Medical University – Pleven

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ASSESSMENT OF VITAL MYOCARDIUM AS A RECOMMENDED CRITERION IN THE TREATMENT OF PATIENTS WITH ISCHEMIC HEART DISEASE WITH OR WITHOUT CHRONIC HEART FAILURE

ABSTRACT

on

DISSERTATION

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The materials for the presentation of the dissertation work are available in the Department of "Propaedeutics of Internal Diseases" at the Faculty of Medicine of the Medical University – Pleven.

CONTENTS

LIST OF ABBREVIATIONS USED

ATP – adenosine triphosphate

ECG – electrocardiography

CHD – coronary heart disease

CAD – coronary artery disease

LV – left ventricular

MI – myocardial infarction

USA – United States of America

EF – ejection fraction

COPD – chronic obstructive pulmonary disease

CHF – chronic heart failure

ACC – American College of Cardiology

AHA – American Heart Association

ACE – angiotensin-converting enzyme

ARB – angiotensin receptor blockers

CABG – coronary bypass

FDG – fluorodeoxyglucose

JACC – Journal of the American College of Cardiology

NYHA – New York Heart Association

PCI – percutaneous coronary intervention

PET – positron emission tomography

INTRODUCTION

Chronic heart failure (CHF) is one of the biggest problems in cardiology. The main reason for this is the high mortality in these patients. The main causes of CHF are ischemic heart disease (CHD) and hypertension.

There is some controversy regarding therapy in patients with systolic and diastolic dysfunction. There are also significant contradictions regarding the treatment of the elderly, as well as regarding patients with a significant number of accompanying diseases. However, with tremendous advances in both cardiac surgery and the field of invasive cardiology, these two therapeutic approaches are rapidly and aggressively entering both the diagnosis and treatment of patients with CHF.

However, over time and with the accumulation of experience, it appears that in groups of patients with multiple risk factors (including age), as well as in individuals with a past acute coronary event and the presence of a small volume of viable myocardium, invasive treatment is not the most appropriate.

In certain groups of patients, the treatment of CHF with drugs alone, without invasive procedures, leads to better results, especially in terms of life expectancy. Nuclear medicine is a valuable method for assessing both cardiac contractility and cardiac muscle viability. Through the use of nuclear (nuclear) medical research, the volume of invasive and treatment procedures for these patients can be significantly limited. This would benefit both the patient and healthcare as a whole.

There is a number of controversies regarding the correct therapeutic behaviour in patients with heart disease and advanced left ventricular systolic dysfunction. There is also controversy regarding the treatment of elderly patients or those with medical contraindications to the use of more aggressive therapy. Should they be treated with a procedure - whether angioplasty/stent or coronary artery bypass grafting (CABG) or should they only undergo conservative (drug) therapy. There is also a group of patients who are not suitable for a diagnostic procedure due to multiple risk factors, such as age, weakened general condition, renal dysfunction, etc. In these cases, the question arises whether in the given group of patients the risk of performing coronary angiography or computed tomography of the coronary vessels should be taken, provided that coronary angiography is impossible or undesirable due to advanced age and coronary calcifications, or non-invasive testing such as nuclear evaluation of possible pathology/ischemia should be resorted to.

It is generally accepted that patients with left ventricular dysfunction and bi- or tri vessel coronary artery disease should undergo CABG. Patients with single or double uncomplicated coronary pathology and left ventricular (LV) dysfunction should receive angioplasty/stenting.

Left ventricular (LV) dysfunction with an ejection fraction of 35% is considered by most treatment-biased studies as the starting point for deciding on therapeutic behaviour in these patients.

Assessment of survival – a basis for treatment to each patient

In the last 2-3 decades, drug treatment for patients with coronary artery disease and left ventricular dysfunction has significantly improved. Starting with the administration of angiotensin inhibitors, followed by angiotensin 2-receptor blockers, acetylsalicylic acid, non-selective beta-blockers, followed by selective beta-blockers and diuretics, such as diuretics affecting the loop of Henle; aldactone antagonists; F-channel receptor blockers; long-acting nitrates; peripheral vasodilators (hydralazine) – all of these drug therapies are available inexpensively worldwide for the treatment of patients with coronary artery disease and associated left ventricular dysfunction. Over the past decade, the advent and advancement of resynchronization therapy (and implantable defibrillators) have improved the quality of life and longevity of many patients who were previously thought to have intractable heart failure with or without angina.

Educating patients about lifestyle, as well as treating symptoms when they first appear as an outpatient, reduces the overall hospital stay of those patients who had a history of prolonged hospitalization. The advent of implantable defibrillators has reduced the risk of sudden cardiac death in patients with CAD and significant LV dysfunction. It should be noted, however, that revascularization alone in patients with significant LV dysfunction does not reduce the incidence of death and ventricular fibrillation, unless the patient is additionally implanted with a defibrillator. This statement is intended to emphasize that **reducing mortality and improving quality of life is the primary goal in the treatment of a patient with heart disease**. It cannot be considered successful therapy – whether surgery or angioplasty – in a patient with immediate 30-day mortality.

Patient groups covered in the study

The first group in our present study was selected among patients undergoing coronary angiography who were examined in a single practice. The follow-up period was 6 years. The study was approved by the ethics committee of Arwyp Hospital - Republic of South Africa. Both studied groups were elderly, with significant co-morbidities. In the group in which primary and/or secondary (additional) nuclear research was performed, the accompanying pathology was more severe. The studies were carried out in collaboration with the Department of Nuclear Medicine, where these patients were examined for myocardial ischemia or viability. According to the results - in the presence of medium (30% involvement) myocardial viability, patients with ischemia were suggested to undergo surgical or PCI treatment. In the presence of a lower percentage of viable myocardium, our hypothesis is that the patient should first undergo drug therapy with follow-up. In the second group of patients in our study, the presence of coronary artery disease was evaluated, with an examination for ischemia. Patients were selected based on their significant comorbidity or inability for one reason or another to undergo coronary angiography. In the absence of myocardial ischemia, angiography is not necessary. The presence of ischemic myocardium suggests the performance of coronary angiography. In our study, this is a small group of patients, some of whom subsequently underwent CABG or PCI. To proceed to one of the two procedures, the amount of ischemic myocardium had to be significant (the presence of a limited amount of ischemic myocardium suggests drug therapy).

THE AIM AND OBJECTIVES

The aim

The aim of the present study is to determine when interventional or surgical treatment should be applied and when drug therapy is preferable or not in patients with coronary pathology and/or CHF.

Tasks

1. To determine the most appropriate approach to achieve the goal.
2. To establish possible indications and contraindications for invasive treatment in elderly patients with or without CHF.
3. To demonstrate that the possible indications in patients with significant perioperative risk (obesity, COPD, advanced renal disease) lead to early fatal outcome and no procedure.
4. To specify the desired percentage of viable myocardium available to proceed to direct angiographic coronary evaluation.
5. Is coronary angiography necessary in patients with CHF, and if so, when?
6. How to approach patients who have undergone revascularization (interventional or bypass) but have angina with or without CHF.
7. How should the same patients be approached when they are of advanced age and/or with co-morbidities?
8. Which methodology is most suitable for answering these tasks?
9. Acceptance of drug therapy in which patients is more appropriate, including to reduce perioperative mortality.
10. What are the additional benefits for avoiding complications (bleeding, nephropathy, etc.) from the application of the therapeutic non-invasive approach.

MATERIAL AND METHODS

Patients

A total of 207 patients were included in the study. Of them, 56 were women and 151 were men.

The age groups are as follows: 28-44 years - 9 people, 45-60 years - 79 people, 61-76 years - 86 people, 77-92 years - 33 people.

The group with contraindications for angiography consisted of 50 people.

The group that underwent angiography included 157 patients.

Patients without acute coronary syndrome were included in both groups.

All patients were referred by their attending physicians for further treatment and possible intervention.

All patients had indications of angina or a recent myocardial infarction.

The occurrence in the past of a myocardial infarction was established by two of three classical indicators:

a) pain and ECG changes;

b) elevated cardiac enzymes and pain and/or

c) ECG changes;

We divided our study groups into two for a specific reason.

One group includes patients with coronary artery disease who are being screened with technetium to assess the need for an in-line bypass procedure or PCI. **The second group** covers patients with undiagnosed disease, but with an increased risk and clinical evidence of angina pectoris. They underwent a technetium scan to assess the need for a coronary angiogram. The aim is to determine the need of initial non-interventional testing, which carries essentially no significant risk, in the evaluation of patients at high risk for coronary angiography testing due to comorbidities.

When the study shows a significant area of ischemia or infarct, coronary angiography is performed. If left ventricular dysfunction is not suspected to be due to an unknown cause, coronary angiography is not performed, because even in the presence of coronary artery disease, it is not necessary for the patient to undergo coronary angiography, as there is no need to take further action. Coronary angiography does not actually pose a significant risk to the general patient population. The risk arises in the group of elderly patients (increasing the possibility of dissection, fragile vessels with many calcifications in them, as well as difficult anatomy, need for partial anaesthesia, curvature, presence of unsuspected disease of the aorta in the abdominal area, ectasia), especially in the over seventy age group. On the other hand, obese patients with pulmonary comorbidities are at risk of bleeding or are challenging to place on the angiographic table due to their inability to lie supine. Patients with decompensated or partially compensated heart failure also have difficulty lying down. We should not forget the purely technical reason that the load capacity of the majority of catheterization tables is calculated to withstand a weight of up to 180 kg (and some of them even up to 160 kg). Some of the older catheterization equipment cannot handle even this weight.

We should also mention the possibilities for the assessment of ischemic heart disease using MRI images. This methodology has the potential to assess the myocardium, function, and coronary circulation with a single image. It's called a one-stop shop. The overall assessment is done by one tool. The sensitivity for detecting coronary artery disease is compared with planar thallium scintigraphy 201. The sensitivity for the presence of double vessel disease is up to 90%. This technique is not widespread and not generally accepted by clinicians.

We also looked at another group of patients - kidney patients with transplantation. They are part of our general patient group and have often participated in scintigraphy for obvious reasons. The presence of coronary disease in these patients is up to 47%. In general, exercise stress tests do not reveal much - as these patients cannot be exercise due to mobility difficulties Adequate metabolic units were not reached due to general fatigue and inability to perform the stress test. Stress test prediction in this group was approximately 71%. Angiographically determined coronary artery disease in such patients increases the likelihood of cardiac events. Coronary angiography is associated with complaints, but since approximately 50% of these patients have significant disease, it does not seem reasonable to perform angiography on every one of them.

Methodology

1. Clinical history: Patients had a detailed history taken. It included the history of the current illness – whether the patient presented with angina pectoris or heart failure. Patients were questioned about risk factors and these were included in the patient risk profile. Comorbid diseases were identified - special attention was paid to kidney diseases associated with renal failure.

2. ECG. All patients had a resting ECG. Those who could exercise were subjected to a stress test according to the following protocols - Bruce, modified Bruce, Cornell (depending on the physical capabilities of the patient). ECG was performed according to a standard protocol with peripheral four electrodes and precordial six electrodes. If a stress test was performed, the same position of the electrodes was maintained. The goal with any exercise test, when done, is to achieve at least 80% of target heart rate (220 bpm – age – 15%).

Description of radioactive exposure

Most patients, as well as clinicians, do not know what radiation dose is associated with the performance of the examination. Typically, the dose is equivalent to a transcontinental flight or a CT scan or similar form of background radiation. In recent years, when airports are full of scanners that scan every passenger, and in some airports where there is a radioactive check, exposure to radiopharmaceuticals can set off the alarm because they radiate from the body for up to three months.

What to avoid before the test – heavy meals should be avoided. Some drugs that may affect stress test responses (antianginal drugs, narcotics, dipyridamole/dipyridamole-containing drugs – e.g. antistenocardine) (165). The patient should refrain from caffeine-containing drugs or beverages (166).

The injection of the radionuclide tracer is administered through a protected venous line. The injection can be given at an interval of 30 minutes. The simultaneous administration of the pharmacological medication with the indicator should be avoided. When an injection is given at rest, it should ideally be given after administration of a sublingual nitrate. This is very important to perform in patients in whom acute myocardial ischemia is suspected or in the elderly. This application is relevant because sublingual nitrate helps reveal infarction or ischemia in areas of reduced perfusion at rest (167).

Advantages and disadvantages of Tl-201 and Tc-m99

- Uptake and excretion in the splanchnic are higher for Tl-201. This makes interpretation of the distribution in the lower walls difficult.
- The absorption of Tc-m99 is less strong compared to Tl-201 (which means that some defects will be less defined).
- Two injections of the indicator are needed - one at rest and one at stress.
- For personnel – exposure is less with Tc-m99.
- Tc-m99 has higher energy and consequently better imaging.
- Less attenuation and dispersion:
- Tc-m99 has a shorter half-life – this technically gives additional information.

Adverse effects

- Mild transient rash, flushing, metallic taste and vasovagal reactions are most common
- Very few of the side effects need treatment.
- For Tl-201 – extravasation should be avoided as it causes tissue necrosis.
- Several cases of anaphylaxis, angioedema, erythroderma have been reported for Tc-m99.

Stress test – overview of the procedure

When coronary artery disease is suspected, a stress test is the first choice. Patients should reach the target heart rate (220 beats/min minus age).

Dynamic exercise should not be performed in patients who cannot achieve an adequate response due to various reasons, such as lung diseases, diseases of the peripheral blood vessels, problems with the musculoskeletal system, neurological problems, etc. Some patients lack the stamina and motivation to perform a test. In them, one should switch to pharmacological perfusion testing.

All tests must be supervised by a physician or appropriately trained technician.

The selected load test may differ. Different cycles can be used to achieve the required physical loading. Effort tolerance information should be obtained before the test is conducted. For some patients, it is impossible to achieve an optimal load due to various medical problems or due to poor motivation. Patients who are unable to exercise, who have lung disease, arthritis, amputation, or neurological disease undergo pharmacological testing. This is a good alternative. There are two groups of drugs used as a substitute for exercise - vasodilators (dipyridamole and adenozine), both of which create hyperemia of the coronary arteries. The second group are drugs (dobutamine) that increase coronary oxygen demand. Patients should prepare appropriate clothing and footwear for the stress test. All stress test procedures must be supervised by a trained professional - doctor, nurse or technologist.

When introducing medical stress factors, the direct supervision of a doctor is necessary. The laboratory technician conducting the stress test should be able to select the most appropriate protocol. Adequate facilities for cardiovascular resuscitation are mandatory. There should also be personnel with advanced life support - resuscitation capabilities and materials for this.

Preparation before the stress test examination:

– Clinical history, i.e. indication, symptoms, risk factors.

– If the patient has diabetes – diet and insulin dosage should be optimized. It may be a good idea to test the patient's blood sugar before the test.

– The patient must be hemodynamically stable for 48 hours before the test.

– Cardiac medications that interfere with the test should be stopped before the test, and this decision should be left to the referring physician.

– Caffeinated beverages and foods as well as medications (some pain relievers have caffeine as well as diet shakes) should be stopped for 24 hours before they antagonize the vasodilator effect. Only if really needed adenosine can be given, neutralizing the effect of caffeine.

– The intake of drugs containing methylxanthine should be re-established for a time equal to at least five times the half-life of the drug.

stress test procedure

Indications. The procedure is usually safe. Myocardial infarction and death are reported in 1:10,000 procedures. However, this depends on the combination of cases. The combination of patients at higher risk with reaching the target heart rate carries a higher risk of complications during the test. Clinical judgment should prevail. ECG, blood pressure and heart rate are recorded at baseline before exercise.

The patient should be monitored for complaints, as ST changes, arrhythmias, and especially symptoms may occur.

Electronic equipment and protocols

Both a treadmill and an ergometer are used. Several protocols are available for treadmill use. The most popular are the Bruce protocol, as well as the modified Bruce protocol. The purpose of the test is to achieve maximal myocardial hyperemia and myocardial perfusion. The protocol used for this is not that important. A generally accepted range of 85% of target heart rate is considered acceptable. In addition to heart rate, blood pressure and oxygen consumption should be monitored. There is a so-called pressure-rate product (heart rate x blood pressure). Values above 25,000 (mm Hg/min) indicate acceptable, and above 30,000 – excellent myocardial hyperemia. It is important to remember that the exercise test should be symptom limited (safety first), but the target should be 15% lower than the predicted target heart rate. When it is very important to achieve the target heart rate, it is necessary to switch from an exercise test to a pharmacological increase in heart rate. If the patient has symptoms for which they are referred – a pharmacologic option should still be considered.

Absolute contraindications for a test with physical effort

– acute coronary syndrome – at least 48 hours after (if the symptoms are acceptable);

– acute pulmonary embolism;

– severe pulmonary hypertension;

– acute dissection of the aorta;

– symptomatic severe aortic stenosis;

– hypertrophic obstructive cardiomyopathy;

– uncontrolled cardiac arrhythmias;

– acute myocarditis or pericarditis;

– active endocarditis.

Relative contraindications

– patients with decompensated heart failure;

– active deep vein thrombosis;

– left femoral block (exercise ECG can be done and related to symptoms);

– hypertension – arterial pressure above 200/100 mm Hg;

– recent stroke or transient ischemic attack;

– moderate to severe aortic stenosis.

The maximal effort test should adhere to the following steps:

– A venous line should be placed prior to efforts to administer radiopharmaceuticals;

– ECG should be followed during exercise and 5 minutes during recovery (12 leads);

– The ECG should be checked every 2-3 minutes of the exercise;

– Exercise should be limited by symptoms or if the patient achieves 85% of the target heart rate;

– The radiopharmaceutical should be injected at peak effort. The patient should continue with physical activity for at least another minute or two afterwards.

Absolute termination indication

– pronounced ST-depression (> 3 mm);

– ST-elevation greater than 1 mm in leads without Q-waves;

– tachyarrhythmia;

– supraventricular tachycardia or atrial fibrillation – new;

– drop in systolic blood pressure by more than 20 mm Hg;

– marked increase in blood pressure - over 250 mm Hg or diastolic 130 mm Hg;

– troubling angina;

– syncope or near syncope or any neurological complications;

– onset of ventricular tachycardia;

– inability of the patient to continue the test.

Relative indications for premature termination of the effort

– horizontal ST-depression of 2 mm or lowering of ST-depression;

– arrhythmias, especially if they are symptomatic;

– fatigue;

– new start of branch block.

It should be noted that dipyridamole increases tissue adenosine levels by preventing intracellular adenosine reuptake and deamination (168).

Vasodilators cause a moderate increase in heart rate. So is their effect on systolic and diastolic blood pressure. So the logic states that a myocardium that has reduced its reserve due to a diseased coronary artery - causes ischemia and "steal phenomenon".

We have already mentioned some drugs and food products, the intake of which should be stopped before the examination. There are several others. Pentocsyphilin and clopidogrel - no need to stop. Newer agents, such as Ticagrelor, which is a direct inhibitor of the P2Y12 adenosine receptor, however, significantly increase the level of plasma adenosine. This leads to an adverse effect with dipyridamole (169, 170). The interaction between adenosine and regadenoson is not yet known.

Indications

This is a very important part of our research. The main indication is patients who are unable to reach their maximum or 85% of their maximum predicted heart rate during exercise.

Also, if patients have a left bundle branch block – the chemical test is preferable.

When all modalities and agents are considered, there is no specific preference for a particular agent that is used in the chemistry test (171, 172).

Absolute contraindications for a vasodilator stress test

– Same as stress test – if the patient is considered stable 48 hours after acute coronary syndrome – and if the risk is considered acceptable – a radiopharmaceutical test can be done.

– Severe COPD.

– Greater than first degree heart block or sick sinus syndrome.

– Symptomatic aortic stenosis.

– Hypertrophic cardiomyopathy (obstructive).

– Low systolic blood pressure (below 90 mm Hg).

– Neurological problems – any type of cerebral ischemia.

Relative contraindications

- Mild to moderate asthma (adenosine, dipyridamole, regadenoson);
- Sinus bradycardia below 40 beats/min;

– Use of dipyridamole in the last 24 hours;

– Severe atherosclerotic lesion in any artery except the brain.

Significant stenosis of the carotid artery

We will pay particular attention to dipyridamole, as this is the substance used in our test population.

Dipyridamole was administered as a continuous infusion at 140 micrograms/kg/min over 4 minutes. Four minutes after the injection, the radiopharmaceutical is administered. It should be noted that dipyridamole is not licensed for use throughout the European Union.

Administration of vasodilators should be stopped when there is:

– severe hypotension;

– second or third degree permanent heart block;

– wheezing or other chest symptoms;

- chest pain of anginal type.

Approximately 50% of patients develop flushing, chest pain, dizziness, drop in blood pressure, or headache.

The duration of the effect is about 20 minutes. If necessary, theophylline or aminophylline can be given - dose between 125-250 mg i.v.

99mTc – sestamibi and tetrofosmin

Sestamibi and tetrofosmin are essentially fixed in the myocardium without redistribution, and separate injections are made to assess resting stress and perfusion. The six-hour half-life of 99mTc means that the two tests should ideally be performed on different days to allow for activity to decrease from the first injection

Two-day protocol

It is preferable. It provides image quality. Each activity is on its own – both the research under stress and at rest. A stress test should be done first. If it shows your result is normal, there is no need for a study at rest.

One-day protocol

It generally depends on the nature of the research if it will be done in one day. If the question is to detect viable myocardium, it may be preferable to perform the study first in a rest state. When looking for ischemia it is best to do a stress study first.

Imaging diagnostics

It should start 30 to 60 min after the injection. The reason is hepatobiliary clearance. Longer delays are seen with imaging in rest as well as when vasodilator stress is used due to the higher subdiaphragmatic activity of 99Tc.

Nitrates

As with Thallium 201, the injection can be administered under a nitrate cover. It is important to consider redistribution as well as its absence when assessing myocardial viability. This may underestimate areas of reduced perfusion.

Liquids

They can be used to remove bowel activity from the subdiaphragmatic area. In some centers, fatty foods may be given to accelerate clearance from the subdiaphragmatic area. The value of this method is uncertain.

Image acquisition

Gamma camera system

Detectors: Myocardial perfusion imaging can be performed using a single, dual, or triple detector system. We used a single detector system.

