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Group: 33

CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH REDUCED, MID-RANGED AND PRESERVED LEFT VENTRICULAR EJECTION FRACTION

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SUMMARY

Author’s name: Ahmad Hussein.

Research title: Clinical characteristics and outcomes of patients with reduced, mid-ranged and preserved left ventricular ejection fraction.

Research aim: This study aims to describe the clinical characteristics and outcomes of patients with HFpEF, HFmrEF and HFrEF in Lithuanian university of health sciences’ (LUHS) Kaunas clinics and light-up the difference in prescribed treatment in each type of heart failure.

Objectives: 1. To compare gender and age differences in HF patients. 2. To compare demographic and cardiovascular risk factors in HF patients. 3. To compare instrumental tests results among them. 4. To compare the treatment given to each type of HF patients.

Methodology: A prospective study was conducted in LSMU Kaunas clinics, which included 124 HF patients, who were admitted to the Cardiology department during 2018 and 2019. These patients were classified into three groups: HFrEF (EF<40%), HFmrEF (EF 40% to 50%) and HFpEF (EF>50%). Demographical information of patients was taken, as well as chief complaints, concomitant diseases and risk factors which could contribute to HF development. Results of the laboratory and instrumental tests were analyzed, and treatment was given accordingly. Statistical studies were made using IBM SPSS statistics program.

Results: 73 males (58.9%) and 51 females (41.1%) were hospitalized due to HF symptoms. The mean age of patients was 74±3, 69±6 and 68±12 (p value= 0.034) in HFpEF, HFmrEF and HFrEF patients respectively. 15 patients had HFpEF (19%), 31 had HFmrEF (39.2%) and 33 had HFrEF (41.8%). 40% of patients with HFrEF had RF and 54.54% had Afib when 22.58% of patients with HFmrEF had RF and 51.61% had Afib and 13.33% of patients with HFpEF had RF and 26.6% had Afib. 15% of patients with HFpEF had rales in their lungs while 31% of patients with HFmrEF and 33% of those with HFrEF had it. 40% of HFpEF patients presented with chest pain and 33.3% with dyspnea same as in patients with HFmrEF. Echo results showed that patients with HFrEF were more likely to have MR and TR compared to those who had an HFpEF (75.75% and 26.6%) and (75.75% and 20%) respectively, while AR was seen in those with HFmrEF (19.35%) whom 51.61% of them had MR as well. For treatment, patients with HFrEF were given low dose diuretics with high doses of ACEI and B-blockers and spironolactone, while patients with HFpEF profited from a low dose of diuretics, ACEI and B-blockers, patients with HFmrEF, were prescribed the same treatment as for those with HFpEF except for a higher dose of B-blockers.
Conclusions:

1. Patients with HFpEF are older and more often women.
2. Patients with HFrEF suffer more from RF, Afib, and rales in lungs while HFpEF patients suffer more from AH, HFmrEF patients had a more similar clinical aspect of those with HFpEF.
3. Enlarged ventricles along with mitral and tricuspid regurgitation were more pronounced in HFrEF.
4. HFrEF patients are prescribed a low dose of diuretics, high dose of ACEI and B-blockers, and spironolactone. HFpEF patients are best treated with a low dose diuretic, a low dose of ACEI and a low dose of B-blockers, spironolactone is less prescribed in this group. HFmrEF patients have prescribed the same treatment as for those with a preserved EF but with a higher dose of B-blockers.
CONFLICTS OF INTEREST

The author reports no conflicts of interest.

ETHICS COMMITTEE APPROVAL

Title: Clinical characteristics and outcomes of patients with reduced ejection fraction and preserved left ventricular ejection fraction.

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ABBREVIATIONS LIST

HF: Heart Failure.
HFpEF: Heart Failure with Preserved Ejection Fraction.
HFmrEF: Heart Failure with mid-range Ejection Fraction.
HFrEF: Heart Failure with Reduced Ejection Fraction.
EF: Ejection Fraction.
LVEF: Left Ventricular Ejection Fraction.
RF: Renal Failure.
AFib: Atrial Fibrillation.
CAD: Coronary Artery Disease.
MI: Myocardial Infarction.
DM: Diabetes Mellitus.
NSAIDs: Non-Steroidal anti-inflammatory drugs.
LAVI: Left Atrial Volume Index
LVMI: Left Ventricular Mass Index
TRV: Tricuspid Regurgitation Velocity
LVEDV: Left Ventricular End Diastolic Volume.
LVESV: Left Ventricular End Systolic Volume.
LVEDD: Left Ventricular End Diastolic Diameter.
MR: Mitral Regurgitation.
TR: Tricuspid Regurgitation.
AR: Aortic Regurgitation.
LVAD: Left Ventricular Assisting Device.
LA: Left Atrium.
RA: Right Atrium.
TERMS

There were no specific or rarely used terms.
INTRODUCTION

Heart failure (HF) is a common phenomenon around the world accounting for 31% of all global deaths [13], this syndrome can be caused by any anatomical or functional disorder which decreases the ability of the ventricle to either fill or eject blood. Diseases of the myocardium, pericardium, endocardium or heart valves are the leading causes of heart insufficiency. Nevertheless, metabolic disorders like hyperthyroidism, diabetes, and obesity play a leading role in heart failure occurrence [1].

Previously patients were classified into two main classes: heart failure with reduced ejection fraction (HFrEF) where the left ventricular ejection fraction (LVEF) is less than 40% and heart failure with preserved ejection fraction (HFpEF) in which LVEF is above 50% [2].

In 2016 the publication of the European Society of Cardiology guidelines introduced a new classification for the patients who were previously counted as "grey area." These patients were either excluded from the researches or were included in the other groups which caused diminished information about the characteristics and prognosis of these patients. The new class is known as heart failure with mildly reduced ejection fraction (HFmrEF), which includes the patients who have LVEF more than 40% but lower than 50% [2].

The main goal of adding this new group was to clear this “grey area” and give its patients their rights by including them into the researches and studies since they were not included in HFpEF or HFrEF groups of patients into any studies. Going back to the previous studies and reanalyzing them according to the new classification of HF showed that there is a compelling difference when compared to HFrEF and HFpEF patients plus when it comes to treatment, the response to medication differs between each class of HF patients in terms of effectiveness. A controversy was initiated upon where do HFmrEF patients fit in, some studies have shown that they perfectly fit in between HFpEF and HFrEF patients in terms of mortality rate, while other studies have shown that HFmrEF patients’ phenotype resembles one of the HFrEF patients and have the same prognosis as patients with HFpEF [3]

Studies have shown that patients with HFrEF are younger, more likely to be men, more likely to have coronary artery disease and less likely to have hypertension and atrial fibrillation.

