18 Patient Birthyear - 1959

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II) I 27.2 – Secondary pulmonary hypertension, I 36.1 – Tricuspid valve regurgitation, non-rheumatic.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 25.2 – Old myocardial infarction, I 48 – Atrial fibrillation, K 25.7 – Gastric ulcer, Q 67.5 – Congenital deformity of the spine, E 89.0 – Hypothyroidism caused by medical procedures.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Myocardial infarction in 2018 and coronary artery stenting with 4 stents implantation. Exudative pericarditis in 2016, Pulmonary Tuberculosis in 1970, Thyroid removal in 1990 does not take medications regularly. Appendectomy in 1955, tonsillectomy in 1960, scoliosis, gastric ulcer – treated.

ECG – Sinus rhythm, QRS electrical axis normal, no acute ischemic changes are visible.

LVEDd - 52 mm	LVESd - 38 mm	FS – 25 %	IVS – 12 mm	PW – 11 mm
LVEDV -129 ml	LVESV – 62 ml	EF – 50 %	LA - 43 mm	RV – 38 mm

IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

19 Patient Birthyear - 1937

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II - III)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 25.2 – Old myocardial infarction,

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

N/P

ECG – Sinus rhythm, QRS electrical axis left deviation, QS III, Qr II, aVF, qR V6.

LVEDd – 52 mm	LVESd - 44 mm	FS – 20 %	IVS – 12 mm	PW - 11 mm
LVEDV - 129 mm	LVESV- 70 ml	EF – 40 %	LA - 48 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

20 Patient Birthyear - 1951

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 35.2 – Aortic valve stenosis with regurgitation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right

coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Uterus removal in 2000, right knee surgery with prosthetics in 2018, coronary artery angiography in 2017.

ECG – Sinus rhythm, QRS electrical axis deviation to the left, no acute ischemic changes are present.

LVEDd - 54 mm	LVESd - 38 mm	FS – 29 %	IVS – 12 mm	PW – 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF - 56 %	LA - 45 mm	RV - 41 mm
IVC - 13 mm	> 50 % collapses			RA - 40 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

21 Patient Birthyear - 1938

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II) I 44.4 – Left anterior bundle of Hiss block

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 25.2 – Old myocardial infarction, Z 82.1 – Blindness because of cataracts in both eyes.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Rubella, appendectomy, pneumonia, cholecystectomy, myocardial infarction in 2004.

ECG – Sinus rhythm, QRS electrical axis deviated to the left, heart rate 60, Left anterior bundle of Hiss hemiblock.

LVEDd - 54 m	LVESd - 41 mm	FS – 23 %	IVS – 14 mm	PW - 11 mm
LVEDV - 141 ml	LVESV – 74 ml	EF – 47 %	LA - 40 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

22 Patient Birthyear - 1959

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 42.9 – Cardiomyopathy

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 36.1 – Tricuspid valve regurgitation, I 48 – Atrial fibrillation (paroxysmal form).

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Cholecystctomy 2010, removal of right ovary because of cysts 2000.

ECG – Atrial fibrialtion, heart rate 140, QRS electrical axis normal, signs of left ventricular hypertrophy, ST segment depression in V4-V6; II; III; AVF;

LVEDd - 62 mm	LVESd - 50 mm	FS - 20%	IVS – 13 - 14 mm	PW - 11 mm
LVEDV - 100 ml	LVESV - 40 ml	EF - 38 %	LA - 50 mm	RV - 43 mm
IVC - 13 mm	> 50 % collapses			RA - 40 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation

+1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

23 Patient Birthyear - 1936

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) I 48 – Atrial fibrillation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Atrial fibrillation, tachysystole, QRS electrical axis normal, incomplete right bundle bunch block.

LVEDd - 52 mm	LVESd - 39 mm	FS – 24 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV - 66ml	EF - 48 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

24 Patient Birthyear - 1948

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) I 34.0 – Mitral regurgitation, I 48 – Atrial fibrillation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Rubella, mumps.

ECG – Atrial fibrillation, tachycardia, heart electrical axis normal.

LVEDd - 50 mm	LVESd - 39 mm	FS – 22 %	IVS – 11 mm	PW – 11 mm
LVEDV - 118 mm	LVESV – 66 ml	EF - 46 %	LA - 45 mm	RA - 44 mm
IVC - 13 mm	> 50 % collapses			RA - 45 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

25 Patient Birthyear - 1962

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH), R 73.0 – Positive glucose tolerance test.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Coronary artery stenting in 2017, tonsillectomy in childhood.

ECG – Sinus rhythm, heart rate 65, QRS electrical axis horizontal, QS (-T) III; qR (-T) AVF

LVEDd - 50 mm	LVESd - 35 mm	FS – 28 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV – 51 ml	EF – 56 %	LA - 38 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

26 Patient Birthyear - 1946

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) E 11.8 – Diabetes Meletus type 2, E 66.0 – Obesity caused by excess caloric intake

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right

coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Strumectomy in 2017, takes 100mg of thyroxine, pneumonia – 2017, extrauterine pregnancy in 1973.

ECG – Sinsu rhythm, QRS el. Axis deviation to the left, QS in V2 – 3 - 4 leads.

LVEDd - 48 mm	LVESd - 34 mm	FS – 27 %	IVS – 13 – 14 mm	PW – 11 mm
LVEDV - 107 ml	LVESV – 47 ml	EF - 55 %	LA - 38 mm	RV - 30 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

27 Patient Birthyear - 1937

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) G 45.0 – Vertebra-basilar syndrome, J 44.9 – Chronic obstructive lung disease, R 73.0 – Positive fasting glucose test.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Maniac depressive episodes since 1986.

ECG – Sinus rhythm, heart rae 73, QRS eel. Axis horizontal, R wave incomplete progression in V2 – V4 leads, no acute ischemic changes are present.

LVEDd – 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 13 mm	PW - 11 mm
LVEDV - 129 ml	LVESV- 58 ml	EF – 55 %	LA - 40 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

28 Patient Birthyear - 1961

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow. Past medical history

Gastric ulcer with bleeding in 2019, treated. Appendectomy, tonsillectomy, parathyroid gland removal.

ECG – Sinus rhythm, heart rate 72, QRS el. Axis deviation to the left. PR – 147 ms, QRS – 100 ms, QT - 432 ms.

LVEDd - 50 mm	LVESd - 38 mm	FS - 30 %	IVS – 15 mm	PW – 12 m
LVEDV -118 ml	LVESV - 74ml	EF - 55 %	LA - 42	RV - 34 mm
IVC - 16 mm	> 50 % collapses			RA - 39 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation

+1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

29 Patient Birthyear - 1953

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension grade III (ESH/ESC) I 67.4 – Hypertensive encepalophaty I 83.9 – Varicose disease of the lower limbs without ulcers and complications.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Transient ischemic attack in 2016.

ECG – Sinus rhythm, QRS axis of the heart horizontal, no acute ischemic changes are visible.

LVEDv - 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV – 58 ml	EF – 55 %	LA – 40 mm	RV -37 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Mild dilatation of the left atrium. Systolic function normal EF – 55 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP normal. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I 0.020

30 Patient Birthyear - 1947

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension grade II (ESH/ESC)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. First Obtuse Marginal branch has a 40% stenosis, others without stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections.

ECG – Sinus rhythm, QRS axis of the heart normal. Negative T wave in lead II. Incomplete R wave progression in V1 – V4 leads.

LVEDv - 52 mm	LVESd - 36 mm	FS – 27 %	IVS – 16 mm	PW – 11 mm

LVEDV - 129 ml	LVESV – 55 ml	EF – 57 %	LA – 42 - 45 mm	RV -37 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Mild – moderate dilatation of the left atrium. Systolic function normal EF – 57 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta mild dilation and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I 0.019

31 Patient Birthyear - 1942

ICD 10 Main probable diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension grade II (ESH/ESC) I 34.0 – Mistral valve regurgitation, I 48 – Atrial fibrillation, I 36.1 – Tricuspid valve insufficiency, I 50 – Congestive heart failure.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – 40% stenosis medial and 30% proximal parts. Diagonal branches no visible stenosis. Circumflex artery – no visible stenosis. First Obtuse Marginal branches without stenosis. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Gastroesophageal reflux disease, treated (2017).

ECG – Rhythm atrial fibrillation. I, aVL – R (+T), II aVF – R (-/+T), III -rS (-/+T), V2 - V6 - Rs, HR - 119, QRS - 90, QT - 342

LVEDv - 52 mm	LVESd - 41 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV – 74 ml	EF – 44 %	LA – 45 mm	RV - 40 mm
IVC - 13 mm	> 50 % colapses			

Conclussion – Moderate dilatation of the left atrium. Systolic function moderately decreased EF – 44 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta mild dilation and aortic arch normal. Aortic valve tricuspid, calcified. Mild mitral and tricuspid valve regurgitation +2/+4. Pulmonary artery pressure PASP 30 elevated. Inferior vena cava collapses > 50 %. Pericardial cavity normal.

Cardiac Troponin I < 0.019 ng/ml

32 Patient Birthyear - 1952

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 44.4 – Left anterior bundle of Hiss hemiblock.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) J 44.9 – Chronic obstructive lung disease.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible

stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Right inguinal hernia in 2004.

ECG – Sinsu rhythm, Left anterior hemiblock of the left bundle of Hiss.

LVEDd - 54 mm	LVESd - 38 mm	FS – 27 %	IVS – 12 mm	PW - 11mm
LVEDV - 141 ml	LVESV - 62ml	EF - 56 %	LA - 43 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

33 Patient Birthyear – 1951

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) I 48 – Atrial fibrillation I 34.0 – Mitral valve regurgitation I36.1 – Tricuspid valve regurgitation I27.2 – Pulmonary hypertension E 66.0 – Obesity because of high caloric intake (BMI – 29).

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

ECG – Atrial fibrialtion, tachysistoly (110), frequent premature ventricular contraction.

LVEDd - 63 mm	LVESd - 48 mm	FS – 23 %	IVS – 15 mm	PW - 11 mm
LVEDV - 202 ml	LVESV – 107 ml	EF - 47 %	LA - 53 mm	RV - 46 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function moderately decreased EF - 47 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

34 Patient Birthyear - 1969

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Gallbladder stones treated.

ECG – Sinus rhythm, pulse 75, RS (-T) V2 - V3 rS (+T) V5 – V6. No acute ischemic changes are present.

LVEDd – 52 mm	LVESd - 37 mm	FS – 26 %	IVS – 13 mm	PW - 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF - 55 %	LA – 41 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			RA – 37 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 55 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

35 Patient Birthyear - 1960

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH), R 73.0 – Positive glucose tolerance test.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS axis normal, no acute ischemic changes are present.

LVEDd - 54 mm	LVESd – 39 mm	FS – 26 %	IVS – 12	PW - 11 mm
LVEDV -141 ml	LVESV - 66 ml	EF - 53 %	LA – 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function mildly decreased EF - 53 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +2/+4. Pulmonary artery pressure PASP normal. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

36 Patient Birthyear - 1976

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) I 34.0 – Mitral valve regurgitation I36.1 – Tricuspid valve regurgitation

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Cholecystitis in 2014, 2016, not treated.

ECG – Sinus rhythm, - T wave in aVR, aVL waves, R wave incomplete progression in V1 – V4 waves.

LVEDd - 57 mm	LVESd - 42 mm	FS – 25 %	IVS – 14 mm	PW - 11mm
LVEDV - 100 ml	LVESV - 40 ml	EF- 50 %	LA - 45 mm	RV- 38 mm
IVC - 13 mm	> 50 % collapses			RA – 38 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function moderately decreased EF - 50 %. Diastolic function normal. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid

valve regurgitation +1/+4. Pulmonary artery pressure PASP elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

37 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH), N 20.2 – Kidney and urethral stones, K 76.0 – Fatty liver.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS heart axis left deviation. No acute ischemic changes are visible.

LVEDd - 50 mm	LVESd - 34 mm	FS – 27 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV – 47 ml	EF – 60 %	LA - 42 mm	RV - 38 mm
IVC -13 ∂∂	>50% kolab.			

Conclusion – Left atrium mild dilation. Systolic function normal EF - 60 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +2/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

38 Patient Birthyear - 1960

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) J 44.9 – Chronic obstructive pulmonary disease

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Acute pneumonia in 2000, uterine bleeding because of myomas.

ECG – Sinus rhythm, QRS heart axis normal, no ischemic changes are visible.

LVEDd - 50 mm	LVESd - 34 mm	FS – 28 %	IVS – 12 mm	PW - 10 mm
LVEDV -118 ml	LVESV - 47ml	EF – 56 - 57 %	LA - 38 mm	RV - 37 mm
IVC - ∂∂	>50% kolab.			RA-38∂∂

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

39 Patient Birthyear - 1970

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 27.2 – Secondary pulmonary hypertension.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) J 44.9 – Chronic obstructive pulmonary disease

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

J44.9 – Chronic obstructive pulmonary disease, F45.3 – Somatotropic autonomic (vegetative) disfunction.

ECG – Sinus rhythm, QRS heart axis normal, negative T wave in I, aVL, R wave incomplete progression in V1 – V3 leads.

LVEDd – 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 12 mm	PW - 11 mm
LVEDV - 129 ml	LVESV – 58 ml	EF – 55 %	LA-42 mm	RV-38 mm
IVC - 13 mm	> 50 % collapse			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 55 %. Diastolic disfunction type II. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP moderately elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

40 Patient. Birthyear - 1968

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH), F 45.3 – Autonomic (vegetative) disfunction.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis.

Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections, mumps.

ECG – Sinus rhythm, QRS heart axis normal, negative T wave in III lead, R wave incomplete progression in V1- V3 leads.

LVEDd - 53 mm	LVESd - 38 mm	FS – 27 %	IVS – 11 mm	PW - 10 mm
LVEDV - 136 ml	LVESV- 58 ml	EF – 56 %	LA - 40 mm	RV – 34 mm
IVC - 13 mm	> 50 % collapses			RA - 34 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

41 Patient Birthyear - 1972

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 05.1 – Rheumatic mitral regurgitation, moderate

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) F 45.3 – Autonomic (vegetative) disfunction.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, QRS heart axis normal, - T wave and R wave incomplete progression in leads V1 – V5.

LVEDd - 50 mm	LVESd – 38 mm	FS – 26 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV - 62 ml	EF – 47 %	LA - 41 mm	RV - 35 mm
IVC - 13 mm	> 50 % collapses			RA - 35 mm

Conclusion – Left atrium moderate dilation. Systolic function moderately decreased EF - 47 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1+2/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

42 Patient Birthyear - 1954

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) E 03.9 – Hypothyroidism

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Appendectomy in teenage years.

ECG – Sinus rhythm, QRS electrical axis left deviation, complete right bundle bunch block, signs of left ventricular hypertrophy.

LVEDd - 50 mm	LVESd - 35 mm	FS – 27 %	IVS – 12 mm	PW – 11 mm
LVEDV - 118 ml	LVESV- 51 ml	EF – 56 %	LA - 39 mm	RV - 36 mm
IVC - 13 mm	> 50 % kolab.			

Conclusion – Left atrium and right atrium mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +2/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

43 Patient Birthyear - 1955

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I 45.0 – Complete block of right bundle of Hiss

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH), I 89.0 Lymphedema

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Apendectomy, tonsillectomy.

ECG – Sinus rhythm, QRS electrical axis normal, pulse 71, PQ - 0.13 QRS - 0.09 QT - 0.44 rS (-T)I II, rs (-T) V1, Rsr (-T) V2 RS (-T) V3

LVEDd - 49 mm	LVESd - 33 mm	FS – 27 %	IVS – 11 mm	PW – 10 mm
LVEDV - 112 mm	LVESV - 40 ml	EF - 60 %	LA - 40 mm	RV – 35 mm
IVC - 13 mm	> 50 % collapses			RA - 35 mm

Conclusion – Left atrium normal. Systolic function normal EF - 60 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary

artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

44 Patient Birthyear - 1966

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I, I 44.7 – Complete left bundle bunch block.

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II) I 27.2 – Secondary pulmonary hypertension

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) E 11.8 – Insulin dependent Diabetes Meletus type 2 E 66.0 Obesity caused by excess caloric intake (BMI 32), E 78.8 – Hypercholesteremia,

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Appendectomy in childhood, tonsillectomy.

ECG – Sinus rhythm, heart rate 105, Complete left bundle bunch block.

LVEDd - 64 mm	LVESd - 52 mm	FS – 19 %	IVS – 13 mm	PW – 11 mm
LVEDV - 209 ml	LVESV – 129 ml	EF – 38 %	LA - 47 mm	RV- 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium moderate dilation. Systolic function normal EF - 38 %. Diastolic disfunction type II. No hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

45 Patient Birthyear - 1962

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, sinus arrythmia, heart rate 68, left anterior fascicular block, no acute ischemic changes are present.

LVEDd - 54 mm	LVESd - 39 mm	FS – 26 %	IVS – 13 mm	PW – 11 mm
LVEDV - 141 ml	LVESV – 66 ml	EF - 53 %	LA - 40 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right atrium mild dilation. Systolic function mildly decreased EF - 53 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, calcinotic. Mild mitral valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

46 Patient Birthyear - 1967

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome I

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II) I 27.2 – Secondary pulmonary hypertension, I 36.1 – Tricuspid valve regurgitation.

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 25.2 – Old myocardial infarction, I 48 – Atrial fibrillation, K 25.7 – Gastric ulcer.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible

stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Myocardial infarction and coronary artery stenting with 2 stents implantation. Appendectomy, tonsillectomy.

ECG – Sinus rhythm, QRS electrical axis normal, no acute ischemic changes are visible.

LVEDd - 52 mm	LVESd - 38 mm	FS – 25 %	IVS – 12 mm	PW – 11 mm
LVEDV -129 ml	LVESV – 62 ml	EF – 50 %	LA - 43 mm	RV – 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Right atrium mild dilation. Systolic function mildly decreased EF - 50 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1.5/+4. Pulmonary artery pressure PASP normal. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

47 Patient Birthyear - 1939

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) I 25.2 – Old myocardial infarction,

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Hospitalized for pneumonia about 10 years ago.

ECG – Sinus rhythm, QRS electrical axis left deviation, heart rate 87.

LVEDd – 52 mm	LVESd - 44 mm	FS – 20 %	IVS – 12 mm	PW - 11 mm
LVEDV - 129 mm	LVESV- 70 ml	EF – 40 %	LA - 48 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function moderately decreased EF - 40 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

48 Patient Birthyear - 1954

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 35.2 – Aortic valve stenosis with regurgitation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Coronary artery angiography in 2015, 2017.

ECG – Sinus rhythm, QRS electrical axis deviation to the left, no acute ischemic changes are present.

LVEDd - 54 mm	LVESd - 38 mm	FS – 29 %	IVS – 12 mm	PW – 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF - 56 %	LA - 45 mm	RV - 41 mm
IVC - 13 mm	> 50 % collapses			RA - 40 mm

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve moderate stenosis with mild regurgitation. Tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

49 Patient Birthyear - 1941

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I) I 44.4 – Left anterior bundle of Hiss block

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 25.2 – Old myocardial infarction.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

N/A

ECG – Sinus rhythm, QRS electrical axis deviated to the left, heart rate 70, Left anterior bundle of Hiss hemiblock.

LVEDd - 54 m	LVESd - 41 mm	FS – 23 %	IVS – 14 mm	PW - 11 mm
LVEDV - 141 ml	LVESV – 74 ml	EF – 47 %	LA - 40 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right atrium normal. Systolic function normal EF - 47 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, calcinotic. Mild mitral valve stenosis. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

50 Patient Birthyear - 1961

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA II)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 36.1 – Tricuspid valve regurgitation, I 48 – Atrial fibrillation (paroxysmal form).

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Uterine surgery of fibromas.

ECG – Atrial fibrillation, heart rate 140, QRS electrical axis normal, no acute ischemic signs.

LVEDd - 62 mm	LVESd - 50 mm	FS - 20%	IVS – 13 - 14 mm	PW - 11 mm
LVEDV - 120 ml	LVESV - 40 ml	EF - 38 %	LA - 50 mm	RV - 43 mm
IVC - 13 mm	> 50 %			RA - 40 mm

	collapses			

Conclusion – Left atrium and right atrium moderate dilation. Systolic function severely decreased EF - 38 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

51 Patient Birthyear - 1938

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH) I 48 – Atrial fibrillation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Atrial fibrillation, tachysystole, QRS electrical axis normal, premature ventricular contraction.

LVEDd - 52 mm	LVESd - 39 mm	FS – 24 %	IVS – 12 mm	PW – 11 mm
LVEDV - 129 ml	LVESV - 66ml	EF - 48 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function moderately decreased EF - 48 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve bicuspid, calcinotic, mild stenosis. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

52 Patient Birthyear - 1949

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH) I 34.0 – Mitral regurgitation, I 48 – Atrial fibrillation.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques.

Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

N/A

ECG – Atrial fibrillation, tachycardia, heart electrical axis normal.

LVEDd - 50 mm	LVESd - 39 mm	FS – 22 %	IVS – 11 mm	PW – 11 mm
LVEDV - 118 mm	LVESV – 66 ml	EF - 46 %	LA - 45 mm	RA - 44 mm
IVC - 13 mm	> 50 % collapses			RA - 45 mm

Conclusion – Left atrium normal. Systolic function moderately decreased EF - 46 %. Diastolic function normal. No hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, normal. Mild mitral valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated (high normal). Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

53 Patient Birthyear - 1960

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH), R 73.0 – Positive glucose tolerance test.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis.

Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Gallbladder removal in 2004, tonsillectomy in childhood.

ECG – Sinus rhythm, heart rate 95, QRS electrical axis horizontal, QS in aVF

LVEDd - 50 mm	LVESd - 35 mm	FS – 28 %	IVS – 12 mm	PW - 11 mm
LVEDV - 118 ml	LVESV – 51 ml	EF – 56 %	LA - 38 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 56 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

54 Patient Birthyear - 1944

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension III (ESC/ESH) E 11.8 – Diabetes Meletus type 2, E 66.0 – Obesity caused by excess caloric intake

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Extrauterine pregnancy, 2 medical abortions.

ECG – Sinus rhythm, QRS el. Axis deviation to the left, QS in V2 – 3 - 4 leads.

LVEDd - 48 mm	LVESd - 34 mm	FS – 27 %	IVS – 13 – 14 mm	PW – 11 mm
LVEDV – 107 ml	LVESV – 47 ml	EF - 55 %	LA - 38 mm	RV - 30 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium and right cavity mild dilation. Systolic function normal EF - 55 %. Diastolic disfunction type I. Mild hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

55 Patient Birthyear - 1945

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension I (ESC/ESH), J 44.9 – Chronic obstructive lung disease.

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Childhood infections

ECG – Sinus rhythm, heart rate 63, QRS el. Axis horizontal, R wave incomplete progression in V1 – V4 leads, no acute ischemic changes are present.

LVEDd – 52 mm	LVESd - 37 mm	FS – 27 %	IVS – 16 mm	PW - 11 mm
LVEDV - 129 ml	LVESV- 58 ml	EF – 55 %	LA - 40 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Conclusion – Left atrium normal. Systolic function normal EF - 55 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, fibrotic. Mild mitral and tricuspid valve regurgitation +1/+4. Pulmonary artery pressure PASP mildly elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.021 ng/ml

56 Patient Birthyear - 1972

ICD 10 Main possible diagnosis

I 20.0 – Acute coronary syndrome

ICD 10 Possible complications

I 50.0 – Congestive heart failure (NYHA I)

ICD 10 Comorbidities

I 10 – Primary hypertension II (ESC/ESH)

Coronary artery angiography

FNDC1A – Left coronary artery, without any stenosis. Divides into two branches: Left anterior desending and Circumflex artery. Left anterior descending artery – without any hemodinamicaly significant stenosis. Diagonal branches show no visible stenosis. Circumflex artery – no visible stenosis. Obtuse marginal branches – no significant stenotic lesions. Right coronary artery – without any stenotic lesions or plaques. Recommendation – Continue treatment with medications, no invasive procedure is necessary. Right dominant blood flow.

Past medical history

Partial parathyroid gland removal.

ECG – Sinus rhythm, heart rate 85, QRS el. Axis deviation to the left. No acute ischemic changes are present.

