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# A PROSPECTIVE OBSERVATIONAL STUDY ON DRUG MILRINONE TO PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

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## ABSTRACT

**Background:** Heart failure with reduced ejection fraction (HFrEF) is a clinical syndrome characterized by impaired ventricular function, leading to insufficient cardiac output. Milrinone, a phosphodiesterase-3 inhibitor with inotropic and vasodilatory properties, is commonly used in acute decompensated heart failure to improve hemodynamics. However, its role, efficacy, and safety in patients with HFrEF remain areas of ongoing evaluation. **Objective:** This study aimed to assess the clinical outcomes, hemodynamic effects, and safety profile of milrinone in patients diagnosed with HFrEF. **Methods:** A prospective observational study was conducted over a defined period in a tertiary care setting. Patients with confirmed HFrEF receiving milrinone as part of their therapeutic regimen were enrolled. Data on patient demographics, baseline characteristics, ejection fraction, dosage and duration of milrinone therapy, and outcomes including symptom relief, hospitalization duration, adverse events, and mortality were collected and analyzed. **Results:** Among the enrolled patients, significant improvement in clinical symptoms and hemodynamic parameters was

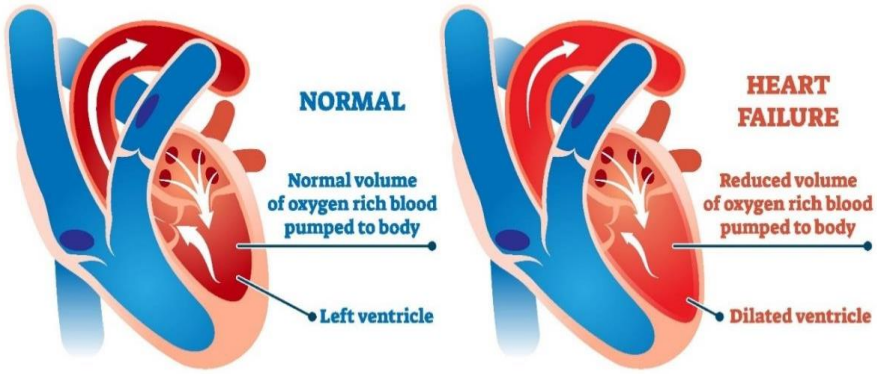
observed in a majority of cases. Adverse effects were noted in a subset of patients, including arrhythmias and hypotension. Milrinone was generally well-tolerated, and its use was associated with short-term improvement in cardiac output. **Conclusion:** Milrinone may offer symptomatic and hemodynamic benefits in selected patients with HFrEF. While it appears to be effective in acute settings, careful patient selection and monitoring are essential to minimize adverse effects. Further randomized controlled studies are recommended to validate these findings.

**KEYWORDS:** Heart failure with reduced ejection fraction (HFrEF), Milrinone, Inotropic agents, Phosphodiesterase inhibitors, Acute decompensated heart failure, Hemodynamics, Prospective observational study.

## INTRODUCTION

### HEART FAILURE

- Congestive heart failure (CHF), is "a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood." Ischemic heart disease is the leading cause of death world wide and the leading cause of CHF.
- CHF is a common disorder worldwide with a high morbidity and mortality rate.




- It is imperative to diagnose and effectively treat the disease to prevent recurrent hospitalizations, decrease morbidity and mortality, and enhance patient outcomes.
- The etiology of heart failure (HF) is variable and extensive. The general management aims at relieving systemic and pulmonary congestion and stabilization of hemodynamic status, regardless of the cause. The treatment of HF requires a multifaceted approach involving patient education, optimal medication administration, and decreasing acute exacerbations.

Left ventricle ejection fraction (LV EF) is used to classify HF.

- HF with **reduced** ejection fraction (HFrEF): LV EF ≤ 40%
- HF with **mildly reduced** ejection fraction: LV EF 41% - 49% and evidence of HF (elevated cardiac biomarkers or elevated filling pressures)
- HF with **preserved** ejection fraction (HFpEF): LV EF ≥ 50% and evidence of HF (elevated cardiac biomarkers or elevated filling pressures)
- HF with **improved** ejection fraction: LV EF >40%, with previously documented LV EF ≤ 40%

Patients with HFpEF have traditionally been underdiagnosed but comprise between 44% and 72% of CHF cases. On echocardiogram (echo), LV EF ≥ 50% with evidence of impaired diastolic function. The most significant risk factor is hypertension (HTN), and other risk factors include older age, female sex, and diabetes.

The ACC (American college of cardiology) and the AHA (American heart association) together classify HF by stages, with the first 2 stages being asymptomatic and the second 2 being classified by severity of symptoms.

**ACC/AHA Heart Failure Stages**

- Stage A: At risk for HF. No symptoms, structural heart disease, or evidence of elevated cardiac biomarkers, but risk factors are present. Risk factors include hypertension, diabetes, metabolic syndrome, cardiotoxic medications, or having a genetic variant for cardiomyopathy.
- Stage B: Pre-HF. Patients have no signs or symptoms of HF but have structural heart disease, evidence of elevated filling pressures (by invasive or noninvasive assessment), or persistently elevated cardiomarkers in the absence of other reasons for elevated markers, like chronic kidney disease or myocarditis.
- Stage C: Patients with structural heart disease and current or past history of HF symptoms.
- Stage D: Patients with refractory symptoms that interfere with daily life or recurrent hospitalization despite targeted guideline-directed medical therapy.

**Physiology of Heart Failure**

Cardiac contractility (force and velocity of contraction), ventricular performance, and myocardial oxygen requirements are determined by

- Preload

- Afterload
- Substrate availability (eg, oxygen, fatty acids, glucose)
- Heart rate and rhythm
- Amount of viable myocardium
- Cardiac output (CO) is the product of stroke volume and heart rate; it is also affected by venous return, peripheral vascular tone, and neurohumoral factors.

**Preload** is the loading condition of the heart at the end of its relaxation and filling phase (diastole) just before contraction (systole). Preload represents the degree of end-diastolic fiber stretch and end-diastolic volume, which is influenced by ventricular diastolic pressure and the composition of the myocardial wall. Typically, left ventricular (LV) end-diastolic pressure, especially if higher than normal, is a reasonable measure of preload. LV dilation, hypertrophy, and changes in myocardial distensibility (compliance) modify preload.

Afterloadis the force resisting myocardial fiber contraction at the start of systole. It is determined by LV chamber pressure, radius, and wall thickness at the time the aortic valve opens. Clinically, systemic systolic blood pressure at or shortly after the aortic valve opens correlates with peak systolic wall stress and approximates afterload.

The Frank-Starling principle describes the relationship between preload and cardiac performance. It states that, normally, systolic contractile performance (represented by stroke volume or CO) is proportional to preload within the normal physiologic range (see figure Frank-Starling principle). Contractility is difficult to measure clinically (because it requires cardiac catheterization with pressure-volume analysis) but is reasonably reflected by the ejection fraction (EF), which is the percentage of end-diastolic volume ejected with each contraction (stroke volume/end-diastolic volume). EF can generally be adequately assessed noninvasively with echocardiography, nuclear imaging, or MRI.

The force-frequency relationship refers to the phenomenon in which repetitive stimulation of a muscle within a certain frequency range results in increased force of contraction. Normal cardiac muscle at typical heart rates exhibits a positive force-frequency relationship, so a faster rate causes stronger contraction (and corresponding greater substrate requirements). During some types of heart failure, the force-frequency relationship may become negative, so that myocardial contractility decreases as heart rate increases above a certain rate.

Cardiac reserve is the ability of the heart to increase its performance above resting levels in response to emotional or physical stress; body oxygen consumption may increase from 250 to≥ 1500 mL/minute during maximal exertion.

**Mechanisms include**

- Increasing heart rate
- Increasing systolic and diastolic volumes
- Increasing stroke volume
- Increasing tissue extraction of oxygen (the difference between oxygen content in arterialblood and in mixed venous or pulmonary artery blood)

In well-trained young adults during maximal exercise, heart rate may increase from 55 to 70 beats/minute at rest to 180 beats/minute, and CO may increase from 6 to ≥ 25 L/minute. At rest, arterial blood contains about 18 mL oxygen/dL of blood, and mixed venous or pulmonary artery blood contains about 14 mL/dL. Oxygen extraction is thus about 4 mL/dL. When demand is increased, oxygen extraction may increase to 12 to 14 mL/dL. This mechanism also helps compensate for reduced tissue blood flow in heart failure.

***Frank-Starling principle***

Normally (top curve), as preload increases, cardiac performance also increases. However, at a certain point, performance plateaus, then declines. In heart failure (HF) due to systolic dysfunction (bottom curve), the overall curve shifts downward, reflecting reduced cardiac performance at a given preload, and as preload increases, cardiac performance increases less. With treatment (middle curve), performance is improved, although not normalized.