So, our study aimed to compare the clinical characteristics, risk factors and outcomes of each type of HF patients according to the new classification.
Aim: The aim of this study is to describe the clinical characteristics and outcomes of patients with HFpEF, HFmrEF and with HFrEF in Lithuanian university of health sciences' (LUHS) Kaunas clinics and light-up the difference in prescribed treatment in each type of heart failure.

Objectives:

- To compare gender and age differences in HF patients.
- To compare demographic and cardiovascular risk factors in HF patients.
- To compare instrumental tests results among them.
- To compare the treatment given to each type of HF patients.
LITERATURE REVIEW

HF is a dominant health issue around the world with a prevalence over 23 million worldwide, even though mortality due to HF is reducing, hospitalization and readmission due to HF are still increasing. To reduce the number of readmissions of HF patients, predictors of it should be characterized along with the influence of multimorbidity related to coexisting conditions. Patient-centered care had shown that when primary prevention of HF was applied, the incidence of this syndrome has decreased while improving the medical care would increase the chances of survival, and on the other hand, the prevalence of HF would be increasing too [4].

HF is generally classified into acute and chronic HF. However, since 2016 there is a new classification regarding the LVEF: HF with preserved ejection fraction (HFpEF) (when EF > 50%) previously called as diastolic heart failure, heart failure with mid-range ejection fraction (HFmrEF) (EF: 40-49%), a term which was newly introduced to cover the patients with an EF between 40% and 49% to include them in the studies as they were either excluded from the researches or included with other types of heart failure, therefore, they were called to be in the "grey area", and heart failure with reduced ejection fraction (HFrEF) previously called systolic heart failure where EF is < 40%, according to the latest European guidelines which were published in 2016 [14].

HF is classified according to the severity of the patients’ symptoms, as reported by the New York Heart Association (NYHA), into:

Class I (Mild): the patient has a cardiac disease, which does not affect his physical activity.

Class II (Mild): the patient has a cardiac disease which slightly affects his physical activity, but no symptoms are present at rest. The everyday activity would lead to weakness, palpitation, dyspnea or anginal pain.

Class III (Moderate): the patient has a cardiac disease which considerably limits his physical activity, and no complaints are present at rest. Minimal actions would result in fatigue, palpitation, dyspnea or anginal pain.

Class IV (Severe): a patient has a cardiac disease which causes discomfort on any physical activity. Symptoms of heart insufficiency or ischemia might be seen even at rest.

Moreover, according to the objective assessment into:

Class A: No objective sign of cardiovascular disease and no symptoms which affect regular daily activity.
Class B: an objective sign of underlying cardiovascular disease. Mild symptoms which marginally affect daily life activity. Symptoms are relieved at rest.

Class C: objective signs of intermediately severe cardiovascular disease. Natural daily life activity is also affected. Symptoms are alleviated at rest.

Class D: Objective signs of severe cardiovascular disease. Daily life activity is severely limited; symptoms are felt even at rest[14].

HEART FAILURE PATHOPHYSIOLOGY

Heart insufficiency can be caused by either the failure of the cardiac muscle to eject blood or by increased demand even in the presence of almost normal cardiac function. Heart failure would always lead to circulatory failure. Meanwhile, the opposite is not always the case as seen in case of shocks (e.g., Hypovolemic, septic or anaphylactic shock) where shocks cause circulatory failure but the cardiac function could be still preserved to preserve the pumping function of the heart, compensatory mechanisms occur, such as increasing the blood volume, cardiac filling pressure, heart rate, and cardiac muscle mass. Nonetheless, even in the occurrence of these compensatory mechanisms, there is still a progressive decline in the capability of the heart to contract and relax leading to worsening heart failure [1].

The decrease in stroke volume caused by systolic and diastolic heart failure lead to activation of central and peripheral baroreflexes and chemoreflexes, therefore, increasing the sympathetic activity [5][6].

The augmentation of norepinephrine levels is directly proportional to the degree of cardiac dysfunction and has significant prognostic values. Norepinephrine is responsible for various signal-transduction abnormalities like downregulation of beta1-adrenergic receptors, uncoupling of beta2-adrenergic receptors and increased activity of inhibitory G-protein. These changes lead to myocardial hypertrophy [1].

Atrial natriuretic peptide and B-type natriuretic peptide are released endogenously when the pressure is increased in the atrium, or In the ventricle, released from there, they promote vasodilation and natriuresis. They lead as well to decrease cardiac preload and afterload by reducing ventricular filling pressures. BNP, specifically, activate selective afferent arteriolar vasodilation and constrain sodium reabsorption at the proximal convoluted tube, inhibits renin and aldosterone release along with adrenergic activation. ANP and BNP levels are high in chronic heart failure. BNP, in particular, has a high diagnostic, therapeutic and prognostic values [1].
The pathophysiology behind diastolic and systolic heart failure is the same, but each responds to a distinct set of hemodynamic and circulatory factors that reduce heart output [7].

The high ventricular afterload is responded by a modification in ventricle relaxation and augmentation of its stiffness which is caused by a slow calcium uptake by the myocyte sarcoplasmic reticulum and delayed calcium efflux from the myocyte. The defected relaxation of the ventricle then leads to the impairment of the diastolic filling of the left ventricle. This occurs in heart failure with preserved ejection fraction [1].

A study conducted by Morris et al. found that diastolic or systolic dysfunction in the right ventricle is commonly seen in patients with HFpEF. This dysfunction which is accompanied by the same fibrotic processes that are seen in the subendocardial layer of LV may be the primary cause in the symptomatology of patients with HFpEF [8].

**ETIOLOGY OF HEART FAILURE**

HF causes, in a practical point of view, can be classified into four main categories [1]:

I-Underlying causes: this category includes structural abnormalities, congenital and acquired, which affect peripheral and coronary arterial circulation, pericardium, myocardium or even cardiac valves, therefore precipitating hemodynamic burden or myocardial or coronary insufficiency. These factors mostly lead to heart failure with preserved ejection fraction [1]. These causes include:

Causes that lead to systolic heart failure:

- Coronary artery disease (CAD)
- Diabetes mellitus (DM)
- Hypertension
- Valvular diseases
- Arrhythmias
- Myocarditis
- Congenital heart diseases
- Idiopathic cardiomyopathy
- Drugs (such as alcohol, cocaine, doxorubicin) [1].