Crystals

201Tl or 99Tc imaging can be performed on thin or thicker crystals. Crystals up to 25 mm thick should be used if FDG is used, as well as for using 511-keV gamma rays. This can be tuned to the energy of 99Tc.

Collimators

They are used for studies with 201Tl. Low energy collimators with high resolution are mostly used for 99Tc studies.

Energy windows

201Tl 20% resolution (PC) at 72 keV and 20% PC at 167 keV.

99Tc 15% RS at 140 keV for systems with better than 10% energy resolution and 20% RS at 140 keV.

Patient positioning

The patient is in a supine position with the arms raised above the head and supported in this position. Reduction of movements, so it is desirable to have a firm support for the hands. In the supine position, the posture can reduce the distraction of the inferior wall. However, the supine position makes infradiaphragmatic attenuation of the scatter difficult. This position can give septal defects. It is important that the comparison between rest and stress is made with the same position of the patient. To remove the bra - for female patients. Chest strapping is recommended for female patients as well as some male patients.

Orbit

180 or 360-degree rotation. Systems detector, 45-degree rotation on the right front, inclined to 45 degrees. For the rest, the rear inclined axle is used. For 180-degree acquisition, the dual detectors must be in a 90-degree configuration. In terms of resolution, 180 degrees typically gives higher contrast resolution but more geometric distortion than a 360-degree orbit.

Acquisition type

"Step and shoot" is the most common mode, but it can be "continuous step and shoot". This is when continuous mode is available

Number of projections

For 201Tl, it is sufficient to use 32 projections per 180 degrees. 64 projection views can also be used. For 99mTc, views of 64 to 128 projections are recommended.

Projection time

There is always a mismatch between the moving patient and the improved acquisition. A total acquisition time of less than 30 minutes is recommended. Gated imaging, as well as attenuation and scattering, will slightly increase the examination time.

Quality control

The gamma camera must be in equal operating mode.

The operational level of one camera is in SPECT mode.

Calibrations specific to SPECT

The original data to be obtained must also be preserved in "raw form".

Data processing

Uniformity with 201Tl and 99Tc

There should not be more than a 2% difference between the equipment being used. Differential uniformity should be in the range of 2-3%. It is necessary to take a suitable radioactive source.

A statistically valid quantitative measurement should be obtained from a single image that contains about 10,000 pixel counts, a 120 million count image acquired in a 128 x 128 matrix.

When checking the source of 99Tc, a sufficient correction card should be available. The validity of the uniformity should be tested periodically by performing a 360-degree SPECT study on a cylinder filled with a uniform solution of 99mTc. A typical acquisition is a 64 x 64 matrix, the same pixel size as used clinically, for a total of 60 projections.

360-degree rotation

500,000 pieces per projection for a 20 cm long phantom.

Sensitivity

For multiple detector systems, the sensitivities of the collimated detector heads should not differ by more than 5%

Center of rotation

The centre of rotation should be done according to the manufacturer's recommendations.

The centre of rotation should not vary more than 0.5 pixels for a 128 x 128 matrix over 360 degrees.

It should be within 0.5px of the previous measurement.

The frequency of calibration depends on the stability of the SPECT system.

Tilting the detector head

During the acquisition, the detector head must remain parallel to the axis of rotation. The centre of rotation should not vary more than 3-4 mm over 360 degrees.

Acquired, original and processed data

The data should be reviewed before the patient leaves the ward. This is with a view to correcting the results obtained, as well as possible re-acquisition of data if the first examination is not suitable.

Reconstruction models

Myocardial perfusion imaging appears to be relatively uncomplicated. Even a lot of software is available to adjust motion, fade and spread, but this software cannot create miracles. The raw data from the image acquisition is the most important factor. This is before the reconstruction begins.

Projection data is essential because the activity image reflects the nearest tracer distribution. Two main categories are available today the analytical method and the interactive reconstruction method.

Analytical method

In the past, it was the main reconstruction method used in SPECT, having been adapted from techniques used in radio astronomy. The methods use rapid and relatively non-intensive research. The main physical processes of emission tomography that can be included in the statistical algorithms are noted. Spatial resolution reduces noise at the expense of high-frequency components. Such assessment must be based on statistical data.

There are several questions that are compelling in the analysis:

– processed negative numbers that appear in reconstructive imaging due to specimen filtering;

– the most common action is to truncate values to zero.

Quantification is important (quantification of volume in gated imaging). The same number is counted as acquired images. Analytical models do not eliminate artifacts completely. Line artefacts must be taken into account.

Interactive reconstruction methods

Reconstruction methods have been available for the past few years. In addition to analytical methods, they can be projected forward into interactive methods.

The comparison between the measured projection data and the projection data calculated from the image matrix is important. The correction is formed by multiplying the original guess after normalization.

Summary of Methods

Both linear and iterative methods are useful. Interactive methods are preferred as they give better modeling.

Cut filtering should not be changed. If the count rate is too low, then the acquisition time must be adjusted. The filter roll-off is taken as the count at which the amplitude drops to 0.70. Some manufacturers expect the drop to be 0.5 from the original.

Gated myocardial perfusion imaging has two advantages:

1. Estimating the ejection fraction and weak motion;

2. Improves the quality of images.

When triggered by ECG, it is mandatory:

1. The patient should have a fairly normal heart rhythm. If he has atrial fibrillation, sinus arrhythmia, premature contraction or has a pacemaker in place – ECG triggering should not be used.

2. Sufficient density. Special attention is paid to low acquisitions. The R-wave is used as a "trigger". The size of the R-wave is required to be 3 times larger than the P- or T-wave.

Screening time

Each step of the camera rotation requires a fixed length of time, or a fixed number of cardiac cycles taken. The projection time must be adjusted to achieve an adequate myocardial count rate per exposure interval. Again, the total acquisition time should be noted. No more than 30 minutes. Otherwise, there is patient movement. The gated 99Tc study time should not exceed the ungated SPECT.

Motion artifacts – gated studies are sensitive to patient motion, even when it is minimal. Gives an incorrect definition of the myocardial border.

Filtering

Filter selection is essentially the same as for non-stepped images. It is recommended to use the same filter parameters.

Reconstruction

Two methods – linear and interactive.

Image analysis

The best analysis of wall movement is visual. Automatic programs strive to estimate it but fail to estimate regional wall motion and thickening.

Analysis should consider pathophysiological as well as physiological variations, such as:

- in healthy individuals there is reduced wall motion at the base compared to the apex;
- there is more movement in the basal sidewall compared to the basal septum;
- paradoxical septal motion seen in patients with LBBB.

Description of wall motion is as: “normal,” “reduced,” “absent,” or “paradoxical.”

After the computer analyses it, the result still needs to be visually evaluated.

Wall thickening - can be 'normal', 'reduced' or 'absent'. Thickening is assessed by the difference in number between systole and diastole.

Normal regional function is when wall thickening, and motion are normal.

Area of "hypokinesia" – thickening and movement are reduced.

"Akinesia" where there is no wall thickening and movement.

"Dyskinesia" is the absence of thickening in the presence of paradoxical septal motion.

Measurement of ejection fraction and ventricular volumes

Left ventricular end-systolic volume as well as end-diastolic volume are calculated automatically. However, they should be assessed visually, as should the volumes when they are too low and the ejection fraction too high in the small ventricles.

The minimum display is: apical, midventricular and basal short-axis views, and midventricular horizontal and ventricular long-axis views in end-systole and end-diastole.

Thickening can be assessed as well as wall motion in the Gray scale variation. Linear grayscale is probably a promising idea. A colour continuous scale can be used to assess wall motion thickening.

Data evaluation and integration

LV function data should not be evaluated from small segments because of the risk of passive motion.

Wall motion, wall thickening in fixed perfusion defects helps distinguish between disruption or attenuation artifacts.

When post-stress LV dysfunction is not present, stress imaging improves sensitivity for the presence of coronary artery disease. If there is LV dysfunction after stress, it has an independent prognosis.

Attenuation and dispersion compensation

"Attenuation" – different parts of the body can reduce the intensity of the signal reaching the camera. It is considered to have a negative effect depending on the type of tissue, radiation energy, body thickness.

"Scatter" – degrades image contrast and affects quantification of activity and relative distribution of perfusion. Scatter compensation is achieved by using one or more additional energy windows, reducing the primary energy window, modeling the scatter based on emission data.

Loss of resolution with depth

Depth-dependent algorithms are used. It is necessary to have an even distribution in the myocardium.

How image quality is achieved

– Attenuation and scatter compensation improves image quality.

– Attenuation and compensation depend on the specific software.

– Studies should be considered from their compensated and uncompensated side.

Visual interpretation

The original raw data should be reviewed together with the calculated data. In addition, the viewpoints of the photographs should also be evaluated.

A polar map display ("bull's eye") is a 1D/2D image. The rest part and the stress part are subtracted from each other. Ventricular size, however, is not shown in the polar map.

The 3D display is better, and other data can be included from the patient's assessment.

Perfusion defects

The distribution of the indicator can be characterized as:

– normal > 70%;

– slightly reduced – 69-50%;

– moderately reduced 49-30%;

– greatly reduced 29-10%;

– absent < 10%.

– according to A. R. Shehata (173) and K. F. Van Train (174).

Size and function of the left ventricle

Left ventricular function is classified as:

– normal;

– hypokinetic;

– akinetic;

– dyskinetic (paradoxical);

– thickening is classified as normal, reduced or absent;

- dimensions and function of the left ventricle;
- transient dilatation of the left ventricular cavity.

Description of coronary angiography

All catheterizations were performed through a right inguinal approach.

The Seldinger technique was used to access the right femoral artery. Cannulation of the artery was done through a Cordis Sheath 6 Fr. Diagnostic catheterization was done with left and right Judkins catheters. The catheters used were 5 Fr or 6 Fr. Rarely, in extreme anatomy, other catheters were used.

Left ventriculography was performed in a standard 30 degree RAO.

The left coronary artery was visualized in right cranial 30 degrees, left cranial 20 degrees, right caudal 30 degrees, left apical 60 degrees with 14 degrees of cranial angulation. Left lateral position 90 degrees was used only in certain cases.

RESULTS

To realize the objectives of the study, 3 groups of results have been defined. The initial group was from the evaluations at the inclusion of the patients in the study. All subjects were on prescribed therapy. All patients included in the study were referred to the Clinic by their attending physician, and some of them had undergone a surgical procedure before being referred to the Clinic. The second group of data is called a conditional group of primary tracking, i.e. the initial group of patients collected for the study was divided into two subgroups. Angiography was performed on one part of the respondents, and on the other, due to the presence of contraindications on the part of the patients, it was not performed. In the initial (primary) follow-up group, a nuclear (nuclear) study was assigned. After its completion and depending on the data obtained from it, the patients are prescribed drug treatment or sent for a procedure (the majority of the examined persons were prescribed drug therapy after the nuclear examination).

The third group of results is from the additional follow-up, with the entire study group being followed for 5-year survival after the assigned therapy at the initial follow-up.

1. Data at enrollment for initial treatment

The obtained results as an absolute value and as a frequency distribution are presented in tabular form.

Table 1-1. Gender distribution of the original group

Gender * Initial_Management Cross-tabulation		**Initial_Management**			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Gender	**Female**	48	4	4	**56**
	Male	122	11	18	**151**
Total		170	15	22	**207**
Relative value	**% within Gender**	**Medical**	**PCI**	**CABG**	
Gender	**Female**	85,7%	7,1%	7,1%	**100,0%**
	Male	80,8%	7,3%	11,9%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

The data in table 1-1 show the gender distribution of the selected patients. As expected, the male gender predominates, and women are three times less. In the relative values of the table, it can be seen that, both in particular and in general, the initial drug treatment prevails, which was applied in more than 80% of the cases. It can also be seen that the initial treatment of patients other than medication was almost the same for the group that had bypass surgery and angioplasty.

Table 1-2. Allocated to patients from the original group depending on the angiography indicator

Angio * Initial_Management Cross-tabulation		**Initial_Management**			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Angio	**No**	42	1	4	**47**
	Yes	128	14	18	**160**
Total		170	15	22	**207**
Relative value	**% within Gender**	**Medical**	**PCI**	**CABG**	
Angio	**No**	89,4%	2,1%	8,5%	**100,0%**
	Yes	80,8%	8,8%	11,3%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

The data in Table 1-2 show that during the initial selection of patients, only 47 of them did not have an angiography performed. These are patients for whom angiography was contraindicated for one reason or another - such as advanced disease, obesity, renal failure, etc. As a percentage, their previous treatment did not differ significantly from the patients in this group, with about 80% of them receiving drug therapy and only a small proportion of the study participants having undergone angioplasty or bypass surgery .

The data in Table 1-3 give an idea of one of the risk factors – diabetes. There were no differences between patients with and without diabetes with regard to therapy. Again, there is concordance of data depending on whether patients are diabetic or not in terms of their treatment, either pharmacologic or interventional at baseline, prior to their stratification and determination of their future therapy.

Regarding the variable "hypertension" from Table 1-4, it can be seen that it is a determining risk factor for coronary artery disease. Despite the small number of hypertensives in the study, it is evident that they have a higher proportion of coronary disease necessitating invasive treatment. Again, it can be seen that drug treatment predominates for this variable at baseline (before stratification).

Table 1-3. Distribution in the initial group by indicator presence/absence of diabetes as a risk factor

Diabetic * Initial_Management Crosstabulation		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Diabetic	No	162	14	21	**197**
	Yes	8	1	1	**10**
Total		170	15	22	**207**
Relative value	% within	Medical	PCI	CABG	
Diabetic	No	82,2%	7,1%	10,7%	**100,0%**
	Yes	80,8%	10,0%	10,0%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-4. Distribution in the initial group according to presence/absence of hypertension as a risk factor

Hypertension * Initial_Management Crosstabulation		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Hypertension	No	160	11	20	**191**
	Yes	10	4	2	**16**
Total		**170**	**15**	**22**	**207**
Relative value	% within	Medical	PCI	CABG	
Hypertension	No	83,8%	5,8%	10,5%	**100,0%**
	Yes	62,5%	25,0%	12,5%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-5. Distribution in the initial group according to presence/absence of angina pectoris

Angina * Initial_Management Crosstabulation		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Angina	No	91	4	6	**101**
	Yes	79	11	16	**106**
Total		**170**	**15**	**22**	**207**
Relative value	% within	Medical	PCI	CABG	
Angina	No	90,1%	4,0%	5,9%	**100,0%**
	Yes	74,5%	10,4%	15,1%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-5 shows the distribution of respondents depending on the initial treatment and the presence/absence of angina pectoris in them.

Operative treatment prevails in patients with angina. It is observed that in cases with angioplasty or bypass, 73% of patients have angina (angina pectoris). Those who initially underwent drug therapy were, for the most part (54%), free of angina pectoris.

	Medical	PCI	CABG
No	54%	27%	27%
Yes	46%	73%	73%
Total	100%	100%	100%

Table 1-6. Distribution in the initial group according to presence/absence of myocardial infarction

MI * Initial_Management Cross-tabulation		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
MI	No	115	10	15	**140**
	Yes	55	5	7	**67**
Total		**170**	**15**	**22**	**207**
Relative value	% within	Medical	PCI	CABG	
MI	No	82,1%	7,1%	10,7%	**100,0%**
	Yes	82,1%	7,5%	10,4%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-6 shows the distribution of patients with myocardial infarction from the ***initial group*** depending on the way they were treated. It can be seen that mainly after a myocardial infarction, most of them are on drug therapy, of which a relatively small relative share are referred for additional angioplasty (this description does not include emergency procedures such as a procedure for acute myocardial infarction and emergency angioplasty) or for additional bypass surgery.

Table 1-7. Distribution in the initial group by echocardiographic finding

Normal_Echo * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Normal_Echo	Normal	110	10	17	**137**
	Not normal	40	4	3	**47**
	No information	20	1	2	**23**
Total		**170**	**15**	**22**	**207**
Relative value	% within	Medical	PCI	CABG	
Normal_Echo	Normal	80,3%	7,3%	12,4%	**100,0%**
	Not normal	85,1%	8,5%	6,4%	**100,0%**
	No information	87,0%	4,3%	8,7%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-7 presents patient distribution according to echocardiographic findings and subsequent treatment outcome at baseline. The echocardiographic findings generally do not determine the therapeutic approach, but it is interesting to see that in the so-called initial groups did not differ significantly in terms of whether they had a good or a bad echocardiographic finding. The initial therapy is almost identical (this is one of our main differences with the STICH study – where a poor echocardiographic finding is more likely to be operative than a good echocardiographic finding). It is also interesting to see that in terms of patient numbers, the angioplasty group was almost equal to the primary bypass surgery group in the initial stratification. This is important to demonstrate that when patients were included in our study, they were not primarily on initial operative treatment to predetermine their subsequent primary pharmacotherapy.

From Table 1-8, it can be seen that for patients allocated mainly to drug treatment at the beginning, this treatment is maintained with the largest relative share during the subsequent follow-up.

Table 1-8 Distribution in the initial group according to data after Cardiolit examination (Cardiolit)

Normal_Cardiolite * Initial_Management Crosstabulation		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Normal_Cardiolite	Normal	72	9	11	**92**
	Not normal	68	6	5	**79**
	No information	30	0	6	**36**
Total		**170**	**15**	**22**	**207**
Relative value	% within	Medical	PCI	CABG	
Normal_Cardiolite	Normal	78,3%	9,8%	12,0%	**100,0%**
	Not normal	86,1%	7,6%	6,3%	**100,0%**
	No information	83,3%		16,7%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

The data in Tables 1-9 reveal that whether or not to have a Cardiolite nuclear medicine study is not determined by how the patients were treated—whether drug therapy or surgery at baseline; before being stratified for inclusion in the study. This indicates that regardless of whether or not a previous procedure was performed on these patients, they were included in the study without that previous procedure being a determinant of their inclusion.

The results illustrated in Table 1-10 are important in determining patients for enrolment in nuclear testing. The following trends are visible:

✓ Diagnostic angiography is one of the main indicators requiring additional nuclear (nuclear) examination.

✓ It can then be seen that another major indicator requiring the application of a nuclear (nuclear) study is the presence of angina.

✓ No less significant indicator of nuclear (nuclear) examination are the anatomical changes that were established during the performed angiography.

✓ The determination of the so-called angina pectoris - whether it is an objective finding or not.

✓ The presence of a myocardial infarction is not decisive for the performance of a nuclear (nuclear) examination (this is also a rather important difference between our study and the STICH study, as the latter one has the additional nuclear (nuclear) examinations, which are to determine whether or not revascularization is needed).

✓ In addition, the presence of chest pain is not decisive for conducting a nuclear (nuclear) examination, but the clinical symptomatology of angina pectoris is important (although it may seem like the same thing, it is not).

The data presented in the Table 1-10, show that the number of angiographies performed for diagnostic reasons is almost equal to the amount of those performed in patients with heart failure. This reveals, on the one hand, that angiograms were not performed without a need for them, and that (as would be logically expected) patients with myocardial infarction and ischemia had the highest rates of stenting (34 and 35%) compared to those in whom the procedure was diagnostic (5%) and in those in whom it was performed due to the presence of heart failure (5.9%). The data in this table also demonstrate that the presence of angina was not a determinant of stenting.

It can also be seen that the presence of postinfarction angina with or without myocardial infarction was the main determining factor for referring patients to surgery (21% and 23%, respectively).

The results in the Table 1-11 show the number and relative proportion of patients allocated after the initial evaluation to persanthin tested with , and the number of patients subjected to the no-load test. One, perhaps side trend, appears to be that initially there are many patients who cannot do a normal stress test for various reasons. This also leads to careful interpretation of exercise stress testing data, because nowadays fewer and fewer patients for one reason or another manage to reach optimal exercise due to age, high body weight and various other diseases.

Table 1-9. Distribution of patients depending on the conduct of a nuclear medicine examination with Cardiolite

Normal_Cardiolite * Initial_Management Cross-tabulation		**Initial_Management**			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Reason_Cardiolite	Diagnostic	48	2	1	**51**
	Angina	21	1	3	**25**
	Angio Findings	28	0	0	**28**
	Severe Angina	1	0	0	**1**
	Suspected coronary artery disease	10	2	2	**14**
	Cardiac Failure	1	0	1	**2**
	Coronary Artery Disease	30	3	3	**36**
	Viability	1	0	0	**1**
	Ischeamia	2	2	0	**4**
	Angina Pectoris	1	1	1	**3**
	Suspect CAD	21	1	5	**27**
	Chronic ischeamic heart dis-ease	0	1	1	**2**
	Suspected Ischeamia	1	0	0	**1**
	Chest Pain	2	1	3	**6**
	Acute Myocardial Infarction	0	1	1	**2**
	Myocardial infarct	1	0	0	**1**
	No information	2	0	1	**3**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Reason_Cardiolite	Diagnostic	94,1%	3,9%	2,0%	**100,0%**
	Angina	84,0%	4,0%	12,0%	**100,0%**
	Angio Findings	100,0%			**100,0%**
	Severe Angina	100,0%			**100,0%**
	Suspected coronary artery disease	71,4%	14,3%	14,3%	**100,0%**
	Cardiac Failure	50,0%		50,0%	**100,0%**
	Coronary Artery Disease	83,3%	8,3%	8,3%	**100,0%**
	Viability	100,0%			**100,0%**
	Ischeamia	50,0%	50,0%		**100,0%**
	Angina Pectoris	33,3%	33,3%	33,3%	**100,0%**
	Suspect CAD	77,8%	3,7%	18,5%	**100,0%**
	Chronic ischeamic heart dis-ease		50,0%	50,0%	**100,0%**
	Suspected Ischeamia	100,0%			**100,0%**
	Chest Pain	33,3%	16,7%	50,0%	**100,0%**
	Acute Myocardial Infarction		50,0%	50,0%	**100,0%**
	Myocardial infarct	100,0%			**100,0%**
	No information	66,7%		33,3%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-10. Allocation of patients for other reasons

Reason Variable * Initial_Management		Initial_Management			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Reason Variable	Diagnostic	84	5	9	**98**
	MI	1	1	1	**3**
	Angina	23	3	7	**33**
	Ischemia	3	2	0	**5**
	Heart disease/Fail-ure	59	4	5	**68**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Reason Variable	Diagnostic	85,7%	5,1%	9,2%	**100,0%**
	MI	33,3%	33,3%	33,3%	**100,0%**
	Angina	69,7%	9,1%	21,2%	**100,0%**
	Ischemia	60,0%	40,0%		**100,0%**
	Heart disease/Fail-ure	86,8%	5,9%	7,4%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-11. Distribution of patients according to testing

Exercise_or_Persantin * Initial_Management		**Initial_Management**			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Exercise_or_Persantin	Exercise	107	13	17	**137**
	Persantin	36	2	3	**41**
	Resting	27	0	1	**28**
	No information	0	0	1	**1**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Exercise_or_Persantin	Exercise	78,1%	9,5%	12,4%	**100,0%**
	Persantin	87,8%	4,9%	7,3%	**100,0%**
	Resting	96,4%		3,6%	**100,0%**
	No information			100,0%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

From table 1-12 it can be seen that patients with pharmacotherapy as a relative proportion are almost equal to the group without ischemia that is referred for a certain procedure such as angioplasty or bypass. The moderate ischemia group is relatively small and patients in it were not assigned procedures. The treatment in all groups was mainly medicinal, independent of the extent of the disease they had, but it should not be forgotten that these are data from the preliminary follow-up, and not after a final diagnosis was made.