LVEDd - 50 mm	LVESd - 38 mm	FS - 30 %	IVS – 15 mm	PW – 12 m
LVEDV -118 ml	LVESV - 74ml	EF - 55 %	LA - 42	RV - 34 mm
IVC - 16 mm	> 50 % collapses			RA - 39 mm

Conclusion – Left atrium moderate dilation. Systolic function normal EF - 55 %. Diastolic disfunction type I. Moderate hypertrophy of the interventricular septum. Ascending aorta and aortic arch normal. Aortic valve tricuspid, mild regurgitation. Mild mitral and tricuspid valve regurgitation +1+2/+4. Pulmonary artery pressure PASP moderately elevated. Inferior vena cava collapses more than 50 %. Pericardial cavity normal.

Cardiac troponin I < 0.017 ng/ml

Patient 1 STEMI

ICD 10 diagnosis

I 21.0 – Anterior wall MI I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP II)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 11.8 – Diabetes Meletus type 2, E 66.0 – obesity because of excess caloric intake, I 65.2 – carotid artery occlusion and stenosis.

Coronary artery angiography

FNSA01 – Left coronary artery normal. Left anterior descending artery – medial segment stenosis 95%, distal segment syenosis 70%. I diagonal branch occlusion proximally.

Circumflex artery – proximal stenosis 80%, distal stenosis 80%. I Obtuse Marginal branch medial stenosis 90%.

Right coronary artery – medial stenosis 70%, distal stenosis 80%. Posterior descending artery – stenosis 95% proximal, lateral branch 80%.

Recommendation – cardiac surgeon consult. imediatelly.

ECG – Sinus rhythm, QRS el. Axis horizontal, ST segment elevation 2 – 4mm (+/- T) I II AVL V2 - V6. HR - 72. QRS - 100. QT - 445

LVEDd - 52 mm	LVESd - 41 mm	FS – 22 %;	IVS – 16 mm	PW - 11 mm
LVEDV - 129 ml	LVESV- 74 ml	EF – 43 %	LA - 40 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Troponin I (AQT90) BL.7.8 0.075 (0.01-0.023) µg/l

Patient 2 STEMI Birthyear 1976

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Pneumothorax and lung injury due to a knife injury in 2001.

Coronary artery angiography

FNDC1A – Left coronary artery normal. Left anterior descending artery – proximal stenosis 30 %, medial 80 %, distal 30%.

Right coronary artery – proximal stenosis with thrombi masses. Medical stenosis 60%, distal total occlusion.

Right coronary artery re-canalization, balloon angioplasty, 1 stent implantation, TIMI 1 blood flow.

Recommendation: Left anterior descending artery stenting later.

ECG – Sinus rhythm, normal lovltage, QRS el. Axis devisted to the left. Herat rate – 96. QT – 202 ms; QRS – 80 ms; Q T- 332 ms; QS (ST segment elevation 2mm) III. rs (ST segment elevation > 2mm) AVF. ST segment depression 1 mm I, AVL.

LVEDd - 46 mm	LVESd - 30 mm	FS – 27 %	IVS – 10 mm	PW – 11 mm
LVEDV - 100 ml	LVESV - 40 ml	EF - 60 %	LA - 38 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			RA – 37 mm

Cardiac Troponin I 1.7 ng/ml

Patient 3 STEMI Birthyear 1966

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP I) I 27.2 – secondary pulmonary hypertension, I 36.1 – tricuspid valve regurgitation

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 11.8 – Diabetes Meletus type 2, E 66.0 – obesity because of excess caloric intake,

Past medical history

Tonsillectomy, appendectomy in 2020, left heel infected ulcer.

Coronary artery stenting

FNDC1A – Left coronary artery – normal, divides into left anterior descending and circumflex arteries. Left anterior descending artery – proximal 70% stenosis, medial diffuse stenosis and 99% stenosis. I diagonal brunch medial part occlusion.

Circumflex artery – distal part diffuse stenosis 90%. I obtuse marginal branch diffuse stenosis and plaques.

Right coronary artery – without significant hemodynamical occlusions. Posterior descending brunch – medial occlusion and retrograde filling.

Recommendation – heart surgeon consult. immediately.

ECG – Sinus tahcycardia, heart rate 115, QRS el. Axis deviation to the left, ST segment elevation 2 mm - I, II, AVL, V4 - V6. PR – 162 ms, QRS – 95 ms, QT – 315 ms.

LVEDd - 58 mm	LVESd - 46 mm	FS – 20 %	IVS – 12 mm	PW – 11 mm
LVEDV - 166 ml	LVESV - 99 ml	EF - 40 %	LA - 45 mm	RV – 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac Troponin I 0.036 ng/ml

Patient 4 STEMI Birthyear 1952

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 27.2 – secondary pulmonary hypertension

ICD 10 comorbidities

I 10 – primary hypertension I (ESC/ESH), I 34.0 – mitral valve regurgitation, I 36.1 – tricuspid valve regurgitation

Past medical history

Tonsillectomy 1960, left hand fifth finger amputation 2016.

Coronary artery stenting

FNDC1A – Left coronary artery short, normal. Left anterior descending artery – medial stenosisi 80%. Diagonal brunch normal.

Circumflex artery – medial zone occlusion, obtuse marginal brunch 50% stenosis.

Right coronary artery – hypoplastic, no stenosis.

Circumflex artery recanalization with wire, balloon angioplasty, 1 stent implantation.

Recommendation – Left anterior descending and distal circumflex artery stenting.

ECG – Sinus rhythm, QRS el. Axis horizontal, heart rate 85, ST segment depression 3 mm (-T wave II, III, AVF leads).

LVEDd - 55 mm	LVESd - 46 mm	FS – 16 %	IVS – 13 mm	PW – 11 mm
LVEDV - 147 ml	LVESV - 99ml	EF - 33 %	LA - 46 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.37 ng/ml

Patient 5 STEMI Birthyear 1937

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction I 44.7 – left bundle bunch block,

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 25.2 – old myocardial infarction, I 34.0 – mitral valve regurgitation, I 36.1 – tricuspid valve regurgitation, I 27.2 – secondary pulmonary hypertension

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH),

Past medical history

Z 95.5 – coronary artery stenting, inguinal hernia – 1953.

Coronary artery stenting

Left coronary artery – two branches, normal.

Left anterior descending artery – proximal occlusion 95%, medially implanted stent normal.

Circumflex artery – ostial stenosis 80%.

Right coronary artery – proximal chronic occlusion 100%, retrograde filling.

Left anterior descending artery stenting.

Recommendation – Circumflex artery stenting after antiaggregant treatment.

ECG – Sinus rhythm, QRS el. axis severly deviated to the left. LBBB; ST elevation 4mm V2 - V3 , 2 mm V4 leads. ST segment depression 2 mm II, aVF leads.

LVEDd - 57 mm	LVESd - 47 mm	FS – 17 %	IVS – 15 mm	PW – 11 mm
LVEDV - 160 ml	LVESV - 103 ml	EF – 34 - 35 %	LA - 53 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.37 ng/ml

Patient 6 STEMI Birthyear 1960

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH)

Past medical history

Left lower jaw bone infection and surgery 2020.

Coronary artery stenting

Left anterior descending artery – normal. Diagonal branches – normal.

Circumflex artery – medial stenosis 40%. Obtuse marginal brunches normal.

Right coronary artery – medial 99% stenosis.

Right coronary artery stenting with 1 drug eluting stent.

ECG – Sinus rhythm, heart rate 60, ST segment elevation 3 mm II, III, AVF; ST segment depression 0.5 – 1 mm I, AVL, V4 - V6 leads. PR – 190 ms, QRS – 120 ms, QT - 457 ms.

LVEDd - 58 mm	LVESd - 47 mm	FS – 18 %	IVS – 12 mm	PW – 11 mm
LVEDV -166 ml	LVESV - 103 ml	EF – 38 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac Troponin I 2.6 ng/ml

Patient 7 STEMI Birthyear 1968

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34. 0 – mitral valve regurgitation.

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, I 65.2 – carotid artery occlusion and stenosis

Past medical history

I 25.2 – old myocardial infarction

Coronary artery stenting

Left coronary artery – normal.

Left anterior descending artery – ostial 99% stenosis, medial 90% stenosis. Diagonal branches – normal.

Circumflex artery – diffuse plaques, medial segment occlusion, retrograde filling.

Right coronary artery – distal 50% occlusion.

Recommendation – cardiac surgeon consult. immediately.

ECG – Sinus rhythm, heart rate 110, ST segment elevation 4 mm in I, aVL, V5 – V6 leads.

LVEDd – 59 mm	LVESd - 44 mm	FS – 22 %	IVS – 14 – 13 mm	PW – 11 mm
LVEDV - 160 ml	LVESV – 88 ml	EF – 45 %	LA - 46 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			RA – 38 mm

Cardiac Troponin I 1.2 ng/ml

Patient 8 STEMI Birthyear 1953

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP II)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Pneumothorax and lung injury due to a knife injury in 2001.

Coronary artery stenting

Left anterior descending artery – proximal 95% occlusion, medial 40%.

Circumflex artery – medial stenosis 80%, distal 50%.

Right coronary artery – proximal stenosis 80%, medial 70%.

Left anterior descending artery 1 stent implantation.

Recommendation – Right coronary artery stenting after antiplatelet treatment.

ECG – Sinus rhythm ,QRS el. Axis left deviation, ST segment elevation 2 mm in leads V1, V2, V3 – V4 3mm elevation. rS (+T) II, III, aVF;

LVEDd - 54 mm	LVESd - 43 mm	FS – 20 %	IVS – 14 mm	PW – 11 mm
LVEDV - 141 ml	LVESV - 83 ml	EF - 41 %	LA - 40 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 10 ng/ml

Patient 9 STEMI Birthyear 1969

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake, K 80.8 – cholelithiasis

Past medical history

Phlebitis

Coronary artery stenting

Left coronary artery – normal. Divides into two branches.

Left anterior descending – proximal occlusion, retrograde filling.

Circumflex artery – proximal 30 – 40 % stenosis. Obtuse marginal branch – medial stenosis 70 – 80%.

Right coronary artery – proximal thrombus, distal occlusion, retrograde filling.

Recommendation – cardiac surgeon consult. immediately.

EVG – Sinus rhythm, normal volage, ST segment elevation 4 mm in leads V2 – V6, qR (+T) II.

LVEDd - 57 mm	LVESd - 42 mm	FS – 27 %	IVS – 11 mm	PW – 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF – 50 %	LA - 46 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			RA - 40mm.

Cardiac troponin I 0.71 ng/ml

Patient 10 STEMI Birthyear 1949

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH),

Past medical history

Z 95.2 – aortic valve replacement with biologic valve. Appendectomy.

Coronary artery stenting

Left anterior descending artery – proximal stenosis 50%, medial sub-occlusion 99%.

Circumflex artery – medial stenosis 30%.

Left anterior descending artery stenting.

ECG – Sinus rhythm, heart rate 70, left anterior bundle of Hiss block, ST segment depression in V2 – V6 leads 5mm, -T (I, AVL);

LVEDd - 58 mm	LVESd - 45 mm	FS – 22 %	IVS – 13 – 14 mm	PW – 11 mm
LVEDV - 166 ml	LVESV - 92 ml	EF - 44 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.19 ng/ml

Patient 11 STEMI Birthyear 1954

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH),

Past medical history

Hemorrhoids 2018

Coronary artery stenting

Left coronary artery – normal. Divides into two brunches.

Left anterior descending – proximal stenosi 70 – 80 %. Distal 80 – 90 %.

Circumflex artery – normal. Obtuse marginal brunch – proximal stenosis 80 – 90 %, distal 80%.

Right coronary artery – distal occlusion, retrograde filling.

Recommendation – cardiac surgeon consult immediately.

ECG – Sinus rhythm, heart rate, ST segment elevation 3 mm in leads V2 – V5, depression 2mm in leads II, III, aVF.

LVEDd – 50	LVESd – 38	FS – 24	IVS – 17	PW – 11 mm;

mm	mm	%	mm	
LVEDV – 118 ml	LVESV – 63 ml	EF – 46 %	LA – 44 mm	RV – 37 mm; RA – 37/49 mm
IVC – 18 mm	> 50 % kolab.			

Cardiac troponin I 0.013 ng/ml

Patient 12 STEMI Birthyear 1935

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), I 80.0 – lower limb thrombophlebitis, D 51.9 – vit B12 deficiency anemia

Past medical history

Glaucoma 2017, cataracts – 2016.

Coronary artery stenting

Left coronary artery – normal, divides into 3 branches.

Left anterior descending – proximal stenosis 40 %, medial 60 – 70 %. Diagonal brunch – ostial occlusion.

Circumflex artery – distal stenosis 80 %, obtuse marginal brunch – normal.

Intermittent artery – Big vessel, proximal subtotal occlusion.

Right coronary artery – proximal and medical diffuse 90 – 99 % stenosis.

Intermittent artery 2 stent implantation. TIMI – 3.

Recommendation – circumflex artery stenting, after antiplatelet treatment.

ECG – Sinus rhythm, heart rate 70, ST segment elevation 2 mm V5 – V6. R (- T) - I, avL; (+ - T). PR – 182 ms, QRS - 82ms, QT – 447 ms.

LVEDd - 50 mm	LVESd - 38 mm	FS – 23 %;	IVS – 12 mm	PW – 11 mm;
LVEDV - 118 ml	LVESV – 62 ml	EF – 47 %	LA - 38 mm	RV - 36 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 0.22 ng/ml

Patient 13 STEMI Birthyear 1938

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), I 64 – ischemic stroke.

Past medical history

I 25.2 – old myocardial infarction, pneumonia – 2018,

Coronary artery stenting

Left anterior descending artery – proximal 95% stenosis. Medial chronic occlusion. Retrograde filling.

Circumflex artery – distal stenosis 50%, I obtuse marginal branch ostial 95 % stenosis, distal 90 %.

Right coronary artery – proximal chronic occlusion, retrograde filling.

Recommendation – cardiac surgeon consult. immediately.

ECG – sinus rhythm, heart rate 80, QRS el. Axis left deviation, voltage normal, ST segment elevation > 2 mm I, aVL, V2 - V3 - V4 – V 5- V6; rS (+T) III, aVF;

LVEDd – 49 mm	LVESd - 36 mm	FS - 24%;	IVS – 16 mm	PW – 11 mm;
LVEDV – 112 ml	LVESV – 55 ml	EF – 45 %	LA - 38 mm	RV – 30 mm.
IVC - 20 mm	> 50 % kolab.			RA – 32 mm;

Cardiac troponin I 0.022 ng/ml

Patient 14 STEMI Birthyear 1957

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction, I 34.0 – mitral valve regurgitation. I 25.1 – atherosclerotic disease of the heart.

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), S 22.2 – sternal bone fracture. E 11.8 – Diabetes Meletus type 2.

Past medical history

Cholecystitis – in childhood

Coronary artery stenting

Left coronary artery – normal. Divides into two branches.

Left anterior descending- proximal bifurcation stenosis 90% at the diagonal branching area.

Circumflex artery – proximal 80 % stenosis, obtuse marginal artery – normal.

Right coronary artery – diffuse plaques entire length. Distal occlusion.

Right coronary artery 2 stents were implanted. TIMI 3 blood flow.

Recommendation – cardiac surgeon consult.

ECG – sinus rhythm, heart rate 72, normal voltage, ST segment elevation > 2 mm in leads II, 4mm III, aVF; ST segment depression in leads I, avL.

LVEDd - 58 mm	LVESd - 49 mm	FS – 17 %;	IVS – 14 mm	PW – 11 mm
LVEDV - 166 ml	LVESV – 112 ml	EF – 34 – 35 %	LA – 48 – 50 mm	RV – 38 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 1.31 ng/ml

Patient 15 STEMI Birthyear 1956

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 66.0 – obesity because of excess caloric intake,

Past medical history

Z 95.5 – coronary artery stenting 2013 and 2014.

Coronary artery stenting

Left coronary artery – normal. Divides into two branches.

Left anterior descending artery – plaques along entire length. I diagonal branch – 90 % stenosis.

Circumflex artery – ostial 75 % stenosis, diffuse plaques along entire length. Obtuse marginal branch – normal.

Right coronary artery – medial stenosis before old stent.

Right coronary artery stenting with 2 stents. TIMI 3.

Recommendation – after antiplatelet treatment circumflex artery and diagonal artery stenting.

ECG – Sinus rhythm, QRS electrical axis deviated ot the left, heart rate 60, ST segment elevation > 2 mm II, III, AVF leads; ST segment depression 1mm (-+T)I, AVL, V1 - V3 leads.

LVEDd - 52 mm	LVESd – 43 mm	FS – 18 %;	IVS – 13 mm	PW – 11 mm;
LVEDV - 129 ml	LVESV – 83 ml	EF – 36 %	LA – 44 - 45 mm	RV – 38 mm, 42 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 8.3 ng/ml

Patient 16 STEMI Birthyear 1953

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 25.5 – ischemic heart disease

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

I 25.2 – old myocardial infarction 2012, 2015. Z 95.5 – coronary artery stenting 2012, 2015.

Coronary artery stenting

Left coronary artery – normal. Divides into two branches.

Left anterior descending artery – normal. I diagonal brunch – ostial 40% stenosis.

Circumflex artery – proximal 50% stenosis, obtuse marginal brunch – 99% stenosis.

Right coronary artery – proximal old stent 90 % re-stenosis,

Right coronary artery proximal part re-stenting.

ECG – sinus rhythm, heart rate 55 bradycardia, qR (-T)II, III, aVF, rS (+T) V2 - V3, ST segment elevation > 2 mm in leads (-T) I, V5, V6.

LVEDd – 72 mm	LVESd - 65 mm	FS – 10 %;	IVS – 13 mm	PW – 11 mm;
LVEDV - 272 ml	LVESV- 216 ml	EF – 20 %	LA - 50 mm	RV - 40 mm; 46 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 0.19 ng/ml

Patient 17 STEMI Birthyear 1973

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Appendectomy, tonsillectomy, ischemic stroke 2015.

Coronary artery angiography

FNSA01 – Left coronary artery normal. Left anterior descending artery – medial segment stenosis 95%, distal segment syenosis 70%. I diagonal branch occlusion proximally.

Circumflex artery – proximal stenosis 80%, distal stenosis 80%. I Obtuse Marginal branch medial stenosis 90%.

Right coronary artery – medial stenosis 70%, distal stenosis 80%. Posterior descending artery – stenosis 95% proximal, lateral branch 80%.

Recommendation – cardiac surgeon consult. imediatelly.

ECG – sinus rhythm, heart rate 90, premature ventricular contractions, bigeminy, ST segment elevation in leads II III; V1; ST segment depression I, AVL; V2 - V6

LVEDd - 60 mm	LVESd - 47 mm	FS – 21 %;	IVS – 13 – 14 mm	PW – 11 mm;
LVEDV - 181 ml	LVESV – 103 ml	EF - 43% - 44%	LA - 46 mm	RV - 38 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 1.5 ng/ml

Patient 18 STEMI Birthyear 1957

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction, I 71.2 – thoracic aortic aneurism, I 34.0 – mitral valve regurgitation, I 35.1 – aortic valve regurgitation.

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

K 26.7 – duodenal ulcer, without rupture or bleeding.

Coronary artery angiography

FNDC1A – Left coronary artery normal. Left anterior descending artery – proximal stenosis 30 %, medial 80 %, distal 30%.

Right coronary artery – proximal stenosis with thrombi masses. Medical stenosis 60%, distal total occlusion.

Right coronary artery re-canalization, balloon angioplasty, 1 stent implantation, TIMI 1 blood flow.

Recommendation: Left anterior descending artery stenting later.

ECG – sinus rhythm, heart rate 75, QRS el. Axis severe left deviation, ST segment elevation 2 – 4 mm in leads II, III, aVF, (-T) V4 - V6.

LVEDd - 48 mm	LVESd – 33 mm	FS - 20 %;	IVS – 16 mm	PW – 12 mm
LVEDV – 107 ml	LVESV - 44 ml	EF – 53 %	LA - 44 mm	RV - 28 mm
IVC - 16 mm	> 50 % kolab.			RA – 36 mm

Cardiac troponin I 0.54 ng/ml

Patient 19 STEMI Birthyear 1954

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Z 95.5 – coronary artery stenting 2015, I 25.2 – old myocardial infarction 2015. Pneumonia – 2019, appendectomy.

Coronary artery stenting

FNDC1A – Left coronary artery – normal, divides into left anterior descending and circumflex arteries. Left anterior descending artery – proximal 70% stenosis, medial diffuse stenosis and 99% stenosis. I diagonal brunch medial part occlusion.

Circumflex artery – distal part diffuse stenosis 90%. I obtuse marginal branch diffuse stenosis and plaques.

Right coronary artery – without significant hemodynamical occlusions. Posterior descending brunch – medial occlusion and retrograde filling.

Recommendation – heart surgeon consult. immediately.

ECG – sinus rhythm, heart rate 75, voltage normal, QRS el. Axis normal, ST segment elevation > 2 mm in leads V4 – V6.

LVEDd – 56 mm	LVESd - 41 mm	FS – 25 %;	IVS – 12 mm	PW – 11 mm;
LVEDV - 148 ml	LVESV - 74 ml	EF - 50 %	LA - 46 mm	R V- 38 mm;
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 7.4 ng/ml

Patient 20 STEMI Birthyear 1971

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension I (ESC/ESH), I 34.0 -mitral valve regurgitation.

Past medical history

I 25.2 – old myocardial infarction 2020, Z 95.5 – coronary artery stenting 2020,

Coronary artery stenting

FNDC1A – Left coronary artery short, normal. Left anterior descending artery – medial stenosisi 80%. Diagonal brunch normal.

Circumflex artery – medial zone occlusion, obtuse marginal brunch 50% stenosis.

Right coronary artery – hypoplastic, no stenosis.

Circumflex artery recanalization with wire, balloon angioplasty, 1 stent implantation.

Recommendation – Left anterior descending and distal circumflex artery stenting.

ECG – Sinus rhythm, QRS el. Axis horizontal, heart rate 85, ST segment depression 3 mm (-T wave II, III, AVF leads).

ECG – sinus rhythm, heart rate 85, qrs electrical axis deviated to the left, ST segment elevation 2 – 3 mm II, III, AVF; ST segment depression 1 - 2∂∂ I, AVL, V1 -V4 leads.

LVEDd – 55 mm	LVESd - 43 mm	FS – 27 %;	IVS – 14 mm	PW – 11 mm;
LVEDV - 147 ml	LVESV - 8 3ml	EF- 43 %	LA - 45 mm	RV - 38 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 15 ng/ml

Patient 21 STEMI Birthyear 1969

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH),

Past medical history

Duodenal ulcer (at age 30).

Coronary artery stenting

Left coronary artery – two branches, normal.

Left anterior descending artery – proximal occlusion 95%, medially implanted stent normal.

Circumflex artery – ostial stenosis 80%.

Right coronary artery – proximal chronic occlusion 100%, retrograde filling.

Left anterior descending artery stenting.

Recommendation – Circumflex artery stenting after antiaggregant treatment.

ECG – sinus rhythm, heart rate 68, QRS el. Axis normal, ST segment elevation 2 – 4 mm V2 - V4; (-T) I, aVL, V5 - V6.

LVEDd - 55 mm	LVESd - mm	FS - 20 %;	IVS – 19 mm	PW – 17 mm;
LVEDV - ml	LVESV - ml	EF - 40 %	LA - 42 mm	RV - 34 mm;
IVC -17 mm	> 50 % kolab.			RA – 43 mm

Cardiac troponin I 1.5 ng/ml

Patient 22 STEMI Birthyear 1964

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP II)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 11.8 – Diabetes Meletus type 2.

Past medical history

I 25.2 – old myocardial infarction,

Coronary aartery stenting

Left coronary artery – normal.

Left anterior descending artery – ostial 99% stenosis, medial 90% stenosis. Diagonal branches – normal.

Circumflex artery – diffuse plaques, medial segment occlusion, retrograde filling.

Right coronary artery – distal 50% occlusion.

Recommendation – cardiac surgeon consult. immediately.