Causes that lead to diastolic heart failure:

- CAD
- DM
- Hypertension
- Valvular diseases
- Hypertrophic cardiomyopathy
- Amyloidosis, sarcoidosis
- Constrictive pericarditis [1].

II-Fundamental causes: fundamental causes consist of biochemical and physiologic mechanisms that would lead to increased hemodynamic stress or impairment of cardiac contraction due to oxygen insufficiency [1].

III-Precipitating causes: precipitating causes of heart failure are conditions that already existed but compensated their worsening aids in heart failure progression. Examples of such conditions are [1]:

- Worsening of valve stenosis
- Fever
- Anemia
- Medications such as NSAIDs, chemotherapy
- Thyrotoxicosis
- Cor pulmonale
- Glomerulonephritis
- Obesity
- Pregnancy [1].

IV-Genetics of cardiomyopathy: It has been shown that genetic causes play a major role in dilated and arrhythmic right ventricular cardiomyopathy. Restrictive cardiomyopathies are irregular and correlated with the gene for cardiac troponin I. Patients who have first degree relatives who are diagnosed with cardiomyopathy are recommended to be screened. The screening consists of the following: an electrocardiogram and an echocardiogram. LV dysfunction, even in asymptomatic ones should be documented and treated [1].

A stable, compensated condition of a patient with HF can deteriorate and lead to a clinically seen heart failure when an intrinsic process has reached a critical point where it cannot be compensated anymore, e.g., continuous mitral/aortic valve stenosis [1].

A prevalent cause of decompensation of a previously compensated heart failure is not getting rid of risk factors like increased dietary sodium and low physical activity or not taking the medication properly.
The second most common cause is uncontrolled hypertension, which is followed by cardiac arrhythmias, as ventricular, for example, can be lethal [1].

Other cases, when the patient has controlled hypertension, and an asymptomatic left ventricular hypertrophy, heart failure can be decompensated when an MI occurs, thus precipitating the original condition [1].

Studies have shown as well that systemic infections can also precipitate heart failure, as fever increases the total metabolism, along with cough, they increase cardiac stress. A more severe condition is a septic shock, as cardiac contractility is affected by the released endotoxins [1].

A cardiac infection like myocarditis or endocarditis can directly affect the heart function and exacerbate existing heart failure as such infections are usually associated with tachycardia, anemia, and fever, which are stressful factors for the heart and deteriorate its function [1].

Patients with heart failure usually prefer bed rest, which put them into a high risk of forming a pulmonary embolus which then increases the hemodynamic burden on the right ventricle by increasing the right ventricular systolic pressure and some cases are associated with fever and tachycardia thus adding more stress on the heart and by that worsening the already existing heart failure [1].

Other existing diseases like (profound anemia, thyrotoxicosis, myxedema, glomerulonephritis, obesity, pregnancy, and some nutritional deficiencies) can exacerbate the clinical presentation of the existing heart failure as in these cases there is an increased myocardial oxygen demand and consumption to critical level [1].

HEART FAILURE DIAGNOSIS

Two main procedures take place when diagnosing HF: detailed history taking along with the physical examination and instrumental work.

A careful history should be taken as HF symptoms are usually not specific and can be hard to detect in patients with chronic lung diseases, obese patients and in elderly. HF is rarely diagnosed in patients with no past cardiac diseases which might damage the heart, on the other hand a previous myocardial infarction increases the chances of heart insufficiency diagnosis in a patient presenting with dyspnea, tachycardia, cough, reduced ability to exercise and leg edema, thus a detailed history and careful physical examination are critical in heart failure diagnosis.
A typical HF patient would present with symptoms like breathlessness, wheezing, palpitations, syncope, orthopnea, paroxysmal nocturnal dyspnea, reduced the tolerance for exercising, ankle swelling and fatigue. A more specific sign is elevated jugular venous pressure, a lateral displaced apical impulse, and gallop rhythm.

Next step in HF failure diagnosis, not in the acute setting is NT-proBNP plasma measurement, an essential factor in HF diagnosis exclusion, and it can lead to the further management and diagnosis plan. Patients with numbers less than the cut-point for excluding cardiac dysfunction do not need echocardiography and patients with normal plasma natriuretic peptide values are most likely not to have HF.

NPs are elevated not only in case of heart failure, its level can be increased in case of AF, renal failure and in elderly and can be disproportionally low in obese patients; therefore it is not a sensitive indicator of heart failure, but it helps excluding it.

The highest range of B-type natriuretic peptide in a non-acute situation is 35pg/ml, for N-terminal pro-BNP is 125 pg/ml. In acute situation, numbers used are higher: normal BNP values are <100 pg/ml and for NT-proBNP<300 pg/m.

Next step in patients with suspected HF diagnosis is echocardiography that is a simple and widely available method to evaluate the ventricular function in systole and diastole, wall thickness and valve function.

In echocardiography, the following should be assessed:

- Left atrial volume index (LAVI) >34 ml/m²
- Left ventricular mass index (LVMI) ≥115 g/m² in males and ≥95 g/m² in females.
- Tricuspid regurgitation velocity (TRV)
- Left ventricular ejection fraction (LVEF)

The latter makes it possible to classify the patients into patients with heart failure with preserved ejection fraction who have LVEF≥50%, patients with heart failure with mid-range ejection fraction who have LVEF within 40 and 49%, and patients with heart failure with reduced ejection fraction who have LVEF <40%.

To measure LVEF, the modified biplane Simpson's rule is usually used where two parameters, left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV), is obtained from two different views: apical view where four chambers are seen and two chamber view.
Another part of the usual echocardiography examination is the assessment of the right ventricle structure and function, and that is done by measuring the right atrial dimension, checking the RV systolic efficacy and pulmonary arterial pressure, not forgetting the importance of tricuspid annular plane systolic excursion (TAPSE, normal values: >17 mm, a value <17mm indicates a right ventricular systolic dysfunction).

Stress echocardiography is also always a choice to assess inducible ischemia and heart muscle viability by exercising or by inducing it pharmacologically.

A chest X-ray can always be performed for differential diagnosis purposes to determine if a pulmonary disease is the origin of the patient’s symptoms plus it shows signs of pulmonary congestion or edema in HF patients. On the other hand, cardiac magnetic resonance is agreed to be the gold standard for cardiac function assessment in terms of ventricles’ volumes and EF measurements. Using late gadolinium enhancement in T1 images makes it possible to determine the HF etiology making the CMR the preferred imaging method in checking myocardial fibrosis, ischemia, amyloidosis, sarcoidosis, and CAD.