Table. 1-12 Distribution of patients from the initial group according to ischemia factor

Ischemia Variable * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Ischemia Variable	Small	22	3	3	**28**
	Mild	29	3	3	**35**
	Moderate	2	0	0	**2**
	Nothing	117	9	16	**142**
Total		170	15	22	207
Relative value	% within	Medical	PCI	CABG	
Ischemia Variable	Small	78,6%	10,7%	10,7%	**100,0%**
	Mild	82,9%	8,6%	8,6%	**100,0%**
	Moderate	100,0%			**100,0%**
	Nothing	82,4%	6,3%	11,3%	**100,0%**
Total		82,1%	7,2%	10,6%	**100,0%**

Data on the distribution of the examined persons (number/percentage) in the initial treatment group before a nuclear (nuclear) examination, and what therapy was assigned to these patients after the completion of this examination are presented in the Table 1-13. It can be seen that 53 of the patients had a positive test for ischemia from the nuclear (nuclear) examination, and in 117 such was not established. The percentage ratio in the distribution of these patients depending on the method of their subsequent treatment – pharmacotherapy, angioplasty or bypass, to a certain extent does not differ from the distribution in their initial treatment.

Table 1-13. Distribution of patients depending on ischemia detected by nuclear medicine examination

Ischemia_sestamibi * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Ischemia_sestamibi	No	117	9	16	**142**
	Yes	53	6	6	**65**
Total		170	15	22	207
Relative value	% within	Medical	PCI	CABG	
Ischemia_sestamibi	No	82.4%	6.3%	11.3%	**100,0%**
	Yes	81.5%	9.2%	9.2%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-14 shows that the majority of the group without prior procedures – a total of 106 people, or 82%, did not have a heart attack, followed by a group of 37 people (without prior procedures) , in which an average one has been established. In the drug-treated group, only 23 people had a large heart attack. This again means that in the initial stratification, a nuclear study was not performed only in the large infarct group (to find a reason for revascularization), as was done in STICH.

Table 1-14. Distribution of the initial group according to the size of the registered heart attack

Infarct Variable * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Infarct Variable	Small	4	0	2	**6**
	Medium	37	5	8	**50**
	Large	23	0	0	**23**
	Nothing	106	10	12	**128**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Infarct Variable	**Small**	66,7%		33,3%	**100,0%**
	Medium	74,0%	10,0%	16,0%	**100,0%**
	Large	100,0%			**100,0%**
	Nothing	82,8%	7,8%	9,4%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

In the Table 1-15 it can be seen that the presence or absence of an infarct in the original group did not have a determining importance for the treatment of the patient before his stratification. The patients continued their drug therapy. The size of the infarct had a decisive role in the choice of the therapeutic approach, as can be seen from the other tables.

The data in Table 1-16, showing the distribution of therapeutic approaches in the group depending on the body weight of the patients, are not essential for the purposes of the present study, but illustrate the fact that in a group with high body flow there are more -some bypass operations. This is probably due to the increased risk that is conditioned for them, as well as the refusal of surgeons to perform similar procedures in this contingent of patients, due to their unfavourable results.

The young age group, as might be expected, had a low procedure frequency (Table 1-17). In the middle age group, the procedure frequency slightly increases and as can be expected, is relatively highest in the group from 60 to 76 years old (Table 1-17).

Table 1-18 shows the distribution of the initial group depending on their SYNTAX score. It should be noted again that this determination is before the start of our research. That is, in patients who underwent angiography and had a previous bypass, such a score could not be calculated. These patients fall into the “Post CABG” group.

Study participants who did not have angiography were patients who had an initial nuclear (nuclear) test to see if they needed such a test. This is nearly a quarter of the persons examined. In the initial group, the patients with a high SYNTAX score were about 20 (9 + 12). Patients who had an average score (between 6 and 20) were about 55 people, or a third of the group with angiography and a quarter of the total group (including those without previous angiography). The presence of more than 30% viability of the myocardium gives an idea of which patients had an angiography performed (ie, the so-called "nihilous" cases were not performed).

Table 1-15. Distribution of the initial group according to the presence/absence of a heart attack

Infarct * Initial_Managemen		Initial_Management			Total
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Infarct	**No**	107	10	13	**130**
	Yes	63	5	9	**77**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Infarct	**No**	82,3%	7,7%	10,0%	**100,0%**
	Yes	81,8%	6,5%	11,7%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-16. Distribution of the initial group according to body mass index

Weight_group * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Weight_group	40-68	24	2	2	**28**
	68-96	53	2	10	**65**
	96-124	28	3	4	**35**
	124-152	10	0	1	**11**
	152-180	2	0	0	**2**
Total		**117**	**7**	**17**	**141**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Weight_group	40-68	85,7%	7,1%	7,1%	**100,0%**
	68-96	81,5%	3,1%	15,4%	**100,0%**
	96-124	80,0%	8,6%	11,4%	**100,0%**
	124-152	90,9%		9,1%	**100,0%**
	152-180	100,0%			**100,0%**
Total		**83,0%**	**5,0%**	**12,1%**	**100,0%**

Table 1-17. Distribution of the initial group according to age

Age_groups * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
Age_groups	28-44	8	0	1	**9**
	44-60	68	5	6	**79**
	60-76	68	5	13	**86**
	76-92	26	5	2	**33**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Age_groups	28-44	88,9%		11,1%	**100,0%**
	44-60	86,1%	6,3%	7,6%	**100,0%**
	60-76	79,1%	5,8%	15,1%	**100,0%**
	76-92	78,8%	15,2%	6,1%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-18. Allocations according to SYNTAX score

SyntaxScore_groups * Initial_Management		**Initial_Management**			**Total**
Absolute value	**Count**	**Medical**	**PCI**	**CABG**	
Syntax Score_groups	0-5	38	2	9	**49**
	6-10	23	5	1	**29**
	11-15	21	4	1	**26**
	16-20	9	0	0	**9**
	21-55	11	1	0	**12**
	above 25	6	0	0	**6**
	No Angio	49	2	7	**58**
	PCI Done	0	1	0	**1**
	Post CABG	13	0	4	**17**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
Syntax Score_groups	0-5	77,6%	4,1%	18,4%	**100,0%**
	6-10	79,3%	17,2%	3,4%	**100,0%**
	11-15	80,8%	15,4%	3,8%	**100,0%**
	16-20	100,0%			**100,0%**
	21-55	91,7%	8,3%		**100,0%**
	above 25	100,0%			**100,0%**
	No Angio	84,5%	3,4%	12,1%	**100,0%**
	PCI Done		100,0%		**100,0%**
	Post CABG	76,5%		23,5%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

Table 1-19 shows the distribution of initial treatment in the different ejection fraction (EF) group. The group with extremely low EF is very small and the patients in it have a previous procedure. This does not mean that it was made before nuclear investigation. In the following groups, it is evident that the treatment was mainly pharmacotherapy and independent of any previous procedure.

Table 1-19. Allocation of patients from the initial group according to echocardiographic data and ejection fraction

EF_Echo_groups * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
EF_Echo_groups	less than 10	2	1	1	**4**
	11-20	11	0	1	**12**
	21-30	6	1	0	**7**
	31-40	12	2	1	**19**
	41-50	16	1	0	**12**
	51-60	19	3	5	**27**
	61-70	75	3	10	**88**
	71-80	7	0	0	**7**
	81-90	2	0	0	**2**
	91-100	0	2	0	**2**
	No information	20	1	2	**23**
Total		**170**	**15**	**22**	**207**
Relative value	**% within**	**Medical**	**PCI**	**CABG**	
EF_Echo_groups	**less than 10**	**50,0%**	**25,0%**	**25,0%**	**100,0%**
	11-20	91,7%		8,3%	**100,0%**
	21-30	85,7%	14,3%		**100,0%**
	31-40	75,0%	12,5%	12,5%	**100,0%**
	41-50	84,2%	10,5%	5,3%	**100,0%**
	51-60	70,0%%	11,1%	18,5%	**100,0%**
	61-70	85,2%	3,4%	11,4%	**100,0%**
	71-80	100,0%			**100,0%**
	81-90	100,0%			**100,0%**
	91-100		100,0%		**100,0%**
	No information	87,0%	4,3%	8,7%	**100,0%**
Total		**82,1%**	**7,2%**	**10,6%**	**100,0%**

From Table 1-20, it can be seen that pharmacotherapy predominates in patients referred for nuclear testing. Participants who have had previous procedures are relatively few. Only the 71 to 80 age group, which is relatively small, had a higher rate of previous surgical/interventional treatment. However, the data are not statistically significant.

Table 1-20. Allocation of patients to initial treatment group according to ejection fraction and nuclear imaging data

EF_Cardiolite_sestamibi_groups * Initial_Management		Initial_Management			Total
Absolute value	Count	Medical	PCI	CABG	
EF_Cardiolite_sestamibi_groups	less than 10	1	0	0	**1**
	11-20	9	1	0	**10**
	20-30	11	1	2	**14**
	31-40	19	2	0	**21**
	41-50	28	2	4	**34**
	51-60	29	4	7	**40**
	61-70	37	3	2	**42**
	71-80	4	2	1	**7**
	81-90	1	0	0	**1**
Total		**139**	**15**	**16**	**170**
Relative value	% within	Medical	PCI	CABG	
EF_Cardiolite_sestamibi_groups	less than 10	100,0%			**100,0%**
	11-20	90,0%	10,0%		**100,0%**
	20-30	78,6%	7,1%	14,3%	**100,0%**
	31-40	90,5%	9,5%		**100,0%**
	41-50	82,4%	5,9%	11,8%	**100,0%**
	51-60	72,5%	10,0%	17,5%	**100,0%**
	61-70	88,1%	7,1%	4,8%	**100,0%**
	71-80	57,1%	28,6%	14,3%	**100,0%**
	81-90	100,0%			**100,0%**
Total		**81,8%**	**8,8%**	**9,4%**	**100,0%**

2. Follow-up of the patients

The follow-up period is about 6 (six) years after initial treatment. The follow-up was carried out through a telephone interview or when the patient appeared at the Clinic.

The data presented in Table 2-1 show the distribution of patients in our study according to the therapeutic approach (pharmacotherapy or bypass surgery) they received and what the survival of these patients was during the course of follow-up. In the medical group there was a 25% mortality, in the bypass group - 18% mortality (it should be noted that the pharmacotherapy group was significantly greater than the other group).

Table 2-1. Survival data by initial therapy at 5-year follow-up

Initial_Management * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Initial_Management	Medical	45	125	**170**
	PCI	1	14	**15**
	CABG	4	18	**22**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Initial_Management	Medical	26,5%	73,5%	**100,0%**
	PCI	6,7%	93,3%	**100,0%**
	CABG	18,2%	81,8%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-2 provides information on the post-nuclear study decision for the therapy undertaken in the study patients. Again, it should be noted that the drug therapy group was almost 20 times larger than the surgical group. Attention should also be paid to the data in the table. 2-3, from which the opposite trend is evident during the follow-up – the individuals on drug therapy from the initial group demonstrate better long-term survival compared to those treated surgically.

Table 2-3 shows the relative proportion of mortality after a follow-up of more than 6 months. Although not statistically significant because the group was extremely small, the interventional procedure resulted in higher mortality at 6-month follow-up.

Mortality is lower in men. This confirms the well-known fact that women have a higher mortality in the presence of coronary disease than men (Table 2-4).

Table 2-2. Tracking data regarding the absolute number and the relative survival value depending on the therapy

Follow_up_Management * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Follow_up_Management	Medical	50	142	**192**
	PCI	0	5	**5**
	CABG	0	10	**10**
Total		**50**	**157**	**207**
Relative value	% within	Deceased	Alive	Total
Follow_up_Management	Medical	26,0%	74,0%	**100,0%**
	PCI		100,0%	**100,0%**
	CABG		100,0%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-3. Patient distribution data for their continued treatment at follow-up

Follow_Management * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Follow_Management	Medical	46	153	**199**
	PCI	3	2	**5**
	CABG	1	2	**3**
Total		**50**	**157**	**207**
Relative value	% within	Deceased	Alive	Total
Follow_Management	Medical	23,1%	76,9%	**100,0%**
	PCI	60,0%	40,0%	**100,0%**
	CABG	33,3%	66,7%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-4. Tracking the influence of gender on treatment outcomes at follow-up

Gender * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Gender	Female	20	36	56
	Male	30	121	151
Total		50	157	207
Relative value	% within	Deceased	Alive	Total
Gender	Female	35,7%	64,3%	100,0%
	Male	19,9%	80,1%	100,0%
Total		24,2%	75,8%	100,0%

Table 2-5. Distribution of patients by age group and follow-up of survival

Age_groups * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Age_groups	28-44	1	8	9
	44-60	14	65	79
	60-76	21	65	86
	76-92	14	19	33
Total		50	157	207
Relative value	% within	Deceased	Alive	Total
Age_groups	28-44	11,1%	88,9%	100,0%
	44-60	17,7%	82,3%	100,0%
	60-76	24,4%	75,6%	100,0%
	76-92	42,4%	57,6%	100,0%
Total		24,2%	75,8%	100,0%

As expected, the highest mortality was observed in the older age group in contrast to the younger age groups (Tables 2-5).

Mortality at follow-up was higher in the higher body weight groups as well as in the underweight group (Tables 2-6). The likely explanation for this observation regarding the low body mass group is that in this case we are dealing with individuals with advanced heart failure.

The group presented on the Table 2-7 is interesting. Patients were divided according to whether or not they had a previous angiography before the nuclear examination. Although considered in one table, these groups differ from each other. In the group in which angiography was not performed before their inclusion in the study, a significantly higher mortality was observed than in the group in which angiography was performed. The explanation for this fact is that this group had significant comorbidity and for this reason they did not undergo coronary angiography in the first place.

Table 2-6. Distribution of patients by body weight/mortality at follow-up

Weight_group * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Weight_group	40-68	10	18	**28**
	68-96	8	57	**65**
	96-124	6	29	**35**
	124-152	2	9	**11**
	152-180	0	2	**2**
Total		**26**	**115**	**141**
Relative value	% within	Deceased	Alive	Total
Weight_group	40-68	35,7%	64,3%	**100,0%**
	68-96	12,3%	87,7%	**100,0%**
	96-124	17,1%	82,9%	**100,0%**
	124-152	18,2%	81,8%	**100,0%**
	152-180		100,0%	**100,0%**
Total		**18,4%**	**81,6%**	**100,0%**

Table 2-7. Distribution of patients at follow-up according to angiography

Angio * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Angio	No	16	31	**47**
	Yes	34	126	**160**
Total		**50**	**157**	**207**
Relative value	% within	Deceased	Alive	Total
Angio	No	34,0%	66,0%	**100,0%**
	Yes	21,3%	78,8%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-8. Data on patient distribution according to telephone follow-up survival and risk facto diabetes

Diabetic * Telephonic_Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Diabetic	No	45	152	**197**
	Yes	5	5	**10**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Diabetic	No	22,8%	77,2%	**100,0%**
	Yes	50,0%	50,0%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

The group presented in table. 2-8, is mixed, but it is evident that a quarter of patients without comorbid diabetes died during the follow-up period, while in the diabetic group, 50% died. As absolute values, these groups are quite different, but it is known that the mortality rate in diabetics is higher, which is also confirmed by our established data.

It is interesting that the logical relationship that generally exists between the presence of hypertension and mortality is not established (Table 2-9). One reason is that hypertension is already treated in these patients (to be noted, if put treated and untreated hypertension into the Framingham Study calculator, the death rate drops in half). The other reason is that the rate is low because of the presence of coronary disease and previously undiagnosed hypertension.

Table 2-9. Patient survival outcomes at follow-up accounting for hypertension

Hypertension * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Hypertension	No	48	143	**191**
	Yes	2	14	**16**
Total		**50**	**157**	**207**
Relative value	% within	Deceased	Alive	Total
Hypertension	No	25,1%	74,9%	**100,0%**
	Yes	12,5%	87,5%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-10. Survival outcomes of telephone-tracked patients and presence of angina pectoris

Angina * Telephonic_Follow_up Cross-tabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Angina	No	30	71	**101**
	Yes	20	86	**106**
Total		**50**	**157**	**207**
Relative value	% within	Deceased	Alive	Total
Angina	No	29,1%	70,3%	**100,0%**
	Yes	18,9%	81,1%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Also of interest are the data we obtained at follow-up when the angina factor is also taken into account (Table 2-10). Patients without angina symptoms have a higher mortality rate than those who have. The difference is significant. This fact can be explained in two ways. One is that patients who have angina have had no complaints due to optimal treatment. The second is that mortality is usually independent of the presence of angina. Angina is a factor that physiologically reduces physical activity to protect the heart. The results presented in Table 2-10 may explain the phenomenon that pharmacotherapy-treated patients with more complications had fewer episodes of angina pectoris.

Table 2-11. Data from the tracking indicator – availability of myocardial infarction during initial treatment

MI * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	**Count**	**Deceased**	**Alive**	
MI	No	30	110	**140**
	Yes	20	47	**67**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
MI	No	21,4%	78,6%	**100,0%**
	Yes	29,9%	70,1%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

The data in the table. 2-11 show the survival at follow-up between admissions with infarcts from the initial group who underwent nuclear examination and those admitted without infarcts. This is an important group of patients. It can be seen that in the group of patients who were admitted with a heart attack, mortality was higher (as a relative proportion) at follow-up, in contrast to the group of patients who were not hospitalized for such an occasion.

Logically, the follow-up results show that the mortality rate is higher in the group with demonstrated echocardiographic changes at initial treatment than in those without echocardiographic changes (Table 2-12).

Table 2-12. Telephone follow-up survival data and Echocardiographic finding at initial treatment

Normal_Echo * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	**Count**	**Deceased**	**Alive**	
Normal_Echo	Normal	24	113	**137**
	Not normal	19	28	**47**
	No information	7	16	**23**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Normal_Echo	Normal	17,5%	82,5%	**100,0%**
	Not normal	40,4%	59,6%	**100,0%**
	No information	30,4%	69,6%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-13. Distribution of follow-up survival and data from the Cardiolite study at initial treatment

Normal_Cardiolite * Telephonic_Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Normal_Cardiolite	Normal	17	75	**92**
	Not normal	24	55	**79**
	No information	9	27	**36**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Normal_Cardiolite	Normal	18,5%	81,5%	**100,0%**
	Not normal	30,4%	69,6%	**100,0%**
	No information	25,0%	75,0%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-13 illustrates the fact that patients with a normal nuclear examination have a lower mortality than those with an abnormality registered by the nuclear examination. Of course, it should also be noted that even in patients with a negative nuclear examination, there is mortality during the follow-up period (*apparently from non-cardiogenic diseases*). This is also one of our endpoints in the study.

Table 2-14. Survival data according to the "other causes" factor

Reason Variable * Telephonic_Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Reason Variable	Diagnostic	23	75	**98**
	MI	2	1	**3**
	Angina	8	25	**33**
	Ischemia	0	5	**5**
	Heart disease/Failure	17	51	**68**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Reason Variable	Diagnostic	23,5%	81,5%	**100,0%**
	MI	66,7%	69,6%	**100,0%**
	Angina	24,2%	75,0%	**100,0%**
	Ischemia		100,0%	**100,0%**
	Heart disease/Failure	25,0%	75,0%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

The results regarding the data from the nuclear study in the original group, shown in table. 2-14, are of interest. In patients where this is done as a diagnostic test, we have a mortality rate of 23%. Approximately the same mortality was observed in patients with angina and the value was almost identical in patients with heart failure. The strange thing about this pattern is that the death rates in the three different groups are almost the same. One possible explanation is that, generally speaking, these are patients with advanced pathology, and we cannot expect large differences in mortality. This perhaps partially proves our hypothesis that mortality is high in various non-cardiac severe pathologies (comorbidity).

In this group (Table 2-15), outcomes are relatively consistent, and as might be expected in patients who can undergo exercise testing, mortality is lower than in those who cannot. they can. Follow-up mortality was highest in patients who had a nuclear scan at rest. The dipyridamole test is done in individuals who are not at extremely high risk. In the latter, an adenosine test was conducted.