***AETIOLOGY***

There are many etiologies of CHF, and coronary artery disease (CAD) causing ischemic heart disease is the most common cause. The etiologies can be broadly classified as intrinsic heart disease and pathologies that are infiltrative, congenital, valvular, myocarditis-related, high-output failure, and secondary to systemic disease.

**Ischemicheart disease**

Is by far the most common cause of CHF worldwide. Ischemia leads to a lack of blood flow to heart muscles, reducing the EF.

**Valvularheart disease**

Is another common intrinsic heart condition that can cause CHF. Rheumatic heart disease is the most common cause of valvular heart disease in children and young adults worldwide. It is caused by an immune response to group A Streptococcus and primarily causes mitral and aortic stenosis. The most common overall cause of valvular disease is age-related degeneration, and the aortic valve is the most commonly affected valve. Women are more likely to experience mitral valve rheumatic heart disease or mitral valve prolapse, while men are more likely to suffer from aortic valve diseases such as regurgitation or stenosis. Endocarditis is also more common in men.

**Hypertension**

Causes CHF even in the absence of CAD or ischemic heart disease. High blood pressure causes mechanical stress by increased afterload and neurohormonal changes that increase ventricular mass. HTN is also strongly associated with other comorbidities for CHF development, and aggressively treating hypertension is shown to lower the incidence of CHF

**Cardiomyopathy**

Is a heterogeneous group of diseases characterized by enlarged ventricles with impaired function not related to secondary causes such as ischemic heart disease, valvular heart disease, hypertension, or congenital heart disease. The most common types of cardiomyopathies are hypertrophic, dilated, restrictive, arrhythmogenic right ventricular, and left ventricular noncompaction. In addition to CHF, cardiomyopathy can present as arrhythmia or sudden cardiac death, further compelling the identification of underlying disorders. Many of these conditions have a genetic basis, and a detailed family history of sudden cardiac death.

**Inflammatory cardiomyopathy:** Is defined by myocarditis along with ventricular remodeling and cardiac dysfunction. The most common cause is viral infection. Other etiologies are bacterial, fungal, or protozoal infections; toxic substances or drugs; and immune-mediated diseases.

**Infiltrative cardiomyopathies**

Cause a restrictive cardiomyopathy pattern (simar to the genetically determined restrictive cardiomyopathy variant), which is notable for normal ventricular systolic function, but with diastolic dysfunction and restrictive filling dynamics of the LV and RV.

**Takotsubo or stress-induced cardiomyopathy** (colloquially broken-heart syndrome)**:**
Is an under recognized cause of CHF, which causes transient left-ventricular wall abnormalities that are not localized to a specific vascular territory.

**Peripartum cardiomyopathy**
Is a significant cause of maternal mortality. During pregnancy, cardiac output is increased by 20% to 30% due to increased heart rate and stroke volume. It presents with CHF due to LV systolic dysfunction during late pregnancy, postpartum, or up to several months after delivery. There is likely an underlying genetic component, and it is more common in women with advanced maternal age, Black race, and multifetal pregnancies. If wall motion abnormalities are present, anticoagulation is essential due to the hypercoagulable state caused by pregnancy. Recovery is variable by global region and inversely correlates with lowered EF.

**Obesity**
Is a leading cause of CHF in patients younger than 40 years, according to the "Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity" (the CHARM study). The "obesity paradox" described elsewhere has significant study flaws and is derived from older data. It is thought that up to 10% of CHF cases are attributable to obesity alone. Patients with obesity are more likely to have HFpEF, possibly secondary to adipose-produced cytokines such as IL-1b, IL-8, and TNFα.

**Tachycardia and arrhythmia**
Can induce a low-output CHF state. There is usually dilation of all cardiac chambers, and there is preservation or thinning of biventricular wall thickness. Electrophysiologic changes, including prologued duration and decreased amplitude of action potentials in the myocytes, accompany this.

**Thyrotoxicosis**
Is a rare cause of HF despite initiating a hyperdynamic circulatory state. This may be partially due to activation of the renin-angiotensin-aldosterone axis, causing sodium and water retention, as well as up regulation of erythropoietin-stimulating agent, both of which will cause increased blood volume. Sustained tachycardia with or without atrial fibrillation can also cause CHF.

**High-output cardiac failure**

Can be associated with thiamine deficiency, which is a rare condition found primarily among patients who are elderly, homeless, or have alcohol abuse disorder. Thiamine deficiency causes decreased ATP production with an accumulation of adenosine, which causes systemic vasodilation. This leads to lowered systemic vascular resistance and increased cardiac output. This evolves to weakened myocardium and decreased EF.

**Epidemiology**

The global magnitude of the disease cannot be accurately assessed given the significant differences in geographical distribution, assessment methods, lack of imaging modalities, and non-adherence to the uniform staging and diagnosis of the disease. Approximately 1.2 million hospitalizations were due to CHF in 2017, with an increase in the percentage of patients with HFpEF compared to HFrEF.

By some reports, the incidence rate has plateaued; however, the prevalence increases as more patients receive therapy. This has not translated to improved quality of life or a decrease in the number of hospitalizations for patients with CHF. According to the Global Health Data Exchange registry, the current worldwide prevalence of CHF is 64.34 million cases. This translates to 9.91 million years lost due to disability (YLDs) and 346.17 billion US dollars in healthcare expenditure.

Age is a major determinant of HF. Regardless of the cause or the definition used to classify patients with HF, the prevalence of HF increases steeply with age. The Framingham Heart Study showed CHF prevalence to be 8 per 1000 males aged 50 to 59 years, with an increase to 66 per 1000 males aged 80 to 89. The incidence of HF in men doubles with each 10-year age increase after the age of 65, whereas in women, for the same age cohort, the incidence triples. Men have higher rates of heart disease and CHF than women worldwide.

The global registry also notes a predilection for a race with a 25% higher prevalence of HF in Black patients than in White patients. HF is still the primary cause of hospitalization in the elderly population and accounts for 8.5% of cardiovascular-related deaths in the United States. International statistics regarding the epidemiology of HF are similar. The incidence increases dramatically with age, metabolic risk factors, and a sedentary lifestyle. Ischemic cardiomyopathy and hypertension are significant causes of HF in developing countries. A notable difference based on a review of small cohort studies from these nations is a higher

prevalence of isolated right HF. The theoretical cause of this is thought to be due to the higher prevalence of tuberculous, pericardial, and lung diseases. There is a lack of robust data to verify these claims.

## PATHOPHYSIOLOGY

HF is a progressive disease. Any acute insult to cardiac structure or acute alteration secondary to genetic mutation, cardiac tissue infiltration, ischemia, valvular heart disease, myocarditis, or acute myocardial injury may initiate the compensatory mechanism, which, once exhausted, results in maladaptation.

In the initial stages of CHF, several compensatory mechanisms attempt to maintain cardiac output and meet the systemic demands. The chronic activation of the sympathetic nervous system results in reduced beta-receptor responsiveness and adrenaline stores. This results in changes in myocyte regeneration, myocardial hypertrophy, and myocardial hypercontractility. The increased sympathetic drive also results in the activation of the renin-angiotensin-aldosterone system (RAAS) system, systemic vasoconstriction, and sodium retention.

A decrease in cardiac output and increased sympathetic drive stimulate the RAAS, leading to increased salt and water retention, along with increased vasoconstriction. These further fuels the maladaptive mechanisms in the heart and causes progressive HF. In addition, the RAAS system releases angiotensin II, which has been shown to increase myocardial cellular hypertrophy and interstitial fibrosis, contributing to myocardial remodeling.

A decrease in cardiac output stimulates the neuroendocrine system with a release of epinephrine, norepinephrine, endothelin-1 (ET-1), and vasopressin. These mediators cause vasoconstriction, leading to increased afterload. There is an increase in cyclic adenosine monophosphate (cAMP), which causes an increase in cytosolic calcium in the myocytes. This increases myocardial contractility and further prevents myocardial relaxation. Increased afterload and myocardial contractility with impaired myocardial relaxation increase myocardial oxygen demand. This paradoxical need for increased cardiac output to meet myocardial demand eventually leads to myocardial cell death and apoptosis. As apoptosis continues, a decrease in cardiac output with increased demand leads to a perpetuating cycle of increased neurohumoral stimulation and maladaptive hemodynamic and myocardial responses. The loss of myocytes decreases EF (cardiac contractility), which leads to

incomplete LV emptying. Increased LV volume and pressure cause pulmonary congestion.

Renal hypoperfusion causes the release of antidiuretic hormone (ADH), further potentiating sodium and water retention. Increased central venous and intraabdominal pressure causes reduced renal blood flow, further decreasing GFR.