ECG – sinus rhythm, heart rate 97, ST segment elevation 2 mm in precordial leads, qR (-T) III, AVF,

LVEDd - 53 mm	LVESd - 45 mm	FS – 15 %;	IVS – 12 – 13 mm	PW – 11 mm;
LVEDV - 136 ml	LVESV - 92 ml	EF - 32 %	LA - 43 mm	RV - 36 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 0.74 ng/ml

Patient 23 STEMI Birthyear 1938

ICD 10 diagnosis

I 21.0 – inferior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 27.2 – secondary pulmonary hypertension.

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake, I 48 – atrial fibrillation,

Past medical history

Nose reconstructive surgery in 1970.

Coronary artery stenting

Left anterior descending artery – proximal 95% occlusion, medial 40%.

Circumflex artery – medial stenosis 80%, distal 50%.

Right coronary artery – proximal stenosis 80%, medial 70%.

Left anterior descending artery 1 stent implantation.

Recommendation – Right coronary artery stenting after antiplatelet treatment.

ECG – Rhythm atrial fibrillation, tachycardia, QRS el. Axis deviated to the left, ST segment elevation 2 mm in leads V4 - V6 -T I, AVL, V2 - V6 leads.

LVEDd - 52 mm	LVESd – 38 mm	FS – 27 %;	IVS – 17 mm	PW – 13 mm;
LVEDV - 129 ml	LVESV – 62 ml	EF – 50 %	LA 45 - 50 mm	RV - 42 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 0.2 ng/ml

Patient 24 STEMI

ICD 10 diagnosis

I 21.0 – Anterior wall MI I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP II)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 11.8 – Diabetes Meletus type 2, E 66.0 – obesity because of excess caloric intake, I 65.2 – carotid artery occlusion and stenosis.

Coronary artery angiography

FNSA01 – Left coronary artery normal. Left anterior descending artery – medial segment stenosis 95%, distal segment syenosis 70%. I diagonal branch occlusion proximally.

Circumflex artery – proximal stenosis 80%, distal stenosis 80%. I Obtuse Marginal branch medial stenosis 90%.

Right coronary artery – medial stenosis 70%, distal stenosis 80%. Posterior descending artery – stenosis 95% proximal, lateral branch 80%.

Recommendation – cardiac surgeon consult. imediatelly.

ECG – Sinus rhythm, QRS el. Axis horizontal, ST segment elevation 2 – 4mm (+/- T) I II AVL V2 - V6. HR - 72. QRS - 100. QT - 445

LVEDd - 52 mm	LVESd - 41 mm	FS – 22 %;	IVS – 16 mm	PW - 11 mm
LVEDV - 129 ml	LVESV- 74 ml	EF – 43 %	LA - 40 mm	RV – 36 mm
IVC - 13 mm	> 50 % collapses			

Troponin I (AQT90) BL.7.8 0.075 (0.01-0.023) µg/l

Patient 25 STEMI Birthyear 1976

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Pneumothorax and lung injury due to a knife injury in 2001.

Coronary artery angiography

FNDC1A – Left coronary artery normal. Left anterior descending artery – proximal stenosis 30 %, medial 80 %, distal 30%.

Right coronary artery – proximal stenosis with thrombi masses. Medical stenosis 60%, distal total occlusion.

Right coronary artery re-canalization, balloon angioplasty, 1 stent implantation, TIMI 1 blood flow.

Recommendation: Left anterior descending artery stenting later.

ECG – Sinus rhythm, normal lovltage, QRS el. Axis devisted to the left. Herat rate – 96. QT – 202 ms; QRS – 80 ms; Q T- 332 ms; QS (ST segment elevation 2mm) III. rs (ST segment elevation > 2mm) AVF. ST segment depression 1 mm I, AVL.

LVEDd - 46 mm	LVESd - 30 mm	FS – 27 %	IVS – 10 mm	PW – 11 mm
LVEDV - 100 ml	LVESV - 40 ml	EF - 60 %	LA - 38 mm	RV - 37 mm
IVC - 13 mm	> 50 % collapses			RA – 37 mm

Cardiac Troponin I 1.7 ng/ml

Patient 26 STEMI Birthyear 1966

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP I) I 27.2 – secondary pulmonary hypertension, I 36.1 – tricuspid valve regurgitation

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), E 11.8 – Diabetes Meletus type 2, E 66.0 – obesity because of excess caloric intake,

Past medical history

Tonsillectomy, appendectomy in 2020, left heel infected ulcer.

Coronary artery stenting

FNDC1A – Left coronary artery – normal, divides into left anterior descending and circumflex arteries. Left anterior descending artery – proximal 70% stenosis, medial diffuse stenosis and 99% stenosis. I diagonal brunch medial part occlusion.

Circumflex artery – distal part diffuse stenosis 90%. I obtuse marginal branch diffuse stenosis and plaques.

Right coronary artery – without significant hemodynamical occlusions. Posterior descending brunch – medial occlusion and retrograde filling.

Recommendation – heart surgeon consult. immediately.

ECG – Sinus tahcycardia, heart rate 115, QRS el. Axis deviation to the left, ST segment elevation 2 mm - I, II, AVL, V4 - V6. PR – 162 ms, QRS – 95 ms, QT – 315 ms.

LVEDd - 58 mm	LVESd - 46 mm	FS – 20 %	IVS – 12 mm	PW – 11 mm
LVEDV - 166 ml	LVESV - 99 ml	EF - 40 %	LA - 45 mm	RV – 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac Troponin I 0.036 ng/ml

Patient 27 STEMI Birthyear 1952

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 27.2 – secondary pulmonary hypertension

ICD 10 comorbidities

I 10 – primary hypertension I (ESC/ESH), I 34.0 – mitral valve regurgitation, I 36.1 – tricuspid valve regurgitation

Past medical history

Tonsillectomy 1960, left hand fifth finger amputation 2016.

Coronary artery stenting

FNDC1A – Left coronary artery short, normal. Left anterior descending artery – medial stenosisi 80%. Diagonal brunch normal.

Circumflex artery – medial zone occlusion, obtuse marginal brunch 50% stenosis.

Right coronary artery – hypoplastic, no stenosis.

Circumflex artery recanalization with wire, balloon angioplasty, 1 stent implantation.

Recommendation – Left anterior descending and distal circumflex artery stenting.

ECG – Sinus rhythm, QRS el. Axis horizontal, heart rate 85, ST segment depression 3 mm (-T wave II, III, AVF leads).

LVEDd - 55 mm	LVESd - 46 mm	FS – 16 %	IVS – 13 mm	PW – 11 mm
LVEDV - 147 ml	LVESV - 99ml	EF - 33 %	LA - 46 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.37 ng/ml

Patient 28 STEMI Birthyear 1937

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction I 44.7 – left bundle bunch block,

ICD complications

I 50.0 – Congestive heart failure (KILLIP II) I 25.2 – old myocardial infarction, I 34.0 – mitral valve regurgitation, I 36.1 – tricuspid valve regurgitation, I 27.2 – secondary pulmonary hypertension

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH),

Past medical history

Z 95.5 – coronary artery stenting, inguinal hernia – 1953.

Coronary artery stenting

Left coronary artery – two branches, normal.

Left anterior descending artery – proximal occlusion 95%, medially implanted stent normal.

Circumflex artery – ostial stenosis 80%.

Right coronary artery – proximal chronic occlusion 100%, retrograde filling.

Left anterior descending artery stenting.

Recommendation – Circumflex artery stenting after antiaggregant treatment.

ECG – Sinus rhythm, QRS el. axis severly deviated to the left. LBBB; ST elevation 4mm V2 - V3 , 2 mm V4 leads. ST segment depression 2 mm II, aVF leads.

LVEDd - 57 mm	LVESd - 47 mm	FS – 17 %	IVS – 15 mm	PW – 11 mm
LVEDV - 160 ml	LVESV - 103 ml	EF – 34 - 35 %	LA - 53 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.37 ng/ml

Patient 29 STEMI Birthyear 1960

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH)

Past medical history

Left lower jaw bone infection and surgery 2020.

Coronary artery stenting

Left anterior descending artery – normal. Diagonal branches – normal.

Circumflex artery – medial stenosis 40%. Obtuse marginal brunches normal.

Right coronary artery – medial 99% stenosis.

Right coronary artery stenting with 1 drug eluting stent.

ECG – Sinus rhythm, heart rate 60, ST segment elevation 3 mm II, III, AVF; ST segment depression 0.5 – 1 mm I, AVL, V4 - V6 leads. PR – 190 ms, QRS – 120 ms, QT - 457 ms.

LVEDd - 58 mm	LVESd - 47 mm	FS – 18 %	IVS – 12 mm	PW – 11 mm
LVEDV -166 ml	LVESV - 103 ml	EF – 38 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac Troponin I 2.6 ng/ml

Patient 30 STEMI Birthyear 1968

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34. 0 – mitral valve regurgitation.

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, I 65.2 – carotid artery occlusion and stenosis

Past medical history

I 25.2 – old myocardial infarction

Coronary artery stenting

Left coronary artery – normal.

Left anterior descending artery – ostial 99% stenosis, medial 90% stenosis. Diagonal branches – normal.

Circumflex artery – diffuse plaques, medial segment occlusion, retrograde filling.

Right coronary artery – distal 50% occlusion.

Recommendation – cardiac surgeon consult. immediately.

ECG – Sinus rhythm, heart rate 110, ST segment elevation 4 mm in I, aVL, V5 – V6 leads.

LVEDd – 59 mm	LVESd - 44 mm	FS – 22 %	IVS – 14 – 13 mm	PW – 11 mm
LVEDV - 160 ml	LVESV – 88 ml	EF – 45 %	LA - 46 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			RA – 38 mm

Cardiac Troponin I 1.2 ng/ml

Patient 31 STEMI Birthyear 1953

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP II)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake,

Past medical history

Pneumothorax and lung injury due to a knife injury in 2001.

Coronary artery stenting

Left anterior descending artery – proximal 95% occlusion, medial 40%.

Circumflex artery – medial stenosis 80%, distal 50%.

Right coronary artery – proximal stenosis 80%, medial 70%.

Left anterior descending artery 1 stent implantation.

Recommendation – Right coronary artery stenting after antiplatelet treatment.

ECG – Sinus rhythm ,QRS el. Axis left deviation, ST segment elevation 2 mm in leads V1, V2, V3 – V4 3mm elevation. rS (+T) II, III, aVF;

LVEDd - 54 mm	LVESd - 43 mm	FS – 20 %	IVS – 14 mm	PW – 11 mm
LVEDV - 141 ml	LVESV - 83 ml	EF - 41 %	LA - 40 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 10 ng/ml

Patient 32 STEMI Birthyear 1969

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH), R 73.0 – positive glucose tolerance test, E 66.0 – obesity because of excess caloric intake, K 80.8 – cholelithiasis

Past medical history

Phlebitis

Coronary artery stenting

Left coronary artery – normal. Divides into two branches.

Left anterior descending – proximal occlusion, retrograde filling.

Circumflex artery – proximal 30 – 40 % stenosis. Obtuse marginal branch – medial stenosis 70 – 80%.

Right coronary artery – proximal thrombus, distal occlusion, retrograde filling.

Recommendation – cardiac surgeon consult. immediately.

EVG – Sinus rhythm, normal volage, ST segment elevation 4 mm in leads V2 – V6, qR (+T) II.

LVEDd - 57 mm	LVESd - 42 mm	FS – 27 %	IVS – 11 mm	PW – 11 mm
LVEDV - 100 ml	LVESV – 40 ml	EF – 50 %	LA - 46 mm	RV - 40 mm
IVC - 13 mm	> 50 % collapses			RA - 40mm.

Cardiac troponin I 0.71 ng/ml

Patient 33 STEMI Birthyear 1949

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH),

Past medical history

Z 95.2 – aortic valve replacement with biologic valve. Appendectomy.

Coronary artery stenting

Left anterior descending artery – proximal stenosis 50%, medial sub-occlusion 99%.

Circumflex artery – medial stenosis 30%.

Left anterior descending artery stenting.

ECG – Sinus rhythm, heart rate 70, left anterior bundle of Hiss block, ST segment depression in V2 – V6 leads 5mm, -T (I, AVL);

LVEDd - 58 mm	LVESd - 45 mm	FS – 22 %	IVS – 13 – 14 mm	PW – 11 mm
LVEDV - 166 ml	LVESV - 92 ml	EF - 44 %	LA - 42 mm	RV - 38 mm
IVC - 13 mm	> 50 % collapses			

Cardiac troponin I 0.19 ng/ml

Patient 34 STEMI Birthyear 1954

ICD 10 diagnosis

I 21.1 – posterior wall myocardial infarction

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension III (ESC/ESH),

Past medical history

Hemorrhoids 2018

Coronary artery stenting

Left coronary artery – normal. Divides into two brunches.

Left anterior descending – proximal stenosi 70 – 80 %. Distal 80 – 90 %.

Circumflex artery – normal. Obtuse marginal brunch – proximal stenosis 80 – 90 %, distal 80 %.

Right coronary artery – distal occlusion, retrograde filling.

Recommendation – cardiac surgeon consult immediately.

ECG – Sinus rhythm, heart rate, ST segment elevation 3 mm in leads V2 – V5, depression 2mm in leads II, III, aVF.

LVEDd – 50 mm	LVESd – 38 mm	FS – 24 %	IVS – 17 mm	PW – 11 mm;
LVEDV – 118 ml	LVESV – 63 ml	EF – 46 %	LA – 44 mm	RV – 37 mm; RA – 37/49 mm
IVC – 18 mm	> 50 % kolab.			

Cardiac troponin I 0.033 ng/ml

Patient 35 STEMI Birthyear 1935

ICD 10 diagnosis

I 21.0 – anterior wall myocardial infarction, I 34.0 – mitral valve regurgitation

ICD complications

I 50.0 – Congestive heart failure (KILLIP I)

ICD 10 comorbidities

I 10 – primary hypertension II (ESC/ESH), I 80.0 – lower limb thrombophlebitis, D 51.9 – vit B12 deficiency anemia

Past medical history

Glaucoma 2017, cataracts – 2016.

Coronary artery stenting

Left coronary artery – normal, divides into 3 branches.

Left anterior descending – proximal stenosis 40 %, medial 60 – 70 %. Diagonal brunch – ostial occlusion.

Circumflex artery – distal stenosis 80 %, obtuse marginal brunch – normal.

Intermittent artery – Big vessel, proximal subtotal occlusion.

Right coronary artery – proximal and medical diffuse 90 – 99 % stenosis.

Intermittent artery 2 stent implantation. TIMI – 3.

Recommendation – circumflex artery stenting, after antiplatelet treatment.

ECG – Sinus rhythm, heart rate 70, ST segment elevation 2 mm V5 – V6. R (- T) - I, avL; (+ - T). PR – 182 ms, QRS - 82ms, QT – 447 ms.

LVEDd - 50 mm	LVESd - 38 mm	FS – 23 %;	IVS – 12 mm	PW – 11 mm;
LVEDV - 118 ml	LVESV – 62 ml	EF – 47 %	LA - 38 mm	RV - 36 mm
IVC - 13 mm	> 50 % kolab.			

Cardiac troponin I 0.22 ng/ml

Work performed

Methodology

Patients, selection of samples

Taking patient's blood samples for measurement of UB, CXCR4 and SDF1 required substantial work and interaction with patients and sometimes with their close relatives. We are proud to say we managed this task successfully. Patients who came to the clinic complaining of chest pain and had coronarography/angioplasty performed we visited them during their hospital stay. We explained to them that we were performing research to find alternative markers to troponin for a selected group of patients where troponin could not be used. The success of this research could point the way for better diagnostic marker development and help save their lives just like the lives of the current patients were saved. We asked the permission to view their medical records to see if they are eligible for our research, of course all access to their personal info (including full names, ID numbers etc.) would be restricted to us from the start as first this info was not necessary for our research and second would minimize the chances of leaking of private information. We also explained that if they agreed part of their blood taken by the clinic for diagnostic tests would be used for ELISA testing. The emphasis was done on the fact that only left-over serum samples will be used for testing as usually a couple extra milliliters of blood is taken for diagnostic tests by hospital and our ELISA required 0.5 milliliter or less and no additional invasive procedures (e.g. venous blood aspiration) would be performed on the patients. First, we wanted to measure UB, CXCR4 and SDF1 levels from the same serum sample that Troponin was measured and second removing additional unpleasant procedures helped increase compliance for patients to participate in our research. The patients who agreed to participate signed the written consent.

Preparation of blood samples

The sample types were all serum taken from venous blood. The serum samples were prepared in the serum separator kit and allowed to clot for two hours at room temperature, centrifuged at 1000g (or 3000rpm) for 15 minutes and frozen at -20C degrees for storage.

ELISA test and kit description

As described above UB CXCR4 and SDF1 serum levels were all measured by ELSIA method. ELISA kits for UB CXCR4 and SDF1 were purchases from the MyBioSource company (Catalog numbers: MBS726848, MBS264286, MBS2885086) and test was performed in accordance with the instructions given. The UB kit is a competitive ELSIA, while the CXCR4 and SDF1 are sandwich kits.

ELISA is an enzyme linked immunosorbent assay invented and used by Engvall and Perlmann in 1971. It has both qualitative and quantitative measures meaning it can not only detect the presence of the substance of interest but also the amount with great precision. As the name suggests it requires the interaction of the antibody and antigen and usually is done in the polystyrene micropipette plates (wells). The general idea of ELISA is that we pour the liquid of interest in the wells where the proteins we are looking for are attached to the bottom of the well (if present of course) directly or with the help of antibodies. Later monoclonal antibodies are added to the well. The antibodies are specific to the molecule we are looking for and will only stay inside the well if attached to the molecule of interest, otherwise they are washed out. The specific enzyme is attached to the antibodies (most often horseradish peroxidase) which can interact with a specific substrate and make a product that changes color to yellow amber blue etc. The substrate is usually added in the last step of the ELSIA to detect the color changes of the solution hence the presence of the molecule of interest. The simple change of color can be detected by human eye but to detect the exact amount of molecule of interest in different samples the spectrophotometry method is used that detects the specific amounts by measuring the absorption of the color. The method described is called direct ELSIA. However, there

are four ELSIA methods in total. Indirect ELISA is similar to the direct one the key difference being that there are two antibodies added. In sandwich ELISA the well is coated with antibodies specific for the molecule of interest and if present it will attach to the antibodies rather than the well directly while the other molecules will be washed out. In competitive ELISA a set number of antibodies are mixed with the solution that may contain the molecule of interest and form an antigen-antibody complexes. The solution is poured into the well where only the free antibodies will stay while the antigen-antibody complexes will be washed out. The less antibodies there are inside the well the more antigen-antibody complexes were washed away, meaning the higher the concentration of the molecule of interest in the solution (209-212).

After the desired number of serum samples were collected, they with the help of portable refrigerator were transported to the laboratory for ELISA, where they were unfrozen at room temperature, pipettes with serum shaken in the shaker machine to prevent sedimentation of proteins and resulting bias. Serum samples were grouped according to diagnosis and/or gender. Each group sample (e.g. MI patients) were measured 3 times and their mean value was taken as a number to further exclude any bias.

Patient number, gender selection criteria, diagnostic tests and treatment

All the patients participating in the research were taken to the same hospital with suspicion of having the ACS and diagnosed and treated with the guidelines according to the European society of cardiology. This includes taking patient history, ECG, trans-thoracic cardiac US, cardiac markers including TnI (method of TnI measurement is described below) and coronarography. In this trial we included 60 patients with no ischemia (30 males and 30 females), 25 patients with NSTEMI (15 males and 10 females) and 35 patients with STEMI (20 males and 15 females). Patients with UA were excluded from this trial as the focus of our research was to compare the diagnostic value of all three (UB, CXCR4, SDF1) protein levels and their correlations to troponin (TnI in this case)

which if high could be later used in MI cases were troponin and CK-MB were falsely elevated (CKF). The fact that all 120 patients had done coronarography (some of them had stenting or CABG as needed) and TnI was measured in all of them during the admission, allows us to state that all of them were selected correctly according to diagnosis. Without coronarography this would have been especially challenging in some patients presenting with suspected cardiac pain and negative TnI tests. But coronarography allowed us to distinguish between ischemic cardiac pain without damage to the myocytes and chest pain caused by other reasons that mimicked ischemia.

All the personal information about the patients except gender and age is classified. For every patient whose blood and medical information was used in our research written informed consent was taken.

Troponin measurement method

The TnI was measured for all patients of our study in hospital with the Automatic immunoassay analyzer AQT90 FLEX (Radiometer Medical). The 99th percentile concentration of TnI which is less than 0.023ng/ml (microgram/liter) was taken as the cutoff point to discriminate between MI and no damage group. The sample types were all serum taken from venous blood, the reagents needed for the test are present in a dry stable form inside the AQT90 FLEX and added to the serum sample during the test. They among others contain the tracer and capture antibodies against TnI which will for the sandwich complexes with TnI. Later the solution is washed out and the assay sample is dried leaving only the sandwiched antibodies and TnI (if present) in the sample cup. The signal of tracer antibodies is measured in a dry form by time-resolved fluorimetry (TRF). The measured signal is converted to lab values by the algorithm present inside the machine thus ensuring the correct results (213).

Description of statistical methods

Before we start examining the results of our measurements, we will briefly mention the statistical methods, models and tools we used to analyze our data. RStudio software has been used (214-217).

Analysis of the distribution shows how the data given is distributed and how the data set is likely to be normally distributed (218, 219).

We used Shapiro-Wilk test to determine the normality for each protein of interest. In Shapiro-Wilk test $P > 0.05$ means normal data distribution, while $P < 0.05$ indicates not normal distribution (220, 221).

If not all data is normal distributed, we use Non-parametrical Mann-Whitney U test (Also known as Wilcoxon test) for calculations. The Mann-Whitney U test, is a non-parametric statistical test used to compare two samples or groups when the data is skewed or distributed non-normally.

The null hypothesis (H0) states that the two populations are equal. The alternative hypothesis (H1) is that the two populations are not equal. Critical value used to accept or reject the null hypothesis is: the alternative hypothesis, if $U \leq$ critical value and null hypothesis if $U >$ than that value correspondingly. In Wilcoxon test (Mann-Whitney U Test) in R studio, U is usually mentioned as W - Wilcoxon test statistic (222).

Other tests which we used for our calculations were non-parametric ANOVA test and Tukey's Honestly Significant Difference (Tukey's HSD) post-hoc test. Non-parametric ANOVA test tells us how non-numerical values affect the variance of distribution. This test was also used in our research to measure how much the diagnosis and sex have the effect on the protein distribution. The F-value shows the variance between the groups and inside the groups too (the higher the F-value the higher the chances that difference between groups is larger than inside the groups). The P-value < 0.05 shows the statistical significance of the F-value (223, 224). ANOVA tells us if there are differences among group means, but not where the differences are. For that Tukey's HSD test for pair wise comparisons were used. We showed the Tukey's HSD results both in the

table and in the graph. The significant groupwise differences are present when the 95% confidence interval doesn't include zero. This is another way of saying that the p-value for these pairwise differences is < 0.05 (225, 226).

Spearman correlation was used in our calculations as our data was nonparametric and Spearman's correlation is always and alternative for Pearson correlation in statistics when nonparametric data is used (227).

ROC curve estimation

We used ROC analysis which is one of the recognized methods for measuring the diagnostic power of biomarkers. The most important parameters of this test are AUC and the cut-point estimation. The curve of the ROC represents the graph with two measurements: sensitivity (true positive) and 1 minus specificity (1-sp) (false positive). To correctly determine the usefulness of the biomarker AUC is used. A biomarker that has AUC equal to 1 will tell the difference between healthy and diseased patients 100% of the time while a biomarker with AUC equal to 0.5 that means the biomarker is useless and not different from flipping a coin to decide if the patient is healthy or not. There are two main components of ROC outcome: cut-point value and diagnostic accuracy. Since not all biomarkers are perfect and do not have an AUC of 1, the cut-point value is determined so it identifies most of the individuals correctly.