Table 2-15. Data on survival at follow-up and stress tests performed at baseline

Exercise_or_Persantin * Telephonic_ Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Exercise_or_Persantin	Exercise	21	116	137
	Persantin	11	30	41
	Resting	17	11	28
	No information	1	0	1
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Exercise_or_Persantin	Exercise	15,3%	84,7%	100,0%
	Persantin	26,8%	73,2%	100,0%
	Resting	60,7%	39,3%	100,0%
	No information	100,0%		100,0%
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-16. Data on survival at follow-up and ischemia score at initial treatment

Ischemia Variable * Telephonic_Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Ischemia Variable	Small	6	22	**28**
	Mild	7	28	**35**
	Moderate	0	2	**2**
	Nothing	37	105	**142**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Ischemia Variable	Small	21,4%	78,6%	**100,0%**
	Mild	20,0%	80,0%	**100,0%**
	Moderate	0	100,0%	**100,0%**
	Nothing	26,1%	73,9%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

The data presented in the table. 2-16 are also an interesting finding . Let's not forget that we have a mixed group of patients. Mortality in persons without and with mild ischemia is similar. From table 2-16 even shows that in the absence of ischemia there is a greater mortality than in the presence of ischemia. This means higher mortality in patients with non-coronary disease than in persons with coronary disease. That is, a relatively greater risk of death is observed in patients with non-coronary disease. So subjecting patients with significant comorbidity to surgical procedures would logically further increase their mortality.

Table 2-17. Follow-up survival data and presence of ischemia at initial nuclear study with sestamibi

Ischemia_sestamibi * Telephonic_Follow_up Crosstabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
Ischemia_sestamibi	No	37	105	**142**
	Yes	13	52	**65**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Ischemia_sestamibi	No	26,1%	73,9%	**100,0%**
	Yes	20,0%	80,0%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

It can be seen from Table 2-17 that when comparing the mortality between the groups that had ischemia and those without ischemia at the time of the nuclear examination. The ischemia group was significantly larger than the non-ischemia group (generally, the ischemia group was collected for logistical reasons or because of suspected ischemia). The percentage ratio and absolute values of living versus deceased are close.

Table 2-18. Data on survival at follow-up and the variable "infarction" in the initial group

Infarct Variable * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	**Count**	**Deceased**	**Alive**	
Ischemia Variable	Small	0	6	**6**
	Medium	15	35	**50**
	Large	10	13	**23**
	Nothing	25	103	**128**
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
Ischemia Variable	Small	0	100,0%	**100,0%**
	Medium	30,0%	70,0%	**100,0%**
	Large	43,5%	56,5%	**100,0%**
	Nothing	19,5%	80,5%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

In the table 2-18 compare the variable "infarct "(present or not, as well as infarct area) to the variable "mortality". A small infarct is irrelevant, and this is logical in terms of mortality. Medium and large infarcts are associated with mortality. It is interesting to note that patients without a heart attack had similar mortality to those with a heart attack (this is because the group without a heart attack was made up of patients who were at risk for other reasons). One must not forget that these are patients with various pathologies who die of non-cardiac causes. Again, in our study, we want to show that the risk of death is not only coronary, and we have to take into account the comorbidity of the patients and their additional risk of death from non-cardiogenic causes. It should be emphasized that our idea is not to send such patients to invasive treatment, since the risk of death is quite high immediately after or later after the operation. Patients with low comorbidity generally always have a better prognosis after such procedures (or at least in most cases).

The data from Table 2-19 confirm that the presence or absence of infarction correlates with no reduction in mortality at follow-up regardless of procedure. Mortality is logically slightly higher in people who have had a heart attack, but not large in area.

Table 2-19. Data on survival at follow-up and presence of infarct at baseline

Infarct * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Infarct	No	27	103	**130**
	Yes	23	54	**77**
Total		**50**	**157**	**207**
Relative value	% within	**Deceased**	**Alive**	**Total**
Infarct	No	20,8%	79,2%	**100,0%**
	Yes	29,9%	70,1%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-20. Suntax score group data at follow-up

SintaxScore_groups * Telephonic_Follow_up Crosstabulation		Telephonic_Follow_up		Total
Absolute value	Count	Deceased	Alive	
Syntax Score_groups	**0-5**	10	39	**49**
	6-10	7	22	**29**
	11-15	4	22	**26**
	16-20	2	7	**9**
	21-25	2	10	**12**
	above 25	2	4	**6**
	No Angio	21	37	**58**
	PCI Done	0	1	**1**
	Post CABG	2	15	**17**
Total		**50**	**157**	**207**
Relative value	% within	**Deceased**	**Alive**	**Total**
Syntax Score_groups	**0-5**	20,4%	79,6%	**100,0%**
	6-10	24,1%	75,9%	**100,0%**
	11-15	15,4%	84,6%	**100,0%**
	16-20	22,2%	77,8%	**100,0%**
	21-25	16,7%	83,3%	**100,0%**
	above 25	33,3%	66,7%	**100,0%**
	No Angio	36,2%	63,8%	**100,0%**
	PCI Done		100,0%	**100,0%**
	Post CABG	11,8%	88,2%	**100,0%**
Total		**24,2%**	**75,8%**	**100,0%**

Data on the Syntax score are presented in the Table 2-20. These results should be interpreted with caution because, in general, the higher the Syntax score, the higher the risk of adverse events. Therefore, with a higher Syntax score, the patient is referred for surgery. We should note again that the Syntax score is an anatomical and not a functional score. This applies to Syntax score I, while Syntax score II also includes anatomical – comorbidity assessment. It is logical to ask why we should not use Logistic Clinical Syntax score or Syntax score II or Syntax score 2020 when interpreting the data and evaluating our results. These are scores using parameters such as anatomical changes and comorbidity in a procedure. Procedures are rarely used in our research. It is not ethical to use angiography where logistic regression analysis gives the risk and then claim that our therapeutic approach is less risky. Of course, the mortality during operative treatment and immediately after it is higher. Somehow in our research we want to show that a risk in our therapeutic choice that is smaller logically gives a greater survival (Table 2-20).

The data in Table 2-20 show the 6-year survival by Syntax score and mortality. It is obvious that the mortality in the group without angiography and without Syntax score is higher than that in the group with calculated Syntax score. Is this observation illogical? In fact, it is quite logical. It shows that comorbidity in patients with co-morbidities is high, and although patients with a calculated Syntax score had perhaps a slightly lower mortality, in the other group (patients that we should in principle undergo angiography, but we are not) in almost a third of patients' death was from non-cardiac causes. Another interesting conclusion from table 2-20 is the data on the values of the Syntax score and what is the percentage of deaths. One cannot fail to notice that between 0 and 25 (25 being a relatively high value) the death rate is almost the same. However, it jumps sharply for the group with a Syntax score above 25, which is however very small. What conclusion can be drawn from this data? The conclusion is obvious - with predominant drug treatment in a group with myocardial dysfunction and a high Syntax score, mortality is relatively identical, regardless of whether the patient underwent a surgical procedure or not. This directly contradicts the claims of the STICH study that patients should undergo surgery to prolong their lives. The other thing that strengthens this opinion is the data on the mortality of patients without angiography. It is higher (these patients were suspected of having coronary disease, but it was not found in them). This subgroup of patients has the highest mortality.

Table 2-21 also demonstrates interesting findings. As can be expected (and this group is from people who were on ideal medical modern treatment) the mortality even as a small relative number - the mortality after 6 years is 50%. Logically, the death rate drops proportionally after that (giving a small jump between 41-60% EF). This may be due to cardiac or non-cardiac causes. What is important from the data in this table is that we have a logical fall in mortality as EF rises. However, if we return to the previous table 2-20, we will notice that the so-called "no angiography" group, where there was significant mortality. What can we possibly conclude from this observation? Regardless of whether EF is determined or not, if the patient has significant co-morbidities, this is certainly a factor for a poor prognosis. Although this is a known fact, it is important for the present study from the point of view of the discussion, we stop at the proposal by the STICH study to send any type of patients for operative treatment.

Table 2-21. Tracking data for fractional correlation of Echocardiogram ejection and survival

EF_Echo_groups * Telephonic_Follow_up Cross-tabulation		**Telephonic_Follow_up**		**Total**
Absolute value	**Count**	**Deceased**	**Alive**	
EF_Echo_groups	less than 10	2	2	4
	11-20	5	7	12
	21-30	2	5	7
	31-40	3	13	16
	41-50	6	13	19
	51-60	7	20	27
	61-70	18	70	88
	71-80	0	7	7
	81-90	0	2	2
	91-100	0	2	2
	No information	7	16	23
Total		**50**	**157**	**207**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
EF_Echo_groups	less than 10	50,0%	50,0%	100,0%
	11-20	41,7%	58,3%	100,0%
	21-30	28,6%	71,4%	100,0%
	31-40	18,8%	81,3%	100,0%
	41-50	31,6%	68,4%	100,0%
	51-60	25,9%	74,1%	100,0%
	61-70	20,5%	79,5%	100,0%
	71-80		100,0%	100,0%
	81-90		100,0%	100,0%
	91-100		100,0%	100,0%
	No information	30,4%	69,6%	100,0%
Total		**24,2%**	**75,8%**	**100,0%**

Table 2-22 offers data on FI when assessed by nuclear (nuclear) testing. In addition to data on the expected high mortality, which is in very low indicators, it can be seen that, mainly with pharmacotherapy, the mortality in the different groups is basically the same after a follow-up of 6 years.

Table 2-22. Ejection fraction Cardiolyte_sestamibi_groups * Telephone follow-up

Absolute value		Telephonic_Follow_up		
EF_Cardiolite_sestamibi_groups	Count	Deceased	Alive	Total
	less than 10	1	0	**1**
	11-20	4	6	**10**
	20-30	3	11	**14**
	31-40	7	14	**21**
	41-50	8	26	**34**
	51-60	8	32	**40**
	61-70	7	35	**42**
	71-80	2	5	**7**
	81-90	0	1	**1**
Total		**40**	**130**	**170**
Relative value	**% within**	**Deceased**	**Alive**	**Total**
EF_Cardiolite_sestamibi_groups	**less than 10**	**100,0%**	**60,0%**	**100%**
	11-20	40,0%	78,6%	**100%**
	20-30	21,4%	66,7%	**100%**
	31-40	33,3%	76,5%	**100%**
	41-50	23,5%	80,0%	**100%**
	51-60	20,0%	83,3%	**100%**
	61-70	16,7%	71,4%	**100%**
	71-80	23,5%	100,0%	**100%**
	81-90	28,6%	76,5%	**100%**
Total				**100%**

3. Frequency distribution

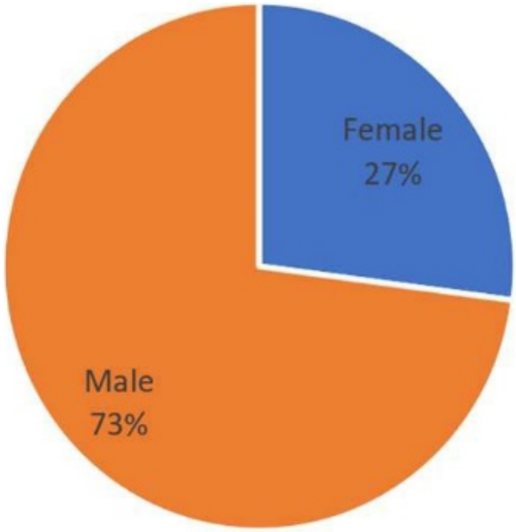


Chart 1. Frequency distribution by gender

The gender distribution presented in graph 1 shows that, as one might logically assume, there are more men than women.

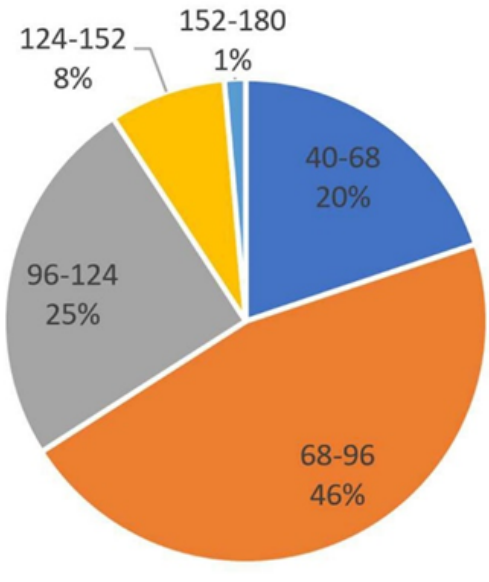


Chart 2. Frequency distribution of patients according to their body weight values

On Chart 2, it can be seen that in terms of weight, we have a logical distribution – with the largest relative share are patients with a weight that is much above or below the norm, and the second may be due to heart failure.

It can be seen that patients in the middle age range predominate (heart problems are registered most often in this group).

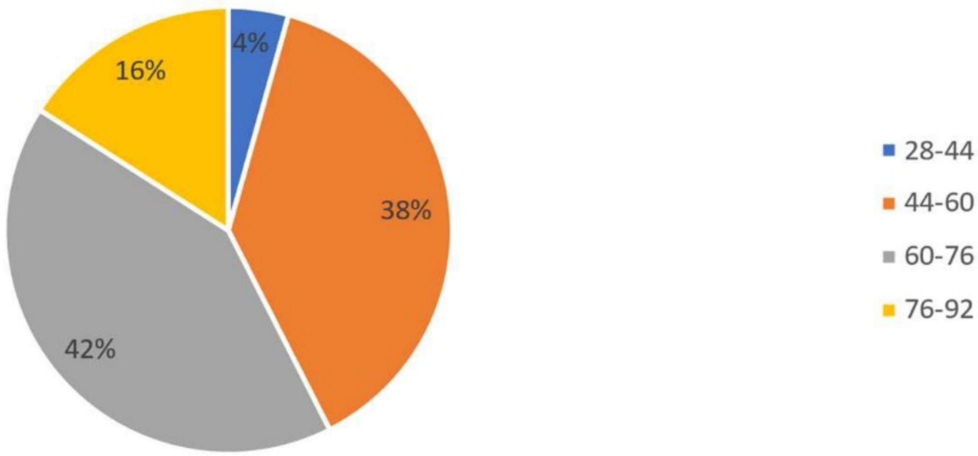


Chart 3. Distribution by age

In Chart 4 it can be seen, and this is logical to some extent from Chart 2, that the patients who were not suitable for angiography were about a quarter of all.

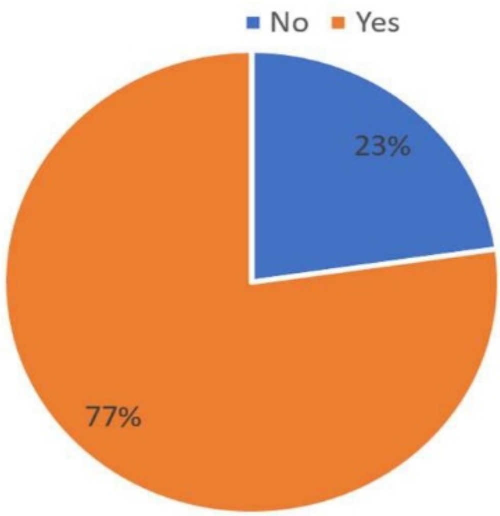


Chart 4. Relative share of eligible respondents or not for angiography

It gives the incidence of diabetics which is not high (this is good because of the relative exclusion of diabetes as a major cause of death).

Chart 6 shows the relative share of hypertensives. They are a relatively small percentage of the total group. However, it should be noted that this indicator is not significant, since the study was initially retrospective and the data on the presence of hypertension were taken from the patients' files. They may have been on prior therapy.

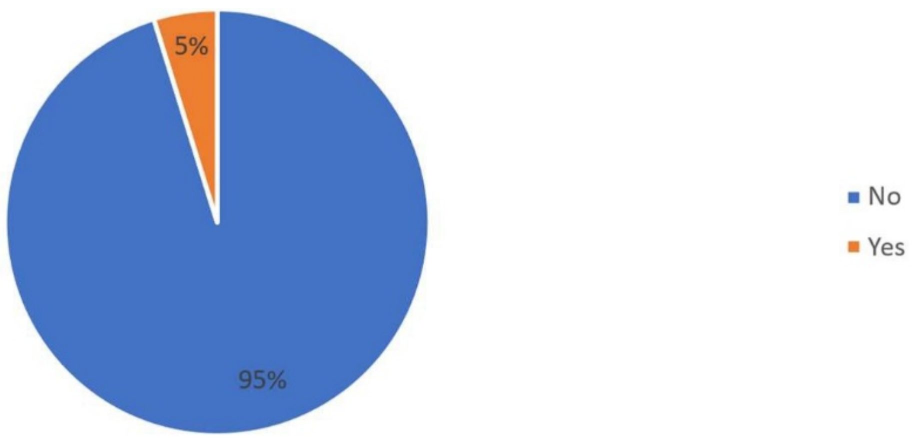
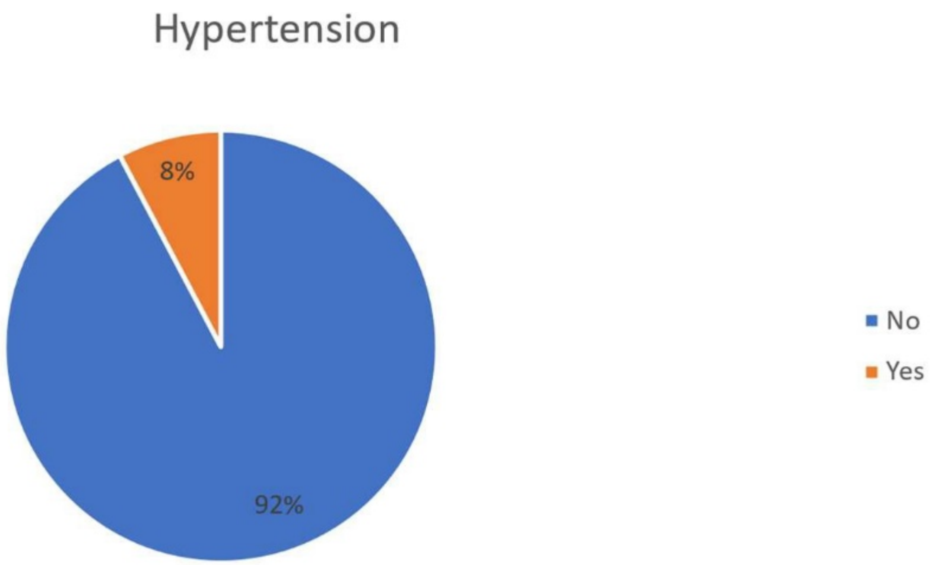


Chart 5. Distribution of patients depending on the presence of diabetes



Graph 6. Relative share of hypertensives

Regarding the distribution according to the functional class of HF from graph 7, it is evident that in our study, the patients in the second functional class, i.e., have the largest relative share. functionally they were not severely affected.

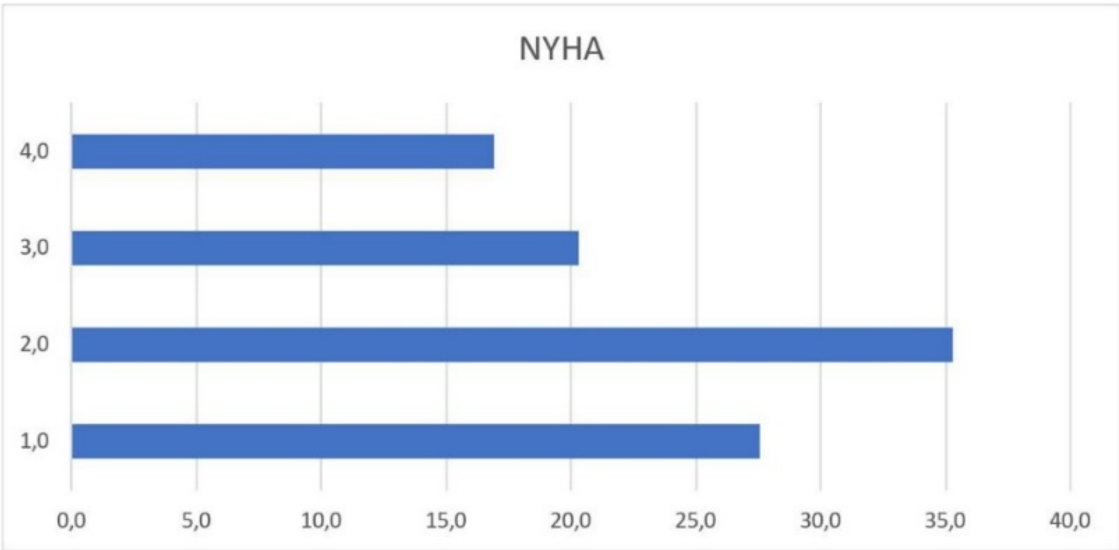


Chart 7. Functional class of HF according to the NYHA classification

Data on the relative share of patients with angina in our study are presented in Chart 8. This is the qualitative presence or absence of angina. Half of the patients had complaints defined as clinical "angina".

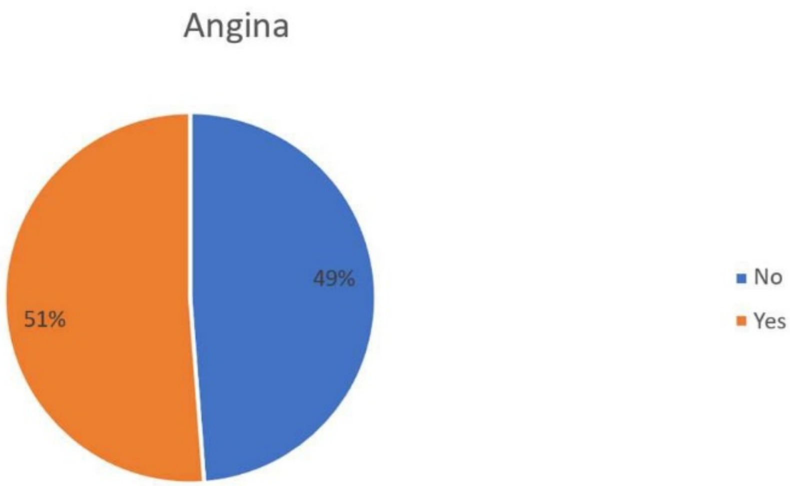


Chart 8. Distribution of patients depending on the presence or absence of angina pectoris (%)

The first and second classes are most common in patients with angina pectoris. The frequency falls towards the 3rd and 4th classes (Chart 9).