In case of a patient suffering from angina pectoris unresponsive to treatment, or having a history of ventricular arrhythmia, coronary angiography is recommended which has both significances in diagnosing CAD indicating its severity and treating it, which could be exacerbating the HF condition. Another indication for coronary angiography is HF patients showing ischemia signs in non-invasive stress tests so we could determine the reason for ischemia and the proper treatment.

Another way of visualizing the status of coronary arteries is by performing a cardiac computed tomography, done in patients when suspecting CAD.

An excellent but invasive technique in heart failure diagnosis is right heart catheterization. This tool plays a critical role in the diagnosis procedure as it gives hemodynamic data, from which we can calculate cardiac output, check intracardiac shunts and valves’ condition. This technique is known to be the gold standard method for diagnosing pulmonary hypertension, as well as playing a significant role in patients’ assessment before and after heart and/or lung transplantation [9].

HEART FAILURE TREATMENT AND PROGNOSIS
HF treatment is a complex treatment which starts with lifestyle changes along with medications, then surgery and heart-assisting devices are the adapted option in more severe cases or when the pharmacological treatment is not enough[12].

Lifestyle changes: following a specific lifestyle including changes in the daily diet, exercising and another routine would help in alleviating heart failure symptoms, slowing the disease's progression and boost everyday life [12].

Lifestyle changes consist of:

- Quitting smoking
- Losing weight
- Decreasing or abstaining caffeine and alcohol consumption
- Healthy diet
- Increase physical activity
- Reduce stress
- Enough rest
- Regular blood pressure measurement [12].

Pharmacological treatment:

Diuretics:

Diuretics or so-called ‘water pills’ are a class of drug which enhances the water loss. This process occurs through different ways which include inhibiting sodium reabsorption from the kidneys thus sodium level increases in the urine which leads to water loss, that's the mechanism of loop diuretics, while thiazide diuretics act on increasing the excretion of both sodium and chloride, resulting in water loss, whereas potassium-sparing diuretics act on blocking the exchange of sodium for potassium, leading in a little loss of potassium compared to loss of sodium, again resulting in excretion of more urine [19].

In symptomatic treatment of heart failure patients with lung congestion or peripheral edema, ascites and raised jugular vein pressure, patients are given diuretics to relieve symptoms caused by fluid overload like dyspnea or peripheral edema, as studies have proved their effectiveness in alleviating physical signs, and improvement in cardiac function the same as in body ability to tolerate physical activity. Treatment is always started with low dose diuretic and the dosage increases gradually until urinary output increases, and the weight goal is achieved, then diuretics are continued to prevent recurrent fluid retention. In more severe HF cases, or when patients do not respond adequately to one
diuretic or intravenous administration, then a combination of diuretics like thiazides with metolazone, which have a symbiotic effect along with a loop diuretic, should be considered. When using diuretics, attention should be given to avoid side effects which can be caused by diuretics overdoses like electrolyte disbalance, hypotension, and azotemia, or for a possible interaction with other drugs like when giving potassium-sparing diuretics along with angiotensin-converting enzyme inhibitors (ACE inhibitors) which would lead to hyperkalemia. Even when symptoms are controlled, diuretics are not given as monotherapy, but they should be given with ACE inhibitor or a B-blocker [10].

ACE inhibitors:

ACE inhibitors block the conversion mechanism of angiotensin I to angiotensin II which therefore leads to bradykinin degradation. When this occurs, ACE inhibitors are shifting the balance from the vasoconstriction, salt retention, and hypertrophic effects of angiotensin II towards the vasodilation effect of bradykinin. Considerable studies and clinical trials were made to check ACE inhibitors effect, and the following was proven: ACE inhibitors augment the chances of survival in HF patients and decrease the need of frequent hospitalization, as well as their effect in relieving dyspnea and increasing the exercise tolerance and the ventricular function was also shown [10].

B-blockers:

B-blockers inhibit the effect caused by the activation of B adrenoreceptors which would be harmful to the failing heart. These drugs were contraindicated in HF due to their negative, but recent studies have proven their effectiveness in alleviating symptoms, improving the cardiac function and survival rate. Plus metoprolol has shown a significant effect in improving the LV function in dilated cardiomyopathy and the patient's tolerance to exercising [11].

MRA:

Mineralocorticoid receptor antagonist like spironolactone is an example of a potassium-sparing diuretic, its mechanism of action is described above, plus it inhibits the effect of aldosterone on the heart which makes it preferable over other potassium-sparing diuretics [20]. It could be used with another diuretic to have a synergetic effect and increase the diuresis. It has been widely used in dialysis patients to reach blood pressure goals, and it is showing good results so far. We should mention as well that spironolactone has been proven to reduce the risk of cardiovascular mortality [21].

Ivabradine:
Depolarization of the sinoatrial node which is initiated by opening of ion channels is blocked by Ivabradine thus slowing the heart rate. Not having effects on inotropy, blood pressure and vascular resistance make it a preferable drug over B-blockers [22].

**ARNI:**

Formerly, inhibition of neprilysin alone was attempted, its inhibition leads to increase the excretion of ANP in the urine which would subsequently decrease the blood pressure but increases the levels of angiotensin II thus the blood pressure drop was not sustained; therefore results were considered not to be satisfactory. For that reason, a dual neprilysin and ARB were made, which have shown great results in reducing and maintaining the blood pressure low, as ARB were blocking the side effects of neprilysin inhibitors [23].

**Digitalis:**

It acts by increasing the sodium delivery to the distal tubules which therefore leads to the renin secretion suppression and activation of the parasympathetic system. Although it is widely used in HF treatment, digitalis usage is still a controversy especially when the patient does not suffer from atrial fibrillation (AFib), as then it would be indicated. Due to this debate, many studies were done to check the digitalis effect, and one of them called (RADIANCE) the conclusion was that digoxin would prevent clinical deterioration of the patient and enhances the LV function. [10] on the other hand, some other studies like (DIG) were made on over 6800 patients with HF but without AFib and it showed no difference in mortality rate but there was a significant decrease in hospitalization due to worsening of HF, so the conclusion is to continue using digoxin in HF patients regardless of having Afib or not [10].

**CRT implantation:**

Cardiac resynchronization therapy is mainly used in patients with reduced EF and bundle branch block. This technique consists of biventricular pacing, but it could involve pacing of the left ventricle alone. Patients with failing ventricles are at risk of dyssynchrony of the ventricle which can worsen its function, therefore, resynchronization may help to improve the failing ventricle’s function, it even reverses the remodeling process thus improving the quality of life and decreases the amount of rehospitalization and give the HF patients a better prognosis [24].