Decompensated CHF is characterized by peripheral vasoconstriction and increased preload delivery to the overburdened heart. The natriuretic peptides BNP and ANP are secreted but are ineffective in counteracting the excess sodium and water retention.

Neprilysin is an enzyme that breaks down several hormones, including BNP, ANP, and bradykinin; it targets several novel therapeutics. It is always used with an angiotensin receptor blocker because it increases angiotensin II levels, and when administered with an ACE inhibitor, it causes significant angioedema.

Causes of CHF are split about equally between HFrEF and HFpEF but require different treatment plans. In HFpEF, there is a decrease in myocardial relaxation and an increase in the stiffness of the ventricle due to an increase in ventricular afterload. This perpetuates a similar maladaptive hemodynamic compensation and leads to progressive HF. Patients with HFpEF tend to be older, female, and hypertensive. Atrial fibrillation and anemia are also more likely co-occurring conditions. There is some evidence that the prognosis is worse than those with HFrEF. It is possible that appropriate targets have not been identified for optimal therapeutic interventions

***COMPLICATIONS***

- Reduced quality of life
- Arrhythmia and sudden cardiac death
- Cardiac cachexia
- Cardiorenal disease
- Liver dysfunction
- Functional valvular insufficiencies (such as functional MR or TR)
- Mural thrombi and risk of thrombo embolism (brain, kidney, lung, major limb vessels)
- Recurrent hospitalizations and nosocomial infection

***TREATMENT***

**NON-PHARMACOLOGICALTREATMENT**

- Choose high fiber grain products and aim to eat 25–35 gm fiber per day
- Limit whole eggs to2to3per week
- Choose low fat dairy products more often
- Limit intake of statured and trans fats
- Getactive–for example brisk walking will help you burncalories, sleepbetter, increase your energy and improve your overall heart health
- Improve blood sugar, bone density
- Improve ability to cough with stress and decrease anxiety and depression
- Avoid exercises where you hold your breath
- Try to get 8 hours of sleep every night during the recovery period be physically active very day to help reduce the effects of stress.

***COMPLICATIONS***

There is a wide spectrum of complications from ischemic cardiomyopathy. The most common complication is the development of clinical congestive heart failure which is often the most common form of presentation for ICMP as the cardiac chambers dilate, innate conduction system of the heart changes leading to abnormal heart rhythms which could be life-threatening.

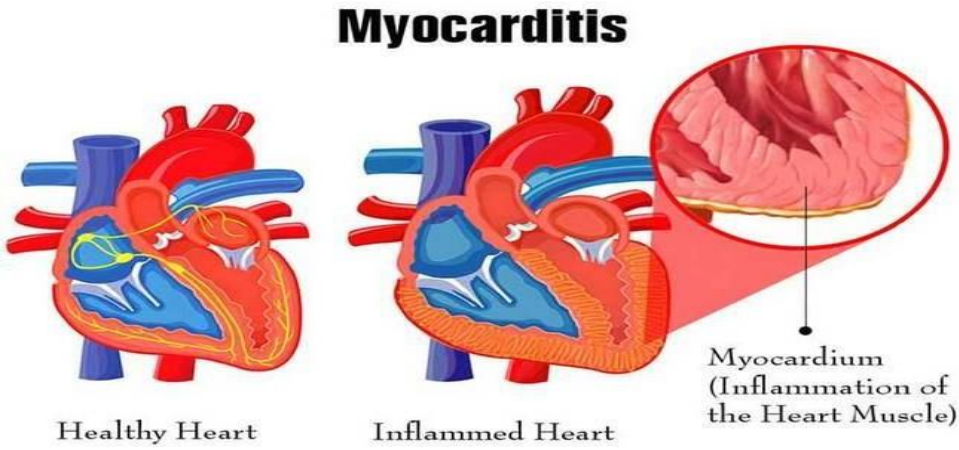
**Myocarditis**

**Myocarditis**, also known as **inflammatory cardiomyopathy**, is an acquired cardiomyopathy due to inflammation of the heart muscle. Symptoms can include shortness of breath, chest pain, decreased ability to exercise, and an irregular heartbeat. The duration of problems can vary from hours to months. Complications may include heart failure due to dilated cardiomyopathy or cardiac arrest.

Myocarditis is most often due to a viral infection. Other causes include bacterial infections, certain medications, toxins and autoimmune disorders. A diagnosis may be supported by an electrocardiogram (ECG), increased troponin, heart MRI, and occasionally a heart biopsy An ultrasound of the heart is important to rule out other potential causes such as heart valve problems.

Treatment depends on both the severity and the cause. Medications such as ACE inhibitors, beta blockers, and diuretics are often used. A period of no exercise is typically

recommended during recovery. Corticosteroids or intravenous immunoglobulin (IVIG) may be useful in certain cases. In severe cases an implantable cardiac defibrillator or heart transplant may be recommended.




Since myocarditis is often due to a viral illness, many patients experience symptoms consistent with a recent viral infection including a fever, rash, loss of appetite, abdominal pain, vomiting, diarrhea, joint pains, and easily becoming tired. Additionally, myocarditis is often associated with pericardit is and many people with myocarditis present with signs and symptoms that suggest myocarditis and pericarditis at the same time.

Children primarily present with the aforementioned symptoms associated with a viral infection. Later stages of the illness can involve the respiratory system and lead to increased work of breathing. These are often mistaken for asthma.

Myocarditis can be distinguished as either fulminant or acute based on the severity of symptoms on presentation, as well as the time course over which symptoms develop and persist. This categorization can help predict the treatment, outcomes, and complications of myocarditis.

Fulminant myocarditis is defined as sudden and severe myocarditis that is associated with signs and symptoms of heart failure while at rest. More specifically, fulminant myocarditis is characterized by a distinct, rapid onset of severe heart failure symptoms, such as shortness of breath and chest pain, that develop over the course of hours to days. Additionally, treatment requires the use of medications or mechanical devices to improve heart function.

Acute non-fulminant myocarditis has a less distinct onset in contrast to fulminant myocarditis,

and evolves over days to months. While the symptoms of acute myocarditis overlap with those of fulminant myocarditis, they do not typically occur at rest, and treatment does not require the use of mechanical circulatory support.

Most forms of myocarditis involve the infiltration of heart tissues by one or two types of pro-inflammatory blood cells, lymphocytes and macrophages plus two respective descendants of these cells, NK cells and macrophages. Eosinophilic myocarditis is a subtype of myocarditis in which cardiac tissue is infiltrated by another type of pro-inflammatory blood cell, the eosinophil. Eosinophilic myocarditis is further distinguished from non-eosinophilic myocarditis by having a different set of causes and recommended treatments.

The pathophysiology of viral myocarditis is not well understood, but it is believed to involve cardiotropic viruses (viruses with a high affinity for the heart muscle) gaining entry to cardiac muscle cells, usually via binding to a transmembrane receptor. Over approximately the next 1–7 days the virus replicates and causes inflammation leadings to necrosis and apoptosis of cardiac muscle cells (myocytes) and activation of the innate immune system. Over the next 1–4 weeks, viral replication continues with subsequent activation of the acquired immune system leading to T cell infiltration and the formation of antibodies, including possibly auto-antibodies. Over the next few months to years, this process either resolves and concludes with viral clearance or it may progress to cause permanent heart damage such as dilated cardiomyopathy, ventricular dysfunction or other cardiomyopathies. Coxsackie B, specifically B3 and B5, has been found to interact with coxsackievirus-adenovirus receptor (CAR) and decay-accelerating factor (DAF). However, other proteins have also been identified that allow Coxsackieviruses to bind to cardiac cells. The natural function of CAR and mechanism that the Coxsackievirus uses to infect the cardiac muscle is still unknown. The mechanism by which coxsackie B viruses (CBVs) trigger inflammation is believed to be through the recognition of CBV virions by Toll-like receptors.

The binding of many types of coronaviruses, including the SARS-CoV-2 virus, through ACE2 receptors present in heart muscle may be responsible for direct viral injury leading to myocarditis. In a study done during the 2002-2004 SARS outbreak, SARS viral RNA was detected in the autopsy of heart specimens in 35% of the patients in the Toronto, Canada area who had died due to SARS. It was also observed that an already diseased heart has increased expression of ACE2 receptor contrasted to healthy individuals which may lead to greater viral infiltration in the heart muscle. Hyperactive immune responses in COVID-19 patients may lead

to the initiation of the cytokine storm. This excess release of cytokines may lead to myocardial injury. In addition to direct cardiac myocyte (heart muscle cell) damage due to SARS-CoV-2 viral infiltration and inflammation, there are other suspected mechanisms that Covid-19 may indirectly cause myocarditis. During COVID-19, the other indirect mechanisms thought to contribute to myocarditis include: oxygen supply-demand mismatch to the heart muscle leading to myocardial (heart muscle) injury; microvascular thrombi, or blood clots in the small blood vessels of the heart causing injury; the systemic hyperinflammatory state in Covid-19 leading to heart muscle injury; or the virus causing indirect damage to the heart by inducing auto- immune mediated damage to the heart muscle (and frequently other organs).