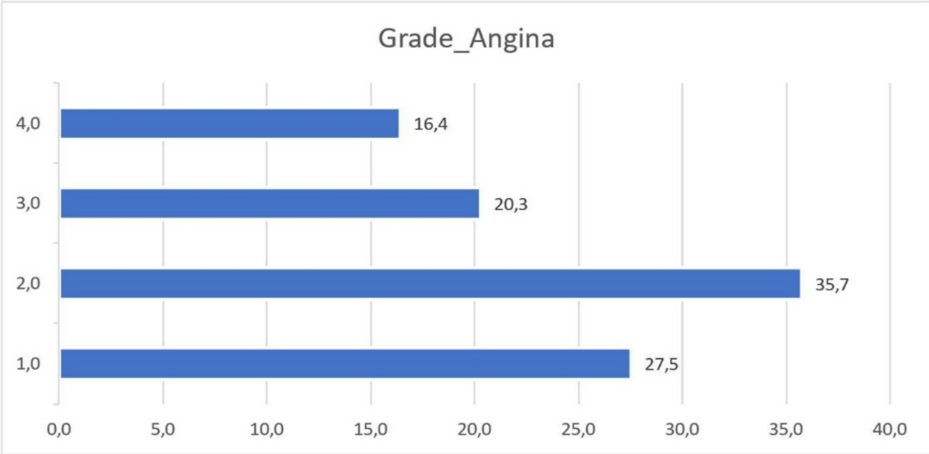


Chart 9. Degree of angina

32% of patients had a myocardial infarction. According to data from the nuclear examination, the remaining persons in the study were without myocardial infarction (Chart 10).

The functional class coincides to some extent with the NYHA classification. And as you might expect, the results are very close (this is more of a comparison with the American Heart Association) (Chart 11).

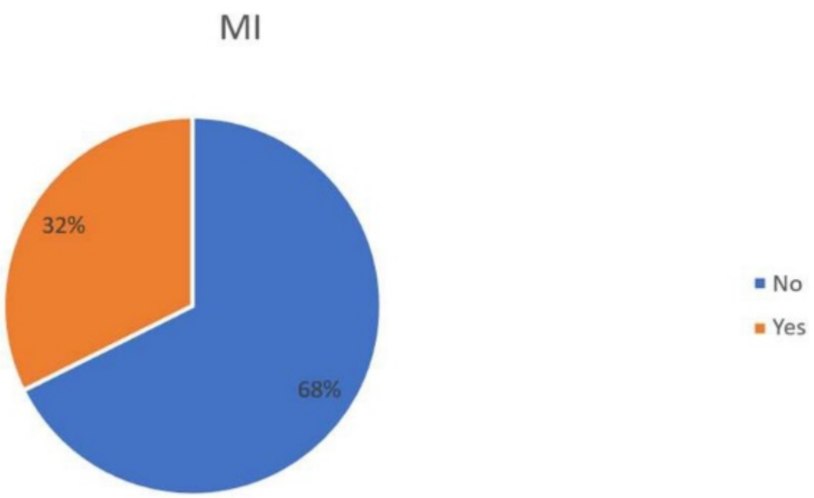


Chart 10. Relative share of patients with myocardial infarction in the study

The data in Chart 12 are of particular importance. They show the treatment with which these patients came to us for the first examination. What they had before. It can be seen from this graph that the interventional treatment was extremely small. 11% had a previous bypass and 7% had a previous angioplasty. The rest were mainly new, undiagnosed patients who came for a specific problem - mainly chest pain.

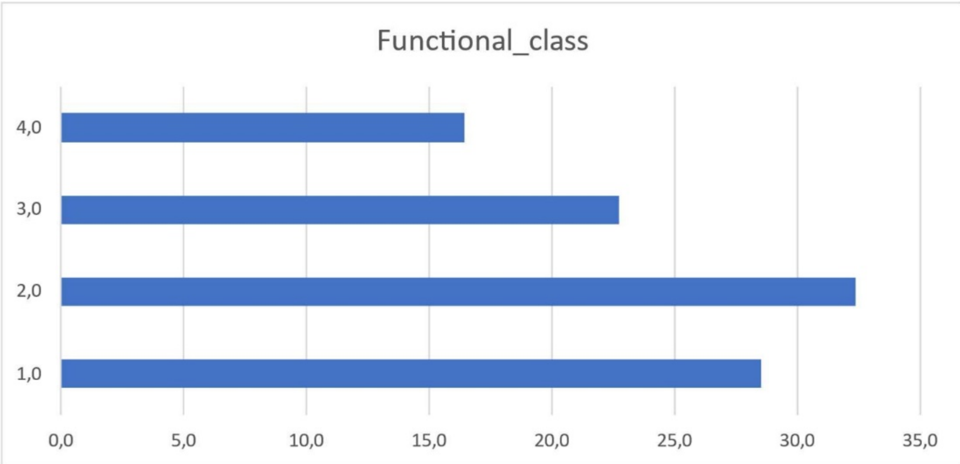


Chart 11. Functional class

The data in Chart 13 demonstrate that most of the patients had a normal echocardiographic finding (66%). In 23%, the finding showed pathological changes. The unknowns come from the fact that the researchers did not have the patient's ultrasound data at initial enrolment in the program.

From Chart 14 it can be seen that the patients are mainly distributed in the normal EF group and smaller groups are towards the medium and high medium to low values for EF. In other words, the group was generally average, with no predominance of patients with completely normal ejection fractions, nor with absolutely abnormal ones.

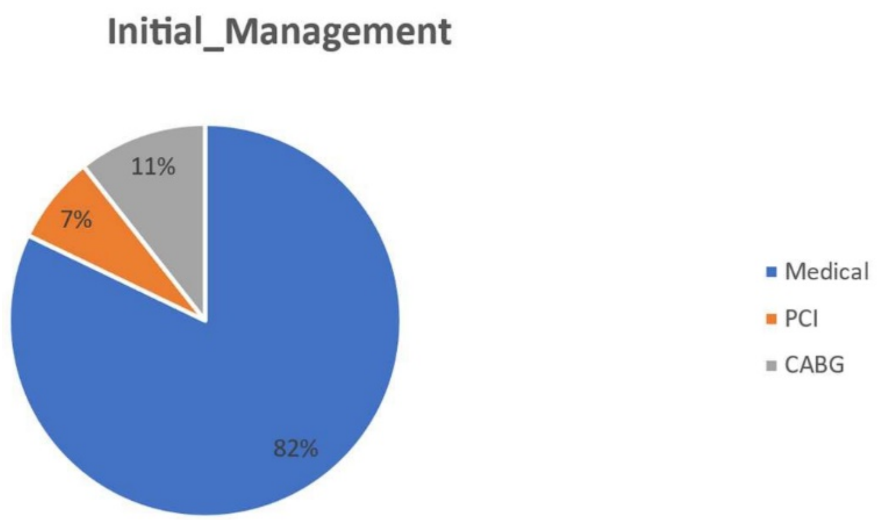


Chart 12. Initial treatment

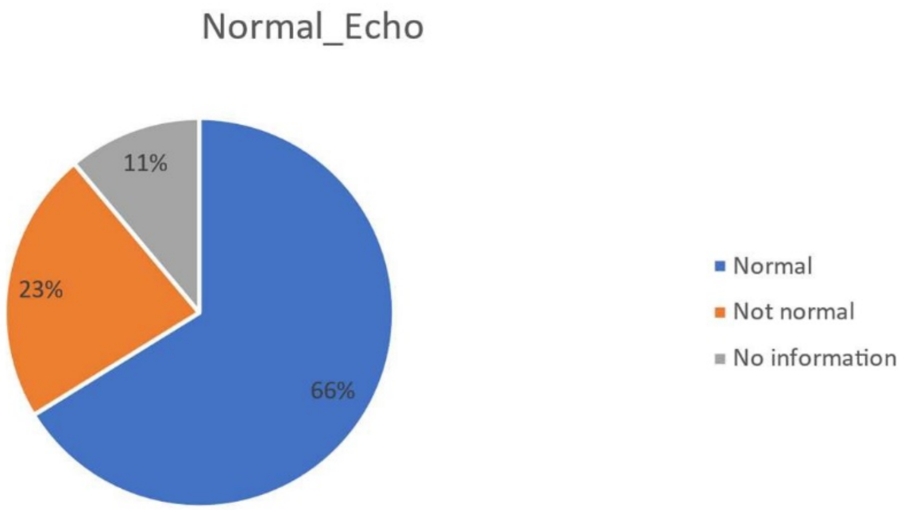


Chart 13. Distribution of patients in the study depending on their echocardiographic findings

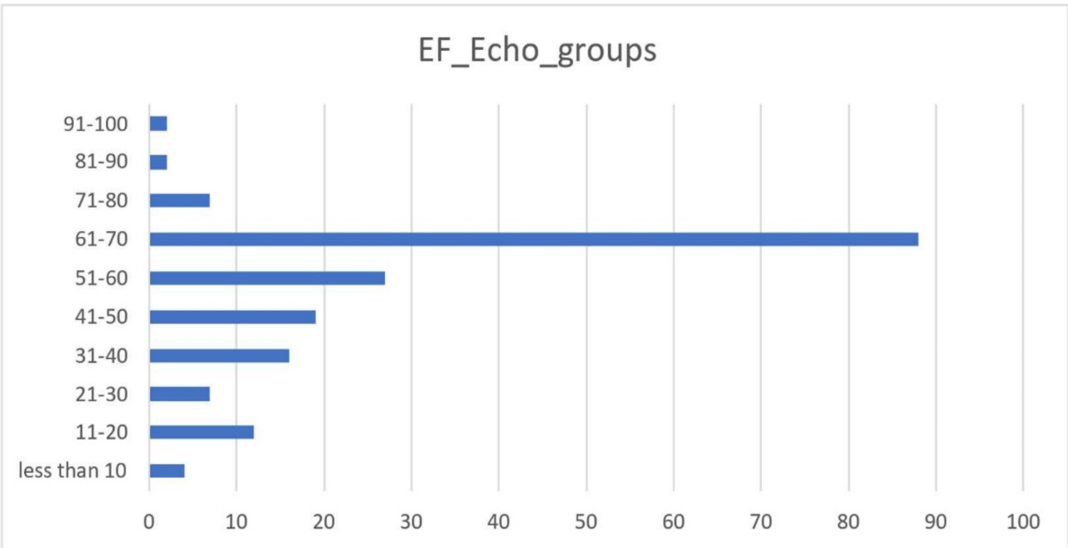


Chart 14. Distribution of patients depending on FI

A normal nuclear examination without evidence of ischemia was present in 45% of cases (Chart 15). This means that in patients with clinically or interventionally proven coronary disease, ischemia is not proven. The pathological and clinical findings were present (for example, in patients who did not undergo coronary angiography, clinical evidence of ischemia was accepted in the presence of two of the three criteria - "pain", "ECG changes", "positive cardiac enzymes"); information" means that the data from the nuclear examination were contradictory or were not "conclusive" for making a final diagnosis.

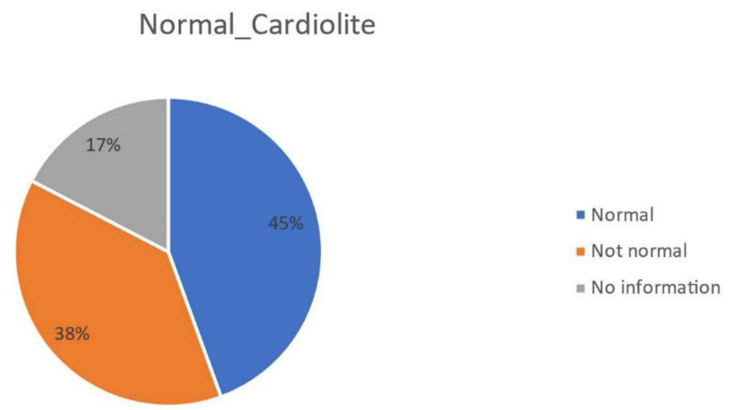


Chart 15. Distribution of FI in nuclear research

The data in Chart 16 somewhat overlaps with the EF chart studied with Echocardiography. Here again it can be seen that the main distribution of patients according to EF values is generally in normal or near normal values.

The data in Chart 17 is of extreme importance. From this chart you can see the ways in which our patients were treated. 93% of treatment is medical. Angioplasty was performed in 2% and bypass surgery was performed in 5%. An extremely large percentage is the sample of the study group that was treated with pharmacotherapy. Interventional treatment - whether bypass or angioplasty - is prescribed in a very small percentage of patients. This comparison with many other studies is below the threshold of interventional therapy in patients who, again we must point out, had coronary disease – clinically or anatomically.

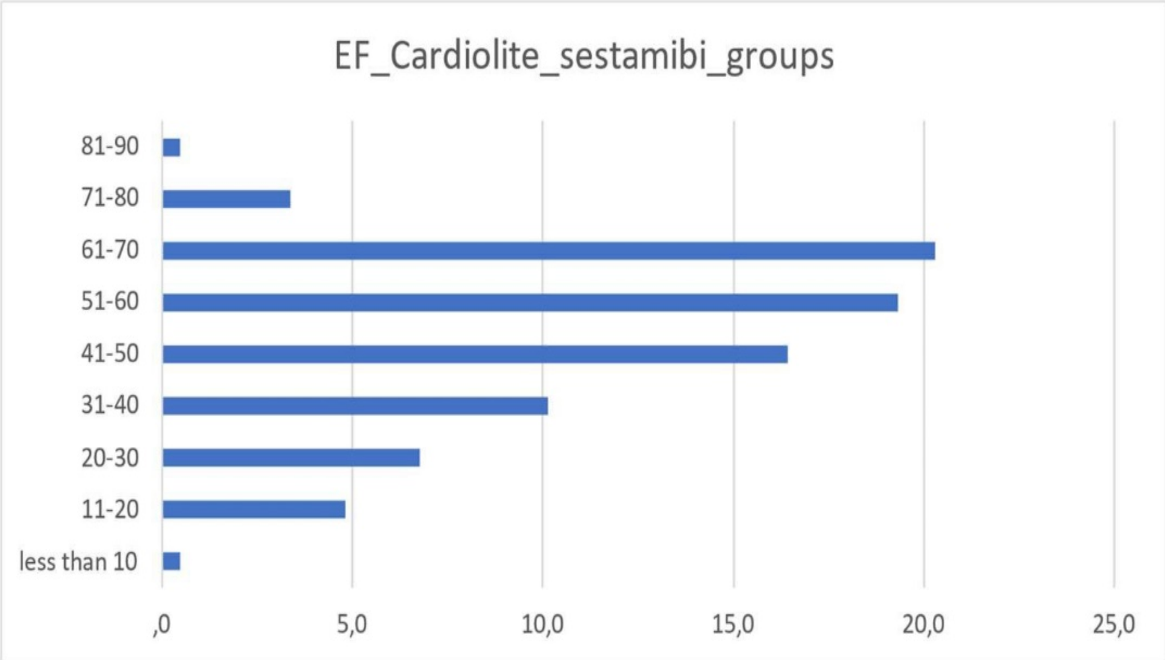


Chart 16. Distribution of FI values in nuclear research

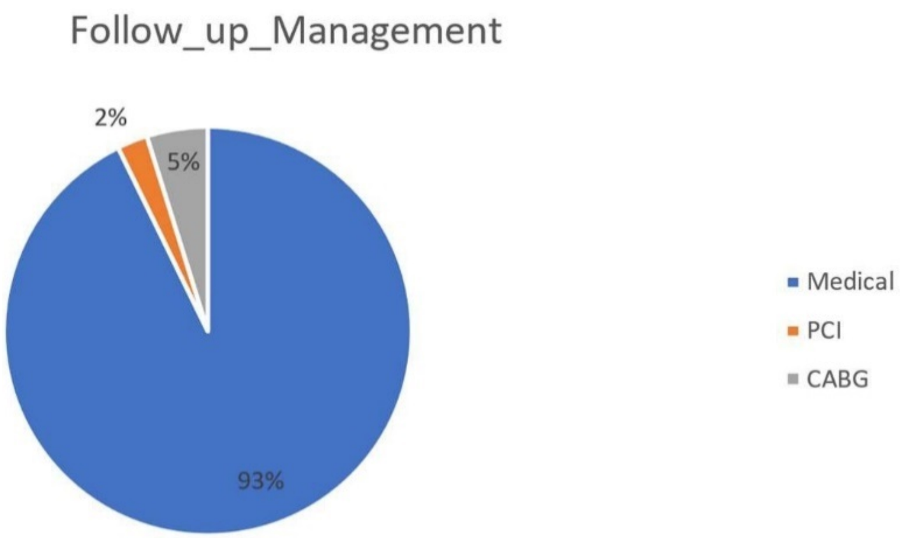


Chart 17. Distribution of patients by dependency from the therapeutic approach

Chart 18 is indicative of Chart 17. It explains why we did nuclear research. From this graph, it can be seen that the least reason was diagnostic in patients who had evidence of coronary artery disease on clinical grounds. Further we can see from this graph that the other indications are – vitality, heart failure with evidence of coronary disease, previous heart attack, etc.

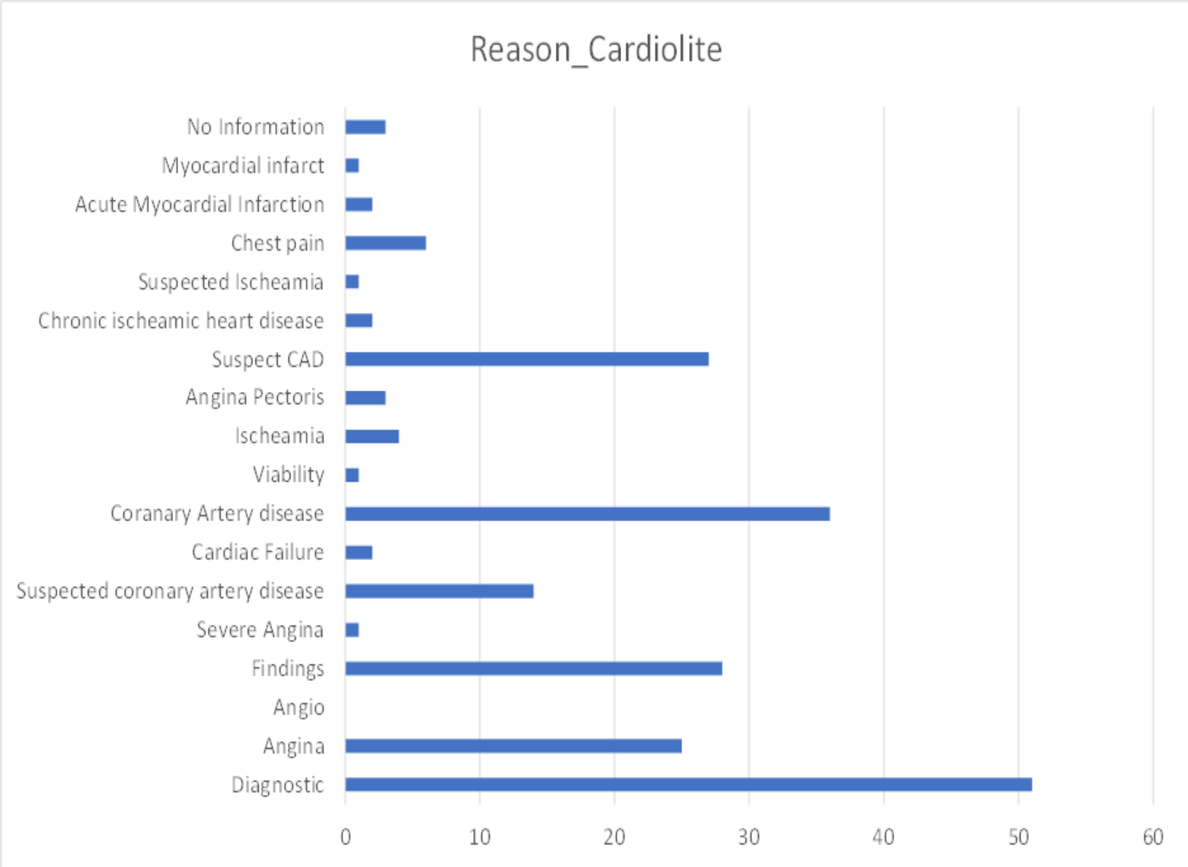


Chart 18. Reasons for conducting nuclear research

From the data in graph 19, the two main reasons for nuclear (nuclear) research can be seen:

- Clinical or anatomical evidence of coronary disease;
- Heart failure.

Angina pectoris ranks third.

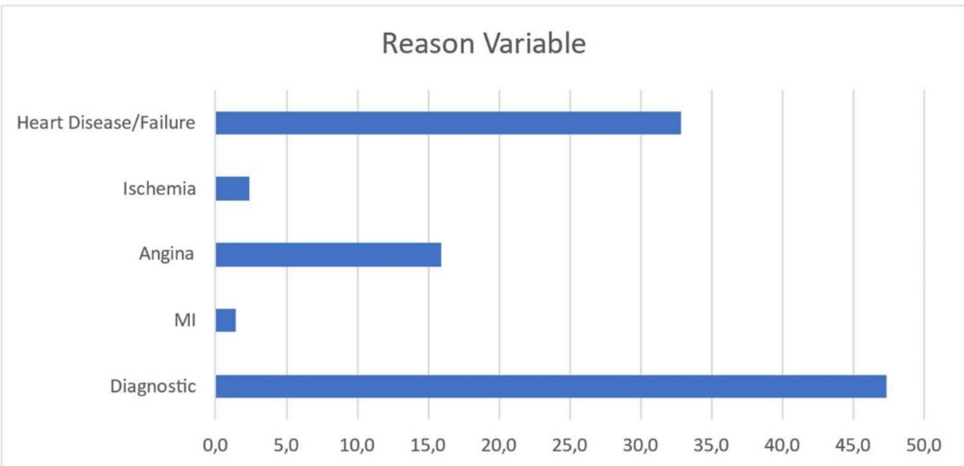


Chart 19. Main reasons for nuclear (nuclear) research

Chart 20 gives an idea of the use of one or another type of test in our patients. Here we must point out that there is a certain overlap between the two tests – with "persantine" and "rest", in time over the years. At first, only persanthin is used. Recently, the research with "Adenocor" came in. This is adenosine, which also accelerates the heart rate, but it acts quickly and has no significant side effects. It's a chemical test again. We note this for clarification and to avoid artificial data overlap. In cases where it was possible, a physical stress test was used, and this was in the majority of cases.