**Surgical options:**

A widely used device in heart failure patients when the LV is not capable of pumping enough blood anymore is a left ventricular assist device (LVAD), this device is a mechanical pump which needs a
battery to function, and is surgically implanted. They help the LV to maintain their pumping ability [10].

When are they used? They are mainly used in two cases, the first one as "bridge to transplant" when the patient has to wait until he/she gets a suitable heart for transplantation, to take advantage of the present time or in other words "to buy time" LVADs are used during this waiting time since the patient's heart is not capable of functioning enough on its own. The second case is called "destination therapy" when the patient is in end-stage heart failure, and there is no possibility for a heart transplant [10].

When a blockage of one of the coronary arteries is the reason behind the heart failure, a percutaneous coronary intervention (PCI) or angioplasty is the treatment option to improve the heart function and might alleviate HF symptoms, and that is done by either stenting the blocked artery or by inserting a balloon which would open the artery when inflated, this balloon is removed when the artery is fully opened, and this procedure is known as balloon angioplasty [10].

Patients with valve problems causing heart failure can benefit from valve replacement surgeries, which have already shown to be effective in reducing the symptoms of HF and improving the heart capability to work efficiently. Patients are usually given two options in valve replacement, either to get a biological or a mechanical valve [10].

HF prognosis: HF is an irreversible lethal condition, despite if it has been detected early in asymptomatic patients or it is being treated.

Some studies have compared the five years of mortality in HF patients to cancer patients. The Framingham cohort study can be used as an example. According to it, the probability of death for an HF patient within five years was 75% in men and 42% in women while the prognosis for cancer patients for the same duration of time was a 50% chance of death. On the other hand, the similarity of the Framingham population and the exclusion of the older patients, make the presented information inapplicable on a global basis. Another study “Rochester” was made to estimate the prognosis of 141 HF patients, and the results were as follow: the mean age of patients was 75, and five-year mortality was 67%, so although the same diagnostic criteria were used in both studies, but the prognosis in the Rochester study was better than the other [15].
METHODS

A prospective study was conducted in LSMU Kaunas Clinics, which included 124 HF patients, who were admitted to the Cardiology department during 2018 and 2019. These patients were classified into three groups: HFrEF (EF<40%), HFmrEF (EF ranging between 40% to 50%) and HFpEF (EF>50%).

Patients were interviewed on admission for current complaints, concomitant diseases and risk factors (arterial hypertension (AH), diabetes, chronic kidney diseases, previous myocardial infarction (MI), atrial fibrillation (Afib), smoking and drinking behavior). Demographic factors (age and gender) were noted as well. Tests were made, and treatment was given accordingly.

For this research, the chief complaints of patients were taken, important clinical history, which included concomitant diseases, previous PTCA or surgeries, was included too, the body mass index (BMI) was calculated, blood pressure was measured, patients were auscultated for possible rales and valvular diseases. The following blood test results were used for the comparison: hemoglobin (g/l), potassium (mmol/l), creatinine (mmol/l) and cholesterol (mmol/l) levels. These echocardiography parameters: left atrium (LA) size (mm), right ventricle (RV) diameter (mm), right atrium (RA) diameter (mm), interventricular wall diameter (mm), posterior wall diameter (mm), left ventricular end diastolic (LVEDD) diameter (mm) mitral, tricuspid and aortic regurgitation of moderate and severe intensity, were analyzed to show the differences between the three groups of heart failure.

Statistical studies were made using IBM SPSS 22.0 statistics program. To light up the differences, we used the descriptive analysis, comparative tables and Chi-Square test properties. Results were considered significant when p value was less than 0.05.
RESULTS

The research included random 124 patients, 73 males (58.9%) and 51 females (41.1%) who were hospitalized due to HF symptoms in Cardiology department of Kaunas clinics without applying any inclusion or exclusion criteria. The mean age of patients was 74±3, 69±6 and 68±12 in HFpEF, HFmrEF and HFrEF patients respectively (p value= 0.034). We had 15 patients with HFpEF (19%), 31 with HFmrEF (39.2%) and 33 patients with HFrEF (41.8%).

Table 1. Patients’ characteristics by EF groups.

<table>
<thead>
<tr>
<th></th>
<th>OVERALL (N=124)</th>
<th>HREF (EF≤ 40%) (N=33)</th>
<th>HFMREF (EF 41-49%) (N=31)</th>
<th>HFPEF (EF≥50%) (N=15)</th>
<th>P-VALUE</th>
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<tr>
<td>BMI (KG/M²)</td>
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<td>30.33</td>
<td>30</td>
<td>30.29</td>
<td>0.288</td>
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<td>AGE</td>
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<td>68</td>
<td>69</td>
<td>74</td>
<td>0.034</td>
</tr>
<tr>
<td>SBP (MMHG)</td>
<td>134.37</td>
<td>138.01</td>
<td>137.68</td>
<td>138.02</td>
<td>0.51</td>
</tr>
<tr>
<td>DBP (MMHG)</td>
<td>81.72</td>
<td>83</td>
<td>82.74</td>
<td>82.44</td>
<td>0.564</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td>80.23</td>
<td>79.61</td>
<td>79.23</td>
<td>78.88</td>
<td>0.239</td>
</tr>
<tr>
<td>RALES IN LUNGS (%)</td>
<td>9.78</td>
<td>33</td>
<td>31</td>
<td>15</td>
<td>0.03</td>
</tr>
<tr>
<td>POTASSIUM (MMOL/L)</td>
<td>4.58</td>
<td>4.576</td>
<td>4.586</td>
<td>4.583</td>
<td>0.067</td>
</tr>
<tr>
<td>HB (G/L)</td>
<td>131.79</td>
<td>132.11</td>
<td>132.73</td>
<td>132.5</td>
<td>0.185</td>
</tr>
<tr>
<td>CREATININE (MMOL/L)</td>
<td>125.46</td>
<td>133.26</td>
<td>129.16</td>
<td>120.2</td>
<td>0.028</td>
</tr>
<tr>
<td>DIABETES (%)</td>
<td>12.5</td>
<td>21.21</td>
<td>19.35</td>
<td>13.33</td>
<td>0.54</td>
</tr>
<tr>
<td>DYSLIPIDEMIA (%)</td>
<td>45</td>
<td>66.66</td>
<td>64.52</td>
<td>80</td>
<td>0.46</td>
</tr>
<tr>
<td>RENAL INSUFFICIENCY(%)</td>
<td>18.33</td>
<td>40</td>
<td>22.58</td>
<td>13.33</td>
<td>0.04</td>
</tr>
<tr>
<td>ARRHYTHMIA(%)</td>
<td>31.66</td>
<td>54.54</td>
<td>51.61</td>
<td>26.6</td>
<td>0.02</td>
</tr>
<tr>
<td>AHP(%) NO HYPERTENSION</td>
<td>5</td>
<td>9.1</td>
<td>6.45</td>
<td>6.6</td>
<td>0.9</td>
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<tr>
<td>GRADE 1</td>
<td>1.6</td>
<td>0</td>
<td>0</td>
<td>13.33</td>
<td></td>
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<tr>
<td>GRADE 2</td>
<td>41.66</td>
<td>66.66</td>
<td>58.1</td>
<td>66.66</td>
<td></td>
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<tr>
<td>GRADE 3</td>
<td>13.33</td>
<td>15.15</td>
<td>29.03</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>PREVIOUS CAD/MI(%)</td>
<td>31.66</td>
<td>48.5</td>
<td>48.4</td>
<td>46.66</td>
<td>0.78</td>
</tr>
<tr>
<td>PREVIOUS ANGIOPLASTY (%)</td>
<td>43.33</td>
<td>66.66</td>
<td>74.2</td>
<td>46.66</td>
<td>0.32</td>
</tr>
</tbody>
</table>