**Milrinone**

Milrinone is a medication indicated for cardiac support in patients with acute heart failure, pulmonary hypertension, or chronic heart failure. It is often used during cardiac surgeries, including coronary artery bypass graft surgery, cardiac transplantation, and other cardiac surgeries requiring cardiac support. It functions by improving cardiac contractility (inotropy), cardiac relaxation (lusitropy), and inducing vasodilation and has the overall effect of increased cardiac output, improvement of left ventricle-arterial coupling, and enhanced cardiac mechanical efficiency. Its use is primarily in the perioperative and ICU settings, although it also has utility for outpatient therapy in select patient populations. This activity will review its mechanism of action, indications, and potential harm and benefits associated with its use. It will also discuss its role throughout various specialties of medicine, including ICU care, perioperative care, use in pediatric populations, and the now discontinued use in the outpatient setting as an oral medication.

Milrinone is approved for short short-term IV therapy for patients with acute decompensated heart failure with reduced ejection fraction in need of inotropic support.

Milrinone is used chiefly in the ICU and the cardiac unit for cardiac support in patients with acute heart failure, weaning patients with pre-existing left ventricular dysfunction from cardiopulmonary bypass, or as a temporizing agent for patients with plans to undergo cardiac surgery or transplantation.

Milrinone is often used during cardiac surgeries, including coronary artery bypass graft surgery, cardiac transplantation, and other cardiac surgeries requiring cardiac support. Likewise, it has utility in non-cardiac surgeries for patients with acute decompensated left

ventricular heart failure, acute right ventricular heart failure, or pulmonary artery hypertension

***Mechanism of action Phosphodiesterase Inhibition***

Milrinone is the phosphodiesterase inhibitor drug class. Phosphodiesterase is an enzyme that hydrolyzes the second messenger cyclic adenosine monophosphate(cAMP) and guanosine monophosphate(cGMP), terminating their effects in various tissues. There are several phosphodiesterase enzymes throughout the body. Phosphodiesterase III is present in the cardiac sarcoplasmic reticulum, smooth muscle in arteries and veins. Milrinone is selective for phosphodiesterase III at low doses and nonselective at high doses.

***Cardiac Effects of Milrinone***

In the myocardium, PDE III inhibition leads to increased contractility (inotropy) and improverelaxation (lusitropy). This effect leads to improved systolic and diastolic function and optimizes cardiac output. Increased heart rate (chronotropy) also occurs but is less pronounced than the increases in heart rate seen with medications in the catecholamine class. Inhibition of phosphodiesterase III prevents cAMP breakdown, increasing protein kinase A activity, leading to phosphorylation of calcium ion channels in the sarcoplasmic reticulum and increasing calcium availability in myocyte sarcomere. The increased calcium availability manifests in increased cardiac inotropy and chronotropy. Consequently, PDE III inhibition by milrinonecauses increased calcium reuptake into the sarcoplasmic reticulum, resulting in enhanced myocardial relaxation (lusitropy) with improved diastolic function.


Injection milrinone 10 ml ampule

***Vasoactive Effects of Milrinone***

In the vasculature, PDE III inhibition prevents cGMP metabolism in the smooth musculature

and results in vasodilation in both arteries and veins. The vasodilatory effects of milrinone are more potent than beta-2 agonists, including dobutamine and isoproterenol. Milrinone is available in an inhalational formula for directed vasodilation of the pulmonary vasculature to treat pulmonary hypertension.

***Pharmacokinetics***

- Plasma half-life: 2 to 2.5 hours.
- Distribution: The volume of distribution:0.38-0.45 liters/kg, Plasma protein binding: 70%
- Metabolism: Milrinone is metabolized by the liver to O-glucuronide metabolite
- Excretion: The route of excretion of urine and mean renal clearance of milrinone is approximately 0.3 liters/min (90% recovered in urine in 8 hours).

**Administration**

**Dosing options for milrinone include**

**Intravenous Administration**

Infusion: 10ml milrinone combine with 40 ml NS AND GIVEN 2ml/hr

The infusion rate should be modified according to hemodynamic and clinical response.

**Adverse effects**

The most feared adverse effect of milrinone is its potential to induce hemodynamic changes and arrhythmias. Milrinone may cause ventricular tachyarrhythmia, leading to cardiac ischemia or sudden cardiac death. These changes are not shown to follow a dose-dependent relationship. Milrinone can cause an increase in venous vessel capacitance, leading to decreased preload and manifesting as headaches, syncope, and severe hypotension. Unlike tachyarrhythmias, hypotension occurs in a dose-dependent relationship.

Anagrelide may enhance the toxic effect of milrinone. Both milrinone and anagrelide inhibit the phosphodiesterase III enzymes. Therefore anagrelide prescribing information states that clinicians should avoid concomitant use of milrinone with anagrelide.

Besides its hemodynamic and arrhythmogenic effects, milrinone may also affect plateletfunction and inflammatory pathways. It may block platelet aggregation, suppress neointimal hyperplasia associated with endothelial injury, and attenuate the proinflammatory effects of cardiopulmonary bypass.

**Contraindications**

Milrinone is contraindicated in patients with hypersensitivity to any of its components. It is relatively contraindicated in patients with severe heart failure or severe pulmonary hypertension. In severe pulmonary hypertension, generalized vasodilation of pulmonary vasculature may worsen V/Q mismatch and lead to worsened hypoxemia. When considering the use of milrinone in these populations, it is advisable to consult a specialist for expert guidance.

Milrinone is generally contraindicated in patients with acute kidney injury and end-stage renal disease, as it primarily undergoes renal excretion. Hence, Clinicians should reduce the infusion rate in patients suffering from renal impairment.

**Warning**

According to the manufacturer's labeling, milrinone is not safe when given for the longer (greater than 48 hours) treatment of patients with heart failure. Long-term oral treatment with milrinone is associated with an increased risk of hospitalization and death in patients with Class III and IV heart failure. Patients with NYHA Class IV symptoms appeared to be at higher risk. Milrinone is associated with ventricular arrhythmias, including NSVT(nonsustained ventricular tachycardia). In addition, long-term oral use is associated with an increased risk of sudden death.

**Monitoring**

Milrinone is primarily for use in the ICU and perioperative setting. Before initiating this medication, a right heart catheterization may be considered for obtaining hemodynamic measurements to establish the patient's baseline parameters and gauge the patient's response to continuous infusion. Repeat or dosing monitoring is not routine due to the risks associated with repeat vascular access or continuous indwelling catheters. Pulmonary artery catheterization for monitoring pulmonary pressures should be done with discretion and only after considering a case-by-case risk-benefit analysis.

**Toxicity**

Cardiovascular toxicity is primarily seen in chronically milrinone patients and manifests as tachyarrhythmias and sudden cardiac death. At high dosing, patients may also experience hypotension and syncope. Milrinone had a previous use as an oral formulation for outpatient use in patients with NYHA class III and IV chronic heart failure (CHF) to improve symptoms

and decrease the frequency of hospital admissions. However this practice was discontinued following the PROMISE trial in 1991 due to safety concerns. This double-blinded clinical trial assessed patients with CHF class III/IV placed on milrinone or placebo and ended early due to increased mortality in the milrinone group secondary to ventricular tachyarrhythmias and sudden cardiac death.

It is important to note that there is no antidote to milrinone. Therefore in case of overdose the administration of milrinone should be discontinued until the patient's condition stabilizes. Clinicians should treat the overdose symptomatically, focusing on hemodynamic parameters and arrhythmias.