It should also be clarified that dipyridamole and adenosine are very similar in their final action. Dipyridamole blocks the entry of adenosine into the cell. Thus, the extracellular level of adenosine rises. Otherwise, adenosine is given directly intravenously.

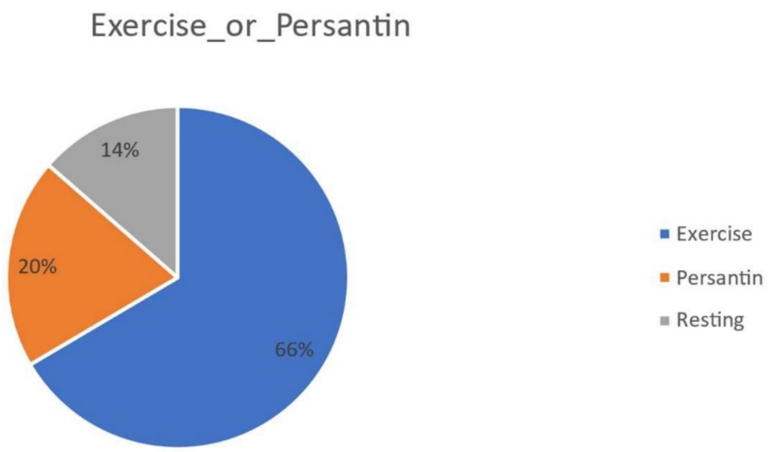


Chart 20. Distribution of patients (%) in dependence from the test performed

Chart 21 again gives very important information about the patients studied. It can immediately be seen that the cases without ischemic changes predominate. Does this mean that nuclear study does not need to be done? Let's not forget that the indication for such an investigation is to have an "a priori" cause - to have a coronary disease proven in some way - clinically or anatomically. This graph reveals that in 69% of cases there is basically no need to take any procedure after that because there is no reason. Separately, it should be discussed in which cases it is imperative to undertake treatment - perhaps, if we are extremely academic or rather conservative, cases in which there is weak or little ischemia - should not undergo procedures. Only 2 cases left – that's 1%!!! In only one percent of patients in whom a good characterization of the ischemia is done, action should be taken! This was known 40 years ago. But with the current infiltration of medicine by the pharmacological branch, this is hardly possible, although it is logical.

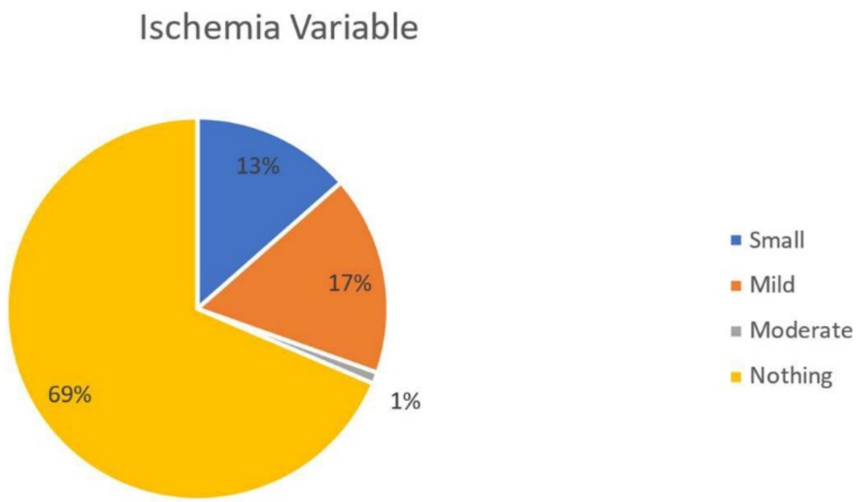


Chart 21. Variability of ischemia

The data on graph 22 are of a purely comparative nature and show, as we have already noted, that in case of clinical suspicion, we have objectively proven ischemia in only 31% of the cases. The other are either anatomical pictures of a pathology, but not of a problem, or subendocardial infarctions, or unstable angina, or a stable one that is controlled by medical therapy.

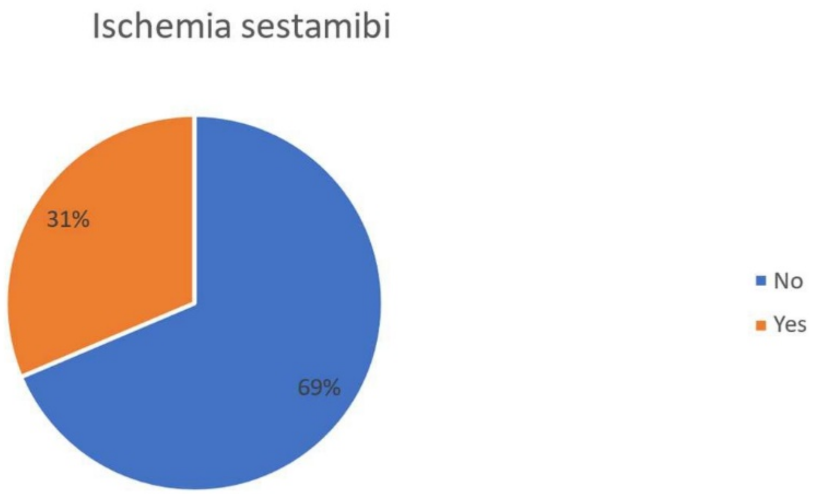


Chart 22. Ischemia confirmed by nuclear examination

The data from Chart 23 provide important information for establishing the thickness of the infarct. Again, we must point out that most of the patients were without heart attacks. Of the patients who had a heart attack, it was large in 11%, medium in 24%, and small in 2.9%. This is logistic-distributed with the total infarct size from the different studies. Its treatment is important for our study. If we combine the terms "large" and "medium" into "significant", this gives about 35%. And the treatment even after invasive follow-up (angioplasty or bypass) is a maximum of 8% at the final follow-up and 1% at the initial follow-up. We are talking about established old heart attacks, not fresh heart attacks!

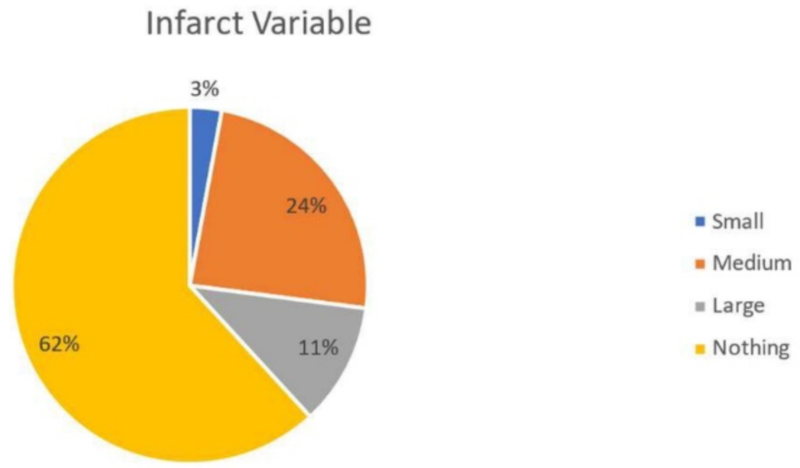


Chart 23. Distribution according to the size of the heart attack

Chart 24 shows what percentage of people had a heart attack (37%). The rest, who had a coronary problem for clinical or anatomical reasons, did not have a past heart attack. The nuclear (nuclear) examination accurately determines the heart attack.

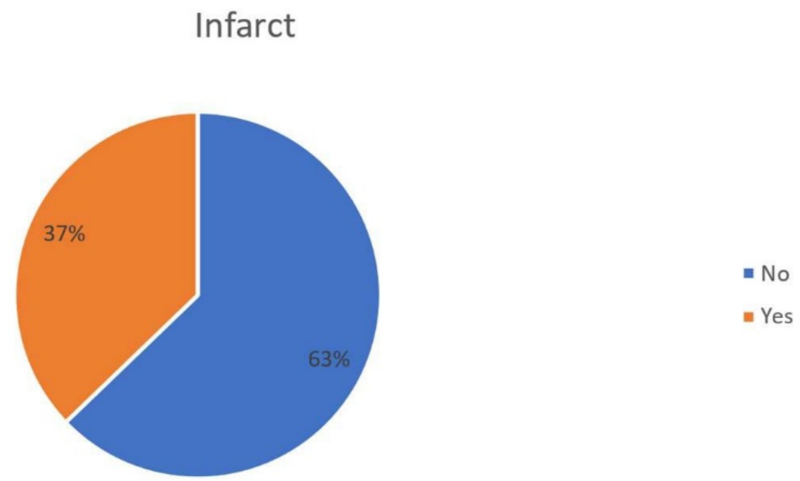


Chart 24. Relative share of presence of heart attack

Chart 25 again represents what our course of treatment was after the initial follow-up of three months. It can be seen that up to three months from the beginning of the follow-up, the therapeutic approach remained almost the same. It is mainly pharmacotherapy, and additionally 5 patients went to angioplasty and 3 to bypass. This still keeps the total invasive therapy group at about 8 people after follow-up.

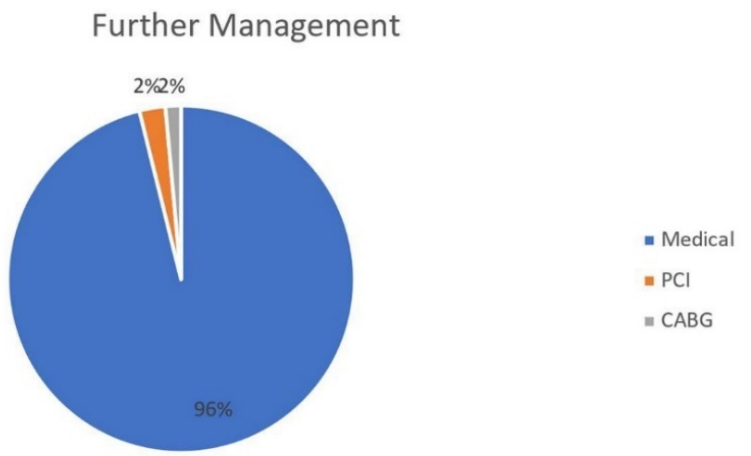


Chart 25. Treatment after initial follow-up

Chart 26 shows the distribution of patients depending on follow-up. Those designated as 0 months of follow-up are stable patients with minimal pathology who do not require further treatment. They were referred back to their treating physicians for follow-up. The 6- and 12-month follow-up groups were patients with significant pathology.

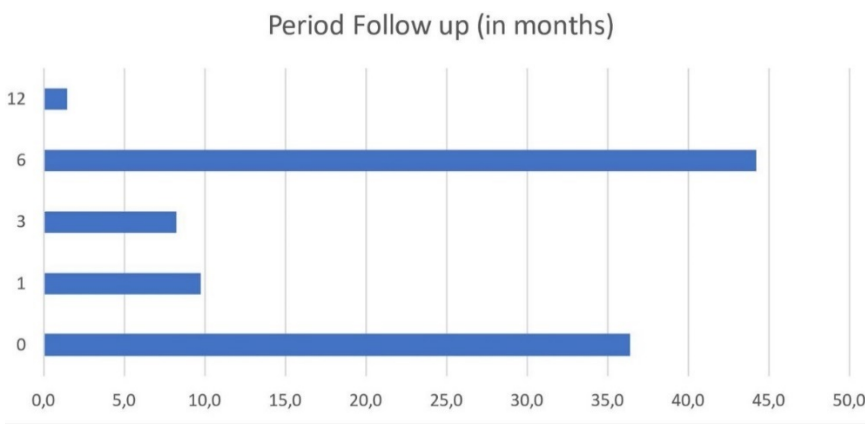


Chart 26. Follow-up period

After 6 months of treatment, no mortality was recorded in the patients followed by us. This is important because studies such as STICH show a high mortality rate in the postoperative period (up to 30%). In our country, this is not observed, because almost all patients are treated with medication.

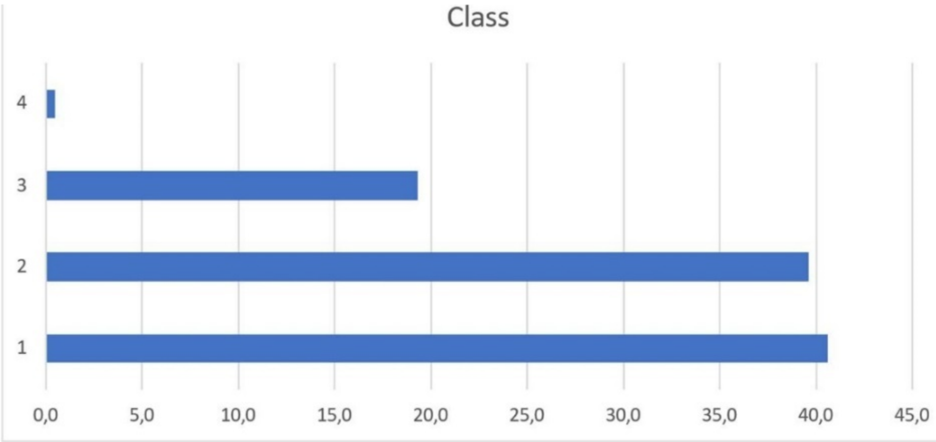


Chart 27. Functional class

The data in Chart 27 shows that we have had a significant improvement in functional class since patients entered the study. If at the beginning of the study there were 57 patients in the first functional class, during the follow-up they grew to 84 people, in the second functional class from 73 they became 82. In thirds, almost the same amount remains. In the fourth, they drop sharply from 35 to 1 person.

This is significant evidence that good pharmacotherapy gives good results and low mortality in high-risk groups.

The follow-up shows (Chart 28) that in the group that was treated with medication we have a 24% mortality rate. Also, 76% survived patients in this heterogeneous group at high risk of mortality when on optimal pharmacotherapy.

Chart 29 shows that the proportion of patients with a high Syntax score is relatively small. Patients with a low Syntax score are a relatively much larger proportion. Again, clearly, these are patients with significant comorbidities as well as patients with heart failure. The number of patients who underwent bypass surgery is relatively small.

The data in Chart 30 shows a very large plethora of different segments of the myocardium that are infarcted or ischemia. The percentage ratio in the groups where they match as regions is quite small. The only thing that stands out clearly is "no ischemia". And these groups include patients who had clinical or morphological evidence of ischemia or heart attack. However, it turns out that after conducting an objective nuclear (nuclear) examination - in many of them, even if there is an anatomical substrate, there is no functional one. This is extremely important in the treatment of these patients. Especially if this treatment will be operative or invasive. This graph clearly shows that it is logical to use pharmacotherapy in most of the cases.

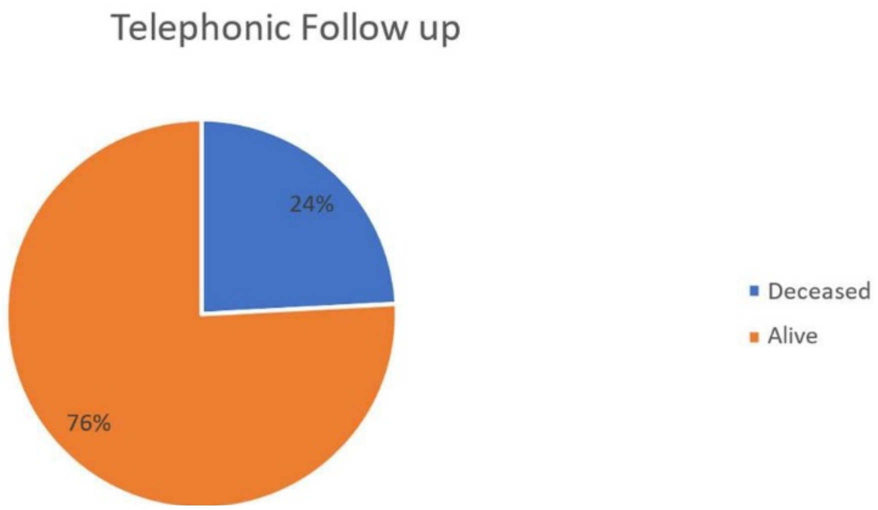
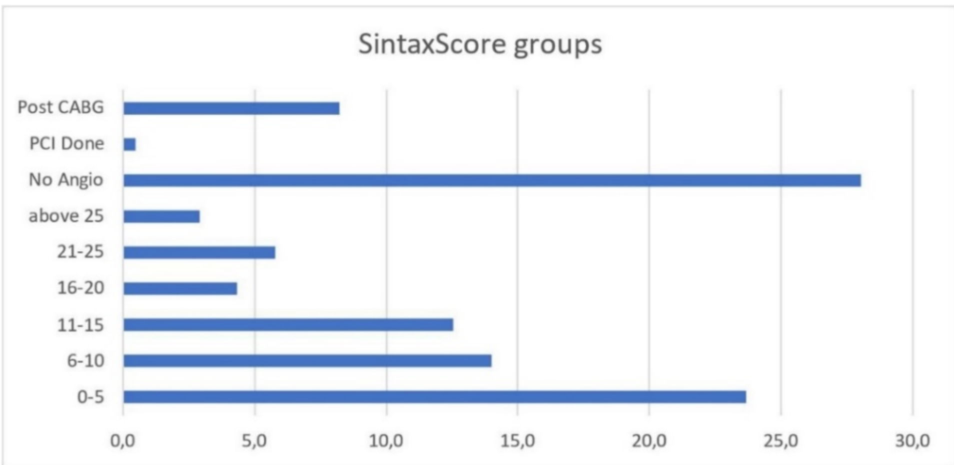


Chart 28. Distribution in the tracked group by indicator survival



Graph 29. Distribution of patients according to Syntax score

Chart 31 shows the distribution of heart attacks. As with ischemia, here too we observe a mixture of different values of the individual indicators. Unless we have more accurate readings, the heart attack is not always as described on the electrocardiography – anterior, posterior, lateral. It is completely multifactorial and multilocalized depending on which area is being studied.

Chart 30. Segments of the myocardium that are infarcted or ischemia

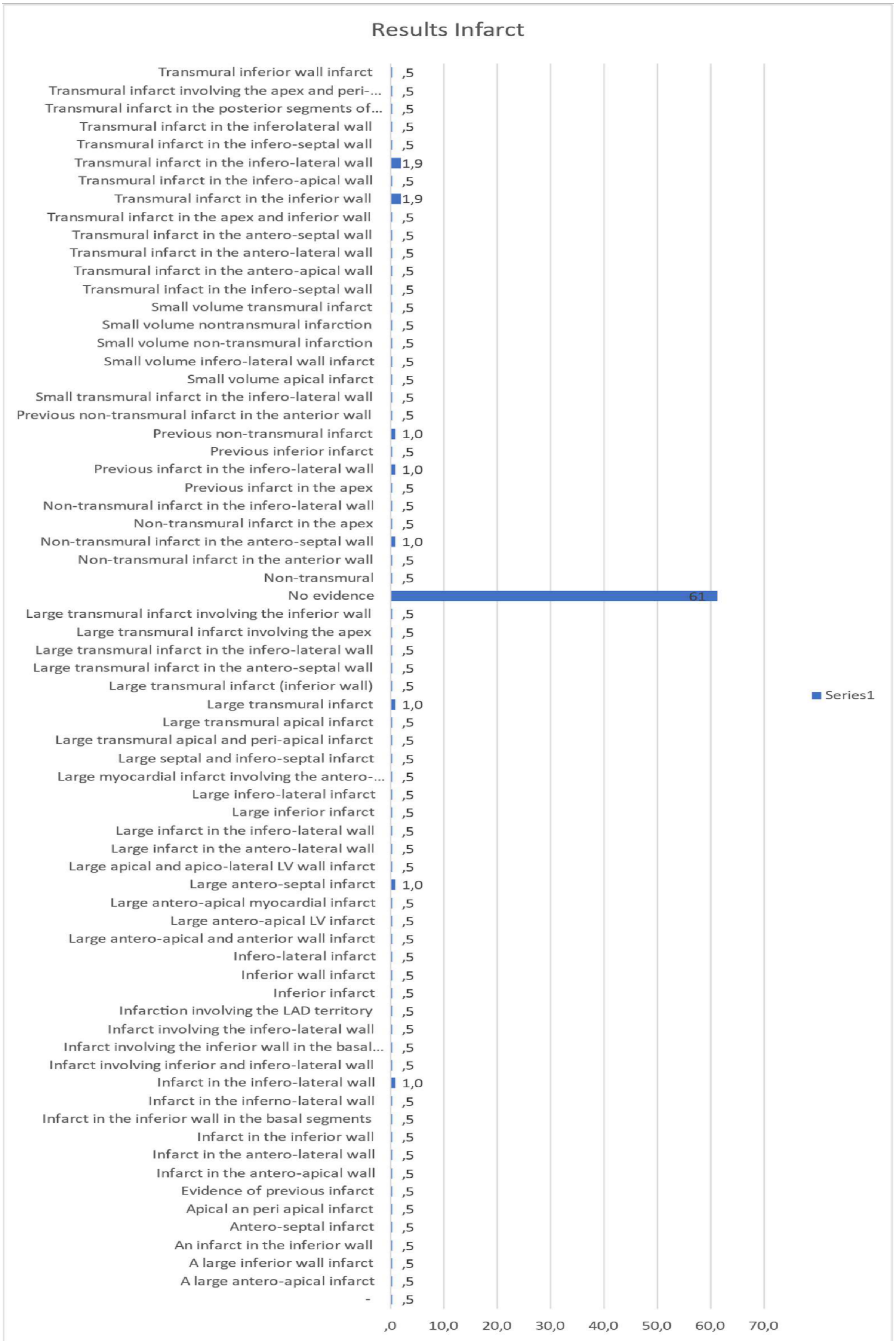


Chart 31. Distribution of the heart attack

4. Hypothesis testing

Hypothesis testing at a risk of error of 5%, whether there is a statistically significant difference between the relative proportions of living and deceased patients in the drug-treated group.