The three significant results were seen in renal insufficiency (RF) atrial fibrillation (Afib) and rales in lungs, where patients with HFrEF where more likely to have RF (40%) and Afib (54.54%) when compared to HFmrEF 22.58% for RF and 51.61% for Afib and 13.33% in patients with HFpEF in RF.
and 26.6% for Afib, p-value 0.04 and 0.02 respectively. 15% of patients with HFP EF, had rales in their lungs while 31% of patients with HFmr EF and 33% of patients with HFr EF had it (p-value 0.03).

Table 2. Patients’ complaints on admission.

<table>
<thead>
<tr>
<th></th>
<th>OVERALL (N=124)</th>
<th>HFREF (EF≤40%) (N=33)</th>
<th>HFMREF (EF 41-49%) (N=31)</th>
<th>HFPEF (EF≥50%) (N=15)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO COMPLAINTS</td>
<td>1 (2.6%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (6.6%)</td>
<td>0.34</td>
</tr>
<tr>
<td>CHEST PAIN</td>
<td>14 (12.9%)</td>
<td>2 (6.06%)</td>
<td>6 (19.35%)</td>
<td>6 (40%)</td>
<td>0.02</td>
</tr>
<tr>
<td>DIZZINESS</td>
<td>1 (2.6%)</td>
<td>0 (0%)</td>
<td>1 (3.2%)</td>
<td>0 (0%)</td>
<td>0.9</td>
</tr>
<tr>
<td>COUGH</td>
<td>1 (2.6%)</td>
<td>0 (0%)</td>
<td>1 (3.2%)</td>
<td>0 (0%)</td>
<td>0.65</td>
</tr>
<tr>
<td>DYSPNEA</td>
<td>17 (13.7%)</td>
<td>8 (24.2%)</td>
<td>4 (12.9%)</td>
<td>5 (33.3%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

When compared to patients with HFR EF, patients who had HFP EF used to present more often with chest pain (40%) and dyspnea (33.3%) same as in patients with HFmr EF.

Table 3. Echocardiographic parameters in HF patients by EF groups.

<table>
<thead>
<tr>
<th>ECHOCARDIOGRAPHIC CHARACTERISTICS</th>
<th>EF</th>
<th>&lt;40</th>
<th>40-49</th>
<th>&gt;50</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA SIZE (MM)</td>
<td></td>
<td>48.11</td>
<td>47.9</td>
<td>47.69</td>
<td>0.27</td>
</tr>
<tr>
<td>RV DIAMETER (MM)</td>
<td></td>
<td>41.63</td>
<td>41.49</td>
<td>41.23</td>
<td>0.04</td>
</tr>
<tr>
<td>RA DIAMETER (MM)</td>
<td></td>
<td>47.78</td>
<td>47.61</td>
<td>47.38</td>
<td>0.37</td>
</tr>
<tr>
<td>INTERVENTRICULAR WALL DIAMETER (MM)</td>
<td></td>
<td>11.38</td>
<td>11.37</td>
<td>11.38</td>
<td>0.572</td>
</tr>
<tr>
<td>POSTERIOR WALL DIAMETER (MM)</td>
<td></td>
<td>11.05</td>
<td>11.02</td>
<td>10.96</td>
<td>0.46</td>
</tr>
<tr>
<td>MITRAL REGURGITATION (%)</td>
<td></td>
<td>75.75</td>
<td>51.61</td>
<td>26.6</td>
<td>0.023</td>
</tr>
<tr>
<td>TRICUSPID REGURGITATION (%)</td>
<td></td>
<td>75.75</td>
<td>58</td>
<td>20</td>
<td>0.039</td>
</tr>
<tr>
<td>AORTIC REGURGITAION (%)</td>
<td></td>
<td>12.12</td>
<td>19.35</td>
<td>6.66</td>
<td>0.09</td>
</tr>
<tr>
<td>LVEDD (MM)</td>
<td></td>
<td>62.0</td>
<td>51.2</td>
<td>45.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
In echocardiography findings, it was found that patients HFP EF have a smaller RV diameter 41.23 mm compared to RV size of patients with HFrEF 41.63 mm and those with HFmrEF had a 41.49 mm size of RV, p-value 0.04. While when it comes to left ventricular end diastolic diameter (LVEDD) patients with HFrEF had a bigger one (62 mm) compared to LVEDD of patients with HFP EF (45.1 mm), again patients with HFmrEF are in between having an average diameter of 51.2 mm, p value<0.001.

Table 4: Treatment of discharge in HF patients by EF groups.