When using a biomarker for determining the state of the patient (MI or Healthy for example) is used a binary classification (Diseased or healthy, Yes or NO). Even though there are only two possible outcomes, the measuring power of the marker is often not perfect so we can get four possible answers from a ROC analysis:

Predicted Negative (0)Predicted Positive (1)

Actual Negative (0) True Negative (TN) False Positive (FP)

Actual Positive (1) False Negative (FN)True Positive (TP)

The cut-off point of the test is the most important aspect of ROC as if chosen incorrectly even a marker with 95 accuracy will have errors. Each

area of the ROC curve can be chosen as a cut-off value and is associated with test sensitivity (Se) and specificity (Sp). Choosing the cut-off point is almost always associated with Se and Sp compromise, but it can be achieved easily when the disease has high mortality (like myocardial infarction), meaning Se is more important than Sp. Generally, a reasonable approach is preferred to have maximal possible Se and Sp. Of course, the perfect (gold-standard) test will have Se and Sp equal to 1. Selection of the cut-off point criteria depends on the situation the test is applied for and the importance of Se and Sp. Usually Se at least 0.8 or more is used to ensure that not many diseased are missed. For estimation of ROC the ROCit package of Rstudio was used (228-230).

Results

Choosing the strategy for statistical evaluation of data

Checking the normality of the distribution

The data we obtained measuring the levels of UB, CXCR4 and SDF1 in serum by ELSIA method is itself inconclusive unless calculated and analyzed by different statistical methods that can show distribution, correlation, performance, classification etc. of our proteins of interest. The results obtained from these calculations will allow us to draw conclusions how the proteins of interest behave in MI and healthy patients and further elaborate if they can be used as disease markers.

Shapiro-Wilk normality test shows a correct approach for further data assessment. The distribution of UB and CXCR4 was not normal (W = 0.86278, p-value = 0.000795 for ubiquitin and W = 0.91851, p-value = 0.01894 for CXCR4) while SDF1 is approximately normally distributed (W = 0.95318, p-value = 0.1773) (Fig. 8.1).

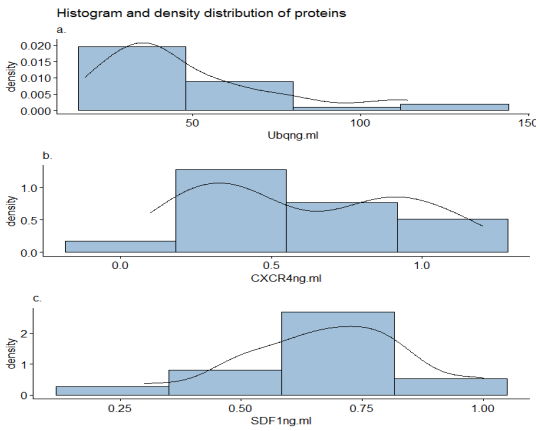

Figure 8.1. Shows density distribution histograms for UB, CXCR4 and SDF1 (a, b and c accordingly). P value and non-bell shape of histograms show non normal distribution of UB and CXCR4 and almost ideal bell-shaped structure for SDF1. W = 0.86278, p-value = 0.000795 for ubiquitin; W = 0.91851, p-value = 0.01894 for CXCR4 and W = 0.95318, p-value = 0.1773 for SDF1.

The correct strategy according to this data is non-parametrical approach for UB, CXCR4 and SDF1.

Non-parametric analysis of UB, CXCR4 and SDF1 proteins in NoDamage and MI groups

For our first calculation we divided the patient serum samples into NoDamage and MI groups (containing both STEMI and NSTEMI) and compared the levels of UB, CXCR4 and SDF1 between the groups (Tab. 8.1, 8.2).

NoDamage			MI		
Ubng.ml	CXCR4ng.ml	SDF1ng.ml	Ubng.ml	CXCR4ng.ml	SDF1ng.ml
28	0.5	0.6	55.5	0.3	0.72
35.5	0.4	0.5	55.5	0.25	0.8
28	0.6	0.81	55.5	0.2	0.72
35.5	0.3	0.7	40	0.9	0.8
28	0.5	0.6	39	0.8	0.3
35.5	0.35	0.5	64	0.9	0.74
25	0.2	0.49	73.2	0.8	0.5
20	0.3	0.51	41	0.9	0.8
19	0.1	0.64	39	0.8	0.3
18	0.9	0.75	62	0.41	0.8
30	0.2	0.49	80	0.43	0.84
25	0.3	0.64	80	0.45	0.8
51	0.1	0.64	100	1	1
40	1.1	0.8	40	1.1	0.65
			114	0.8	0.74

		40	1.2	0.65
		114	1.1	1
		38	1	0.65

Table 8.1. Summary and visualization of the total data set. All numbers are given in nanograms per milliliter. Data set of ELISA results in myocardial infarction (MI) and patients without cardiac damage (NoDamage). All the numbers are arithmetic average of three ELSIA measurements of the same sample group. Each sample has multiple patient serum as levels of UB, CXCR4 and SDF1 were measured in groups of patients with the same parameters. Hence 32 results and 120 initial patients.

Proteins	Diagnosis	n	mean	SD	min	Q1	median	Q3	max
UB ng/ml	MI	18	62.82	25.75	38	40	55.5	78.3	114
	NoDamage	14	29.89	9.02	18	25	28	35.5	51
CXCR4ng/ml	MI	18	0.74	0.32	0.2	0.43	0.8	0.97	1.2
	NoDamage	14	0.42	0.29	0.1	0.22	0.32	0.5	1.1
SDF1 ng/ml	MI	18	0.71	0.19	0.3	0.65	0.74	0.8	1
	NoDamage	14	0.62	0.11	0.49	0.5	0.62	0.69	0.81

Table 8.2. Summary data of all three proteins according to diagnosis. N (number of data), mean, SD (standard deviation), median, min (minimal measurement number), max (maximal measurement number), range, se

(standard error). Data used for evaluation of box plots for UB, CXCR4 and SDF1.

As distribution of variables was not normal for all of the proteins, we used Non-parametrical Mann-Whitney t-test to compare the difference in the amount of proteins in case of different diagnosis. The alternative hypothesis being: true location shift is not equal to 0. As can be seen in Tab. 8.3. the statistically important difference (P value < 0.05) was shown for UB, CXCR4 and SDF1 proteins when comparing MI and NoDamage groups (Fig.8.1).

N	Protein ng/ml	group1	group2	n1Nodamage	n2MI	statistics	*P. value*	*P. value significance*	Effect size	magnitude
1	UB	Healthy	MI	14	18	11.5	0.0001	****	0.77	large
2	CXCR4	Healthy	MI	14	18	60	0.01	*	0.44	moderate
3	SDF1	Healthy	MI	14	18	70.5	0.035	*	0.375	moderate

Table 8.3. The alternative hypothesis: true location shift is not equal to 0. P indicates P value. W indicates W value.

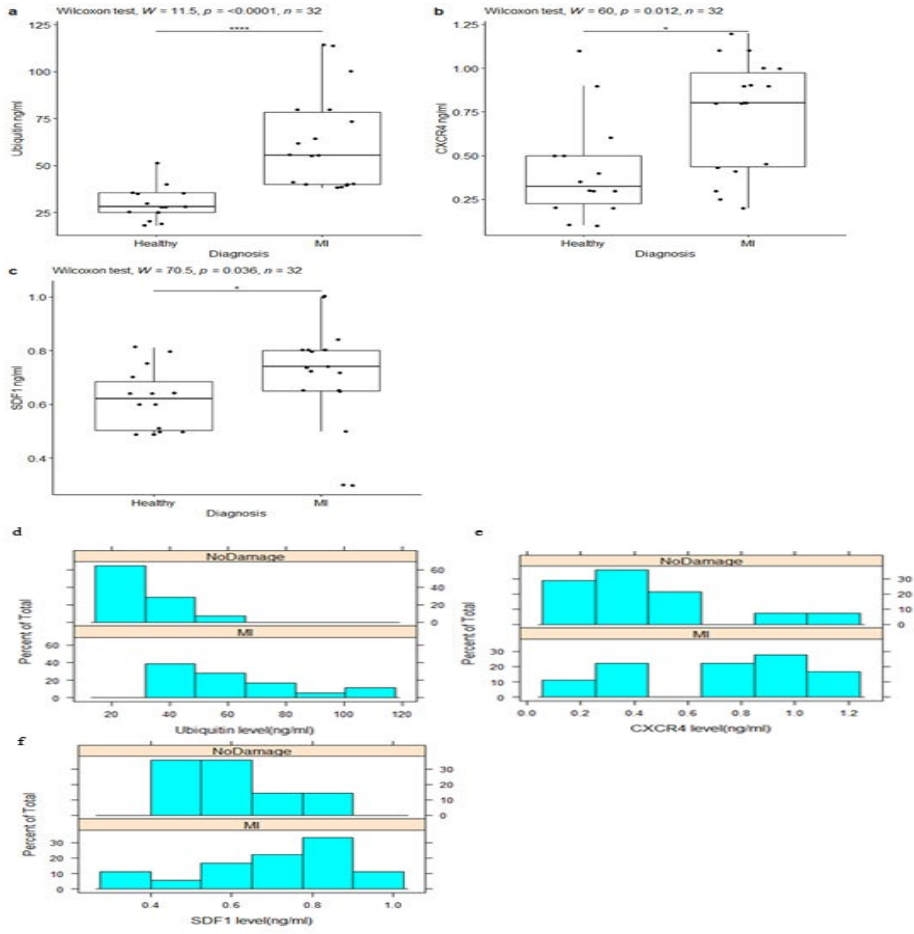

Figure 8.2. a, b and c --- Wilcoxon rank sum test to compare significance of differences of proteins amount for Nodamage and MI groups: UB(a), CXCR4(b) and SDF1(c).

d, e and f --- box plots and distribution of UB (d), CXCR4 (e) and SDF1 (f) for NoDamage and MI groups. The horizontal axis -- concentration of proteins in ng/ml; vertical axis -- the percentage of total protein present.

Fig. 8.2. a, d. indicates that in NoDamage group 80% of Ubiquitin has a low concentration range (from 5 to 15ng/ml) and the approximately 20% is in 16 to 35 ng/ml range. For MI group 100% of the protein is above the

15 ng/ml range, 80% being in the 16 to 35 ng/ml and the rest located even in the higher concentration range. This graph clearly shows that patients with MI have a higher concentration of UB in majority of cases compared to NoDamage group.

Fig. 8.2. b, e. shows that in NoDamage group 75% of protein is distributed in 0.1 to 0.6 ng/ml range. While the remaining 25% lies in 0.6 to 1.3 ng/ml range. The MI group 80% of the protein is in 0.6 to 1.6 ng/ml range and only 20% is in the 0.1 to 0.6 ng/ml range. While there is some overlap in the distribution of proteins in NoDamage and MI groups the 80% of proteins in MI patients has a significantly higher concentration compared to NoDamage group.

Fig. 8.2. c, f. shows that in NoDamage group 75% of proteins are distributed between 0.4 to 0.7 ng/ml ranges. The rest being in the 0.75 to 1.1 ng/ml range. In MI group SDF1 comprises different concentration ranges with approximately 70% of proteins located in the 0.75 to 1.1 ng/ml range. Despite the overlap in MI the SDF1 has higher concentration in 70% and in NoDamage has a lower concentration in 75%.

By analyzing data from Tables 8.1. - 8.3. and Fig. 8.2. we conclude that concentration of UB, CXCR4 and SDF1 differs in MI and NoDamage groups. But to see the statistically significant difference, we used non-parametrical Mann-Whitney test in Tab. 8.3. The test results presented in Tab. 8.3. show the statistically important difference (P value < 0.05) for UB, CXCR4 and SDF1 proteins when comparing MI and NoDamage groups. Which proved our initial conclusions. It should be noted that for all three proteins of interest the concentration in MI group was higher compared to NoDamage group.

Correlation analysis of UB, CXCR4 and SDF1

As all three investigated proteins share the receptor ligand relationship, we analyzed their correlation to see if they have any positive or negative correlation in serum and if this correlation varies according to diagnosis. The correlation test was made by Spearman method. Knowledge of

correlation between UB, CXCR4 and SDF1 could help us in the understanding the variability of molecular relationships caused by diagnosis. This data along with serum levels of proteins can be used in the further medical implementation of our research (Fig. 8.3.).

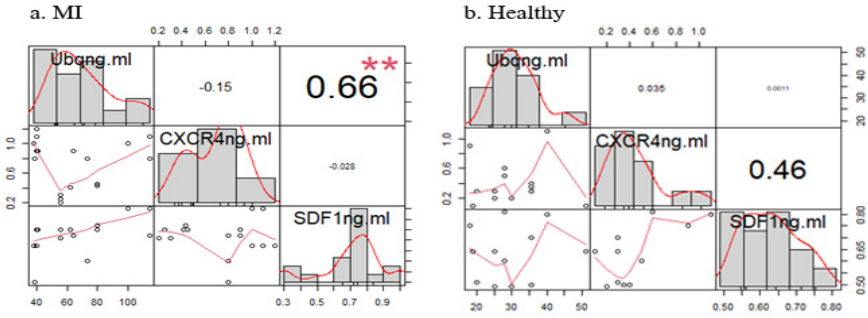

Figure 8.3. Correlation test for proteins of MI (a) and Healthy (b) groups.

It is evident the positive correlation between UB and SDF1 in MI group with Correlation coefficient 0.66, P<0.01. Unlike MI groups no correlation was found in NoDamage group. Even though the correlation coefficient is 0.46 between CXCR4 and SDF1 the P value is >0.05 making it statistically insignificant. By this data we concluded that UB and SDF1 correlate mainly in MI group.

Non-parametric analysis of UB, SDF1 and CXCR4 proteins in NoDamage and MI groups according to sex

Measurement method of troponin levels for diagnosis of MI has same cut-off values for both males and females, due to standard methodology which doesn't take into the account patients' sex. However, levels of many blood and plasma proteins are different in males and females. For example, testosterone, estrogen, hemoglobin, creatinine, etc. For this reason, we divided the serum samples into MI male, MI female, NoDamage male and NoDamage female groups and measured the results to see if sex could be a factor in the fluctuation of serum levels of UB, CXCR4 and SDF1 according to diagnosis. Tab. 9.1 shows the complete data-sets for all four groups.

a

Ubiquitin ng/ml		n	mean	SD	min	Q1	median	Q3	max
Diagnosis	MI	21	64.129	24.034	38	40	60	75	114
	NoDamage	8	28.5	11.576	18	19.75	25	32.5	51
Sex	Female	14	46.586	17.480	18	39	40	60	75
	Male	15	61.500	31.917	20	35	61.5	82	114

b

CXCR4 ng/ml		n	mean	SD	min	Q1	median	Q3	max
Diagnosis	MI	21	0.837	0.318	0.2	0.720	0.9	1.0	1.5
	NoDamage	8	0.4	0.382	0.1	0.175	0.25	0.450	1.1
Sex	Female	14	0.853	0.385	0.1	0.740	0.85	1.1	1.5
	Male	15	0.593	0.343	0.2	0.25	0.5	0.9	1.1

c

SDF1 ng/ml		n	mean	SD	min	Q1	median	Q3	max
Diagnosis	MI	27	0.724	0.188	0.30	0.650	0.735	0.80	1
	NoDamage	14	0.620	0.117	0.49	0.505	0.640	0.68	0.8

Sex	Female	14	0.628	0.159	0.30	0.640	0.65	0.729	0.8
	Male	14	0.757	0.172	0.49	0.67	0.8	0.825	1

Table 9.1 a, b and c Summary data of all three proteins according sex and diagnosis.

As can be seen from Fig. 9.1 while UB and CXCR4 concentrations are higher in MI group both in males and females, the concentration difference is larger in males. As for SDF1, in males it follows the typical pattern being significantly higher in MI compared to NoDamage group, but in females the opposite is observed NoDamage female patients having higher concentration of SDF1 compared to MI group. Data visualization in Fig. 9.1.

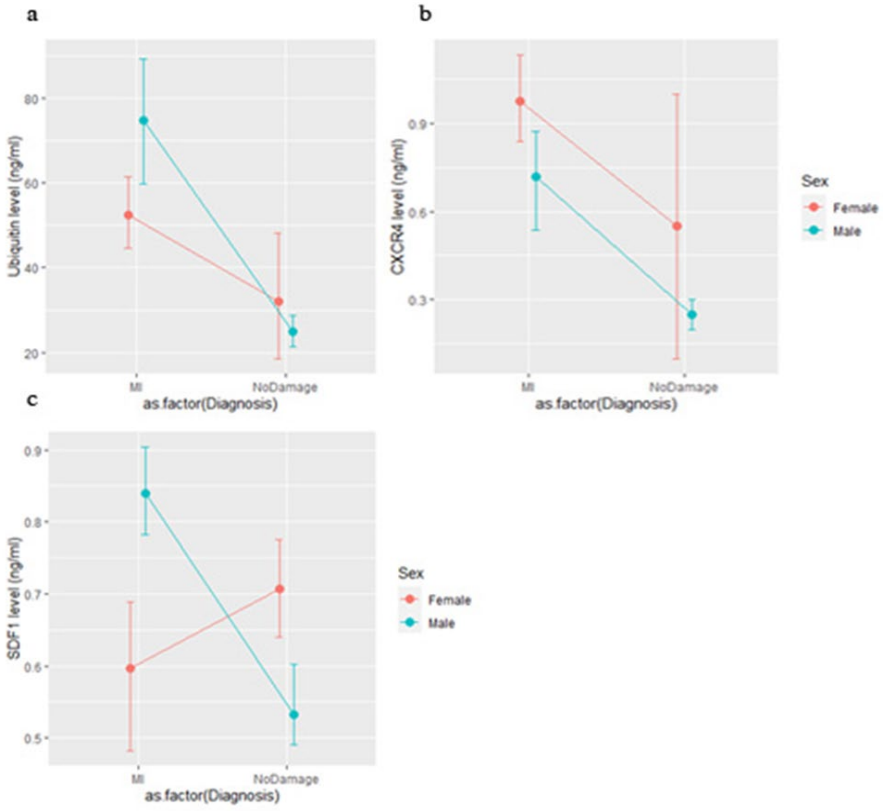

Figure 9.1. UB (a), CXCR4 (b) and SDF1 (c) data according to diagnosis and sex. Female NoDamage – Female MI, Male NoDamage – Male MI groups for the UB, CXCR4 and SDF1 proteins accordingly.

While UB and CXCR4 concentrations are higher in MI group both in males and females, the concentration difference is larger in males. For SDF1, in males it follows the typical pattern being significantly higher in MI compared to NoDamage group, but in females the opposite is observed NoDamage female patients having higher concentration of SDF1 compared to MI group. To prove the significance of the data of comparison of sex and diagnosis relationship we use ANOVA test.

ANOVA test of UB, SDF1 and CXCR4 proteins in NoDamage and MI groups according to sex

UB levels are strongly affected by diagnosis, but diagnosis and sex interaction affect UB levels on the level of statistical tendency, while the Sex itself has no effect on the diagnosis. CXCR4 levels are affected by diagnosis and sex affects CXCR4 levels on the level of statistical tendency, while the Sex itself has no effect on diagnosis. For SDF1 on the contrary sex is the major determinant of SDF1 levels, the diagnosis also has statistical significance and the effect of Sex on the diagnosis is large (large F value) and statistically significant that is in accordance with published data (Tab. 9.2), (231).

a.

Ubiquitin	Df	Df.res	F value	Pr(>F)
Sex	1	25	2.5701	0.121462
Diagnosis	1	25	26.9558	2.2702e-05 ***
Sex: Diagnosis	1	25	3.9847	0.056916 .

b.

CXCR4	Df	Df.res	F value	Pr(>F)
Sex	1	25	3.82408	0.061786 .
Diagnosis	1	25	9.24792	0.005470 **
Sex: Diagnosis	1	25	0.17675	0.677770

c.

SDF1	Df	Df.res	F value	Pr(>F)
Sex	1	25	5.1931	0.03148090 *
Diagnosis	1	25	5.8761	0.02291395 *

Sex : Diagnosis	1	25	18.2565	0.00024528 ***

*Table 9.2. ANOVA analysis for UB(a), CXCR4(b) and SDF1(c). Df, Df.res – degrees of freedom, Pr – P value. The asterisks indicate the number of P value: 0 '***', 0.001 '**', 0.01 '*', 0.05 '.'*

Further Tukey's test distinguished the difference between results of each group (Tab. 9.3.). Here we are interested in the comparison of the same diagnosis groups in case of different sex.

a

Contrast	Estimate	SE	DF	T ratio	P
Female, MI - Female, NoDamage	7.33	3.39	25	2.155	0.1637
Female, MI - Male, MI	-7.16	2.51	25	-2.853	0.04
Female, NoDamage - Male, NoDamage	2.88	4.06	25	0.708	0.8931
Male, MI - Male, NoDamage	17.05	3.35	25	5.176	0.0001

b

Contrast	Estimate	SE	DF	T ratio	P
Female, MI - Female, NoDamage	7.83	4.46	25	1.756	0.3174
Female, MI - Male, MI	4.56	3.29	25	1.387	0.5190
Female, NoDamage - Male, NoDamage	5.88	5.33	25	1.103	0.6910
Male, MI - Male, NoDamage	9.14	4.40	25	2.077	0.1880

c

Contrast	Estimate	SE	DF	T ratio	P
Female, MI - Female, NoDamage	-3.621	3.35	25	-1.082	0.7032
Female, MI - Male, MI	-11.82	2.47	25	-4.806	0.0003
Female, NoDamage - Male, NoDamage	9.12	4.00	25	2.280	0.13
Male, MI - Male, NoDamage	17.39	3.31	25	5.260	0.0001

Table 9.3. Tukey's test for UB(a), CXCR4(b) and SDF1(c). Estimate – calculation coefficient, SE – standard error, DF – degrees of freedom, T ratio – T score, and P is P value.

UB levels are strongly affected by diagnosis, but diagnosis and sex interaction affect UB levels on the level of statistical tendency, while the Sex itself has no effect on the diagnosis.

CXCR4 levels are affected by diagnosis and sex affects CXCR4 levels on the level of statistical tendency, while the Sex itself has no effect on diagnosis.

For SDF1 on the contrary sex is the major determinant of SDF1 levels, the diagnosis also has statistical significance and the effect of Sex on the diagnosis is large (large F value) and statistically significant.

As can be seen from section 8 if we compare MI and Nodamage groups for UB, CXCR4 and SDF1 proteins the statistically important difference was found for all three proteins. However, when we divided the MI and NoDamage patients into male and female groups, more interesting results occurred. For males UB and SDF1 were statistically different in MI and NoDamage, while CXCR4 levels were not. However, for females, UB and CXCR4 were higher in MI than no damage group but without the statistical significance (P value >0.05). For SDF1 female group, not only was the difference in MI and NoDamage groups not statistically

significant but the levels of SDF1 were higher in NoDamage group compared to MI group (Opposite to the SDF1 Male group). This lets us conclude that when we compared the MI to NoDamage group without division by sex the statistically important significance for UB, CXCR4 and SDF1 proteins were due to the male patients.

Correlation analysis of UB, CXCR4 and SDF1 according to diagnosis and sex

As all three investigated proteins share the receptor ligand relationship, we analyzed their correlation to see if they have any positive or negative correlation in serum and if this correlation varies according to diagnosis and sex. Knowledge of correlation between UB, CXCR4 and SDF1 could help us in the understanding the variability of molecular relationships caused by diagnosis. This data along with serum levels of proteins can be used in the further medical implementation of our research. The results are presented in Fig. 9.2. below. The correlation was made by Spearman method.

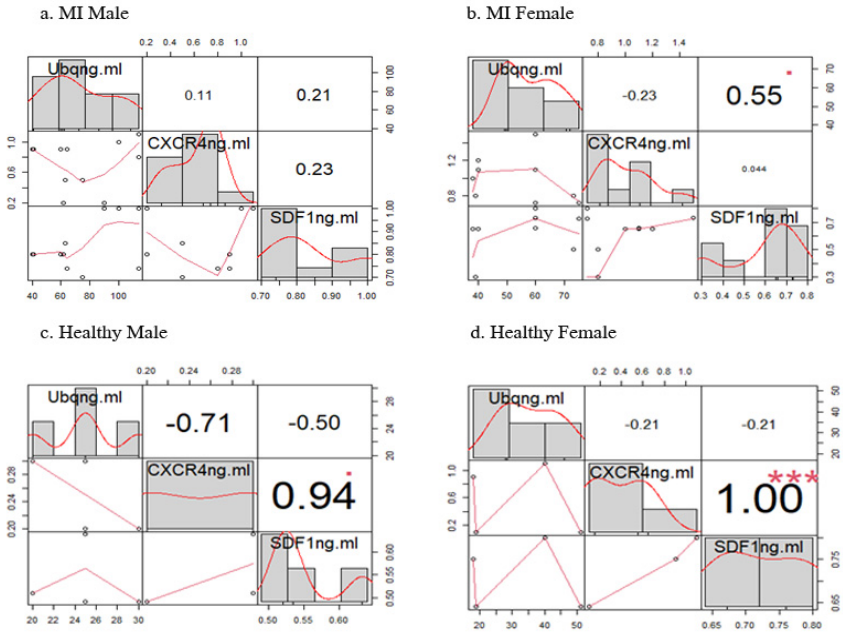

Figure 9.2. Correlation of UB, CXC4 and SDF1 in MI Male group (a). Female MI group (b). NoDamage Male group (c). NoDamage Female group (d).