Table 4-1. Follow-up treatment 2 * Telephone follow-up (Crosstab)

			Telephonic_Follow_up		Total
			Deceased	Alive	
Followup_management2	**Medical**	Count	50	142	**192**
	Surgery	Count	0	15	**15**
Total		**Count**	**50**	**157**	**207**

Defining the hypotheses:

- The null hypothesis states that there is no statistically significant difference in the relative proportions of living and deceased patients in the drug-treated group. As far as such is observed in the specific data, it is due to random factors.
- The alternative hypothesis states that there is an objective difference in the relative proportions of living and deceased patients in the drug-treated group and it is not random.

The risk of first-order error is 5%.

A t-test is used to test the hypothesis.

The empirical characteristic is estimated at 1.94.

Theoretical characteristic:

Since we have reason to reject the null hypothesis in favour of the alternative, i.e. there is an objective, statistically significant difference in the relative proportions of living and deceased patients in the drug-treated group, and it is not due to random factors.

Chi-square analysis for association between two variables

1. Initial management

The study of the relationship between the follow-up of patients and the type of treatment is presented in table. 4-2. The Chi-square method was used to examine the relationship. SPSS statistical software was used for the purposes of the study.

Table 4-2. Distribution of patient follow-up variables and type of treatment

Telephonic_Follow_up * Initial_management 2 Crosstabulation			Initial_management		Total
			Medical	Surgery	
Telephonic_Follow_up	Deceased	Count	45	5	**50**
		Expected Count	41,1	8,9	**50,0**
	Alive	Count	125	32	**157**
		Expected Count	128,9	28,1	**157,0**
Total		Count	170	37	**207**
		Expected Count	170,0	37,0	**207,0**

The presented on the Table 4-2 distribution of the two variables is demonstrated as absolute and theoretical (forecast) values. The distribution of the theoretical (expected) values shows that the model meets the requirements for its application. ***First requirement***: no theoretical values equal to 1. ***Second requirement***: no theoretical frequency that is less than 5. As 0% of cells are found to have values less than 5.

Table 4-3 presents the Pearson coefficient. Due to the level of significance Asymp Sig = 0.095, we accept as true the null hypothesis, which states that the two variables are independent, i.e. there is no legal relationship between them.

Table 4-3. Result of Chi-Square Tests

	Value	df	Asymp. Sig. (2- sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	2,785a	1	,095		
Continuity Correc-tionb	2,122	1	,145		
Likelihood Ratio	3,082	1	,079		
Fisher's Exact Test				,136	,068
Linear-by-Linear Association	2,771	1	,096		
N of Valid Cases	207				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 8,94.
b. Computed only for a 2x2 table

Table 4-4 presents the Cramer coefficient. Its level of significance is Approx. Sig = 0.095, which is greater than the risk of first order error α = 0.05, therefore the coefficient is not statistically significant and cannot be interpreted.

Table 4-4. Cramer coefficient

		Value	Approx. Sig.
Nominal by Nomina	Ph	,116	,095
	Cramer's V	,116	,095
N of Valid Cases		207	

The obtained results confirmed what was found in the hypothesis test.

2. Study of the relationship between patient follow-up and type of treatment (Follow up management)

The Chi-square method was used to examine the relationship. The statistical software SPSS was used for the purposes of the study.

Table 4-5. Distribution of the variables Patient follow-up and Type of treatment

Telephonic_Follow_up		Followup_management 2		Total
		Medical	Surgery	
Deceased	Count	50	0	50
	Expected Count	46,4	3,6	50,0
Alive	Count	142	15	157
	Expected Count	145,6	11,4	157,0
Total	Count	192	15	207
	Expected Count	192,0	15,0	207,0

Table 4-5 presents the distribution of the two variables, giving both absolute and theoretical values. From the distribution of theoretical (predicted) values, it can be seen that, first, there are no theoretical values equal to 1. Second, there is only 1 theoretical frequency that is less than 5, and that is 3.6. Having found that 25% of the cells have values less than 5.

Table 4-6. Chi-square test result

Chi-Square Tests	Value	df	Asymp. Sig. (2- sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	5,150a	1	,023		
Continuity Correctionb	3,827	1	,050		
Likelihood Ratio	8,661	1	,003		
Fisher's Exact Test				,024	,013
Linear-by-Linear	5,125	1	,024		
N of Valid Cases	207				

a. 1 cells (25,0%) have expected count less than 5. The minimum expected count is 3,62.
b. Computed only for a 2 x 2 table

Table 4-6 presents the Pearson coefficient. The level of significance in this test is Asymp Sig = 0.023, but because 25% of the cells were found to have values less than 5 it cannot be interpreted. Therefore, Fisher's Exact test of significance will be used in the analysis. It has an Exact Sig value of 0.024, which is less than the first order error value of α = 0.05. We accept the alternative hypothesis that the two variables are not independent, i.e., there is a natural relationship between them. In other words, whether a patient will have the status alive, or dead is directly dependent on the type of treatment carried out, i.e., with medication or surgery.

Table 4-7 presents the Cramer coefficient. It has a significance level of Exact Sig = 0.024, which is less than the risk of a first order error α = 0.05, therefore the coefficient is statistically significant and can be interpreted. The value of the coefficient is 0.158, which in turn indicates that the relationship under study is weak.

Table 4-7. Cramer coefficient

		Followup_management2		Exact Sig.
		Value	Approx. Sig.	
Nominal by Nomina	Ph	,158	,023	0,24
	Cramer's	,158	,023	0,24

3. Exploring the relationship between continued follow-up of patients and type of treatment (Further management)

The chi-square method was applied to investigate the relationship. The statistical software SPSS was used for the purposes of the study.

Table 4-8 presents the distribution of the two variables, with both absolute and theoretical values presented. The distribution of the theoretical (expected) values shows that the model meets the requirements for its application. First requirement: there are no theoretical values equal to 1. Second requirement: there is only 1 theoretical frequency that is less than 5 and it is 3.6. As 25% of the cells were found to have values less than 5.

Table 4-8. Distribution of patient follow-up variables and type of treatment

Telephonic_Follow_up * Further_management 2 Crosstabulation			Further_management2		Total
			Medical	Surgery	
Telephonic_Follow_up	Deceased	Count	46	4	50
		Expected	48,1	1,9	50,0
	Alive	Count	153	4	157
		Expected	150,9	6,1	157,0
Total		Count	199	8	207
		Expected	199,0	8,0	207,0

Table 4-9 presents the Pearson coefficient. Due to the fact that the Asymp Sig significance level is equal to 0.082, we accept the null hypothesis that the two variables are independent, i.e., there is no legal relationship between them.

Table 4-9. Result of Chi-Square Tests (Chi-Square Tests)

	Value	df	Asymp. Sig. (2- sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	3,034%	1	,082		
Continuity Correc-tionb	1,744	1	,187		
Likelihood Ratio	2,605	1	,106		
Fisher's Exact Test				,0,98	,098
Linear-by-Linear Association	3,020	1	,082		
N of Valid Cases	207				

a. 1 cells (25,0%) have expected count less than 5. The minimum expected count is 1,93.
b. Computed only for a 2 x 2 table

Table 4-10. Cramer coefficient

		Value	Approx. Sig.
Nominal by Nomina	Ph	-,121	,082
	Cramer's V	,121	,082
N of Valid Cases		207	

Table 4-10 presents the Cramer coefficient. Its level of significance is Approx. Sig = 0.082, which is greater than the risk of first order error $\alpha = 0.05$, therefore the coefficient is not statistically significant and cannot be interpreted.

DISCUSSION

In this study, an analysis was made of the relative mortality in patients who did not undergo invasive treatment. These patients are a group, or it would be more accurate to say groups. No two patients are the same – everyone has their own individual characteristics. The study included patients who had clinical evidence of angina pectoris but were not suitable for invasive investigations. The reasons are different: disease, hemodynamic instability, obesity, etc. Cardiovascular causes are often suggested to be the leading cause. But let's ask ourselves why are they leading? Because they are leading diseases in the world? Perhaps the truth is not exactly like that. Philosophically, the heart beats and stops, and that's the end... All the other diseases that may have led to this more than the heart are often considered and recorded as secondary and tertiary causes of death. It is easiest to write "heart failure", "sudden cardiac death" and in the absence of autopsies - this is accepted as the official truth. That's how it gets into the registries and eventually into the WHO's calculations of leading causes of death. For those who doubt this, let's look at what happened to the mortality statistics during the COVID epidemic. Anyone who dies with a positive test for COVID is counted as having died due to COVID. And this is official government policy. And the fact that the patient had multiple other illnesses and COVID was just one additional reason - that was ignored. In the press and in the scientific literature, there have been reports of a greatly increased death rate compared to other years in relation to non-COVID diseases, which do not correspond to official statistics.

So in our study we included a group of patients with angina pectoris. This angina was based on clinical indicators. We divided these patients into two subgroups – patients suitable for angiography and those not suitable for such a procedure.

The separation of patients is based on different indicators, and their morbidity and mortality are monitored. The main treatment is mainly medication, not surgery or angioplasty. Of course, where the patient needed an operation, such was performed, as well as angioplasty.

Another group of patients was examined - kidney patients with transplantation patients. They are part of our general patient group and have often participated in scintigraphy for obvious reasons. The presence of coronary disease in these patients is up to 47%. In general, exercise stress tests do not reveal much - since these patients cannot be exercised. Adequate metabolic units due to general fatigue and inability to perform the stress test were not reached. Stress test prediction in this group was approximately 71%. Angiographically determined coronary artery disease in them increases the likelihood of cardiac events. Coronary angiography is associated with complaints, but since approximately 50% of these patients have significant disease, it does not seem reasonable to perform angiography on every one of them.

Noninvasive methods such as thallium or technetium scintigraphy have been suggested to be of greater value in this group (175).

In order to assess the presence or absence of coronary artery disease in patients, applied myocardial perfusion scintigraphy has a sensitivity of 90%. This helps diagnose significant coronary artery disease and is significantly more informative than a simple stress test. It should be taken into account that the group of patients we included for evaluation by cardiolite were individuals who would not be able to perform a stress test or would not be able to perform adequately on stress measures (176).

The sensitivity for detecting coronary artery disease with Thallium 201 is high, although it does not do a great job of differentiating patients with more severe disease. A study by J. Kwok et al. (177) showed that patients with single-branch disease on scan had extensive coronary artery disease in the remaining vessels, including more than 70% narrowing of the left coronary artery trunk and/or the left anterior descending, right coronary, circumflex, posterior diagonal. An independent predictor of the severity of coronary artery disease was the presence of diabetes mellitus, hypertension, the magnitude of ST-depression achieved in the exercise stress test and the value of the exercises (peak heart rate x peak systolic blood pressure). Another point of interest from the cited study was a group of 474 patients who had a single abnormality on the Thallium test (like the group above). This group Kwok et al. divided into three risk groups - low, medium and high. The follow-up period was 7 years. The 8-year overall survival for the groups (mortality) showed low mortality – 89%, medium - 73%, high - 75%.

A study by M. Verani (178) revealed that non-diabetic and hypertensive patients with a stress test score of > 30,000 (systolic blood pressure times heart rate) may have up to 2 mm of ST-depression and still have an extremely good survival rate. In contrast, hypertensive and diabetic patients with a score < 24,000, even with an ST-depression of 1 mm, had poor survival.

It is important to know the clinical presentation to determine pretesting for disease.

The pharmacologic aspect of adenosine, dobutamine, or dipyridamole testing is more accurate than exercise testing, particularly in patients with left bundle branch block. The disadvantage of the pharmacological study is the lack of assessment of functional capacity.

The specificity of stress perfusion studies is in the interest of all, whether clinicians, patients, or a third party (eg, health insurers, health fund payers, etc.). When a patient has a normal stress perfusion study, whether or not they have coronary artery disease, they have a cumulative risk of less than 1% per year. A patient who has an abnormal scan has a risk of > 7% per year (179).

The greater the perfusion deficit, the greater the risk. (180).

It should be noted that obesity is a significant factor in obtaining incorrect results. This is particularly important for our study, as a significant proportion of patients enrolled in the non-angiography arm were obese. The predictive value for obese patients with a body mass index greater than 30 was 86% versus 92% predictive value (181).

It is believed that the following defects are most likely not important if the patient has a good tolerance to efforts and there are no changes in the ECG or manifesting any symptoms:

– a small posterior perfusion defect in an obese stocky man;

– small anterolateral defect in a woman with large breasts;

– small inferior defect secondary to diaphragm attenuation.

Sharir included in his study 1680 patients who had Tl-201/stress 99mTc sestamibi SPECT. Patients were followed up for 19 months (182). The group that had an ejection fraction greater than 45% had a mortality rate of less than 1% per year, even if there were significant defect abnormalities on the scan. The group whose ejection fraction was less than 45% had a mortality of more than 9% per year even with a mild perfusion defect.

Again, it is important to note that nuclear tests provide an excellent assessment of the patient when exercise testing is limited and impossible. They are very useful when the evaluation includes obesity, limited exercise capacity, patients with obstructive pulmonary disease (183).

The cut-off of the test is different, and it is not very accurate in patients with arrhythmia.

In the selection of patients, it is evident that the male gender predominates, and there are significantly fewer women. But this is observed in the general population. Men are more, but women, especially if they are diabetic, are known to have more severe coronary disease. As can be logically expected, the initial pharmacotherapy was more in men than in women. The groups of men and women who had the procedure matched in number.

As shown in table. 1-2, about 25% of cases had no initial angiography. These patients had certain contraindications and had not been previously treated. They underwent angiography only if the data from the nuclear study showed significant (over 30%) ischemia. Obesity, advanced age and renal failure are the leading reasons for not having an angiography. As a general ratio, it can also be seen from the same table that most (80%) of the patients are on drug treatment and only 20% are after a previous intervention. Why is early intervention important? Most of the pre-interventions predetermine additional interventions in principle. In most doctors' practices, if a patient has chest pain and a blocked graft, this ”99%” (as an expression, not as data) predetermines the performance of an invasive procedure. The presence of closed grafts in most cases leads to reoperation. The anatomical substrate guides the cardiologist's decision on how to proceed with the specific patient. In almost all cases, the determination of the pain as typically anginal (and this can only be done in the presence of functional studies) is not done. This leads to unnecessary morbidity and early mortality, especially in individuals at increased risk.

Regarding diabetes, it is known to be a risk factor. The presence of diabetes does not determine the presence of coronary disease. Having diabetes can aggravate coronary disease. There is no linear relationship between diabetes and coronary heart disease. And this is evident from our data in table 1-3. This table also shows that there is no definite relationship between whether treatment is medical or invasive/operative on patient outcome.

Hypertension is a known risk factor for coronary heart disease. The Framingham study confirmed that there is a correlation between the presence and level of hypertension and coronary disease. The study used regression analysis, so the relationship is not linear. From our data, it can be seen that there is a relationship between hypertension and the development of coronary disease. Given that many of the patients were already on treatment in our study, there is no linear relationship.

In discussing the data in Tables 1-5, we can see that patients without any complaints of angina or chest pain are much more likely to have had a previous procedure. These are the patients at the beginning of our selection, i.e., these are individuals who are included in the study and during the study they will have a nuclear test to see if they really have angina or not. This will be seen below in the discussion of whether angina (positive 99Tc test) was actually present.

In Table 1-6 we have placed two groups of patients. Those who had and those who had not had a myocardial infarction - before their inclusion in the study. Passage of a myocardial infarction is determined by the presence of history or ECG evidence of one. It is interesting to see from these data that although quantitatively there are twice as many persons without a previous heart attack as compared to patients with a previous heart attack, we observe an equal distribution of procedures such as angioplasty and bypass surgery. One possibility for this (these are patients at entry into our study, not the end result) is that unnecessary procedures were performed in the so-called "nihilous" cases. However, we have no evidence for this.

Most of the patients in our study underwent echocardiography (EchoCG). The presence of a impaired echocardiography findings does not determine how these patients should be treated. At the time of their inclusion in our study, most of the patients had a normal Echocardiogram. In 12.4% of the examined persons, a previous bypass was present. It is interesting to observe that their amount is twice that of patients who do not have normal left ventricular function. There, the presence of bypass is twice less. Of course, quantitatively the two groups are not the same. Again, we want to emphasize that these data are from the so-called "group on initial inclusion". If you take data from the STICH study into account, we'll see that you're much more likely to have a low ejection fraction in the baseline group and get a bypass than not. Another finding that is important to discuss is that it is not necessary (and in our study this is clearly evident) to have a "reverse" approach to therapy. That is, if a patient is on bypass at inclusion, at the end of our study he is on drug therapy, or vice versa. In our follow-up, if a patient had insufficiently viable myocardium, then at the end of our study he was on drug therapy.

For inclusion in our study, the presence of a previous procedure is not a determining factor (tables 1-8). Only 12% of those patients with normal nuclear (nuclear) examination parameters had previous bypass. In the case of persons in whom an abnormality was registered during this examination, the percentage is lower - 6.3%. What we want to show with the data in Table 1-8 is that the presence of a bypass does not predict a negative nuclear (nuclear) study later in follow-up. Also, the presence of a procedure is not a determinant of inclusion in the follow-up group. How is it determined whether a patient will be enrolled in a 99Tc trial? From Table 1-9 we can see that the major determinant is angiography. In other words, in the presence of an angiography indicating the presence of coronary disease, and if it is necessary to specify whether this disease should be treated or not - we perform a test with 99Tc. Another indicator that is decisive is the presence of angina. Angina is clinically proven by the specified indicators. As we have already indicated above, the anatomical changes are also decisive, since it is necessary to know which lesion and which region of the myocardium is significantly threatened, and which is not. One of our main differences with the STICH study is the presence of myocardial infarction (MI) and its chronic treatment. The presence of MI in the indicated examination is decisive for performing a nuclear (nuclear) examination, regardless of the patient's symptoms. In our study, only clinical evidence of ischemia was subjected to such an examination. To clarify, while in STICH any disease with possible more than two vessel disease a nuclear or other semi-analog study is done regardless of the patient's symptoms, in our group the patient must have a reason by clinical criteria to be included in the study.

The chest pain. The presence of chest pain did not determine inclusion in the study. It is logical to ask – why not? We must not forget that chest pain can be typical or atypical. We must also not forget that chest pain in 90% of cases is due to heart, stomach or muscle conditions. Very often (if not most of the patients) who are referred for chest pain have atypical chest pain and most often it is due to muscle spasm or stomach discomfort with a good history taking and a well-conducted examination.

On the table 1-10 again shows that the presence of angina is not a determinant of stenting in the initial (input) group of patients. The data also show that the patients who entered our study as a group without angina had almost the same amount of "diagnostic" reasons as those with angina because of the presence of heart failure. It should be mentioned that the presence of heart failure does not predetermine the performance of angiography. Only the presence of HF and evidence or suspicion of coronary disease - such as the presence of angina or equivalent - are decisive. Based on this, we can argue that in our study, angiographies were not performed unnecessarily.

The data in Table 1-10 also show that to prove the above statement, the fact that the proportion of patients with a previous stent or bypass was greater in the diagnostic angiography group (34% and 35%) is telling. The same, but not to such an extent, applies to patients with heart failure (5.9%). Diagnostic angiographies are in 5%.

In Table 1-11 we can see the proportion of patients who had a normal stress test compared to the use of dipyridamole or adenosine. Obviously, performing a dipyridamole test or an adenosine test is significant in number. It should be noted that from a diagnostic and procedural point of view, the stress test is always preferable to the chemical test. It gives a better idea of how the patient takes the physical effort tolerance, there is a good increase in the heart rate, the doctor has a good relative idea of the increase in oxygen consumption in the patient. Unfortunately, the older a person is, the smaller is his possibility for physical exertion. The latter also depends on high weight mass or additional diseases or recent surgical intervention. We must not forget the well-known rule that elderly patients recover up to about 50% of their physical capacity after any operation. The data in the table should be interpreted carefully. 1-12. It should not be forgotten that it refers to patients who are referred for nuclear assessment after the specified procedures, which were performed in the "past time" (this is not specified in the present work, because whether it is 1 month or 10 years before being included in the group, it does not matter how old the surgery was). It is interesting to see that the non-ischemic group had the highest number of bypasses. What could this mean? One possibility (which is the more likely) is that the presence of a bypass immediately predisposes the physician's reasoning (including in our strict angina metrics) to the possible presence of ischemia. The same applies to angioplasty. When looking at these data, on the other hand, we can see that some ischemia is present in about 25% of cases overall (with "minor" ischemia being predominant). Table 1-13 shows a broadly similar distribution of data. Negative results (negative test) from nuclear (nuclear) examinations prevailed in the majority of the group that had prior invasive therapy (bypass or angioplasty). Most (81%) of the patients, before entering the study, were on drug therapy without having had a previous intervention. The remaining 10% and 7% had previous bypass or angioplasty, respectively. In this group, again, it can be seen that only 1/4, or 53 patients, had a more positive (meaning not significant) nuclear test. The others did not.

Another interesting result that can be seen from the data - again, we must not forget that the data from table 1-14 are "post-factum" for the patient, i.e. finding a heart attack - small, medium or large - is after performing a nuclear examination on the patient and visualizing the heart attack. Interestingly, no bypass was placed in the large infarct group (and in terms of the STICH study, this group should have the highest amount of revascularizations, especially surgical ones). The non-heart attack group had the highest number of bypass surgeries. This is interesting as a cause in a general population. The largest amount of bypasses was in patients without a proven heart attack post factum. This is hard to argue as fact or reason. Patients who should not have had a bypass? We don't know, since its existence is already a fact. But one thing is clear and obvious – the patients with large heart attacks were not operated on and this is in clear contradiction with the current research.

Next was the initial treatment group who had a heart attack or not. It should be noted that this group of patients had a heart attack in the past, not a recent heart attack. They were assigned to the group based on the presence of a heart attack in the past. This was established by data from nuclear medicine. From the data, we can see that whether or not they had a heart attack, the percentage of patients who are referred for bypass surgery is close - about 10%. The same applies to patients who have undergone angioplasty. With or without a heart attack, this figure is about 7%. Again, it can be seen that the size of the infarct does not play a decisive role in the treatment of the patient. Also, the presence or absence of a heart attack generally did not determine how the patient would be treated. This is important when our data are compared with data from the STICH study (9), as they contradict the STICH findings.