**PHARMACOLOGICALTREATMENT**

| **Typeof Medicine** | **Namesofmedication** | **HowMedication Works** | **PotentialSide Effects** |
|---|---|---|---|
| **BetaBlockers** | Acebutolol(Rhotral, Sectral) Atenolol(Tenormin)Bisoprolol (Monocor)Carvedilol(Coreg) Labetalol (Trandate)Metoprolol(Betaloc, Lopressor) Nadolol (corgard)Pindolol (Visken)Propronolol (Inderal)Timolol(Blocadren) | • Lowers Bloodpressure& Heartrate<br>• Helps to preventAngina<br>• ImprovesHeartf unction<br>• Slowdownirregularheartrhythms<br>• Decrease the risk offutureHeartAttacks | • Fatigue/Tiredness<br>• Dizziness,<br>• Depression<br>• Wheezing |
| **Angiotensin receptor-neprilysin inhibitor (ARNi)** | sacubitril and valsartan (Entresto) | • Decreaseriskoffuture heartattacks<br>• It reduceses hypertention<br>• Maintain fluid balance | • Angeoedema<br>• Low blood pressure<br>• Diziness<br>• Incresed potassium levels<br>• Devloping cough<br>• Kidney problems |
| PDE 3 INHIBITORS | Milrinone Inamrinone | • Improvingcardiac Contractility<br>• Cardiac ralaxiation<br>• Increased cardiac output | • Ventricular arrhymias<br>• Hypotention<br>• Headache |
| ACE Inhibitors(Angiotensinconvertingenzymeinhibito | Benazepril (Lotensin)Captopril (Capoten)Cilazapril (Inhibace)Enalapril (Monopril)Lisinopril(Zestril,Prinivil)Perindopril | • RelaxesBloodvessels andlowers bloodpressure<br>• Decreases therisk of futureheartattacks<br>• Maintains theheart's shapepromoting | • Cough<br>• Dizziness, Lightheadache<br>• Increasedpotassiumlevel inblood |

| | | | |
|---|---|---|---|
| rs) | (Coversyl)Quinapril (Accupril)Ramipril (Altace) Trandolapril (Mavi k) | normalfunction | • Swelling oflips/face |
| Calcium sensitizer | Levosimendan | • It incrsese the sensitivity of the heart to calcium<br>• Increasing cardiac contactility | • Headache<br>• low blood pressure,<br>• stomach discomfort |
| CalciumChannelblockers | Amlodipine (Norvasc) Felodipine (plendil,Renedil) Nifedipine (Adalat XL) Diltiazem (CardiazemCD,Tiazac) Verapamil(isoptin) | • Lowersbloodp ressure<br>• Lower heartrate(Diltiazem,verapamil)<br>• Helpspreventa ngina<br>• Slows irregular heartrhythms(Diltia zem) | • Dizziness, Light headache<br>• Ftigue/tiredn ess<br>• Swelling of ankles/fee t |
| Angiotensin II Receptor Blockers | Candesartan(Atacama)Irbesartan (Avapro) Losartan (Cozaar) Olmesartan (Olmsted) Telmisartan (Macarids) Valsartan (Diovan) | • Relaxes bloodvessels<br>• Decrease the riskof future heartattack<br>• Alternative to ACEInhibitors | • Dizziness, lightheadedness<br>• Headache<br>• Increasedpotassiumlevel inblood |

## METHODOLOGY

### Study Site

Study has been carried out at Raghava 24 hours emergency hospital, Kakinada.

### Duration of Study

6months

SampleSize:

75cases

### Materials

Casecollection, cardiac markers

### Study Design

A prospective observational study.

### Ethical Committeeapproval

Approval for data collection was obtained from the head of the department of cardiology department from Raghava 24 hours emergency hospital, Kakinada.

## STUDY CRITERIA

### Inclusion Criteria

- Patientsfrom the cardiology department OPD and IPD
- Patientswith different types of heart failure
- Patients with reduced ejection fraction
- Patients with different cardiac contractility
- Patients who have been administered with the drug milrinone.
- Patients who are at a risk of developing heart failure were selected forthestudy.

### Exclusion Criteria

- Patients of heart failure with normal range of ejection fraction
- Patients who were incompliance to management.
- Patients with normal cardiac contractility features.

### Source of Data

Data was collected from the case collection forms from the cardiology department patients with regular follow - up at raghava hosital.

### Work Plan

### Uses

- Socio demographic details of patient like name, age, gender are collected.
- Details like chief complaints, family history, present medicalhistory, Past medicalhistory, personal history, diagnosis are collected.
- Pathological, radiological, biochemical parameters like cardiac markers and 2D echocardiography were collected from the case sheets of the patients in thehospital.
- All the information regarding the medication used in the treatment chart were collected.
- Doses, drugs, andduration of drugs of therapy were noted from the patient's drug chart who are on regular follow up
- Clinical outcome of the patient after using the therapy must be observed and patient data should be collected.
- Estimating the percentage of patients who improved their cardiac contractility and the percentage of ejection fraction after administration of drug milrinone.
- Helping for precise management of patients with risk of heart failure.
- Research helps to reduce the secondary events prevention.

- To create general awareness on risk factors associated with heart failure with reduced ejection fraction.

**Data Analysis**

**Descriptive Analysis Method**

Byusingt-Test: pair two sample, mean values were calculated for ejection fraction and cardiac contractility. Descriptive statistics such as improved ejection fraction, improved cardiac contractility and percentages were calculated and defined in bar graphs, pie charts and histograms.

**Statistical Analysis Method**

t-Test: pair two sample method of statistics was used to determine and calculate the statistical analysis for this prospective observational study about the improved ejection fraction percentage and cardiac contractility of heart failure patients who has been administered with drug milrinone in cardiology patients on regular follow up.

**Ethical Committee Clearance**

Incharge of the institutional ethical committee approved our study, informed consent form was collected from the patient to collect the data.

**RESULTS**

***DESCRIPTIVE DATAANALYSIS***

**AGE**

A total of 75 cases were collected from the hospital. Among them, the study has been categorized the age group into three types.

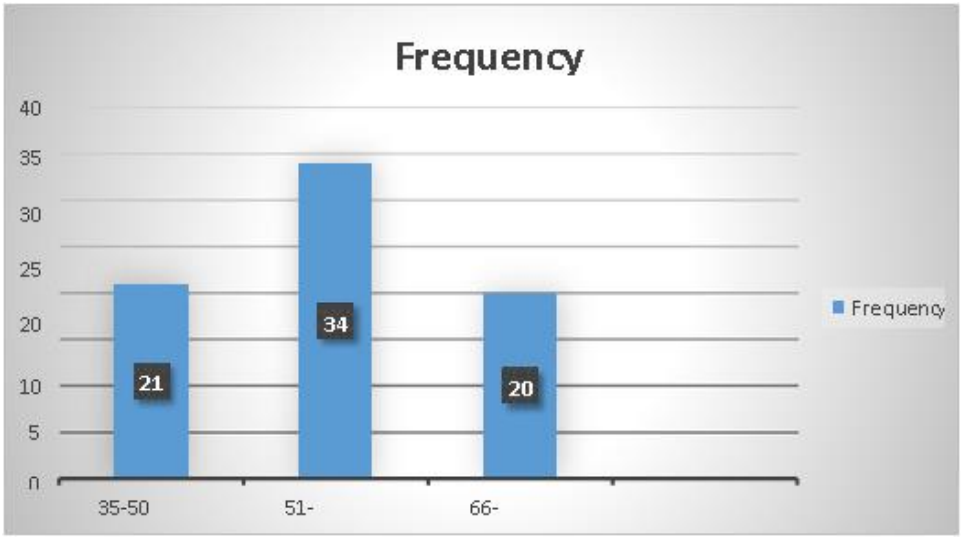
They are: 1). Age group of 35 to 50Years 2). Age group of 51 to 65years 3). Age group of 66 to 80 years

**Frequency table for age group**

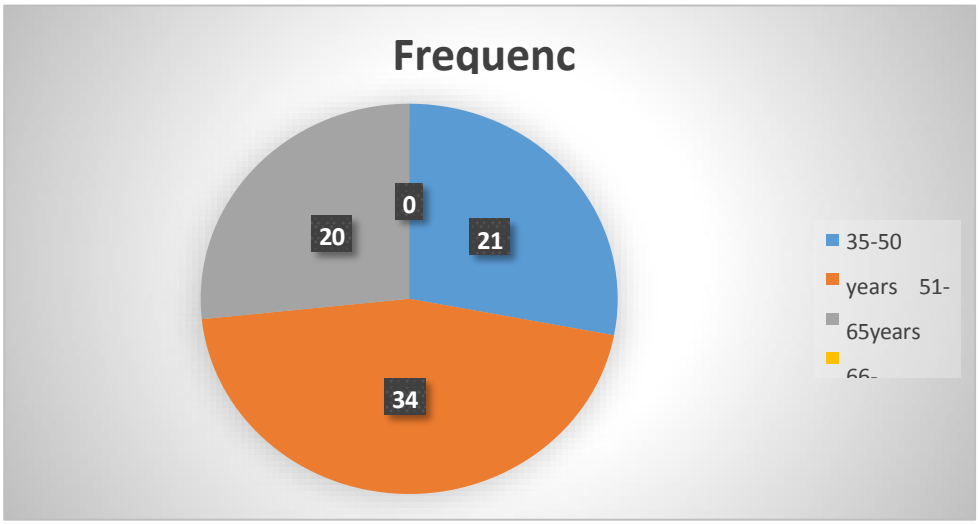
| | Age group | Frequency | Percent |
|---|---|---|---|
| **Valid** | 35–50years | 21 | 28.00 % |
| | 51–65years | 34 | 45.30 % |
| | 66–80years | 20 | 26.70 % |
| **Total** | | **75** | **100** |

**Bar graph representation for age**

The graphical representation of bar graph shows the details of graph with the dataof Age group v/s Number of Patients. Taking Number of patients on X – axis and AgegrouponY– axis.