No statistically significant correlation was observed in MI male group. The positive correlation of UB/SDF1 pair was observed on the level of statistical significance in female MI group. There a perfect correlation coefficient of 1 was obtained in CXCR4/SDF1 pair with a very high level of statistical significance for Nodamage female group.

While we obtained very statistically important correlation between UB and SDF1 in MI group when not dividing the groups by sex we did not see the same correlation when MI groups were divided by sex. This indicates that there is not any statistically important correlation between them. It may have happened because the lack of number of samples. At the same time, we obtained correlation coefficient of 0.94 in NoDamage male group but with only a statistical tendency and same results were not present when measured in NoDamage total groups (male + female). Again, we came to the conclusion that sex may be very important for the correlation of these proteins and requires further investigation to increase the number of groups as every statistical analysis works better with increased number of data.

Non-parametric analysis of UB, SDF1 and CXCR4 proteins in NoDamage, STEMI and NSTEMI groups

As discussed earlier, STEMI and NSTEMI have different treatment guidelines and NSTEMI can be harder to diagnose in patients with diseases where troponin is chronically elevated. For this reason, we divided patients into NoDamage, STEMI and NSTEMI groups to further measure and understand the concentration and correlation differences of UB, CXCR4 and SDF1 in healthy and diseased states. The summary of data sets used for the calculations are presented in Tab.10.1. As can be seen on Fig. 10.1 the concentration of all three proteins is as follows: STEMI>NSTEMI>NoDamage, however there is significant overlap especially for CXCR4 and SDF1 proteins.

Proteins	Diagnosis	n	mean	sd	min	Q1	median	Q3	max
Ubiquitin ng/ml	NoDamage	14	29.89	9.02	18	25	28	35.5	51
	NSTEMI	9	51.41	12.4	39	40	55.5	55.5	73.2
	STEMI	9	74.22	31.02	38	40	80	100	114
CXCR4ng/ml	NoDamage	14	0.42	0.29	0.1	0.22	0.32	0.5	1.1
	NSTEMI	9	0.65	0.3	0.2	0.3	0.8	0.9	0.9
	STEMI	9	0.83	0.32	0.41	0.45	1	1.1	1.2
SDF1 ng/ml	NoDamage	14	0.62	0.11	0.49	0.5	0.62	0.68	0.81
	NSTEMI	9	0.63	0.21	0.3	0.5	0.72	0.8	0.8
	STEMI	9	0.79	0.14	0.6	0.6	0.8	0.8	1

					5	5		4	

Table 10.1. NoDamage, STEMI and NSTEMI groups. Concentration and correlation differences of UB, CXCR4 and SDF1 in healthy and diseased states. The summary of data sets.

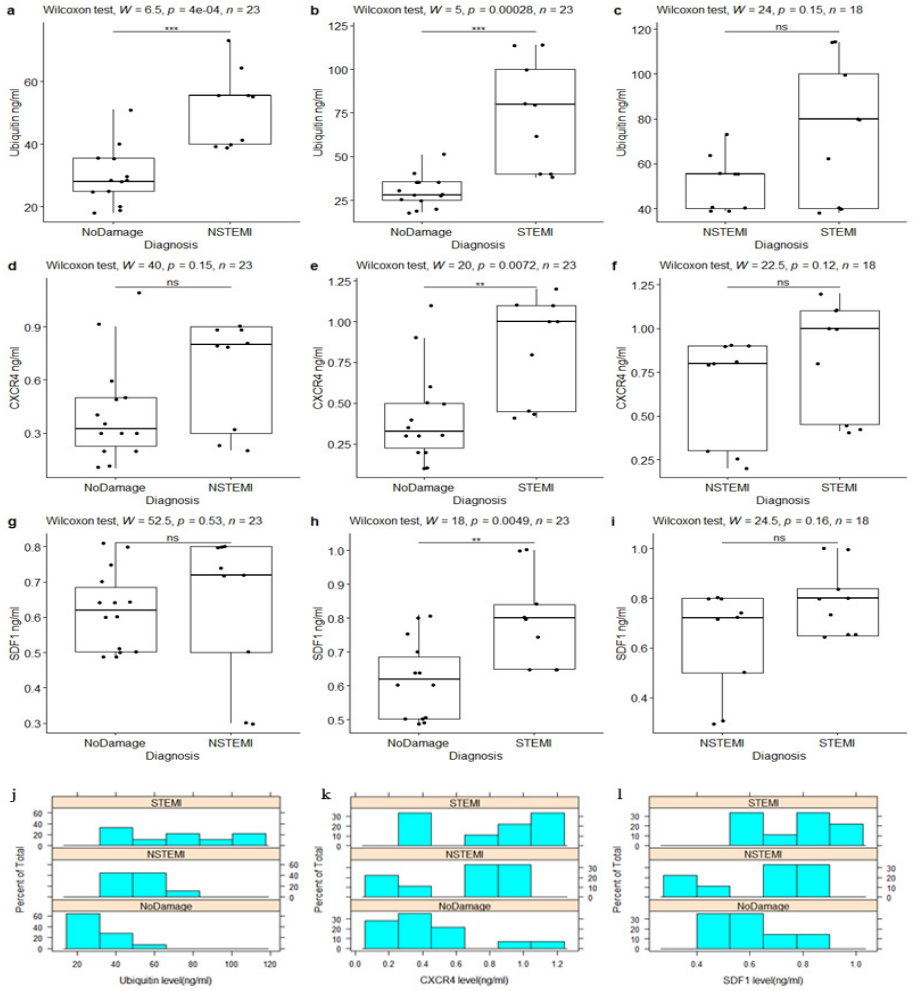

Figure 10.1 a-i – Statistical reliability of UB, CXCR4, SDF1 protein concentration differences in STEMI, NSTEMI and NoDamage groups. J-l - - representing distribution of UB, CXCR4 and SDF1 in NoDamage,

STEMI and NSTEMI groups. The horizontal axis shows concentration of proteins in ng/ml and vertical one shows the percentage of total protein present.

Chart – j - for UB indicates that in NoDamage group 65% of ubiquitin has a low concentration range (from 5 to 15ng/ml) and the approximately 30% is in 15 to 25 ng/ml range. NSTEMI group 60% of UB is distributed above the 25 ng/l range, 40% in the 15-25 ng/ml range. At the same time in STEMI group only 30% of UB is in the range of 15 to 25 ng/ml range while the rest is above 25 ng/ml. This graph clearly shows that patients with STEMI and NSTEMI have a higher concentration of UB in majority of cases compared to NoDamage group.

Chart - k - for CXCR4 shows that in NoDamage group 80% of protein is distributed in 0.1 to 0.7 ng/ml range. While the remaining 20% lies in 0.8 to 1.3 ng/ml range. The NSTEMI group 60% of the protein is located in 0.6 to 1.1 range. The remaining 40% being distributed in the low 0.1-0.5 ng/ml range. In STEMI group 70% of CXCR4 is above the 0.6 ng.ml range while the rest in 0.2-0.4 ng/ml range. While there is some overlap in the distribution of proteins in NoDamage, NSTEMI and STEMI groups the majority of proteins in NSTEMI and STEMI patients still has a higher concentration compared to NoDamage group.

Chart – l - for SDF1 shows that in NoDamage group 80% of proteins are distributed between 0.4 to 0.7 ng/ml range. The rest being in the 0.75 to 1 ng/ml range. In NSTEMI group SDF1 comprises different concentration ranges with approximately 70% of proteins located in the 0.7 to 0.9 ng/ml range while STEMI group SDF1 is relatively equally distributed between 0.5-1.1 ng/ml range. Unlike the graphs a and b, the protein concentration distribution between NoDamage, NSTEMI and STEMI groups seems relatively equal.

We again used Non-parametrical Mann-Whitney t-test to compare the difference in the amount of proteins in case of different diagnosis. The alternative hypothesis being: true location shift is not equal to 0.

Protein	group1	group2	Effect size	n1	n2	magnitude
Ubqng.ml	NoDamage	NSTEMI	0.74	14	9	large
	NoDamage	STEMI	0.76	14	9	large
	NSTEMI	STEMI	0.35	9	9	moderate
CXCR4ng.ml	NoDamage	NSTEMI	0.3	14	9	moderate
	NoDamage	STEMI	0.57	14	9	large
	NSTEMI	STEMI	0.38	9	9	moderate
SDF1ng.ml	NoDamage	NSTEMI	0.139	14	9	small
	NoDamage	STEMI	0.59	14	9	large
	NSTEMI	STEMI	0.34	9	9	moderate

Table 10.2. Mann-Whitney t-test. The statistically important difference (P value < 0.05) was shown in all three proteins when comparing STEMI patients with no damage groups and in UB proteins when comparing NSTEMI and NoDamage groups.

As can be concluded from the data above the statistically important differences for UB are present between NoDamage/STEMI and NoDamage/NSTEMI groups. As for CXCR4 and SDF1 the difference was shown for NoDamage/STEMI groups only.

Correlation analysis of UB, CXCR4 and SDF1 according to STEMI, NSTEMI and NoDamage groups

We built correlation matrix that shows how the distribution of data correlates with each other in a graphical from for every diagnosis group (NoDamage, STEMI, NSTEMI). The correlation was made by Spearman correlation coefficient (Fig. 10.2). In STEMI group the correlation is only between UB and SDF1 (correlation coefficient is 0.75 and P value < 0.05). No other correlation between UB, CXCR4 and SDF1 was observed in STEMI, NSTEMI and NoDamage groups.

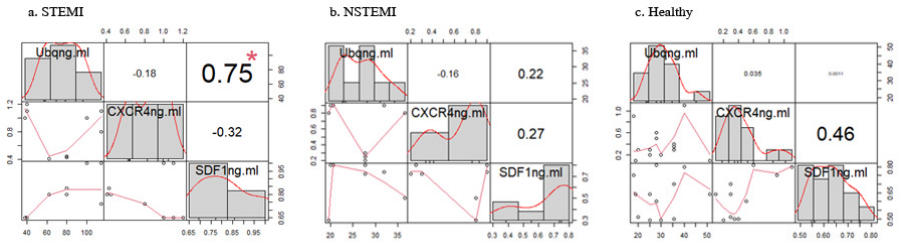

Figure 10.2. STEMI(a), NSTEMI(b) and NoDamage(c) groups. Correlation between protein concentrations respectively. In STEMI group the correlation is only between UB and SDF1 (correlation coefficient is 0.75 and P value <0.05). No other correlation between UB, CXCR4 and SDF1 was observed in STEMI, NSTEMI and NoDamage groups.

Receiver Operating Characteristic Curve (ROC) analysis of protein for NoDamage, STEMI and NSTEMI groups

Finally, we did ROC test to examine the effectiveness of UB, CXCR4 and SDF1 as markers of MI. We also did the ROC test for Troponin to compare our hypothetical markers to the gold standard. Results of STEMI and NSTEMI patients were considered to be positive and results of NoDamage patients negative (same classification is done for all medical tests in general practice). As myocardial infarction is a very serious disease with very high mortality and complication rates, the Sensitivity was the number one concern. We wanted to make a cut-off value so that STEMI and NSTEMI patients were not considered as negative (in short no False Negative patients).

Ubiquitin, SDf1.CXCR4. Troponin data evaluation

Tab. 11.1 represents the predicted probabilities and cut-off point analysis of STEMI, NSTEMI and NoDamage groups for UB, CXCR4, SDF1 and TnI.

Fig. 11.1 is ROC curve for UB, CXCR4, SDF1 and TnI where black line is for STEMI condition and red line – for NSTEMI condition.

All the results are discussed below.

Diagnosis	Protein	ng/ml	Probability	Health status	Cutoff	TP	FP	TN	FN	ACC	SENS	SPEC	FSCR
STEMI - NoDamage	UB	62	0.9478257 6	+	0.2694	9	2	12	0	0.91	1	0.857	0.9
NSTEMI		55.5	0.95259	+	0.393	9	2	12	0	0.91	1	0.85	0.9

- NoD amag e					8						7	
STE MI - NoD amag e	CXC R4	0.4 1	0.223 6995 7	+	0.2 23 7	9	5	9	0	0. 78	1	0. 64 3	0. 78
NST EMI - NoD amag e		0.3	0.258 444	+	0.2 10 8	9	1 2	2	0	0. 48	1	0. 14 3	0. 6
STE MI - NoD amag e	SDF 1	0.8	0.674 429	+	0.2 66 3	9	4	1 0	0	0. 83	1	0. 71 4	0. 82
NST EMI - NoD amag e		0.7 2	0.403 271	+	0.3 51 3	9	1 4	0	0	0. 39	1	0	0. 56
STE MI - NoD amag e	Trop onin	2.5	1	+	1	9	0	1 4	0	1	1	1	1

NSTEMI - NoDamage		0.27	1	+	1	9	0	14	0	1	1	1	1

Table 11.1 Summary data of cutoff analysis for all proteins. Probabilities and corresponding cutoff in concentration units and probabilities are included. TP- True positive rate, FP – False positive rates, TN – True negative rates, FN – False negative rates, ACC – accuracy, SENSE – Sensitivity, SPEC – Specificity, FSCR - Full scale range.

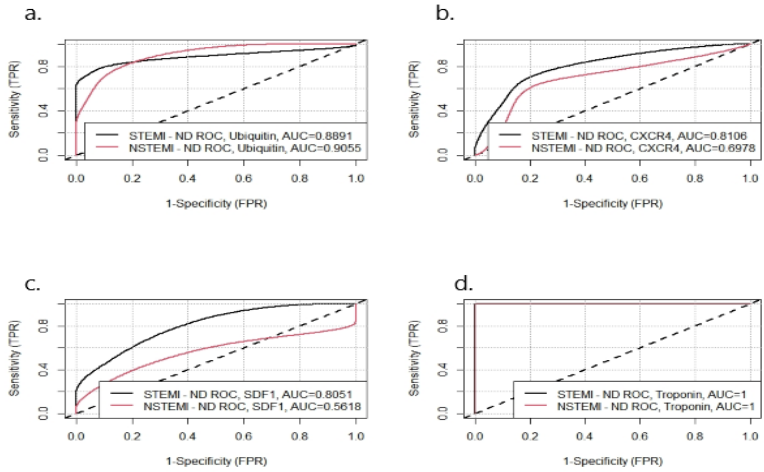

Figure 11.1. a. STEMI - solid black, NSTEMI – solid red ROC curves for ubiquitin; b. STEMI - solid black, NSTEMI – solid red ROC curves for CXCR4; c. STEMI - solid black, NSTEMI – solid red ROC curves for SDF1; d. STEMI - solid black, NSTEMI – solid red ROC curves for troponin.

For UB (Fig. 11.1. a, Tab. 11.1) we saw that the cut-off value was 0.27 and 0.39 for STEMI and NSTEMI respectively. Not only we did not have any

False Negative (FN) patients at this level but the number of False Positive (FP) patients was low: for both STEMI and NSTEMI less than 10% of all patients tested.

Cut-off values have been studied via calculations of minimal FP and maximal TP 38ng/ml and 39ng/ml of UB in serum for STEMI and NSTEMI correspondingly. Meaning the test considers patients having the serum levels of more than UB 38 ng/ml (STEMI) and 39 ng/ml (NSTEMI) to have MI. In the end as seen on Figure 1 STEMI and NSTEMI AUC covers 89% and 90% of the whole area respectively. Indicating the very high positive predictive value of the test.

For CXCR4 (Fig.11.1. b., Tab. 11.1) the cut-off value with no FN patients in STEMI and NSTEMI groups was 0.22 and 0.21 respectively. Meaning the test considers patients having the serum levels of more than CXCR4 0.41 ng/ml (STEMI) and 0.2 ng/ml (NSTEMI) to have MI. The problem was the increased number of FP patients especially for NSTEMI. (5 or 22% of all patients tested were FP for STEMI and 12 or almost 50% of all patients were FP for NSTEMI). The AUC was 81% for STEMI and 70% for NSTEMI indicating it as a poor prognostic marker for MI especially NSTEMI which is usually harder to detect compared to STEMI.

For SDF1 (Fig.11.1. c., Tab. 11.1) the cut-off value where we had 0 FN patients was 0.26 for STEMI and 0.35 for NSTEMI. Meaning the test considers patients having the serum levels of more than SDF1 0.65 ng/ml (STEMI) and 0.35 ng/ml (NSTEMI) to have MI. There the number of FP patients was 4 (or 17%) for STEMI and 14 for NSTEMI. The AUC also supported the analysis showing 80% for STEMI and only 56% for NSTEMI (meaning SDF1 marker for NSTEMI accuracy is close to 50/50 chance of flipping a coin). However, our results showing SDF1 levels in man and women to be opposite should not be neglected (see above). Further research according to gender is required to fully accesses the effectiveness of SDF1 as a marker of MI.

Last but not least the ROC of the gold marker Troponin (Fig.11.1. d., Tab.11.1) showed perfect results. With cut-off value having 0 FN and FP

patients and The AUC being the 100% both for STEMI and NSTEMI. This was expected and we calculated the Troponin ROC only to compare it the markers of interest. It should be remembered that UB CXCR4 and SDF1 are studied as MI markers for cases when Troponin levels are chronically elevated (e.g. CKF) and cannot be used for the diagnostic tests.

Discussions

To choose the correct strategy for our statistical calculations we needed to conduct Shapiro-Wilk test to check normality of distribution for UB, CXCR4, SDF1. As we can see according to Shapiro-Wilk test UB does not follow the normal distribution as P value is less than 0.05. SDF1 has P >0.05 following normal distribution and CXCR4 has a normal distribution on the level of statistical significance (P value = 0.05612). H0 is Hypothesis 0 that states that the data does not follow the normal distribution (P >0.05). The distribution histogram is presented in Figure 7.1. The correct strategy according to this data is to use non-parametrical approach for all further calculations.

First, we divided the patients in MI and NoDamage groups. The full data-set for these groups is presented in Table 8.1. According to Tables 8.1, 8.2 and Figure 8.1, we can conclude that concentration of UB, CXCR4 and SDF1 differs in MI and NoDamage groups. To prove this, we used non-parametrical Mann-Whitney test. Mann-Whitney test shows if there is a statistically significant difference in protein concentration between two groups. The test results presented in Table 8.3 and Figure 8.1 a-c show the statistically important difference (P value <0.05) for UB, CXCR4 and SDF1 proteins when comparing MI and NoDamage groups. It should be noted that for all three proteins of interest the concentration in MI group was higher compared to NoDamage group Figure 8.1.

As all three investigated proteins share the receptor ligand relationship, we analyzed their correlation to see if they have any positive or negative correlation in plasma and if this correlation varies according to diagnosis. The correlation was made by spearman correlation coefficient. Knowledge of correlation between UB, CXCR4 and SDF1 could help us in the understanding the variability of molecular relationships caused by

diagnosis. This data along with serum levels of proteins can be used in the further medical implementation of our research. The correlation results are presented in Fig. 8.2. Fig. 8.2 . a. shows correlation for MI group. Fig. 8.2. b. shows correlation inside the NoDamage group. When divided into groups no statistically significant correlation was observed for NoDamage patients (Fig. 8.2.b) and for MI patients (Figure 8.2.c.) correlation was observed only in UB/SDF1 pair. By this data we can conclude that UB and SDF1 correlate mainly in MI group.

Measurement method of troponin levels for diagnosis of MI has same cut-off values for both males and females, due to standard methodology which doesn't take into the account patients' sex. However, levels of many blood and plasma proteins are different in males and females. For example, testosterone, estrogen, hemoglobin, creatinine, etc. For this reason, we divided the serum samples into MI male, MI female, NoDamage male and NoDamage female groups and measured the results to see if sex could be a factor in the fluctuation of serum levels of UB, CXCR4 and SDF1 according to diagnosis. Table 9.1 show the data-sets for all four groups. As can be seen from Figure 9.1 while UB and CXCR4 concentrations are higher in MI group both in males and females, the concentration difference is larger in males. As for SDF1, in males it follows the typical pattern being significantly higher in MI compared to NoDamage group, but in females the opposite is observed NoDamage female patients having higher concentration of SDF1 compared to MI group.

To explain distribution of variances of of UB, CXCR4 and SDF1 concentration according to groups we used ANOVA test, which showed us if the protein levels were affected by diagnosis, sex and if sex had any effect on diagnosis itself (Table 9.2). UB levels are strongly affected by diagnosis, but diagnosis and sex interaction affect UB levels on the level of statistical tendency, while the Sex itself has no effect on the diagnosis. CXCR4 levels are affected by diagnosis and sex affects CXCR4 levels on the level of statistical tendency, while the Sex itself has no effect on diagnosis. For SDF1 on the contrary sex is the major determinant of SDF1

levels, the diagnosis also has statistical significance and the effect of Sex on the diagnosis is large (large F value) and statistically significant.

Finally to compare the difference between each group we did Tukey's test with results presented in Table 9.3. Since Tukey's test is designed to compare all the groups indiscriminately there, we will consider only the results. There we will discuss only the results that make sense, as for example comparing Male MI group and Female NoDamage group concentration of UB would not be logical. As can be seen from section 8 if we compare MI and NoDamage groups for UB, CXCR4 and SDF1 proteins the statistically important difference was found for all three proteins. However, when we divided the MI and NoDamage patiens into male and female groups, more interesting results occurred. For males UB and SDF1 were statistically different in MI and NoDamage, while CXCR4 levels were not. However, for females, UB and CXCR4 were higher in MI than no damage group but without the statistical significance (P value >0.05). For SDF1 female group, not only was the difference in MI and NoDamage groups not statistically significant but the levels of SDF1 were higher in NoDamage group compared to MI group (Opposite to the SDF1 Male group). This lets us conclude that when we compared the MI to NoDamage group without division by sex the statistically important significance for UB, CXCR4 and SDF1 proteins were due to the male patients.

Last but not least we measured correlation between UB, CXCR4 and SDF1 proteins in Male and Female groups according to diagnosis. Only one positive correlation was shown in MI group in Females between UB and SDF1 on the level of statistical significance. As for NoDamage group while we obtained very statistically important correlation between UB ans SDF1 in MI group when not dividing the groups by sex we did not see the same correlation when MI groups were divided by sex. This indicates that there is not any statistically important correlation between them. It may have happened because the lack of number of samples. At the same time, we obtained correlation coefficient of 0.94 in NoDamage male group but with only a statistical tendency and same results were not

present when measured in NoDamage total groups (male+female). Again, we came to the conclusion that sex may be very important for the correlation of these proteins and requires further investigation to increase the number of groups as every statistical analysis works better with increased number of data. Same can be said for the NoDamage Female group as a perfect correlation coefficient of 1 was obtained in CXCR4/SDF1 pair with a very high level of statistical significance Fig.9.2.

As discussed earlier STEMI and NSTEMI have different treatment guidelines and NSTEMI can be harder to diagnose in patients with diseases where troponin is chronically elevated. For this reason, we divided patients into NoDamage, STEMI and NSTEMI groups to further measure and understand the concentration and correlation differences of UB, CXCR4 and SDF1 in healthy and diseased states. (The data sets used for the calculations are presented in table 10.1.). As can be seen on Fig. 10.1 the concentration of all three proteins is as follows: STEMI>NSTEMI>NoDamage, however there is significant overlap especially for CXCR4 and SDF1 proteins.

Again, we did a non-parametric Mann-Whitney test (distribution of proteins is not normal, Table 10.2) which showed statistically important difference (P value <0.05) in all three proteins when comparing STEMI patients with no damage groups and in UB proteins when comparing NSTEMI and NoDamage groups (Tables 10.2., Fig.10.1.).