<table>
<thead>
<tr>
<th></th>
<th>OVERALL (N=124)</th>
<th>HREF (EF≤40%) (N=33)</th>
<th>HFREF (EF 41-49%) (N=31)</th>
<th>HFPEF (EF≥50%) (N=15)</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose diuretics</td>
<td>34.16</td>
<td>66.6</td>
<td>48.38</td>
<td>26.6</td>
<td>0.03</td>
</tr>
<tr>
<td>High dose diuretics</td>
<td>7.5</td>
<td>12.12</td>
<td>9.67</td>
<td>13.3</td>
<td>0.46</td>
</tr>
<tr>
<td>Low dose ACEI</td>
<td>30.83</td>
<td>33.33</td>
<td>54.84</td>
<td>60</td>
<td>0.36</td>
</tr>
<tr>
<td>High dose ACEI</td>
<td>29.16</td>
<td>63.64</td>
<td>35.5</td>
<td>20</td>
<td>0.02</td>
</tr>
<tr>
<td>Low dose B-blockers</td>
<td>28.33</td>
<td>42.42</td>
<td>35.48</td>
<td>60</td>
<td>0.039</td>
</tr>
<tr>
<td>High dose B-blockers</td>
<td>35</td>
<td>57.6</td>
<td>61.3</td>
<td>40</td>
<td>0.13</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>22.5</td>
<td>45.45</td>
<td>32.25</td>
<td>13.3</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Low dose diuretics*: Toresamide 5-50 mg

High dose diuretics*: Toresamide 50-200 mg,

Low dose ACEI*: perindopril 5mg, ramipril 2.5mg, zofenopril 7.5-15 mg, trandalopril 2mg.

High dose ACEI*: perindopril 10mg, ramipril 10mg, zofenopril 30-60 mg, trandalopril 4mg.

Low dose B-blockers*: Metoprololol ≤25 mg, bisoprolol ≤ 2.5 mg, nebivolol ≤ 2.5 mg, carvedilol ≤ 6.25 mg

High dose B-blockers*: Metoprololol >25 mg, bisoprolol >2.5 mg, nebivolol > 2.5 mg, carvedilol >6.25 mg
Echo results showed as well a significant difference in valvular diseases (p-value: 0.023) in mitral regurgitation and (0.039) in tricuspid regurgitation, which reveals that patients with HFrEF, were more likely to have mitral and tricuspid regurgitation when compared to those who had a HFpEF (75.75% and 26.6%) and (75.75% and 20%) respectively, while aortic regurgitation was mostly seen in those with HFmrEF (19.35%) whom 51.61% of them had mitral regurgitation as well.

On discharge, patients with HFrEF were more prescribed low dose diuretics along with high doses of angiotensin-converting enzyme inhibitors (ACEI) and a high dose of B-blockers and spironolactone, while patients with HFpEF profited from low dose of diuretics with low dose of ACEI and a lower dose of B-blockers, HFpEF patients were less prescribed spironolactone, patients with HFmrEF, were prescribed the same treatment as for those with HFpEF but only with a higher dose of B-blockers (Table 4).

*Figure 1: clustered Bar Mean of age by ejection fraction (%) by gender.*

![Clustered Bar Chart](chart.png)

**P Value:**
0.034
DISCUSSION OF RESULTS

Our prospective study included HF patients who were categorized by their EF according to the latest guidelines issued by the European heart society in 2016. This showed that HFrEF had made the most significant part of the three described groups accounting for 41.8% of the total amount of patients.

In our study, HFrEF patients were more female, older and had a higher chance of having hypertension (Figure 1, Table 1) which matches with a clinical study made in Japan which included 429 patients [16] and another study which was conducted in University of Gondar Referral Hospital (GURH) [18]. While patients with HFrEF were more likely to have atrial fibrillation (Table 1) in our study, a study was done in the US, and the Japanese one contradict these results, where patients with HFrEF were having a history of atrial fibrillation and other diseases like COPD, asthma, and anemia [17].

Regarding dyslipidemia there were no significant differences among the different groups of our HF patients, contrarily to the study made in the US [17].

Our study showed no significance in patients having a history of acute coronary diseases (CAD) or previous myocardial infarction (MI) while the study made on the Japanese patients showed that these factors were less common in HFrEF [16].

Diabetes was seen in all the groups of HF patients, without any significant difference but it was less seen in patients with preserved EF, as it was demonstrated in the Japanese study [16].

The Japanese study found that the prevalence of renal failure was equal in all HF patients [16] meanwhile our study could prove that patients with HFrEF were more likely to have renal insufficiency when compared to HFmrEF or HFrEF patients, which matches with the elevated levels of serum creatinine thus confirming our results.

The echocardiography parameters that were found to be significant in our study are logical: there are more increased sizes of left and right ventricles in HFrEF patients if compared to HFmrEF, and HFrEF patients and our results did match with the results of the study which was done at GURH [18]. A higher number of MR and TR in HFrEF show that patients with HFrEF had a severe left and right ventricular remodeling.

The study made in GURH showed no difference in treatment prescribed for HF patients regarding diuretics, spironolactone, anticoagulants, and statins but generally HFrEF patients were more prescribed ACEI and B-blockers whereas anti-coagulants and calcium channel blockers were kept for HFrEF patients[18], meanwhile in our study, we saw a significance in terms of diuretics, B-blockers and spironolactone prescription, where HFrEF patients were prescribed a low dose of diuretics along
with a high dose of ACEI, high dose of B-blockers and spironolactone, on the other hand, HFpEF patients were given a low dose of diuretics, ACEI, and B-blockers on discharge, spironolactone was less prescribed to the latter group, which is due to the fact that there are no evidence-based techniques for treating HFpEF, on the other hand, calcium channel blockers have shown a significant efficacy in treating this type of patients while being dangerous to be used in patients with a reduced EF[16].

Study limitations:

Our study had few limitations, the first one is being conducted on a relatively small sample, which would explain the insignificant correlations we had in our results, and if done on a larger group of patients, results are expected to be slightly different. The second one is time shortage which made it challenging to assess 1 and 5-year prognosis and mortality, so we have made the insights in prognosis looking at the need for medication at the discharge in different groups. Another study limitation which appeared after the research was done is the usage of LVEDD as parameter to compare the difference in LV size between each group of patients when the best option was to compare the LV end diastolic, systolic volumes and their indexes, which was not thought of when the research was started.