**Pie graph representation of age groups**




***EJECTION FRACTION***

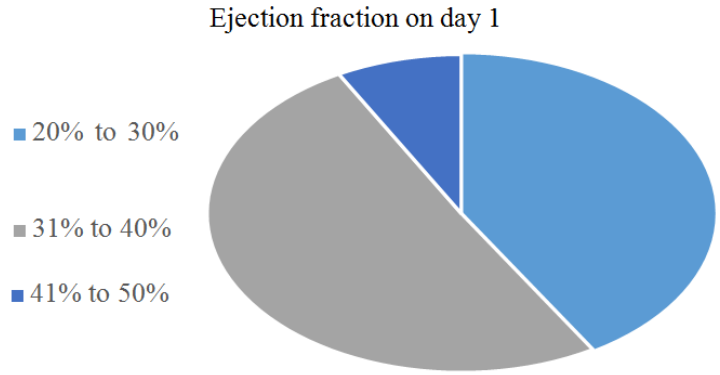
**Range of ejection fraction on day 1**

A total of 75 cases were collected from the hospital. Among them, the range of ejection fraction is as follows

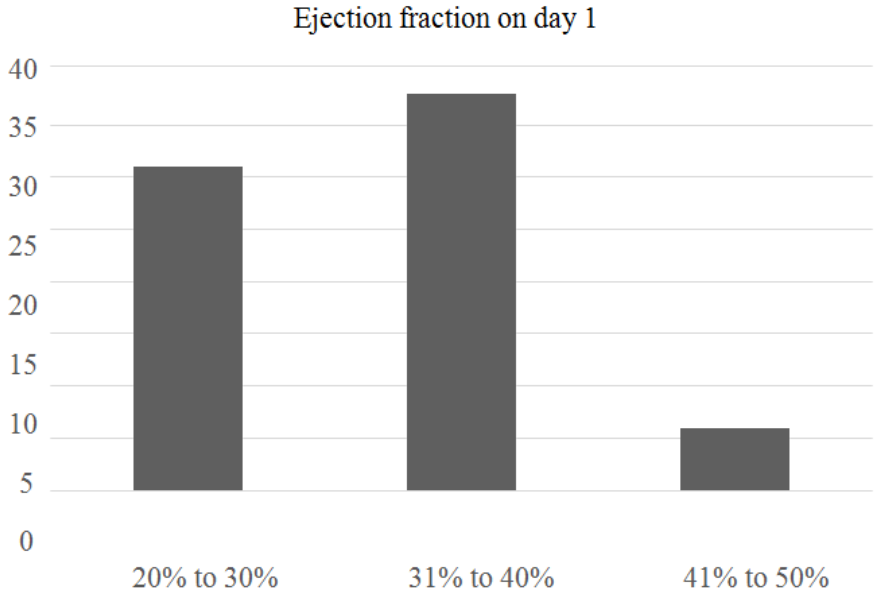
| Range | Frequency | Percent |
|---|---|---|
| 20% to 30% | 31 | 41.30 % |
| 31% to 40% | 38 | 50.60 % |
| 41% to 50% | 6 | 8.10 % |
| **Total** | **75** | **100 %** |

Pie chart representation of patients with decreased range of ejection fraction on day 1 Ejection

fraction on day 1.




**Bar graph representation of patients with decreased range of ejection fraction on day 1**

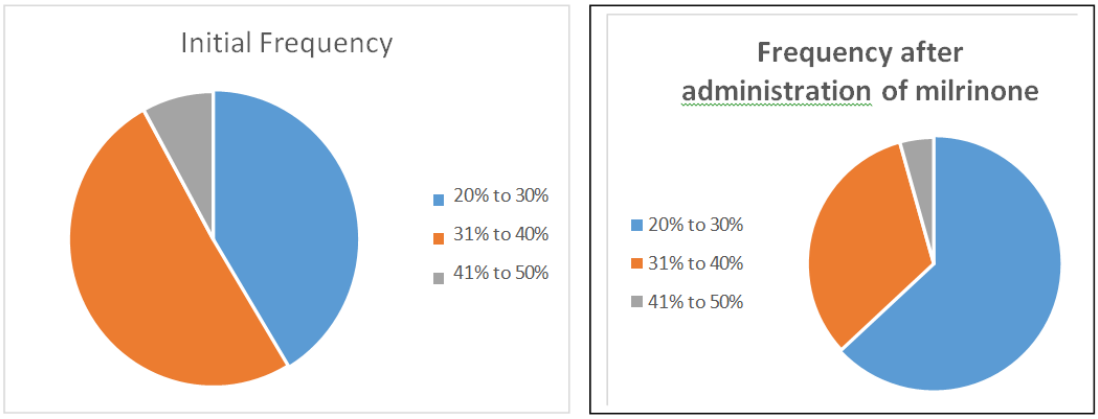



The graphical representation of bar graph shows the details with the data of patients with decreased ejection fraction. By taking ejection fraction on x-axis and total numbers on y-axis.

Range of ejection fraction after administrating drug milrinone:

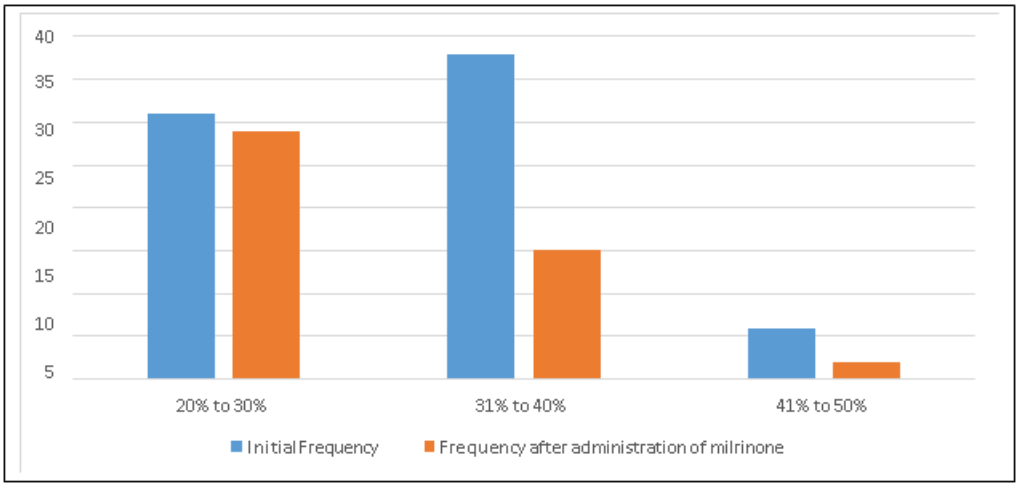
| Range | Initial Frequency | Frequency after administration of milrinone | Percen31t |
|---|---|---|---|
| 20% to 30% | 31 | 29 | 38.00 % |
| 31% to 40% | 38 | 15 | 20.00% |
| 41% to 50% | 6 | 2 | 2.60 % |
| **Total** | **75** | **46** | **61 %** |