We built correlation matrix that shows how the distribution of data correlates with each other in a graphical from for every diagnosis group (NoDamage, STEMI, NSTEMI). The correlation was made by spearman correlation coefficient (Figure 10.5). In STEMI group the correlation is only between UB and SDF1 (correlation coefficient is 0.75 and P value <0.05). No other correlation between UB, CXCR4 and SDF1 was observed in STEMI, NSTEMI and NoDamage groups Fig.10.2.

Finally, we did ROC test to examine the effectiveness of UB, CXCR4 and SDF1 as markers of MI. We also did the ROC test for Troponin to compare our hypothetical markers to the gold standard. We divided the

patients into NoDamage, STEMI and NSTEMI groups. And diseased patients were considered to be positive and NoDamage patients negative (same classification is done for all medical tests in general practice). As myocardial infarction is a very serious disease with very high mortality and complication rates, the Sensitivity was the number one concern. We wanted to make a cut-off value so that no MI patient was considered negative if they had the STEMI or NSTEMI (in short no False Negative patients).

For UB we saw that the cut-off value was 0.27 and 0.39 for STEMI and NSTEMI respectively. Not only we did not have any FN patients at this level but the number of False Positive (FP) patients was low: 2 for both STEMI and NSTEMI less than 10% of all patients tested. Also, as can be seen from Table 1 cut-off values correspond to the 38ng/ml and 39ng/ml of UB in serum. Meaning the test considers patients having the levels of more than UB 38 ng/ml (STEMI) and 39 ng/ml (NSTEMI) to have MI. In the end as seen on Figure 1 STEMI and NSTEMI AUC covers 89% and 90% of the whole area respectively. Indicating the very high positive predictive value of the test.

For CXCR4 the cut-off value with no FN patients in STEMI and NSTEMI groups was 0.22 and 0.21 respectively. Meaning the test considers patients having the serum levels of more than CXCR4 0.41 ng/ml (STEMI) and 0.2 ng/ml (NSTEMI) to have MI. The problem was the increased number of FP patients especially for NSTEMI. (5 or 22% of all patients tested were FP for STEMI and 12 or almost 50% of all patients were FP for NSTEMI). The AUC was 81% for STEMI and 70% for NSTEMI indicating it as a poor prognostic marker for MI especially NSTEMI which is usually harder to detect compared to STEMI.

For SDF1 the cut-off value where we had 0 FN patients was 0.26 for STEMI and 0.35 for NSTEMI. Meaning the test considers patients having the serum levels of more than SDF1 0.65 ng/ml (STEMI) and 0.35 ng/ml (NSTEMI) to have MI. There the number of FP patients was 4 (or 17%) for STEMI and 14 for NSTEMI. The AUC also supported the analysis showing 80% for STEMI and only 56% for NSTEMI (meaning SDF1

marker for NSTEMI accuracy is close to 50/50 chance of flipping a coin). However, our results showing SDF1 levels in man and women to be opposite should not be neglected (see above). Further research according to gender is required to fully accesses the effectiveness of SDF1 as a marker of MI.

Last but not least the ROC of the gold marker Troponin showed perfect results. With cut-off value having 0 FN and FP patients and The AUC being the 100% both for STEMI and NSTEMI. This was expected and we calculated the Troponin ROC only to compare it the markers of interest. It should be remembered that UB CXCR4 and SDF1 are studied as MI markers for cases when Troponin levels are chronically elevated (e.g. CKF) and cannot be used for the diagnostic tests.

Conclusions

1. When comparing MI and NoDamage group concentration of UB, CXCR4 and SDF1 proteins, the statistically significant difference was shown for all of them strengthening our initial assumptions that they could be used as MI markers when Troponin is chronically falsely elevated. The concentrations of all three proteins of interest were higher in MI group compared to NoDamage group.

2. A positive correlation was found between UB and SDF1 in MI patients with a correlation coefficient of 0.66. No correlation was found in NoDamage group. UB and SDF1 correlate mainly in MI group.

3. For males UB and SDF1 were statistically different in MI and NoDamage, while CXCR4 was on the level of statistical significance. For females, UB and CXCR4 were higher in MI than no damage group but without the statistical significance. SDF1 for female group, not only was the difference in MI and NoDamage groups not statistically significant but the levels of SDF1 were higher in NoDamage group compared to MI group (Opposite to the SDF1 Male group). When compared the MI to NoDamage group without division by sex the

statistically important significance for UB, CXCR4 and SDF1 proteins was probably due to the male patients.

4. The correlation between UB, CXCR4 and SDF1 pairs we obtained: positive correlation of UB/SDF1 pair on the level of statistical significance in female MI group, CXCR4/SDF1 pair positive correlation on the level of statistical significance in male NoDamage group and a perfect correlation coefficient of 1 was obtained in CXCR4/SDF1 pair with a very high level of statistical significance for the NoDamage Female group.

5. In STEMI, NSTEMI and NoDamage groups UB proved and excellent marker for MI showing the statistically important difference between NoDamage/STEMI and NoDamage/NSTEMI groups. As for CXCR4 and SDF1 the difference was shown for NoDamage/STEMI groups only.

6. Positive correlation between UB and SDF1 was observed only in STEMI.

7. The ROC test showed the effectiveness of UB, CXCR4 and SDF1 as markers of MI compared to Troponin.

For UB the number of False Positive (FP) patients was low: less than 10% of all patients tested and AUC covers 89% and 90% of the whole area for STEMI and NSTEMI respectively. Indicating the very high positive predictive value of the test (89 and 90 percent sensitivity).
For CXCR4 the problem was the increased number of FP patients especially for NSTEMI (22% of all patients tested were FP for STEMI and almost 50% of all patients were FP for NSTEMI). The AUC was 81% for STEMI and 70% for NSTEMI indicating it as a poor prognostic marker for MI especially NSTEMI which is usually harder to detect compared to STEMI.

For SDF1 the number of FP patients was 17% for STEMI and 44% for NSTEMI. The AUC also supported the analysis showing 80% for STEMI and only 56% for NSTEMI (meaning SDF1 marker for NSTEMI accuracy is close to 50/50 chance of flipping a coin).
However, our results showing SDF1 levels in man and women to be opposite should not be neglected.
The ROC of the gold marker Troponin showed perfect results. With cut-off value having 0 FN and FP patients and the AUC being the 100% both for STEMI and NSTEMI.

8. The results indicate that UB can be an alternative new marker for MI diagnosis. Separate MI study where only patients with CKD will participate should be done to determine the effectiveness of UB. Further studies in males and females are required to determine SDF1 usefulness as an MI marker.

References

Heron. (2021). Deaths: Leading Causes for 2019. National Vital Statistics Reports, 70(9). https://stacks.cdc.gov/view/cdc/107021

Al-Otaiby, M. A., Al-Amri, H. S., & Al-Moghairi, A. M. (2011). The clinical significance of cardiac troponins in medical practice. Journal of the Saudi Heart Association, 23(1), 3–11. https://doi.org/10.1016/j.jsha.2010.10.001

Hamm, C. W., Giannitsis, E., & Katus, H. A. (2002). Cardiac Troponin Elevations in Patients Without Acute Coronary Syndrome. Circulation, 106(23), 2871–2872. https://doi.org/10.1161/01.cir.0000044342.50593.63

Paul O. Collinson. (1998). Troponin T or troponin I or CK-MB (or none?). European Heart Journal, 19 Suppl N, N16-24.

McLaurin, M. D., Apple, F. S., Voss, E. M., Herzog, C. A., & Sharkey, S. W. (1997). Cardiac troponin I, cardiac troponin T, and creatine kinase MB in dialysis patients without ischemic heart disease: evidence of cardiac troponin T expression in skeletal muscle. Clinical Chemistry, 43(6), 976–982. https://doi.org/10.1093/clinchem/43.6.976

Ota, T., Hasegawa, Y., Murata, E., Tanaka, N., & Fukuoka, M. (2020). False-Positive Elevation of CK-MB Levels with Chest Pain in Lung Adenocarcinoma. Case Reports in Oncology, 13(1), 100–104. https://doi.org/10.1159/000505724

Kliza, K., & Husnjak, K. (2020). Resolving the Complexity of Ubiquitin Networks. Frontiers in Molecular Biosciences, 7. https://doi.org/10.3389/fmolb.2020.00021

Yu, X., & Kem, D. C. (2009). Proteasome inhibition during myocardial infarction. Cardiovascular Research, 85(2), 312–320. https://doi.org/10.1093/cvr/cvp309

Kobayashi, M., Higa, J. K., & Matsui, T. (2019). The role of ubiquitin in cardiac ischemia-reperfusion injury. American Journal of Physiology-Heart and Circulatory Physiology, 316(3), H583–H585. https://doi.org/10.1152/ajpheart.00018.2019

Askari, A. T., Unzek, S., Popovic, Z. B., Goldman, C. K., Forudi, F., Kiedrowski, M., Rovner, A., Ellis, S. G., Thomas, J. D., DiCorleto, P. E., Topol, E. J., & Penn, M. S. (2003). Effect of stromal-cell-derived factor 1 on stem-cell homing and tissue regeneration in ischaemic cardiomyopathy. The Lancet, 362(9385), 697–703. https://doi.org/10.1016/s0140-6736(03)14232-8

Ghadge, S. K., Mühlstedt, S., Özcelik, C., & Bader, M. (2011). SDF-1α as a therapeutic stem cell homing factor in myocardial infarction. Pharmacology &Amp; Therapeutics, 129(1), 97–108. https://doi.org/10.1016/j.pharmthera.2010.09.011

Saini, V., Marchese, A., & Majetschak, M. (2010). CXC Chemokine Receptor 4 Is a Cell Surface Receptor for Extracellular Ubiquitin. Journal of Biological Chemistry, 285(20), 15566–15576. https://doi.org/10.1074/jbc.m110.103408

Collet, J. P., Thiele, H., Barbato, E., Barthélémy, O., Bauersachs, J., Bhatt, D. L., Dendale, P., Dorobantu, M., Edvardsen, T., Folliguet, T., Gale, C. P., Gilard, M., Jobs, A., Jüni, P., Lambrinou, E., Lewis, B. S., Mehilli, J., Meliga, E., Merkely, B., . . . Siontis, G. C. M. (2020). 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal, 42(14), 1289–1367. https://doi.org/10.1093/eurheartj/ehaa575

Ibanez, B., James, S., Agewall, S., Antunes, M. J., Bucciarelli-Ducci, C., Bueno, H., Caforio, A. L. P., Crea, F., Goudevenos, J. A., Halvorsen, S., Hindricks, G., Kastrati, A., Lenzen, M. J., Prescott, E., Roffi, M., Valgimigli, M., Varenhorst, C., Vranckx, P., Widimský, P., . . . Gale, C. P. (2017). 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal, 39(2), 119–177. https://doi.org/10.1093/eurheartj/ehx393

Wallentin, L., Lindholm, D., Siegbahn, A., Wernroth, L., Becker, R. C., Cannon, C. P., Cornel, J. H., Himmelmann, A., Giannitsis, E., Harrington, R. A., Held, C., Husted, S., Katus, H. A., Mahaffey, K. W., Steg, P. G., Storey, R. F., & James, S. K. (2014). Biomarkers in Relation to the Effects of Ticagrelor in Comparison With Clopidogrel in Non–ST-Elevation Acute Coronary Syndrome Patients Managed With or Without In-Hospital Revascularization. Circulation, 129(3), 293–303. https://doi.org/10.1161/circulationaha.113.004420

Braunwald, E., & Morrow, D. A. (2013). Unstable Angina. Circulation, 127(24), 2452–2457. https://doi.org/10.1161/circulationaha.113.001258

Chadwick Jayaraj, J., Davatyan, K., Subramanian, S., & Priya, J. (2019). Epidemiology of Myocardial Infarction. Myocardial Infarction. https://doi.org/10.5772/intechopen.74768

Yu, B., Akushevich, I., Yashkin, A. P., & Kravchenko, J. (2021). Epidemiology of Geographic Disparities of Myocardial Infarction Among Older Adults in the United States: Analysis of 2000–2017 Medicare Data. Frontiers in Cardiovascular Medicine, 8. https://doi.org/10.3389/fcvm.2021.707102

Zafari, A. M., MD PhD. (2022, July 13). Myocardial Infarction: Practice Essentials, Background, Anatomy. https://emedicine.medscape.com/article/155919-overview

Sanchis-Gomar, F. (n.d.). Epidemiology of coronary heart disease and acute coronary syndrome. https://atm.amegroups.com. https://atm.amegroups.com/article/view/10896/html

Connolly, M., & Menown, I. (2013). Epidemiology and classification of myocardial infarction. Advances in Myocardial Infarction Management, 6–19. https://doi.org/10.2217/ebo.12.411

Gorenoi, V., & Hagen, A. (2015). Overview of Risk-Estimation Tools for Primary Prevention of Cardiovascular Diseases in European Populations. Central European Journal of Public Health, 23(2), 91–99. https://doi.org/10.21101/cejph.a4004

Bonow, R. O. (2002). Primary Prevention of Cardiovascular Disease. Circulation, 106(25), 3140–3141. https://doi.org/10.1161/01.cir.0000048067.86569.e1

Hajar, R. (2017). Risk factors for coronary artery disease: Historical perspectives. Heart Views, 18(3), 109. https://doi.org/10.4103/heartviews.heartviews_106_17

Stewart, J., Manmathan, G., & Wilkinson, P. (2017). Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. JRSM Cardiovascular Disease, 6, 204800401668721. https://doi.org/10.1177/2048004016687211

Knuuti, J. (2020). 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). Russian Journal of Cardiology, 25(2), 119–180. https://doi.org/10.15829/1560-4071-2020-2-3757

Perk, J. (2017). The 2016 version of the European Guidelines on Cardiovascular Prevention. European Heart Journal - Cardiovascular Pharmacotherapy, 3(1), 9–10. https://doi.org/10.1093/ehjcvp/pvw030

DeVon, H. A., Mirzaei, S., & Zègre-Hemsey, J. (2020). Typical and Atypical Symptoms of Acute Coronary Syndrome: Time to Retire the Terms? Journal of the American Heart Association, 9(7). https://doi.org/10.1161/jaha.119.015539

Fox, K. A. A. (2000, July 1). Acute coronary syndromes: presentation—clinical spectrum and management. Heart. https://heart.bmj.com/content/84/1/93

Rosengren, A., Wallentin, L., Simoons, M., Gitt, A. K., Behar, S., Battler, A., & Hasdai, D. (2006). Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. European Heart Journal, 27(7), 789–795. https://doi.org/10.1093/eurheartj/ehi774

Styczkiewicz, K., Styczkiewicz, M., Myćka, M., Mędrek, S., Kondraciuk, T., Czerkies-Bieleń, A., Wiśniewski, A., Szmit, S., & Jankowski, P. (2020). Clinical presentation and treatment of acute coronary syndrome as well as 1-year survival of patients hospitalized due to cancer. Medicine, 99(5), e18972. https://doi.org/10.1097/md.0000000000018972

Craig Barstow, Matthew S. Rice, & Jonathan D. McDivitt. (2017). Acute Coronary Syndrome: Diagnostic Evaluation. American Family Physician, 95(3), 170–177.

AlGhatrif, M., & Lindsay, J. (2012). A brief review: history to understand fundamentals of electrocardiography. *Journal of Community Hospital Internal Medicine Perspectives*, *2*(1), 14383. https://doi.org/10.3402/jchimp.v2i1.14383

Barold, S. S. (2003). Willem Einthoven and the birth of clinical electrocardiography a hundred years ago. Cardiac Electrophysiology Review, 7(1), 99–104. https://doi.org/10.1023/a:1023667812925

Herring, N. (2006). ECG diagnosis of acute ischaemia and infarction: past, present and future. QJM, 99(4), 219–230. https://doi.org/10.1093/qjmed/hcl025

Wagner, G. S., Macfarlane, P., Wellens, H., Josephson, M., Gorgels, A., Mirvis, D. M., Pahlm, O., Surawicz, B., Kligfield, P., Childers, R., Gettes, L. S., Bailey, J. J., Deal, B. J., Gorgels, A., Hancock, E. W., Kors, J. A., Mason, J. W., Okin, P., Rautaharju, P. M., & van Herpen, G. (2009). AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. Journal of the American College of Cardiology, 53(11), 1003–1011. https://doi.org/10.1016/j.jacc.2008.12.016

Klabunde, R. E. (2017). Cardiac electrophysiology: normal and ischemic ionic currents and the ECG. Advances in Physiology Education, 41(1), 29–37. https://doi.org/10.1152/advan.00105.2016

Okada, J., Fujiu, K., Yoneda, K., Iwamura, T., Washio, T., Komuro, I., Hisada, T., & Sugiura, S. (2020). Ionic mechanisms of ST segment elevation in electrocardiogram during acute myocardial infarction. The Journal of Physiological Sciences, 70(1). https://doi.org/10.1186/s12576-020-00760-3

Belie, N., & Gardin, J. M. (1980). ECG Manifestations of Myocardial Ischemia. Archives of Internal Medicine, 140(9), 1162–1165. https://doi.org/10.1001/archinte.1980.00330200038016

Brady, W. J. (2000). Electrocardiographic abnormalities encountered in acute myocardial infarction. Emergency Medicine Journal, 17(1), 40–45. https://doi.org/10.1136/emj.17.1.40

Li, D., Li, C. Y., Yong, A. C., & Kilpatrick, D. (1998). Source of electrocardiographic ST changes in subendocardial ischemia. Circulation Research, 82(9), 957–970. https://doi.org/10.1161/01.res.82.9.957

Rossello, X., Wiegerinck, R. F., Alguersuari, J., Bardají, A., Worner, F., Sutil, M., Ferrero, A., & Cinca, J. (2014). New Electrocardiographic Criteria to Differentiate Acute Pericarditis and Myocardial Infarction. The American Journal of Medicine, 127(3), 233–239. https://doi.org/10.1016/j.amjmed.2013.11.006

Nickel, C. H., Bingisser, R., & Morgenthaler, N. G. (2012). The role of copeptin as a diagnostic and prognostic biomarker for risk stratification in the emergency department. BMC Medicine, 10(1). https://doi.org/10.1186/1741-7015-10-7

Morgenthaler, N. G., Struck, J., Jochberger, S., & Dünser, M. W. (2008). Copeptin: clinical use of a new biomarker. Trends in Endocrinology & Metabolism, 19(2), 43–49. https://doi.org/10.1016/j.tem.2007.11.001

Keller, T., Tzikas, S., Zeller, T., Czyz, E., Lillpopp, L., Ojeda, F. M., Roth, A., Bickel, C., Baldus, S., Sinning, C. R., Wild, P. S., Lubos, E., Peetz, D., Kunde, J., Hartmann, O., Bergmann, A., Post, F., Lackner, K. J., Genth-Zotz, S., & Nicaud, V. (2010). Copeptin Improves Early Diagnosis of Acute Myocardial Infarction. Journal of the American College of Cardiology, 55(19), 2096–2106. https://doi.org/10.1016/j.jacc.2010.01.029

Möckel, M., Searle, J., Hamm, C., Slagman, A., Blankenberg, S., Huber, K., Katus, H., Liebetrau, C., Müller, C., Muller, R., Peitsmeyer, P., von Recum, J., Tajsic, M., Vollert, J. O., & Giannitsis, E. (2014). Early discharge using single cardiac troponin and copeptin testing in patients

with suspected acute coronary syndrome (ACS): a randomized, controlled clinical process study. European Heart Journal, 36(6), 369–376. https://doi.org/10.1093/eurheartj/ehu178

Reichlin, T., Hochholzer, W., Stelzig, C., Laule, K., Freidank, H., Morgenthaler, N. G., Bergmann, A., Potocki, M., Noveanu, M., Breidthardt, T., Christ, A., Boldanova, T., Merki, R., Schaub, N., Bingisser, R., Christ, M., & Mueller, C. (2009). Incremental Value of Copeptin for Rapid Rule Out of Acute Myocardial Infarction. Journal of the American College of Cardiology, 54(1), 60–68. https://doi.org/10.1016/j.jacc.2009.01.076

Boeddinghaus, J., Reichlin, T., Nestelberger, T., Twerenbold, R., Meili, Y., Wildi, K., Hillinger, P., Giménez, M. R., Cupa, J., Schumacher, L., Schubera, M., Badertscher, P., Corbière, S., Grimm, K., Puelacher, C., Sabti, Z., Widmer, D. F., Schaerli, N., Kozhuharov, N., & Shrestha, S. (2017). Early diagnosis of acute myocardial infarction in patients with mild elevations of cardiac troponin. Clinical Research in Cardiology, 106(6), 457–467. https://doi.org/10.1007/s00392-016-1075-9

Hillinger, P., Twerenbold, R., Jaeger, C., Wildi, K., Reichlin, T., Gimenez, M. R., Engels, U., Miró, O., Boeddinghaus, J., Puelacher, C., Nestelberger, T., Röthlisberger, M., Ernst, S., Rentsch, K., & Mueller, C. (2015). Optimizing Early Rule-Out Strategies for Acute Myocardial Infarction: Utility of 1-Hour Copeptin. Clinical Chemistry, 61(12), 1466–1474. https://doi.org/10.1373/clinchem.2015.242743

Mueller-Hennessen, M., Lindahl, B., Giannitsis, E., Vafaie, M., Biener, M., Haushofer, A. C., Seier, J., Christ, M., Alquézar-Arbé, A., deFilippi, C. R., McCord, J., Body, R., Panteghini, M., Jernberg, T., Plebani, M., Verschuren, F., French, J. K., Christenson, R. H., Dinkel, C., & Katus, H. A. (2019). Combined testing of copeptin and high-sensitivity cardiac troponin T at presentation in comparison to other algorithms for rapid

rule-out of acute myocardial infarction. International Journal of Cardiology, 276, 261–267. https://doi.org/10.1016/j.ijcard.2018.10.084

Mueller, C., Möckel, M., Giannitsis, E., Huber, K., Mair, J., Plebani, M., Thygesen, K., Jaffe, A. S., & Lindahl, B. (2017). Use of copeptin for rapid rule-out of acute myocardial infarction. European Heart Journal: Acute Cardiovascular Care, 7(6), 570–576. https://doi.org/10.1177/2048872617710791

Stallone, F., Schoenenberger, A. W., Puelacher, C., Rubini Gimenez, M., Walz, B., Naduvilekoot Devasia, A., Bergner, M., Twerenbold, R., Wildi, K., Reichlin, T., Hillinger, P., Erne, P., & Mueller, C. (2016). Incremental value of copeptin in suspected acute myocardial infarction very early after symptom onset. European Heart Journal: Acute Cardiovascular Care, 5(5), 407–415. https://doi.org/10.1177/2048872616641289

Vargas, K. G., Kassem, M., Mueller, C., Wojta, J., & Huber, K. (2016). Copeptin for the early rule-out of non-ST-elevation myocardial infarction. International Journal of Cardiology, 223(13), 797–804. https://doi.org/10.1016/j.ijcard.2016.08.304

Wildi, K., Zellweger, C., Twerenbold, R., Jaeger, C., Reichlin, T., Haaf, P., Faoro, J., Giménez, M. R., Fischer, A., Nelles, B., Druey, S., Krivoshei, L., Hillinger, P., Puelacher, C., Herrmann, T., Campodarve, I., Rentsch, K., Steuer, S., Osswald, S., & Mueller, C. (2015). Incremental value of copeptin to highly sensitive cardiac Troponin I for rapid rule-out of myocardial infarction. International Journal of Cardiology, 190(27), 170–176. https://doi.org/10.1016/j.ijcard.2015.04.133

Govindan, S., McElligott, A., Muthusamy, S., Nair, N., Barefield, D., Martin, J. L., Gongora, E., Greis, K. D., Luther, P. K., Winegrad, S., Henderson, K. K., & Sadayappan, S. (2012). Cardiac myosin binding protein-C is a potential diagnostic biomarker for myocardial infarction.