Although our study is considered to be limited, we believe that it still reflects the clinical features of HF patients and it gives us valuable information and could be an example for further studies or follow-up studies.
CONCLUSIONS

Heart failure is a fatal disease with a low 5-year prognosis. HFpEF patients were older and more often women, compared to the other groups. Patients with HFrEF, HFmrEF, and HFpEF have a different symptom and anamnestic profile. HFrEF patients were more likely to complain of dyspnea, and have rales in lungs, renal failure and arrhythmias, while HFpEF patients present with chest pain and would have a history of arterial hypertension. HFmrEF patients had a more similar clinical aspect of those with HFpEF. Enlargement of ventricles along with mitral and tricuspid regurgitation was more pronounced in HFrEF patients. For HF treatment, patients with HFrEF needed more low dose diuretics, high dose ACEI, and B-blockers and spironolactone, while patients with an HFpEF, they benefited from a low dose of diuretics, ACEI and B-blockers. However HFmrEF patients have prescribed a similar treatment as the one given to HFrEF patients showing that milder symptoms profile and better LVEF anyway require kind intensive treatment.
REFERENCES


Annex No.3

**EVALUATION OF THE FINAL MASTER’S THESIS**

(identification No. of the thesis)

**Reviewer’s Examination Form**

Length of the thesis: no. of pages : _____; no. of sources in the list of literature : _____; no. of table(s) : _____; no. of figure(s) : _____; no. of annex(-es) : _____.

<table>
<thead>
<tr>
<th>No.</th>
<th>Fulfillment of the structural and methodological criteria for the thesis</th>
<th>Evaluation</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td>The thesis consists of at least 20 pages (excluding annexes)</td>
<td>Yes/No</td>
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<tr>
<td>2.</td>
<td>The thesis contains all the necessary structural elements</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Titles of chapters and sections are clearly seen</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>The thesis is well-written, logical and concise</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>There are no grammatical errors</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>The volume of the thesis has not been artificially increased</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Literature references have been cited correctly</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>The bibliography has been produced properly</td>
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</tr>
<tr>
<td>9.</td>
<td>At least 70% of the cited references are less than 10 years old</td>
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<tr>
<td>10.</td>
<td>Tables, figures and annexes are presented correctly</td>
<td></td>
</tr>
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**Evaluation criteria of the Final Master’s Thesis**

<table>
<thead>
<tr>
<th>No.</th>
<th>Evaluation (on a 1–10-point scale)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>Literature analysis: the latest and most relevant literature sources are analysed; the key claims of the topic under investigation and research problems are presented.</td>
</tr>
<tr>
<td>12.</td>
<td>Aim and objectives: relevance of a selected scientific problem is explained, the raised hypotheses are described and explained properly, aim and objectives are formulated correctly.</td>
</tr>
<tr>
<td>13.</td>
<td>Methodology: a detailed explanation of the research methodologies is provided, the research instruments are described, an appropriate data collection method is selected and suitable statistical methods for addressing the set objectives are applied</td>
</tr>
<tr>
<td>14.</td>
<td>Results: the presented results are relevant in respect of the research topic. Analysis of the results is presented properly</td>
</tr>
<tr>
<td>15.</td>
<td>Discussion of the results: the obtained results are compared with most recent data by other authors; the student presents their opinion on the topic being analysed</td>
</tr>
<tr>
<td>16.</td>
<td>Conclusions: The findings are relevant to and consistent with the thesis topic and objectives; conclusions are based on the results obtained; suggestions and practical recommendations are submitted</td>
</tr>
</tbody>
</table>

**Final evaluation (mean average of 11-16 point evaluation)**
Reviewer’s comments and questions

Strengths of the Final Master’s Thesis

Weaknesses of the Final Master’s Thesis

Evaluation of the Final Master’s Thesis:

Can be presented/ can be presented after corrections

Can be presented for the defence; evaluation of ________________(on a 5–10-point scale)

Cannot be presented for the defence; evaluation of _______________(on a 1–4-point scale)

Reviewer’s signature:
EVALUATION OF THE FINAL MASTER’S THESIS

Evaluation Form of the Evaluation Commission Member

Final Master’s Thesis title: ______________________________________________________

by the postgraduate __________________________________ from Group ___
of the Medical Study Programme

Evaluation Criteria of the Final Master’s Thesis Presentation

<table>
<thead>
<tr>
<th>No.</th>
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<th>Evaluation (on 1–10-point scale)</th>
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<tbody>
<tr>
<td>1.</td>
<td>The primary research problem of the final master’s thesis is formulated and the aim and objectives are stated</td>
<td></td>
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<td>2.</td>
<td>The work methodology is explained; the main research instruments and data collection methods are indicated</td>
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<tr>
<td>3.</td>
<td>Statistical or other methods for the implementation of the set objectives are clearly specified</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Research results are presented clearly</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Any visual material displayed is clear and informative</td>
<td></td>
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<tr>
<td>6.</td>
<td>Conclusions are based on the achieved results and are associated with the set tasks and objectives</td>
<td></td>
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<tr>
<td>7.</td>
<td>Practical recommendations are presented (where possible)</td>
<td></td>
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<tr>
<td>8.</td>
<td>The presentation has a logical progression</td>
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<tr>
<td>9.</td>
<td>The fundamental idea of the final master’s thesis corresponds to the nature of the Medical Study Programme</td>
<td></td>
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<tr>
<td>10.</td>
<td>Ability to present the thesis</td>
<td></td>
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</table>

Final evaluation (mean evaluation on a 1–10-point scale)

Comments of FMTEvaluationCommission member:

Signature of the Evaluation Commission Member: _____________________
THE EVALUATION JOURNAL FOR THE MASTER'S THESIS OF THE MEDICAL INTEGRATED MASTER'S STUDY PROGRAMME

Date of the defence....................


2.

3.

4.

The thesis is evaluated by 3 members of the Evaluation Commission. If the thesis supervisor is included in the Evaluation Commission, he/she cannot participate in the evaluation

<table>
<thead>
<tr>
<th>Student name, surname</th>
<th>Evaluation by the reviewer</th>
<th>Evaluation by the member of the Evaluation Commission (1)</th>
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</tbody>
</table>

Signature of the head of the department or chairman of the evaluation commission..................................................................................................................................................
Medicinos akademijos (MA)
Vientisų studijų programa – Medicina
VI k. studentui Ahmad Hussein
Darbo vadovė prof. Diana Žaliaduonytė-Pekšiene
LSMUL KK Kardiologijos klinika

DĖL PRITARIMO TYRIMUI

LSMU Bioetikos centras, įvertinęs Ahmad Hussein pateiktus dokumentus, studento tiriamajam darbui tema „Clinical characteristics and outcomes of patients with reduced left ventricular ejection fraction and preserved left ventricular ejection fraction“ pritaria*.

* Pastaba: Šis pritarimas neatliežia tiriamajį mokslinį darbą vykdančių asmenų nuo prievoles laikytis Bendrojo duomenų apsaugos reglamento nuostatų ir nuo atskomybės gautai nacionalinio arba regioninio bioetikos komiteto leidimą, jei teks leidimas būtinas pagal LR Biomedicininės tyrimų etikos įstatymo numatytus reikalavimus.