**Pie chart representation**



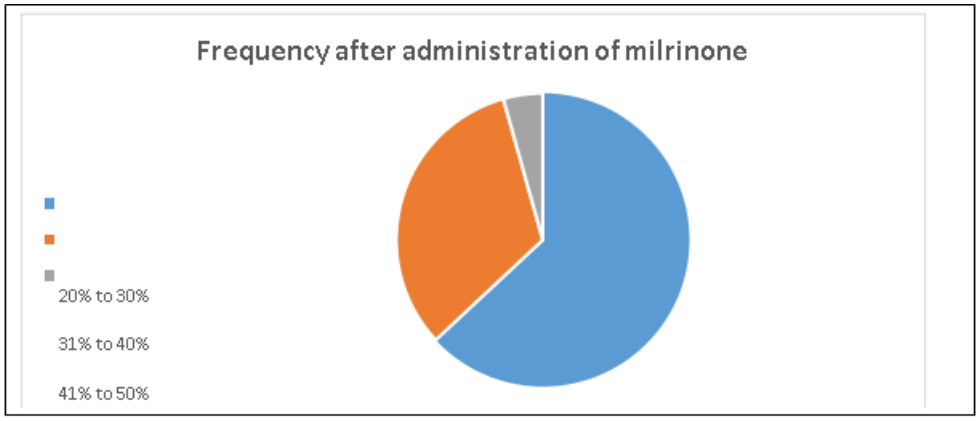

***Bar graph representation***

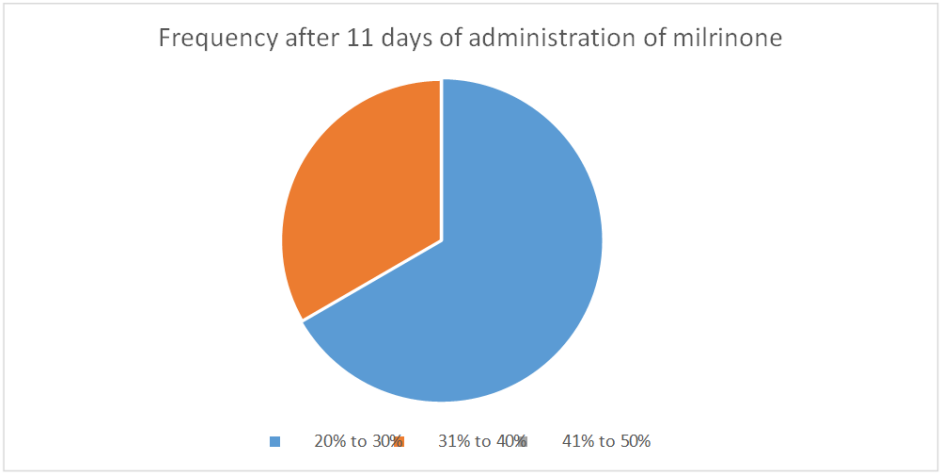
The graphical representation of bar graph shows the details with the data of increased ejection fraction after administrating drug milrinone. By taking range of ejection fraction on x-axis and number of patients on y-axis.



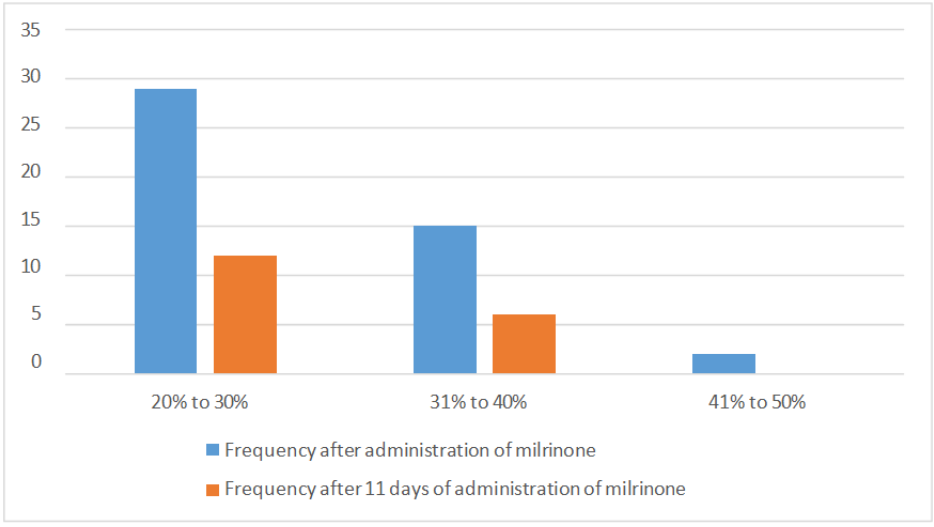

**Range of ejection fraction after 11 days administrating drug milrinone**

| Range | Initial Frequency | Frequency after administration of milrinone | Frequency after 11 days of administration of milrinone | Percentage |
|---|---|---|---|---|
| 20% to 30% | 31 | 29 | 12 | 16.00 % |
| 31% to 40% | 38 | 15 | 6 | 8.00% |
| 41% to 50% | 6 | 2 | 0 | 0 % |
| **Total** | **75** | **46** | **18** | **24 %** |




The graphical representation of bar graph shows the details of graph with the data of ejection fraction after administrating drug milrinone Vs ejection fraction after 11 days of administration of drug milrinone. By taking range of ejection fraction on x-axis and number of patient son y-axis.

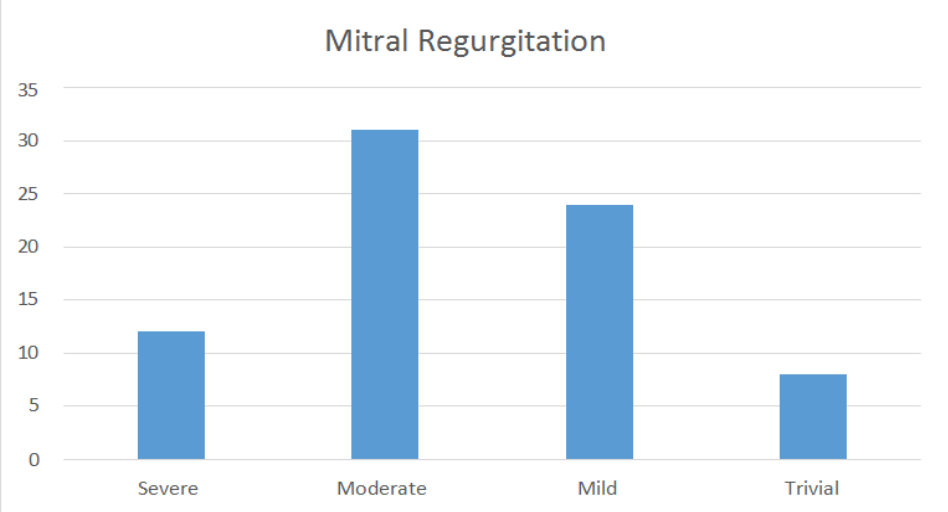


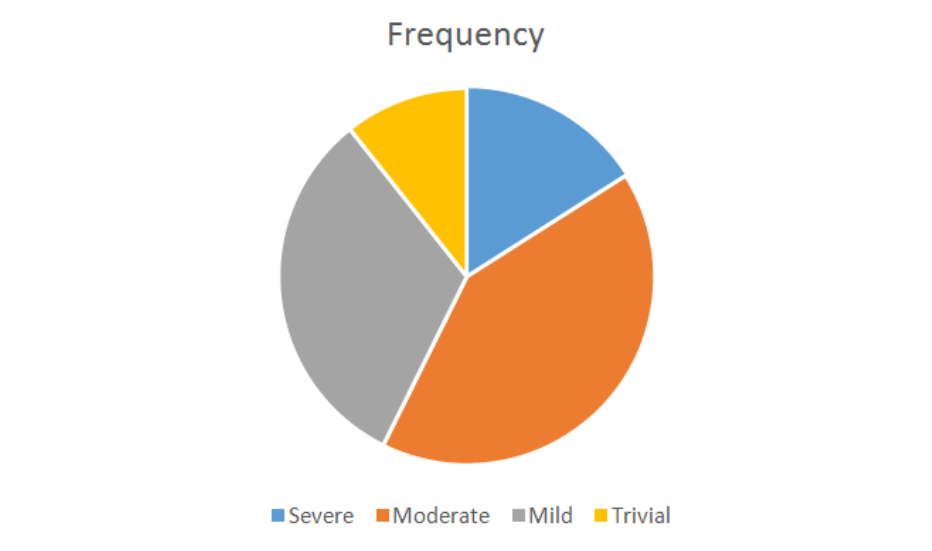
***CARDIAC CONTRACTILITY***

**Patients with range of mitral regurgitation (MR) on day 1**

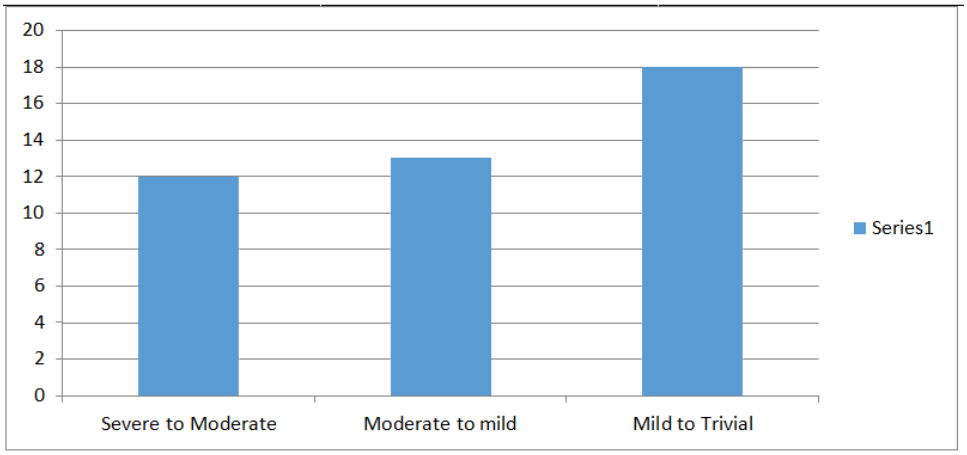
Among the75 patients the observed Mitral regargutation (MR) found to be