Journal of Molecular and Cellular Cardiology, 52(1), 154–164. https://doi.org/10.1016/j.yjmcc.2011.09.011

Flashman, E., Redwood, C., Moolman-Smook, J., & Watkins, H. (2004a). Cardiac Myosin Binding Protein C. Circulation Research, 94(10), 1279–1289. https://doi.org/10.1161/01.res.0000127175.21818.c2

Kaier, T. E., Stengaard, C., Marjot, J., Sørensen, J. T., Alaour, B., Stavropoulou-Tatla, S., Terkelsen, C. J., Williams, L., Thygesen, K., Weber, E., Marber, M., & Bøtker, H. E. (2019). Cardiac Myosin-Binding Protein C to Diagnose Acute Myocardial Infarction in the Pre-Hospital Setting. Journal of the American Heart Association, 8(15). https://doi.org/10.1161/jaha.119.013152

Flashman, E., Redwood, C., Moolman-Smook, J., & Watkins, H. (2004b). Cardiac Myosin Binding Protein C. Circulation Research, 94(10), 1279–1289. https://doi.org/10.1161/01.res.0000127175.21818.c2

Kaier, T. E., Twerenbold, R., Puelacher, C., Marjot, J., Imambaccus, N., Boeddinghaus, J., Nestelberger, T., Badertscher, P., Sabti, Z., Giménez, M. R., Wildi, K., Hillinger, P., Grimm, K., Loeffel, S., Shrestha, S., Widmer, D. F., Cupa, J., Kozhuharov, N., Miró, Ò., & Martín-Sánchez, F. J. (2017). Direct Comparison of Cardiac Myosin-Binding Protein C With Cardiac Troponins for the Early Diagnosis of Acute Myocardial Infarction. Circulation, 136(16), 1495–1508. https://doi.org/10.1161/circulationaha.117.028084

Perryman, M. Benjamin., Strauss, A. W., Buettner, T. L., & Roberts, R. (1983). Molecular heterogeneity of creatine kinase isoenzymes. Biochimica et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology, 747(3), 284–290. https://doi.org/10.1016/0167-4838(83)90107-3

Hornemann, T., Rutishauser, D., & Wallimann, T. (2000). Why is creatine kinase a dimer? Evidence for cooperativity between the two subunits. Biochimica et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology, 1480(1-2), 365–373. https://doi.org/10.1016/s0167-4838(00)00098-4

Baird, M. F., Graham, S. M., Baker, J. S., & Bickerstaff, G. F. (2012). Creatine-Kinase- and Exercise-Related Muscle Damage Implications for Muscle Performance and Recovery. Journal of Nutrition and Metabolism, 2012(5), 1–13. https://doi.org/10.1155/2012/960363

Dahlstedt, A. J., Katz, A., Tavi, P., & Westerblad, H. (2003). Creatine Kinase Injection Restores Contractile Function in Creatine-Kinase-Deficient Mouse Skeletal Muscle Fibres. The Journal of Physiology, 547(2), 395–403. https://doi.org/10.1113/jphysiol.2002.034793

Hettling, H., & van Beek, J. H. (2011). Analyzing the Functional Properties of the Creatine Kinase System with Multiscale "Sloppy" Modeling. PLoS Computational Biology, 7(8), e1002130. https://doi.org/10.1371/journal.pcbi.1002130

Saks, V. (2008). The phosphocreatine-creatine kinase system helps to shape muscle cells and keep them healthy and alive. The Journal of Physiology, 586(12), 2817–2818. https://doi.org/10.1113/jphysiol.2008.155358

Goodman, S. G., Steg, P. G., Eagle, K. A., Fox, K. A. A., López-Sendón, J., Montalescot, G., Budaj, A., Kennelly, B. M., Gore, J. M., Allegrone, J., Granger, C. B., & Gurfinkel, E. P. (2006). The diagnostic and prognostic impact of the redefinition of acute myocardial infarction: Lessons from the Global Registry of Acute Coronary Events (GRACE). American Heart Journal, 151(3), 654–660. https://doi.org/10.1016/j.ahj.2005.05.014

Sandoval, Y., & Apple, F. S. (2014). The Global Need to Define Normality: The 99th Percentile Value of Cardiac Troponin. Clinical Chemistry, 60(3), 455–462. https://doi.org/10.1373/clinchem.2013.211706

Bakker, A. J., Gorgels, J. P. M. C., van Vlies, B., Haagen, F. D. M., & Smits, R. (1993). The Mass Concentrations of Serum Troponin T and Creatine Kinase-MB are Elevated before Creatine Kinase and Creatine Kinase-MB Activities in Acute Myocardial Infarction. Clinical Chemistry and Laboratory Medicine, 31(11). https://doi.org/10.1515/cclm.1993.31.11.715

Ravkilde, J., Nissen, H., Hørder, M., & Thygesen, K. (1995). Independent prognostic value of serum creatine kinase isoenzyme MB mass, cardiac troponin T and myosin light chain levels in suspected acute myocardial infarction. Journal of the American College of Cardiology, 25(3), 574–581. https://doi.org/10.1016/0735-1097(94)00430-x

Kost, G. (1998). A strategy for the use of cardiac injury markers (troponin I and T, creatine kinase-MB mass and isoforms, and myoglobin) in the diagnosis of acute myocardial infarction. Arch Pathol Lab Med, 122(245).

Ohman, E. M. (1999). Troponin and other cardiac markers: role in management of acute coronary syndromes. Australian and New Zealand Journal of Medicine, 29(3), 436–443. https://doi.org/10.1111/j.1445-5994.1999.tb00740.x

Wu, A. H. (1996). Comparison of myoglobin, creatine kinase-MB, and cardiac troponin I for diagnosis of acute myocardial infarction. Annals of Clinical and Laboratory Science, 26(4).

Maisel, A. S., Bhalla, V., & Braunwald, E. (2006). Cardiac biomarkers: a contemporary status report. Nature Clinical Practice Cardiovascular Medicine, 3(1), 24–34. https://doi.org/10.1038/ncpcardio0405

Anand Kumar, G. (2018). Biomarkers in Acute Myocardial Infarction. National Journal of Basic Medical Sciences, 8(3), 137–141. https://doi.org/10.31975/njbms.2018.8303

Odum, E., & Wakwe, V. (2017). Clinical Significance of Creatine Kinase-MB Elevation in Patients with Chronic Kidney Disease before Initiation of Hemodialysis. Cardiology and Angiology: An International Journal, 6(4), 1–7. https://doi.org/10.9734/ca/2017/38020

Peng, A. (2014). Elevated Cardiac Markers in Chronic Kidney Disease as a Consequence of Hyperphosphatemia-Induced Cardiac Myocyte Injury. Medical Science Monitor, 20(43), 2043–2053. https://doi.org/10.12659/msm.890909

Bozbas, H., Yildirir, A., & Muderrisoglu, H. (2006). Cardiac Enzymes, Renal Failure and Renal Transplantation. Clinical Medicine & Research, 4(1), 79–84. https://doi.org/10.3121/cmr.4.1.79

D'Marco, L., Bellasi, A., & Raggi, P. (2015). Cardiovascular Biomarkers in Chronic Kidney Disease: State of Current Research and Clinical Applicability. Disease Markers, 2015(123), 1–16. https://doi.org/10.1155/2015/586569

Mitchell, C., Rahko, P. S., Blauwet, L. A., Canaday, B., Finstuen, J. A., Foster, M. C., Horton, K., Ogunyankin, K. O., Palma, R. A., & Velazquez, E. J. (2019). Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. Journal of the American Society of Echocardiography, 32(1), 1–64. https://doi.org/10.1016/j.echo.2018.06.004

Greaves, S. C. (2002). Role of echocardiography in acute coronary syndromes. Heart, 88(4), 419–425. https://doi.org/10.1136/heart.88.4.419

Sia, Y. T., O'Meara, E., & Ducharme, A. (2008). Role of echocardiography in acute myocardial infarction. Current Heart Failure Reports, 5(4), 189–196. https://doi.org/10.1007/s11897-008-0029-6

Lancellotti, P., Price, S., Edvardsen, T., Cosyns, B., Neskovic, A. N., Dulgheru, R., Flachskampf, F. A., Hassager, C., Pasquet, A., Gargani, L., Galderisi, M., Cardim, N., Haugaa, K. H., Ancion, A., Zamorano, J.-L., Donal, E., Bueno, H., & Habib, G. (2015). The use of echocardiography in acute cardiovascular care: Recommendations of the European Association of Cardiovascular Imaging and the Acute Cardiovascular Care Association. European Heart Journal: Acute Cardiovascular Care, 4(1), 3–5. https://doi.org/10.1177/2048872614568073

Dahlslett, T., Karlsen, S., Grenne, B., Eek, C., Sjøli, B., Skulstad, H., Smiseth, O. A., Edvardsen, T., & Brunvand, H. (2014). Early Assessment of Strain Echocardiography Can Accurately Exclude Significant Coronary Artery Stenosis in Suspected Non–ST-Segment Elevation Acute Coronary Syndrome. Journal of the American Society of Echocardiography, 27(5), 512–519. https://doi.org/10.1016/j.echo.2014.01.019

Grenne, B., Eek, C., Sjoli, B., Dahlslett, T., Uchto, M., Hol, P. K., Skulstad, H., Smiseth, O. A., Edvardsen, T., & Brunvand, H. (2010). Acute coronary occlusion in non-ST-elevation acute coronary syndrome: outcome and early identification by strain echocardiography. Heart, 96(19), 1550–1556. https://doi.org/10.1136/hrt.2009.188391

Ingkanisorn, W. P., Kwong, R. Y., Bohme, N. S., Geller, N. L., Rhoads, K. L., Dyke, C. K., Paterson, D. I., Syed, M. A., Aletras, A. H., & Arai, A. E. (2006). Prognosis of Negative Adenosine Stress Magnetic Resonance in Patients Presenting to an Emergency Department With Chest Pain. Journal of the American College of Cardiology, 47(7), 1427–1432. https://doi.org/10.1016/j.jacc.2005.11.059

Smulders, M. W., Kietselaer, B. L. J. H., Wildberger, J. E., Dagnelie, P. C., Brunner–La Rocca, H.-P., Mingels, A. M. A., van Cauteren, Y. J. M., Theunissen, R. A. L. J., Post, M. J., Schalla, S., van Kuijk, S. M. J., Das, M., Kim, R. J., Crijns, H. J. G. M., & Bekkers, S. C. A. M. (2019). Initial Imaging-Guided Strategy Versus Routine Care in Patients With Non–ST-Segment Elevation Myocardial Infarction. Journal of the American College of Cardiology, 74(20), 2466–2477. https://doi.org/10.1016/j.jacc.2019.09.027

Valbuena-López, S., Hinojar, R., & Puntmann, V. O. (2016). Cardiovascular Magnetic Resonance in Cardiology Practice: A Concise Guide to Image Acquisition and Clinical Interpretation. Revista Espanola de Cardiologia (English Ed.), 69(2), 202–210. https://doi.org/10.1016/j.rec.2015.11.011

Tseng, I. (2016). Introduction to Cardiovascular Magnetic Resonance: Technical Principles and Clinical Applications. Acta Cardiologica Sinica, 32(2). https://doi.org/DOI: 10.6515/acs20150616a

Kumar, A. (2015). Cardiac magnetic resonance in clinical cardiology. World Journal of Cardiology, 7(1), 6. https://doi.org/10.4330/wjc.v7.i1.6

Gardner, B. I., Bingham, S. E., Allen, M. R., Blatter, D. D., & Anderson, J. L. (2009). Cardiac magnetic resonance versus transthoracic echocardiography for the assessment of cardiac volumes and regional function after myocardial infarction: an intrasubject comparison using simultaneous intrasubject recordings. Cardiovascular Ultrasound, 7(1). https://doi.org/10.1186/1476-7120-7-38

Fox, K., Achenbach, S., Bax, J., Cosyns, B., Delgado, V., Dweck, M. R., Edvardsen, T., Flachskampf, F., Habib, G., Lancellotti, P., Muraru, D., Neglia, D., Pontone, G., Schwammenthal, E., Sechtem, U., Westwood, M., & Popescu, B. A. (2018). Multimodality imaging in cardiology: a statement on behalf of the Task Force on Multimodality Imaging of the

European Association of Cardiovascular Imaging. European Heart Journal, 40(6), 553–558. https://doi.org/10.1093/eurheartj/ehy669

Yandrapalli, S., & Puckett, Y. (2020). SPECT Imaging. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK564426/

Abbott, B. G., Case, J. A., Dorbala, S., Einstein, A. J., Galt, J. R., Pagnanelli, R., Bullock-Palmer, R. P., Soman, P., & Wells, R. G. (2018). Contemporary Cardiac SPECT Imaging—Innovations and Best Practices: An Information Statement from the American Society of Nuclear Cardiology. Circulation: Cardiovascular Imaging, 11(9). https://doi.org/10.1161/hci.0000000000000020

Lim, S. H., Anantharaman, V., Sundram, F., Chan, E. S.-Y., Ang, E. S., Yo, S. L., Jacob, E., Goh, A., Tan, S. B., & Chua, T. (2013). Stress myocardial perfusion imaging for the evaluation and triage of chest pain in the emergency department: A randomized controlled trial. Journal of Nuclear Cardiology, 20(6), 1002–1012. https://doi.org/10.1007/s12350-013-9736-9

Nabi, F., Kassi, M., Muhyieddeen, K., Chang, S. M., Xu, J., Peterson, L. E., Wray, N. P., Shirkey, B. A., Ashton, C. M., & Mahmarian, J. J. (2015). Optimizing Evaluation of Patients with Low-to-Intermediate-Risk Acute Chest Pain: A Randomized Study Comparing Stress Myocardial Perfusion Tomography Incorporating Stress-Only Imaging Versus Cardiac CT. Journal of Nuclear Medicine, 57(3), 378–384. https://doi.org/10.2967/jnumed.115.166595

Lu, L., Liu, M., Sun, R., Zheng, Y., & Zhang, P. (2015). Myocardial Infarction: Symptoms and Treatments. Cell Biochemistry and Biophysics, 72(3), 865–867. https://doi.org/10.1007/s12013-015-0553-4

Ryan, T. J., Anderson, J. L., Antman, E. M., Braniff, B. A., Brooks, N. H., Califf, R. M., Hillis, L. D., Hiratzka, L. F., Rapaport, E., Riegel, B. J., Russell, R. O., Smith, E. E., & Weaver, W. D. (1996). ACC/AHA

Guidelines for the Management of Patients With Acute Myocardial Infarction:Executive Summary. Circulation, 94(9), 2341–2350. https://doi.org/10.1161/01.cir.94.9.2341

Mercado, M. (2013). Myocardial infarction: management of the subacute period. Am Fam Physician, 88(9).

Aronow, W. (2019). Medical management after myocardial infarction. Future Cardiology, 15(3). https://doi.org/https://doi.org/10.2217/fca-2019-001

Peng, X. (2017). New Strategies for Myocardial Infarction Treatment. Journal of Cardiology and Therapy, 4(3).

Shannon, A. W., & Harrigan, R. A. (2001). GENERAL PHARMACOLOGIC TREATMENT OF ACUTE MYOCARDIAL INFARCTION. Emergency Medicine Clinics of North America, 19(2), 417–431. https://doi.org/10.1016/s0733-8627(05)70192-9

Schupp, T., Akin, I., & Behnes, M. (2021). Pharmacological Treatment Following Myocardial Infarction: How Large Is the Gap Between Guideline Recommendations and Routine Clinical Care? Journal of the American Heart Association, 10(14). https://doi.org/10.1161/jaha.121.021799

Cheong, V-Lin., Zaman, H., & Annett, S. (2021). Pharmacotherapy of STEMI: a review of international guidelines. Pharmaceutical Journal, 306(7950). https://doi.org/10.1211/pj.2021.1.85645

Lin, V., Holman, J., & Jamieson, B. (2010). Clinical Inquiries: Which drugs should post-MI patients routinely receive? The Journal of Family Practice, 59(9).

Valgimigli, M., Bueno, H., Byrne, R. A., Collet, J.-P., Costa, F., Jeppsson, A., Jüni, P., Kastrati, A., Kolh, P., Mauri, L., Montalescot, G., Neumann, F.-J., Petricevic, M., Roffi, M., Steg, P. G., Windecker, S., Zamorano, J. L., Levine, G. N., Badimon, L., & Vranckx, P. (2017). 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. European Heart Journal, 39(3), 213–260. https://doi.org/10.1093/eurheartj/ehx419

Ahmad, M., Mehta, P., Reddivari, A. K. R., & Mungee, S. (2020). Percutaneous Coronary Intervention. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK556123/

Doll, J. A., Hira, R. S., Kearney, K. E., Kandzari, D. E., Riley, R. F., Marso, S. P., Grantham, J. A., Thompson, C. A., McCabe, J. M., Karmpaliotis, D., Kirtane, A. J., & Lombardi, W. (2020). Management of Percutaneous Coronary Intervention Complications. Circulation: Cardiovascular Interventions, 13(6). https://doi.org/10.1161/circinterventions.120.008962

Mintz, G. S., & Guagliumi, G. (2017). Intravascular imaging in coronary artery disease. The Lancet, 390(10096), 793–809. https://doi.org/10.1016/s0140-6736(17)31957-8

Park, S.-J., & Park, D.-W. (2009). Percutaneous Coronary Intervention With Stent Implantation Versus Coronary Artery Bypass Surgery for Treatment of Left Main Coronary Artery Disease. Circulation: Cardiovascular Interventions, 2(1), 59–68. https://doi.org/10.1161/circinterventions.108.831701

Gach, O., Davin, L., & Lempereur, M. (2019). Diagnostic coronarography. Revue Medicale de Liege, 74(1).

Doenst, T., Haverich, A., Serruys, P., Bonow, R. O., Kappetein, P., Falk, V., Velazquez, E., Diegeler, A., & Sigusch, H. (2019). PCI and CABG for

Treating Stable Coronary Artery Disease. Journal of the American College of Cardiology, 73(8), 964–976. https://doi.org/10.1016/j.jacc.2018.11.053

Beerkens, F. J., Claessen, B. E., Mahan, M., Gaudino, M. F. L., Tam, D. Y., Henriques, J. P. S., Mehran, R., & Dangas, G. D. (2021). Contemporary coronary artery bypass graft surgery and subsequent percutaneous revascularization. Nature Reviews Cardiology, 19(3), 195–208. https://doi.org/10.1038/s41569-021-00612-6

Dimeling, G., Bakaeen, L., Khatri, J., & Bakaeen, F. G. (2021). CABG: When, why, and how? Cleveland Clinic Journal of Medicine, 88(5), 295–303. https://doi.org/10.3949/ccjm.88a.20115

Alexander, J. H., & Smith, P. K. (2016). Coronary-Artery Bypass Grafting. New England Journal of Medicine, 374(20), 1954–1964. https://doi.org/10.1056/nejmra1406944

Spadaccio, C., & Benedetto, U. (2018). Coronary artery bypass grafting (CABG) vs. percutaneous coronary intervention (PCI) in the treatment of multivessel coronary disease: quo vadis? —a review of the evidences on coronary artery disease. Annals of Cardiothoracic Surgery, 7(4), 506–515. https://doi.org/10.21037/acs.2018.05.17

Belley-Côté, E. P., & Devereaux, P. J. (2021). PCI versus CABG for left main coronary artery disease: is the jury still out? The Lancet, 398(10318), 2208–2209. https://doi.org/10.1016/s0140-6736(21)02491-0

Wilms, G., & Baert, A. (1995). The history of angiography. Journal Belge de Radiologie, 78(5).

Neumann, F.-J., Sousa-Uva, M., Ahlsson, A., Alfonso, F., Banning, A. P., Benedetto, U., Byrne, R. A., Collet, J.-P., Falk, V., Head, S. J., Jüni, P., Kastrati, A., Koller, A., Kristensen, S. D., Niebauer, J., Richter, D. J., Seferović, P. M., Sibbing, D., Stefanini, G. G., & Windecker, S. (2018a).

2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal, 40(2), 87–165. https://doi.org/10.1093/eurheartj/ehy394

Cheng, Y., & Regnier, M. (2016). Cardiac troponin structure-function and the influence of hypertrophic cardiomyopathy associated mutations on modulation of contractility. Archives of Biochemistry and Biophysics, 601(601), 11–21. https://doi.org/10.1016/j.abb.2016.02.004

Filatov, V., & Katrukha, A. (1999). Troponin: structure, properties, and mechanism of functioning. Biochemistry, 64(9).

Ohtsuki, I., & Morimoto, S. (2013, January 1). Troponin (W. J. Lennarz & M. D. Lane, Eds.). ScienceDirect; Academic Press. https://www.sciencedirect.com/science/article/pii/B978012378630200195X

Takeda, S. (2005). Crystal structure of troponin and the molecular mechanism of muscle regulation. Microscopy, 54(suppl_1), i35–i41. https://doi.org/10.1093/jmicro/54.suppl_1.i35

Stark, M., & Sharma, S. (2020). Troponin. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK507805/

Marston, S., & Zamora, J. E. (2019). Troponin structure and function: a view of recent progress. Journal of Muscle Research and Cell Motility. https://doi.org/10.1007/s10974-019-09513-1

Katrukha, I. A., & Katrukha, A. G. (2020). Myocardial Injury and the Release of Troponins I and T in the Blood of Patients. Clinical Chemistry, 67(1), 124–130. https://doi.org/10.1093/clinchem/hvaa281

Wu, A. H. B. (2017). Release of cardiac troponin from healthy and damaged myocardium. Frontiers in Laboratory Medicine, 1(3), 144–150. https://doi.org/10.1016/j.flm.2017.09.003

Mair, J., Lindahl, B., Hammarsten, O., Müller, C., Giannitsis, E., Huber, K., Möckel, M., Plebani, M., Thygesen, K., & Jaffe, A. S. (2017). How is cardiac troponin released from injured myocardium? European Heart Journal: Acute Cardiovascular Care, 7(6), 553–560. https://doi.org/10.1177/2048872617748553

deFilippi, C. R., & Mills, N. L. (2021). Rapid Cardiac Troponin Release After Transient Ischemia. Circulation, 143(11), 1105–1108. https://doi.org/10.1161/circulationaha.120.052649

Jaffe, A., & Wu, A. (2011). Troponin release--reversible or irreversible injury? Should we care? Clinical Chemistry, 58(1).

Hammarsten, O., Mair, J., Möckel, M., Lindahl, B., & Jaffe, A. S. (2018). Possible mechanisms behind cardiac troponin elevations. Biomarkers, 23(8), 725–734. https://doi.org/10.1080/1354750x.2018.1490969

Chauin, A. (2021). The Main Causes and Mechanisms of Increase in Cardiac Troponin Concentrations Other Than Acute Myocardial Infarction (Part 1): Physical Exertion, Inflammatory Heart Disease, Pulmonary Embolism, Renal Failure, Sepsis. Vascular Health and Risk Management, Volume 17, 601–617. https://doi.org/10.2147/vhrm.s327661

Solaro, J., & Rosas, P. (2021). Mechanisms of troponin release into serum in cardiac injury associated with COVID-19 patients. International Journal of Cardiology and Cardiovascular Diseases, 1(2). https://doi.org/10.46439/cardiology.1.006

Starnberg, K., Jeppsson, A., Lindahl, B., & Hammarsten, O. (2014). Revision of the Troponin T Release Mechanism from Damaged Human Myocardium. Clinical Chemistry, 60(8), 1098–1104. https://doi.org/10.1373/clinchem.2013.217943

Katus, H. A., Remppis, A., Scheffold, T., Diederich, K. W., & Kuebler, W. (1991). Intracellular compartmentation of cardiac troponin T and its release kinetics in patients with reperfused and nonreperfused myocardial infarction. The American Journal of Cardiology, 67(16), 1360–1367. https://doi.org/10.1016/0002-9149(91)90466-x

Babuin, L. (2005). Troponin: the biomarker of choice for the detection of cardiac injury. Canadian Medical Association Journal, 173(10), 1191–1202. https://doi.org/10.1503/cmaj/051291

Garg, P., Morris, P., Fazlanie, A. L., Vijayan, S., Dancso, B., Dastidar, A. G., Plein, S., Mueller, C., & Haaf, P. (2017). Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Internal and Emergency Medicine, 12(2), 147–155. https://doi.org/10.1007/s11739-017-1612-1

Jaffe, A. S., & Ordonez-Llanos, J. (2013). High-sensitivity Cardiac Troponin: From Theory to Clinical Practice. Revista Española de Cardiología (English Edition), 66(9), 687–691. https://doi.org/10.1016/j.rec.2013.04.020

Antman, E. M. (2002). Decision Making with Cardiac Troponin Tests. New England Journal of Medicine, 346(26), 2079–2082. https://doi.org/10.1056/nejme020049

Brush, J. (2017). A Brief Review of Troponin Testing for Clinicians - American College of Cardiology. American College of Cardiology. https://www.acc.org/latest-in-cardiology/articles/2017/08/07/07/46/a-brief-review-of-troponin-testing-for-clinicians

Jaffe, A. S., Ravkilde, J., Roberts, R., Naslund, U., Apple, F. S., Galvani, M., & Katus, H. (2000). It's time for a change to a troponin standard. Circulation, 102(11), 1216–1220. https://doi.org/10.1161/01.cir.102.11.1216

Santalo, M., & Guindo, J. (2003). Biological Markers of Myocardial Necrosis. Revista Española de Cardiologia, 56(7).