In table 1-16 we can see the distribution of patients according to their body mass. In general, it can be seen that apart from the peak around 70 kg – where there are significantly more patients who are referred for surgical intervention, in the other groups the treatment percentage was approximately the same. The greater the patient's body weight, the more the risk increases for them especially in case of surgical intervention. Therefore, in patients with a higher body mass, surgical intervention is less often resorted to (we must not forget that these patients are less mobile, have a lower tolerance for physical exertion). Because patients are immobile and do not move, they do not increase their heart rate and therefore have fewer angina attacks.

The next assessment is age and surgery. As can be seen from Table 1-17, the highest percentage ratio for surgery is in the 60 to 76 age group. In principle, this is logical. This age group is most often affected by coronary disease. At this age, functional capacity usually begins to decline and patients pay more attention to their symptoms. From table 1-17 it is clear that, in general, the percentages of angioplasty, except in quite old age, where in most cases it is a "life-saving" procedure, in other ages the percentage ratio is approximately the same - about 6%. Considering our overall patient population - 15% for bypass and 6% for angioplasty, in proven patients with previous coronary problems - this is a fairly low rate.

In Table 1-18, we discuss the Syntax score and our initial treatment. Let's recall that, according to generally accepted recommendations, a Syntax score of up to 10 is an indicator for referring the patient for angioplasty. With a Syntax score of 10 to 22, the therapeutic approach is at the discretion of the physician, and above 22, surgery is preferable (5). What can we see from Table 1-18? We have patients referred to us for the first time for a thorough examination for heart pathology after a preventive examination with their treating physician. It may be noted and may cause possible criticism that patients with a low Syntax score are referred for surgical intervention rather than angioplasty (in most cases these are patients with a poor ejection fraction). As the Syntax score increases, the proportion of patients who are referred for procedures drops sharply. The relative share of patients (23%) who were previously bypassed is significant, and they were left on pharmacotherapy and were not sent for operative or interventional treatment.

In the next two tables - 1-19 and 1-20, which are close in meaning, we discuss the ejection fraction, which is estimated in table. 1-19 by echocardiography, and in tab. 1-20 – with nuclear research. What is the difference? Echocardiography usually gives perhaps more deviations from the "true fraction". This is because in most studies it is done on a one-dimensional echo and there are areas that can be overestimated or underestimated. Nuclear research generally provides objective data on the ejection fraction. However, it also has its drawbacks. This is mainly the dispersion observed in the image and the insufficiently linear estimation of the silhouette. So maybe the truth lies somewhere between the two studies. Table 1-19 presents data with an interesting evaluation of the treatment of patients according to their ejection fraction. It should be seen from the relative distribution of patients that perhaps the group below 10% has a high bypass rate, but that is only 1 patient. In the same comparison, the largest group of patients sent for bypass, namely 10, has an ejection fraction of about 60%. The smaller the relative ejection fraction, the fewer patients were referred for operative or interventional treatment. This is very defining for our research. We refer patients for procedures if we are reasonably certain they will survive the procedure. In our research, there is no so-called "dark period" of a month or two after surgery or angioplasty - where there is a so-called MACE of 30 days, in which many studies exclude these patients. We included all patients we assessed at baseline as well as their comorbidities from baseline to the end of the study.

If Tables 1-19 and 1-20 are to be broken down, one can see the difference of significance for the operative group, which is given by echocardiography as 50+ to 60%, while in nuclear examination it is between 40 and 60 %. This is due to the research technique. Again, in the nuclear examination table, it can be seen that in the elderly group there were relatively more procedures, such as angioplasty, which were mainly palliative.

Discussion of follow up

We should point out that the difference between the initial follow up and the later follow up should be noted in these tables. In Table 2-1, we have an initial follow-up that is up to 6 months. The importance of the fact that the pharmacotherapy group was much larger than the surgical or procedure group should be emphasized. At first glance, it can be seen that the lowest mortality is in the group that was operated on. However, as a number, it is very small - 22 people, of which 18 are alive and 4 have died. So the death rate was lowest for the group that was treated with surgery. This is of course relative because this group is very small. The lowest post-procedural mortality is in the angioplasty group, where there is one death and 14 alive – this gives 93%, but again the group is small. The number of deaths in the group left on pharmacotherapy is impressive – 26% (73% alive). Is this perhaps a rather high rate for the drug treatment group? The pharmacotherapy group had a high Euroscore for operative mortality. Also, this group was in many cases not suitable for surgical treatment. Here the data also refer to table 2-2 - the absolute value is given there.

In Table 2-3 we see the additional trace. On average, it was about 3 to 5 years (if the patient was alive until then). Again, let's not forget that these were patients who in most cases were elderly or had significant comorbidities. Most of the patients were not good candidates for angiography. Many had significant comorbidities. In this follow-up, we see how things have turned in terms of mortality. Of the individuals who had angioplasty, only 2 are alive. This also applies to the surgical treatment group. In the pharmacotherapy group, things did not change much. And the status quo from recent and long-term follow-up has remained more or less the same - there are 46 dead and 153 alive. Although the percentage ratio is in favour of the procedures, it can clearly be seen that the drug therapy group has the most survivors.

Long-term follow-up Table 2-4 examines mortality in men and women. Mortality is lower in men than in women. In men it is about 20%, and in women about 36%. In general, the fact that with long-term pharmacotherapy of coronary disease and in the presence of heart failure, mortality in women is higher than in men is known [183]. Our data also confirms this.

In the following age comparison table 2-5 - at follow-up it can be seen that as age increases, so does mortality - from 11% at a young age to 24% at an older age. This is also a known fact (184). It is different that postoperatively at a young age the mortality rate is greater. This is the only major difference for young age in postoperative care. We have no such patients in our study.

The following table, which examines patient weight in relation to mortality - table. 2-6, shows that in the range of very low weight patients, mortality is high because these are patients with advanced heart failure in the stage of cardiac cachexia. After this group we have a slow rise in mortality with increasing overweight. It should be noted that overweight is not a determinant of mortality. Basically, it leads to a significant amount of conditions such as hypertension, diabetes, elevated cholesterol, which are identified as risk factors. Obesity has not been identified as a risk factor.

Table 2-7, where mortality after angiography is assessed, shows that in patients without angiography, it is higher. Of course, the question arises as to why there is a higher mortality in patients who did not have angiography than in those who did. The question is strange, but logical. It is always assumed that the procedural risk is greater than that of no procedure. But of course, we must not forget that patients without angiography were at a higher risk of death from other diseases. Their co-morbidities are also one of the reasons why angiography was not assigned to them, but a study was done - in this case a nuclear (nuclear) study to see if they really need angiography. If these patients were to undergo such a procedure, their mortality would probably be higher.

Table 2-8 examines mortality in patients with diabetes. Diabetic patients are known to have greater mortality and morbidity than other groups. This is especially true for women with diabetes. The latter have a higher mortality rate than men in general when it comes to heart disease and especially when they are also diabetic. There were relatively few diabetics in our group, but their mortality was 50% compared to the other group's 22%. It is logical to have this result especially in diabetics.

Table 2-9 describes mortality in patients with hypertension. Hypertension is a widely recognized risk factor. It has been extensively reviewed in the Framingham study (185). This study in regression statistical form shows us that if hypertension is not treated, it increases the mortality almost twice. If the hypertension is controlled with medication, then this risk is greatly reduced, and the regression analysis shows us that if the hypertension is treated to normal levels, then the death rate is only slightly higher than in the non-hypertensive patients. It is strange that in the results of the patients who do not have hypertension, the mortality is much more than those who have hypertension. We must not forget that the patients in our study were individuals treated by multiple colleagues before entering the study, and in all cases they already had their hypertension treated and controlled. But patients with hypertension, although their number is small, they still have an increased mortality. And that's with controlled hypertension. This again shows us that hypertension of any kind leads to an increase in mortality.

In Table 2-10, we discuss the outcomes of the presence of angina and mortality. Let's not forget that these are patients who have clinically or anatomically proven coronary artery disease. They are on therapy. In our study, most of the patients were on pharmacotherapy. Drug treatment is not maximal, it is optimal. So if the patient does not complain of symptoms of angina, then the treatment is not increased. If there are such complaints, then the treatment is increased. Let us not forget that the presence of angina does not determine mortality. In patients with angina, however, physical activity decreases. When they feel pain, they stop exercising. This is probably one of the reasons why these patients do not exercise. So with these data it can also explain why the patients with less complaints died more because their workload that they did in daily life was more than what they should have done.

Table 2-11 shows that patients initially admitted with myocardial infarction have an approximately 8% higher mortality rate than patients without one. That's not a high percentage. It is generally accepted that patients with myocardial infarction theoretically have a higher mortality rate than those without. And it is also assumed that patients with post-infarction angina have a higher mortality than those without it (186). We have no patients with untreated post-infarction angina, which explains the relatively slightly higher mortality in the group of patients with or without a heart attack. We must not forget that this table includes all patients with myocardial infarction. Those who have heart failure also fall into this group. Heart failure generally leads to an increase in mortality by itself. We did not subanalyze which patients with heart attack had heart failure. This is not the purpose of our study, to determine which patients with heart failure and heart attack have a shorter survival. This quantity is already well known. Our interest is - if the patient has experienced a heart attack and heart failure and is on pharmacotherapy instead of being treated surgically, his chance of survival is greater!

Table 2-12 compares the data of patients with a normal echocardiographic finding with those with an abnormal one. From this table, it is logical to see that patients with a normal ejection fraction have a lower mortality than those with an impaired fraction.

In table 2-14 we can see what the mortality rate is in those patients who had a normal nuclear examination, (no information - means no information about ischemia and cardiac involvement or infarction; negative means - no ischemia). It can be seen that where the comment is - no ischemia - the mortality is the least compared to those for whom there is no evidence of a heart attack. Where the nuclear examination shows pathological findings, the mortality rate is higher.

In the group, a patient with a negative nuclear examination also had mortality, but it was not from heart disease, but from concomitant illness.

In the table 2-15 examines telephone follow up and the mortality that is identified from that follow up. First we need to say how this phone follow up was done and why. When asked how, patients received a phone call on average between 3 and 5 years later. This period was chosen to see if there was any significant survival rate. The format of a telephone interview was chosen, because in many cases these patients are not in the area of our practice, they live far away and go to other regional doctors. With us, they were only for the initial treatment and establishing the diagnosis. They are then referred to their own doctors. The phone call includes a comprehensive questionnaire to the patient - but ultimately it asks basic questions - is the patient alive, is he feeling well, is he having chest pain, what is his functional class (is it more than II on the NYHA), is he adheres to his drug therapy and whether the latter has been changed. A few more general questions follow. In cases where the patient died, it was established when this happened either from information from relatives or from the central information system of the State. The group on which this was done diagnostically - or without preliminary data - was made up of 98 people. Of these, 23 have died (24%), and 75 are alive (77%). That is, it appears that we have mortality in patients in whom this procedure is performed to prove and rule out the finding of significant coronary disease. Next is the heart attack group, which we do not need to evaluate in detail because it is extremely small. The other two significant groups are those with "angina/ischemia" and "heart failure". It can be seen from the data that both groups have almost the same mortality as the diagnostic group. This speaks extremely well for our approach to the treatment of patients, as their mortality (from angina and HF) is the same as the diagnostic group.

The following Table 2-16 looks at how a given test was done and patient survival. It goes without saying that a patient's survival does not depend on the test they are given. But indirectly the conducted test reflects the functionality of the patient. In a stress test, it is clear that the patient was able to undergo this stress. If a persanthin test was performed, the patient was unable to walk but was not in a high-risk group for death since the test was performed (persanthin blocks the entry of ATP into the myocyte and thus it accumulates extracellularly and leads to vasodilation). Administration of adenosine avoids the blocking of ATP channels and this stage of hyperemia passes much more quickly. The latter test has a lower risk than the persanthin test and is used for high-risk patients.

From the data in the table, we see that the patients who were able to do stress test with effort- 85% of them are alive and 15% died. This fell to 73%/27% in the persanthin test group, respectively, and mortality was high in the adenosine group. We emphasize that it is a question of mortality in the follow-up after time, not after the test! It seems that firstly, it was right to do an adenosine test in the high-risk group - they have a high mortality rate, and doing any other test could have resulted in the patient's outcome.

Second, these patients did not necessarily die of heart disease. Overall, this table shows that careful consideration should be given to what test to perform on a patient for an optimal treatment decision.

In Table 2-17, we look at the patients after the nuclear examination and the determination of whether or not they have ischemia. What is the mortality in the definition of small, minimal, moderate ischemia, as well as the absence of ischemia. Interestingly, an average was not observed in our study. The question of why was explained by the fact that the presence of such was determined by clinical indicators (including a normal stress test) and it was not imperative to do a nuclear examination. However, these studies are done to prove or disprove something and because of their very high sensitivity and specificity and giving accurate indicators of the area of ischemia. And so from the indicators in the table. 2-17 we can see that with small, minimal and no ischemia mortality and survival are almost the same. That is, with pharmacotherapy, almost the same result is achieved, both in those without ischemia, established by nuclear (nuclear) examination, and in those with small ischemia. So this shows that in most cases operative or interventional treatment is not required. Drug treatment gives equally good results instead of exposing the patient to the risk of surgical or interventional treatment.

Table 2-18 somewhat complements Table 2-17. The aim is to directly see the presence of ischemia as - YES or NO. Although the number of patients was not the same in the two groups, it was clearly seen that in the ischemia group the mortality was low (20%) and even lower by 3% than that in the non-ischemia group. Again, this gives us reason to argue that pharmacotherapy in high-risk patients with minor angina or ischemia is a much better option than invasive or surgical treatment.

Tables 2-19 and 2-20 we will consider them in general. In the first, heart attacks are divided into small - survival 100%, medium - survival 70%, and large - survival 56%. The latter coincides with mortality and survival in patients with heart failure. In small and medium we do not have heart failure. Interestingly, the group without myocardial infarction had a 10% greater survival rate than the group with myocardial infarction, and it was an average of 80% versus 70%.

Table 2-20 gives the heart attack as a general phenomenon - its presence or absence. In principle, we know (and we also know from the above tables that heart attack is significant for mortality when it is large). We have already seen that small heart attacks do not lead to high mortality. The table shows that in our study, where patients were treated primarily with medication rather than procedures, the mortality rate in the presence of a heart attack was 30%, and in the absence of one - 21%. The difference is statistically significant, but not "astronomical", i.e. – 9% is an acceptable difference to treat the patient with drugs instead of sending him for surgery.

Table 2-21 has a philosophical meaning (and medicine is a part of philosophy, because for a long time there were only two proven sciences - philosophy and mathematics). Here we use Syntax score. But everyone will ask - why use Syntax score, since no procedures will be done. The Syntax score is a procedural calculation of what to do with a particular patient – in terms of risk, ie. if the Syntax score is risk-determining, then why score patients who are not going to have a procedure. The answer is that we did it to show that from low to high Syntax scores, from 0 to 26, the mortality rate differs by approximately 3%. This is after patients have been treated with medication. Of course, the procedural mortality of these patients is significantly higher. With us it is only a few percent. This again demonstrates that pharmacotherapy is much better. The risk is lower. And to summarize, the lowest mortality is in patients with the highest Euroscore. This is completely contrary to any current understanding of interventional cardiology that invasive treatment produces much better results. On the contrary, the more anatomically complicated pathology a patient has and has no complaints, and if this patient is treated with medication, the greater his chance of survival.

Table 2-22 presents the echocardiography data for patients at telephone follow-up. It can be seen that the lower the ejection fraction, the lower the survival in these patients. And that's logical. Mortality depends mainly on heart failure, not angina. And this is the main flaw of research. If a patient has heart failure, then their mortality depends on the heart failure, not on whether they have angina or a small heart attack. The latter does not determine mortality. Heart failure defines it. It is important to mention that heart failure and the presence of angina are predisposing factors for the development of terminal arrhythmias. Where in the column we have missing information, it means that these patients were not classified as having angina or heart attack.

The following table 2-23 is close to the previous one. But the ejection fraction is estimated by nuclear (nuclear) and not by subjective method. Again we see similar results that the better the ejection fraction the better the patient survival. This confirms the echocardiographic findings with greater certainty. Again, let's say - the patient is not dying of angina, he is dying of heart failure (and/or having angina causing an arrhythmia in heart failure). And all interventional treatments lead to the same outcome as drug treatment, which is much less risky.

CONCLUSIONS

1. Patients with advanced left ventricular dysfunction and coronary artery disease do not need an angiogram unless they have marked angina of III-IV functional class.

2. Assessment of their viable myocardium is most important, including to assess the need for planning for possible intervention.

3. Patients who do not have sufficient (above 20-30%) viable myocardium do not need angiography, as there is no need for intervention and the angiogram will delineate the anatomical problem but not the physiological need.

4. Patients with prior coronary artery disease and an intervention related to CABG or angioplasty presenting with chest pain and without obvious coronary pathology are probably better evaluated by noninvasive nuclear testing for the need for performing a procedure.

5. Patients with a previous procedure and/or known coronary artery disease are probably better off undergoing noninvasive testing to assess the need for a procedure, given their advanced age and comorbidities.

6. It is very reasonable to perform non-invasive nuclear (nuclear) studies in suspicious patients who have suspicious complaints and ischemia is not certain, including quantitatively.

7. ECG changes and LV dysfunction in patients with coronary artery disease and a previous procedure (or without it) can be interpreted differently. Nuclear tests yield the best evaluation in these patients.

8. There is a significant reduction in unnecessary procedures when an anatomic problem exists but a physiologic substrate is lacking.

9. There is a significant reduction in perioperative mortality with drug treatment of patients, the risk of perioperative death is also reduced.

10. There is a reduction in morbidity and mortality in patients who would undergo unnecessary percutaneous procedures.

11. There is a reduction in renal nephropathy in these patients (with renal dysfunction) due to a non-performed procedure such as doing angiography or surgery.

12. Arterial hypertension is a greater cause of coronary disease than diabetes.

13. Arterial hypertension, weight, female gender, but also diabetes are important for comorbidity.

14. Coronary artery disease can occur without ischemia.

15. In contrast to the STICH study, after 6 months there was no mortality in the medical treatment, and there was even an improvement in the functional class (the complete lack of mortality is perhaps accidental).

16. Non-coronary ischemia plus comorbidity is more dangerous and here invasive procedures are more dangerous.

17. With left ventricular dysfunction and a high Syntax score, mortality is close to reperfusion and drug treatment.

18. With nuclear (nuclear) examination, there is a reduction in risk for patients, because in angiography, a lot of contrast is given and there is a risk of developing contrast-induced nephropathy. When angiography is not performed, patients receive less fluid and this helps prevent pulmonary edema from developing.

19. There is also technical relief for patients who are over 140 kg and cannot go to the catheterization table.

20. There is also a reduction in perioperative risk in patients with advanced COPD, advanced kidney disease, transplant candidates, multiple co-morbidities.

21 Obese patients with a femoral approach are at significant risk of perioperative bleeding. Avoiding and not performing a procedure that is not necessary in certain patients reduces the risk.

22. Patients with renal failure in all cases benefit enormously because of concomitant contrast-induced nephropathy in 100% of cases with advanced renal failure.

23. Elderly patients are excluded from the risk of a possible complication due to extreme calcifications that they have in their vessels in more than 50% of cases.

24. Patients with left femoral block do not always need angiography to rule out the cause of mild pain. The stress test is inconclusive because it relies only on symptom data. Performing a nuclear (nuclear) study proves the presence or absence of significant coronary disease. This is particularly valuable in individuals who are problematic for one reason or another for coronary angiography.

CONTRIBUTIONS TO SCIENTIFIC WORK

1. Patients with advanced left ventricular dysfunction do not require an angiogram unless they have severe angina.

2. The assessment of the volume of viable myocardium in advanced left ventricular dysfunction is most important for planning a possible intervention.

3. Patients without sufficient (over 20-30%) viable myocardium do not need angiography, as there is no need for intervention and the angiogram will outline the anatomical problem, but not the physiological necessity.

4. Patients with questionable symptoms presenting with anginal symptoms are probably better evaluated by noninvasive nuclear testing for the need for a procedure, especially in the presence of comorbidity.

5. Patients with a previous procedure and/or known coronary artery disease are better off undergoing non-invasive testing.

6. Quantitative assessment of the level of ischemia before an invasive procedure is a reasonable approach to save the patient unnecessary procedures and gives correspondingly better financial results.

7. Nuclear tests yield the best assessment in patients with left ventricular dysfunction.

8. Reduction of perioperative mortality with drug treatment of high-risk patients.

9. There is a reduction in renal nephropathy in patients who did not undergo angiography.

10. Non-coronary ischemia combined with comorbidity is more dangerous and in these patients invasive procedures do not give the desired result.

11. There is a reduction in the risk of pulmonary edema in patients with nuclear examination.

12. Reducing the risk in elderly patients of unnecessary invasive/surgical procedures

13. Patients with left femoral block can be evaluated without angiography.

PUBLICATIONS RELATED TO THE SUBJECT OF THE DISSERTATION PAPER

Publications in scientific periodicals

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2. Goldberg L., Grigorov V., Mekel J., Landless P., Smith D., Varbanova M. Miocardio vitale: meccanismo della reversibilita della disfunzione del miocardio nei casi di malattia delle coronarie. Cardiologia (ISSN 1311-8501), October 2001, № 2, pp. 7-20.
3. Goldberg L., Grigorov V. Infarto del ventricolo destra. Cardiologia (ISSN 1311-8501), Aprile 2002, № 3, pp. 5-18.
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5. Григоров, Вл., Е. Григоров. Оценка на преживяемостта при пациенти с коронарна болест със и без преживян миокарден инфаркт. Сърдечно-съдови заболявания (ISSN 0204-6865), 2022, № 2, с. 34-40.
6. Григоров, Вл. Петгодишна преживяемост при пациенти с подозирана коронарна болест – точност на преценката в зависимост от метода за установяване на заболяването. Медицински преглед (ISSN 1312-2193), 2022**,** № 3, с. 48-54.