Patibandla, S., & Alsayouri, K. (2020). Cardiac Enzymes. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK545216/

Adams, J. E., Abendschein, D. R., & Jaffe, A. S. (1993). Biochemical markers of myocardial injury. Is MB creatine kinase the choice for the 1990s? Circulation, 88(2), 750–763. https://doi.org/10.1161/01.cir.88.2.750

Neumann, F.-J., Sousa-Uva, M., Ahlsson, A., Alfonso, F., Banning, A. P., Benedetto, U., Byrne, R. A., Collet, J.-P., Falk, V., Head, S. J., Jüni, P., Kastrati, A., Koller, A., Kristensen, S. D., Niebauer, J., Richter, D. J., Seferović, P. M., Sibbing, D., Stefanini, G. G., & Windecker, S. (2018b). 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal, 40(2), 87–165. https://doi.org/10.1093/eurheartj/ehy394

Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., White, H. D., Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., White, H. D., Mickley, H., Crea, F., Van de Werf, F., Bucciarelli-Ducci, C., Katus, H. A., & Pinto, F. J. (2018). Fourth universal definition of myocardial infarction (2018). European Heart Journal, 40(3), 237–269. https://doi.org/10.1093/eurheartj/ehy462

Szummer, K., Lundman, P., Jacobson, S. H., Schön, S., Lindbäck, J., Stenestrand, U., Wallentin, L., & Jernberg, T. (2010). Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: data from the SWEDEHEART register. Journal of Internal Medicine, 268(1). https://doi.org/10.1111/j.1365-2796.2009.02204.x

Miller-Hodges, E., Anand, A., Shah, A. S. V., Chapman, A. R., Gallacher, P., Lee, K. K., Farrah, T., Halbesma, N., Blackmur, J. P., Newby, D. E., Mills, N. L., & Dhaun, N. (2018). High-Sensitivity Cardiac Troponin and

the Risk Stratification of Patients With Renal Impairment Presenting With Suspected Acute Coronary Syndrome. Circulation, 137(5), 425–435. https://doi.org/10.1161/circulationaha.117.030320

Skeik, N., & Patel, D. C. (2007). A review of troponins in ischemic heart disease and other conditions. International Journal of Angiology, 16(02), 53–58. https://doi.org/10.1055/s-0031-1278248

Parikh, R. H., Seliger, S. L., & deFilippi, C. R. (2015). Use and interpretation of high sensitivity cardiac troponins in patients with chronic kidney disease with and without acute myocardial infarction. Clinical Biochemistry, 48(4-5), 247–253. https://doi.org/10.1016/j.clinbiochem.2015.01.004

Jafari Fesharaki, M., Alipour Parsa, S., Nafar, M., Ghaffari-Rahbar, M., Omidi, F., & Karimi-Sari, H. (2016). Serum Troponin I Level for Diagnosis of Acute Coronary Syndrome in Patients with Chronic Kidney Disease. Iranian Journal of Kidney Diseases, 10(1), 11–16. https://pubmed.ncbi.nlm.nih.gov/26837675/

Kraus, D., von Jeinsen, B., Tzikas, S., Palapies, L., Zeller, T., Bickel, C., Fette, G., Lackner, K. J., Drechsler, C., Neumann, J. T., Baldus, S., Blankenberg, S., Münzel, T., Wanner, C., Zeiher, A. M., & Keller, T. (2018). Cardiac Troponins for the Diagnosis of Acute Myocardial Infarction in Chronic Kidney Disease. Journal of the American Heart Association, 7(19). https://doi.org/10.1161/jaha.117.008032

Kanderian, A. S., & Francis, G. S. (2006). Cardiac troponins and chronic kidney disease. Kidney International, 69(7), 1112–1114. https://doi.org/10.1038/sj.ki.5000174

Bansal, N. (2012). Clinically silent myocardial infarctions in the CKD community. Nephrology Dialysis Transplantation, 27(9), 3387–3391. https://doi.org/10.1093/ndt/gfs171

Cooper, G. M. (2013). Protein Degradation. Nih.gov; Sinauer Associates. https://www.ncbi.nlm.nih.gov/books/NBK9957/

Ciechanover, A. (2005). Intracellular protein degradation: from a vague idea thru the lysosome and the ubiquitin–proteasome system and onto human diseases and drug targeting. Cell Death & Differentiation, 12(9), 1178–1190. https://doi.org/10.1038/sj.cdd.4401692

Varshavsky, A. (2005). Regulated protein degradation. Trends in Biochemical Sciences, 30(6), 283–286. https://doi.org/10.1016/j.tibs.2005.04.005

Guo, H. J., & Tadi, P. (2020). Biochemistry, Ubiquitination. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK556052/

Callis, J. (2014). The Ubiquitination Machinery of the Ubiquitin System. The Arabidopsis Book, 12, e0174. https://doi.org/10.1199/tab.0174

TANAKA, K. (2009). The proteasome: Overview of structure and functions. Proceedings of the Japan Academy, Series B, 85(1), 12–36. https://doi.org/10.2183/pjab.85.12

Lecker, S. H., Goldberg, A. L., & Mitch, W. E. (2006). Protein Degradation by the Ubiquitin–Proteasome Pathway in Normal and Disease States. Journal of the American Society of Nephrology, 17(7), 1807–1819. https://doi.org/10.1681/asn.2006010083

Jung, T., Catalgol, B., & Grune, T. (2009). The proteasomal system. Molecular Aspects of Medicine, 30(4), 191–296. https://doi.org/10.1016/j.mam.2009.04.001

Sun-Wang, J. L., Yarritu-Gallego, A., Ivanova, S., & Zorzano, A. (2021). The ubiquitin-proteasome system and autophagy: self-digestion for

metabolic health. Trends in Endocrinology & Metabolism, 32(8), 594–608. https://doi.org/10.1016/j.tem.2021.04.015

Wojcik, C., & Di Napoli, M. (2004). Ubiquitin-Proteasome System and Proteasome Inhibition: New Strategies in Stroke Therapy. Stroke, 35(6), 1506–1518. https://doi.org/10.1161/01.str.0000126891.93919.4e

Harrigan, J. A., Jacq, X., Martin, N. M., & Jackson, S. P. (2018). Deubiquitylating enzymes and drug discovery: emerging opportunities. Nature Reviews Drug Discovery, 17(1), 57–78. https://doi.org/10.1038/nrd.2017.152

Amerik, A. Y., & Hochstrasser, M. (2004). Mechanism and function of deubiquitinating enzymes. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 1695(1-3), 189–207. https://doi.org/10.1016/j.bbamcr.2004.10.003
Dharadhar, S., Kim, R. Q., Uckelmann, M., & Sixma, T. K. (2019). Quantitative analysis of USP activity in vitro. Methods in Enzymology, 618, 281–319. https://doi.org/10.1016/bs.mie.2018.12.023

Reyes-Turcu, F. E., Ventii, K. H., & Wilkinson, K. D. (2009). Regulation and Cellular Roles of Ubiquitin-Specific Deubiquitinating Enzymes. Annual Review of Biochemistry, 78(1), 363–397. https://doi.org/10.1146/annurev.biochem.78.082307.091526

National Institute of Diabetes and Digestive and Kidney Diseases. (2019, January 3). Kidney Disease Statistics for the United States | NIDDK. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease

CDC. (2021, March 9). Chronic Kidney Disease in the United States, 2021. Www.cdc.gov. https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html

Klinkmann, H., & Vienken, J. (1995). Membranes for dialysis. Nephrology Dialysis Transplantation, 10(supp3), 39–45. https://doi.org/10.1093/ndt/10.supp3.39

Boure, T. (2004). Which dialyser membrane to choose? Nephrology Dialysis Transplantation, 19(2), 293–296. https://doi.org/10.1093/ndt/gfg508

Bianchi, M. E., & Mezzapelle, R. (2020a). The Chemokine Receptor CXCR4 in Cell Proliferation and Tissue Regeneration. Frontiers in Immunology, 11. https://doi.org/10.3389/fimmu.2020.02109

Saini, V., Marchese, A., & Majetschak, M. (2010). CXC Chemokine Receptor 4 Is a Cell Surface Receptor for Extracellular Ubiquitin. Journal of Biological Chemistry, 285(20), 15566–15576. https://doi.org/10.1074/jbc.m110.103408

Tripathi, A., Saini, V., Marchese, A., Volkman, B. F., Tang, W.-J., & Majetschak, M. (2013). Modulation of the CXC Chemokine Receptor 4 Agonist Activity of Ubiquitin through C-Terminal Protein Modification. Biochemistry, 52(24), 4184–4192. https://doi.org/10.1021/bi400254f

Nguyen, T., Ho, M., Ghosh, A., Kim, T., Yun, S. I., Lee, S. S., & Kim, K. K. (2016). An ubiquitin-binding molecule can work as an inhibitor of ubiquitin processing enzymes and ubiquitin receptors. Biochemical and Biophysical Research Communications, 479(1), 33–39. https://doi.org/10.1016/j.bbrc.2016.09.010

Saini, V., Staren, D. M., Ziarek, J. J., Nashaat, Z. N., Campbell, E. M., Volkman, B. F., Marchese, A., & Majetschak, M. (2011). The CXC Chemokine Receptor 4 Ligands Ubiquitin and Stromal Cell-derived Factor-1α Function through Distinct Receptor Interactions. Journal of Biological Chemistry, 286(38), 33466–33477. https://doi.org/10.1074/jbc.m111.233742

Pawig, L., Klasen, C., Weber, C., Bernhagen, J., & Noels, H. (2015a). Diversity and Inter-Connections in the CXCR4 Chemokine Receptor/Ligand Family: Molecular Perspectives. Frontiers in Immunology, 6, 429. https://doi.org/10.3389/fimmu.2015.00429

Steagall, R. J., Daniels, C. R., Dalal, S., Joyner, W. L., Singh, M., & Singh, K. (2014). Extracellular Ubiquitin Increases Expression of Angiogenic Molecules and Stimulates Angiogenesis in Cardiac Microvascular Endothelial Cells. Microcirculation, 21(4), 324–332. https://doi.org/10.1111/micc.12109

Yao, J. (2020). Role and Mechanism of Free Ubiquitin Activated CXCR4 Pathway in Ischemic Myocardial Repair. National Natural Science Foundation of China, 1(1).

Singh, K. (2021). Investigation of therapeutic potential of exogenous ubiquitin following myocardial ischemia/reperfusion injury. James H Quillen va Medical Center, 1(1).

Kobayashi, M., Higa, J. K., & Matsui, T. (2019). The role of ubiquitin in cardiac ischemia-reperfusion injury. American Journal of Physiology-Heart and Circulatory Physiology, 316(3), H583–H585. https://doi.org/10.1152/ajpheart.00018.2019

Ji, Y., Yao, J., Zhao, Y., Zhai, J., Weng, Z., & He, Y. (2020). Extracellular ubiquitin levels are increased in coronary heart disease and associated with the severity of the disease. Scandinavian Journal of Clinical and Laboratory Investigation, 80(3), 256–264. https://doi.org/10.1080/00365513.2020.1728783

Chen, S-M., Zhang, H-X., Li, Y-G., Wang, D-M., Zhang, G-H., & Tan, C-J. (2008). Expression of Ubiquitin in Peripheral Inflammatory Cells from Patients with Coronary Artery Disease. Journal of International Medical Research, 36(6), 1227–1234. https://doi.org/10.1177/147323000803600609

Vannucci, S. J., Mummery, R., Hawkes, R. B., Rider, C. C., & Beesley, P. W. (1998). Hypoxia—Ischemia Induces a Rapid Elevation of Ubiquitin Conjugate Levels and Ubiquitin Immunoreactivity in the Immature Rat Brain. Journal of Cerebral Blood Flow & Metabolism, 18(4), 376–385. https://doi.org/10.1097/00004647-199804000-00005

Janssens, R., Struyf, S., & Proost, P. (2017). The unique structural and functional features of CXCL12. Cellular & Molecular Immunology, 15(4), 299–311. https://doi.org/10.1038/cmi.2017.107

CXCL12 C-X-C motif chemokine ligand 12 [Homo sapiens (human)] - Gene - NCBI. (2022). Www.ncbi.nlm.nih.gov. https://www.ncbi.nlm.nih.gov/gene/6387

Guyon, A. (2014). CXCL12 chemokine and its receptors as major players in the interactions between immune and nervous systems. Frontiers in Cellular Neuroscience, 8. https://doi.org/10.3389/fncel.2014.00065

Lee, E., Han, J., Kim, K., Choi, H., Cho, E.-G., & Lee, T. R. (2012). CXCR7 mediates SDF1-induced melanocyte migration. Pigment Cell & Melanoma Research, 26(1), 58–66. https://doi.org/10.1111/pcmr.12024

Kucia, M., Jankowski, K., Reca, R., Wysoczynski, M., Bandura, L., Allendorf, D. J., Zhang, J., Ratajczak, J., & Ratajczak, M. Z. (2003). CXCR4–SDF-1 Signalling, Locomotion, Chemotaxis and Adhesion. Journal of Molecular Histology, 35(3), 233–245. https://doi.org/10.1023/b:hijo.0000032355.66152.b8

Bianchi, M. E., & Mezzapelle, R. (2020b). The Chemokine Receptor CXCR4 in Cell Proliferation and Tissue Regeneration. Frontiers in Immunology, 11. https://doi.org/10.3389/fimmu.2020.02109

Otsuka, S., & Bebb, G. (2008). The CXCR4/SDF-1 Chemokine Receptor Axis: A New Target Therapeutic for Non-small Cell Lung Cancer. Journal

of Thoracic Oncology, 3(12), 1379–1383. https://doi.org/10.1097/jto.0b013e31818dda9d

CXCR4 protein expression summary - The Human Protein Atlas. (2022). Www.proteinatlas.org. https://www.proteinatlas.org/ENSG00000121966-CXCR4

Pawig, L., Klasen, C., Weber, C., Bernhagen, J., & Noels, H. (2015b). Diversity and Inter-Connections in the CXCR4 Chemokine Receptor/Ligand Family: Molecular Perspectives. Frontiers in Immunology, 6, 429. https://doi.org/10.3389/fimmu.2015.00429

Walenkamp, A. M. E., Lapa, C., Herrmann, K., & Wester, H.-J. (2017). CXCR4 Ligands: The Next Big Hit? Journal of Nuclear Medicine, 58(Supplement 2), 77S82S. https://doi.org/10.2967/jnumed.116.186874

Hesselgesser, J., & Liang, M. (1998). Identification and characterization of the CXCR4 chemokine receptor in human T cell lines: ligand binding, biological activity, and HIV-1 infectivity. Journal of Immunology, 160(2).

Litman-Zawadzka, A., Łukaszewicz-Zając, M., Gryko, M., Kulczyńska-Przybik, A., Kędra, B., & Mroczko, B. (2020). Specific Receptors for the Chemokines CXCR2 and CXCR4 in Pancreatic Cancer. International Journal of Molecular Sciences, 21(17), 6193. https://doi.org/10.3390/ijms21176193

Peng, L., Zhu, N., Mao, J., Huang, L., Yang, Y., Zhou, Z., Wang, L., & Wu, B. (2020). Expression levels of CXCR4 and CXCL12 in patients with rheumatoid arthritis and its correlation with disease activity. Experimental and Therapeutic Medicine, 20(3). https://doi.org/10.3892/etm.2020.8950

Han, J. H., Ahn, M.-H., Jung, J.-Y., Suh, C.-H., Kwon, J. E., Yim, H., & Kim, H.-A. (2019). The levels of CXCL12 and its receptor, CXCR4, as a

biomarker of disease activity and cutaneous manifestation in adult-onset Still's disease. Clinical and Experimental Rheumatology, 37 Suppl 121(6), 67–73. https://pubmed.ncbi.nlm.nih.gov/31287410/

Łukaszewicz-Zając, M., Mroczko, B., Kozłowski, M., & Szmitkowski, M. (2016). The Serum Concentrations of Chemokine CXCL12 and Its Specific Receptor CXCR4 in Patients with Esophageal Cancer. Disease Markers, 2016, 1–7. https://doi.org/10.1155/2016/7963895

Frayyeh, A. H., Salman, E. D., & Melconian, A. K. (2019). Elevated Serum Level of CXCR4 in Breast Cancer Women. Research Journal of Pharmacy and Technology, 12(8), 3833. https://doi.org/10.5958/0974-360x.2019.00657.7

DĄBROWSKA, E., PRZYLIPIAK, A., ZAJKOWSKA, M., PISKOR, B. M., SIDORKIEWICZ, I., SZMITKOWSKI, M., & LAWICKI, S. (2020). Possible Diagnostic Application of CXCL12 and CXCR4 as Tumor Markers in Breast Cancer Patients. Anticancer Research, 40(6), 3221–3229. https://doi.org/10.21873/anticanres.14303

DÃ¶ring, Y., Pawig, L., Weber, C., & Noels, H. (2014). The CXCL12/CXCR4 chemokine ligand/receptor axis in cardiovascular disease. Frontiers in Physiology, 5. https://doi.org/10.3389/fphys.2014.00212\

Wang, K., Zhao, X., Kuang, C., Qian, D., Wang, H., Jiang, H., Deng, M., & Huang, L. (2012). Overexpression of SDF-1α Enhanced Migration and Engraftment of Cardiac Stem Cells and Reduced Infarcted Size via CXCR4/PI3K Pathway. PLoS ONE, 7(9), e43922. https://doi.org/10.1371/journal.pone.0043922

Penn, M. S., Pastore, J., Miller, T., & Aras, R. (2012). SDF-1 in myocardial repair. Gene Therapy, 19(6), 583–587. https://doi.org/10.1038/gt.2012.32

Ziff, O. J., Bromage, D. I., Yellon, D. M., & Davidson, S. M. (2017). Therapeutic strategies utilizing SDF-1α in ischaemic cardiomyopathy. Cardiovascular Research, 114(3), 358–367. https://doi.org/10.1093/cvr/cvx203

Yu, J., Li, M., Qu, Z., Yan, D., Li, D., & Ruan, Q. (2010). SDF-1/CXCR4-Mediated Migration of Transplanted Bone Marrow Stromal Cells Toward Areas of Heart Myocardial Infarction Through Activation of PI3K/Akt. Journal of Cardiovascular Pharmacology, 55(5), 496–505. https://doi.org/10.1097/fjc.0b013e3181d7a384

Penn, M. S. (2009). Importance of the SDF-1:CXCR4 Axis in Myocardial Repair. Circulation Research, 104(10), 1133–1135. https://doi.org/10.1161/circresaha.109.198929

Zhong, J., & Rajagopalan, S. (2015). Dipeptidyl Peptidase-4 Regulation of SDF-1/CXCR4 Axis: Implications for Cardiovascular Disease. Frontiers in Immunology, 6. https://doi.org/10.3389/fimmu.2015.00477

Alhajj, M., & Farhana, A. (2020). Enzyme Linked Immunosorbent Assay (ELISA). PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK555922/

Aydin, S. (2015). A short history, principles, and types of ELISA, and our laboratory experience with peptide/protein analyses using ELISA. Peptides, 72(1), 4–15. https://doi.org/10.1016/j.peptides.2015.04.012

Lequin, R. M. (2005). Enzyme Immunoassay (EIA)/Enzyme-Linked Immunosorbent Assay (ELISA). Clinical Chemistry, 51(12), 2415–2418. https://doi.org/10.1373/clinchem.2005.051532

The enzyme-linked immunosorbent assay (ELISA). (1976). Bulletin of the World Health Organization, 54(2), 129–139. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2366430/

Radiometer AQT90 FLEX Troponin I METHOD AND SAMPLE COLLECTION 1. PURPOSE AND SCOPE. (2021). https://www.appn.net.au/data/sites/1/appn/02implementation/technicalresources/troponini/radiometeraqt90flextroponinimethodandsamplecollection.pdf

RStudio | Open source & professional software for data science teams. (2020). Rstudio.com. https://www.rstudio.com

Grolemund, G. (2021). Quick list of useful R packages. Posit Support. https://support.posit.co/hc/en-us/articles/201057987-Quick-list-of-useful-R-packages

R Packages. (2022). Rstudio.com. https://www.rstudio.com/products/rpackages/

RStudio Open-Source Packages. (2022). Www.rstudio.com. https://www.rstudio.com/about/rstudio-open-source-packages/

Korstanje, J. (2020, February 17). 6 ways to test for a Normal Distribution — which one to use? Medium. https://towardsdatascience.com/6-ways-to-test-for-a-normal-distribution-which-one-to-use-9dcf47d8fa93

Weisstein, E. W. (2020). Normal Distribution. Mathworld.wolfram.com. https://mathworld.wolfram.com/NormalDistribution.html

SHAPIRO, S. S., & WILK, M. B. (1965). An analysis of variance test for normality (complete samples). Biometrika, 52(3-4), 591–611. https://doi.org/10.1093/biomet/52.3-4.591

Stephanie. (2014, November 19). Shapiro-Wilk Test: What it is and How to Run it. Statistics How To. https://www.statisticshowto.com/shapiro-wilk-test/

McClenaghan, E. (2022, July 6). Mann-Whitney U Test: Assumptions and Example. Informatics from Technology Networks. https://www.technologynetworks.com/informatics/articles/mann-whitney-u-test-assumptions-and-example-363425

Jiang, X. (2018). Parametric and Non-parametric ANOVA. Jbhender.github.io. https://jbhender.github.io/Stats506/F18/GP/Group3.html

Wobbrock, J. O., Findlater, L., Gergle, D., & Higgins, J. J. (2011). The aligned rank transform for nonparametric factorial analyses using only anova procedures. Proceedings of the 2011 Annual Conference on Human Factors in Computing Systems - CHI '11. https://doi.org/10.1145/1978942.1978963

Salkind, N. (2010). Encyclopedia of research design. Encyclopedia of Research Design, 1(1). https://doi.org/10.4135/9781412961288

Bevans, R. (2020, March 20). Two-way ANOVA | When and How to Use it, With Examples. Scribbr. https://www.scribbr.com/statistics/two-way-anova/

Schober, P., Boer, C., & Schwarte, L. A. (2018). Correlation Coefficients: Appropriate Use and Interpretation. Anesthesia & Analgesia, 126(5), 1763–1768. https://doi.org/10.1213/ane.0000000000002864

Habibzadeh, F., Habibzadeh, P., & Yadollahie, M. (2016). On determining the most appropriate test cut-off value: the case of tests with continuous results. Biochemia Medica, 26(3), 297–307. https://doi.org/10.11613/bm.2016.034

Unal, I. (2017). Defining an Optimal Cut-Point Value in ROC Analysis: An Alternative Approach. Computational and Mathematical Methods in Medicine, 2017, 1–14. https://doi.org/10.1155/2017/3762651

Hard Classification. (2020). R-Packages. https://cran.r-project.org/web/packages/ROCit/vignettes/my-vignette.html?fbclid=IwAR0AxESIHkb9Lc5u4T5KyxDlMA3BlSb987CiWG4qKDBrpd4qlJamw32f8Cg

Xiao, Q., Ye, S., Oberhollenzer, F., Mayr, A., Jahangiri, M., Willeit, J., Kiechl, S., & Xu, Q. (2008). SDF1 Gene Variation Is Associated with Circulating SDF1α Level and Endothelial Progenitor Cell Number–The Bruneck Study. PLoS ONE, 3(12), e4061. https://doi.org/10.1371/journal.pone.0004061