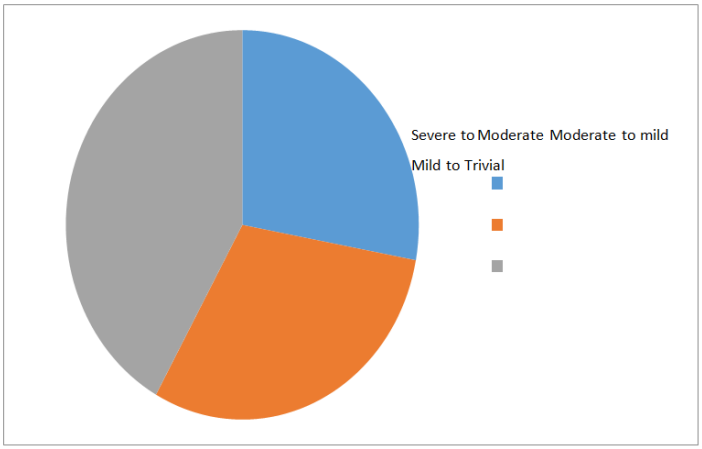
| Range | Frequency | Percent |
|---|---|---|
| Severe | 12 | 16.0 % |
| Moderate | 31 | 41.30 % |
| Mild | 24 | 32.00 % |
| Trivial | 8 | 10.70 % |
| **Total** | **75** | **100 %** |




| Range | Frequency | Percent |
|---|---|---|
| Severe to Moderate | 12 | 15.90 % |
| Moderate to mild | 13 | 17.50 % |
| Mild to Trivial | 18 | 23.90 % |
| Total | 43 | 56.59% |




***STATISTICAL DATAANALYSIS***

As per the study, Statistica data analysis was per formed by t-Test: pair two sample for means to calculate the data of our study on role of milrin one on patients with reduced ejection fraction and reduced cardiac contractility.

**Total no. of cases**

***Case processing summary***

| | Cases | | | | | |
|---|---|---|---|---|---|---|
| | Valid | | Missing | | Total | |
| | N | Percent | N | Percent | N | Percent |
| Total no. Of cases | 75 | 100% | 0 | 0% | 75 | 100% |

**Age group**

**Age processing summary**

| | Agegroup | Frequency | Percent |
|---|---|---|---|
| **Valid** | 35–50years | 21 | 28.00 % |
| | 51–65years | 34 | 45.30% |
| | 66–80years | 20 | 26.70% |
| **Total** | | **75** | **100** |

t-Test: Paired Two Sample for Means

| | *Frequency* | *Percent* |
|---|---|---|
| Mean | 1.916666667 | 8.241666667 |
| Variance | 9.71969697 | 183.1844697 |
| Observations | 12 | 12 |
| Pearson Correlation | 0.999755045 | |
| Hypothesized Mean Difference | 0 | |
| Df | 11 | |
| t Stat | -2.10315044 | |
| P(T<=t)one-tail | 0.029638036 | |
| tCriticalone-tail | 1.795884819 | |
| P(T<=t)two-tail | 0.059276072 | |
| t Critical two-tail | 2.20098516 | |

***EJECTION FRACTION***

**Range of ejection fraction on day 1**

A total of 75 cases were collected from the hospital. Among them, the range of ejection fraction is as follows.

| **Range** | **Frequency** | **Percent** |
|---|---|---|
| 20% to 30% | 31 | 41.30 % |
| 31% to 40% | 38 | 50.60 % |
| 41% to 50% | 6 | 8.10 % |
| **Total** | **75** | **100 %** |

**t-Test: Paired Two Sample for Means**

| | *Frequency* | *Percent* |
|---|---|---|
| Mean | 26 | 33.33333333 |
| Variance | 149 | 155.8433333 |
| Observations | 3 | 3 |
| PearsonCorrelation | 0.21869999 | |
| Hypothesized Mean Difference | 0 | |
| Df | 2 | |
| t Stat | 4.6386075556 | |
| P(T<=t)one-tail | 0.0232674 | |
| tCriticalone-tail | 2.91998558 | |
| P(T<=t)two-tail | 0.04148646 | |

**Range of ejection fraction after administrating drug milrinone**

A total of 75 cases were collected from the hospital. Among them, 46 patients are found to be

| Range | Initial Frequency | Frequency after administration of milrinone | Percent |
|---|---|---|---|
| 20% to 30% | 31 | 29 | 38.00 % |
| 31% to 40% | 38 | 15 | 20.00% |
| 41% to 50% | 6 | 2 | 2.60 % |
| **Total** | **75** | **46** | **61 %** |

t-Test: Paired Two Sample for Means

| | *Frequency* | *Percent* |
|---|---|---|
| Mean | 19 | 50 |
| Variance | 5202 | 3680.82 |
| Observations | 2 | 2 |
| PearsonCorrelation | 1 | |
| HypothesizedMeanDifference | 0 | |
| Df | 1 | |
| t Stat | 0.16283946 | |
| P(T<=t)one-tail | 0.016199533 | |
| tCriticalone-tail | 6.313751515 | |
| P(T<=t)two-tail | 0.707984322 | |
| tCriticaltwo-tail | 12.70620474 | |

Range of ejection fraction after 11 days administrating drug milrinone:

Among the105 patients with risk factors,46 patients are grouped into 45 to 55years.

| Range | Initial Frequency | Frequency after administration of milrinone | Frequeny after 11 days of administration of milrinone | Percentage |
|---|---|---|---|---|
| 20% to 30% | 31 | 29 | 12 | 16.00 % |
| 31% to 40% | 38 | 15 | 6 | 8.00% |
| 41% to 50% | 6 | 2 | 0 | 0 % |
| **Total** | **75** | **46** | **18** | **24 %** |

t-Test: Paired Two Sample for Means

| | *Frequency* | *Percent* |
|---|---|---|
| Mean | 3.583333333 | 8.341666667 |
| Variance | 41.17424242 | 222.817197 |
| Observations | 02 | 12 |
| PearsonCorrelation | 0.999998503 | |
| HypothesizedMeanDifference | 0 | |
| Df | 11 | |
| t Stat | -1.93685617 | |
| P(T<=t)one-tail | 0.039431034 | |
| tCriticalone-tail | 1.795884819 | |
| P(T<=t)two-tail | 0.078862068 | |
| tCriticaltwo-tail | 2.20098516 | |

## CARDIAC CONTRACTILITY

Patients with range of mitral regurgitation (MR) on day 1:

Among the 75 patients with risk factors, 39 patients are grouped into 56 to 65years.

| **Range** | **Frequency** | **Percent** |
|---|---|---|
| Severe | 12 | 16.0 % |
| Moderate | 31 | 41.30 % |
| Mild | 24 | 32.00 % |
| Trivial | 8 | 10.70 % |
| **Total** | **75** | **100 %** |

| | ***Frequency*** | ***Percent*** |
|---|---|---|
| Mean | 2.53 | 8.333333333 |
| Variance | 30.38636364 | 199.3824242 |
| Observations | 04 | 12 |
| PearsonCorrelation | 0.999999394 | |
| HypothesizedMeanDifference | 0 | |
| Df | 11 | |
| t Stat | -2.04569862 | |
| P(T<=t)one-tail | 0.032729405 | |
| tCriticalone-tail | 1.795884819 | |
| P(T<=t)two-tail | 0.065458809 | |
| tCriticaltwo-tail | 2.20098516 | |

| **Range** | **Frequency** | **Percent** |
|---|---|---|
| Severe to Severe | 4 | 5.30 % |
| Severe to Moderate | 8 | 10.60 % |
| Moderate to Moderate | 4 | 5.30 % |
| Moderate to mild | 9 | 12.20 % |
| Mild to mild | 7 | 9.30 % |
| Mild to Trivial | 3 | 4.00 % |
| Trivial | 8 | 10.60 % |
| **Total** | 43 | **57.30 %** |

t-Test: Paired Two Sample for Means

| | *Frequency* | *Percentage* |
|---|---|---|
| Mean | 21 | 34.06666667 |
| Variance | 1423 | 1190.613333 |
| Observations | 7 | 3 |
| PearsonCorrelation | 0.21999541 | |
| HypothesizedMeanDifference | 0 | |
| Df | 2 | |
| t Stat | 1 | |
| P(T<=t)one-tail | 0.211324865 | |
| tCriticalone-tail | 2.91998558 | |
| P(T<=t)two-tail | 0.040257265 | |
| tCriticaltwo-tail | 2.364624252 | |

## DISCUSSION

### *ON EJECTION FRACTION (EF)*

Among the 75 cases collected from the hospital the age group with highest frequency of heart failure with reduced ejection fraction(EF) was observed to be 51-65 years which present upto (45.30%) and the remaining age group frequencies were observed 35-50 years which present upto (28.00%) and 66-80 years which present upto (26.70%).These results were represented in Bar graph and pie chart.

### *Range of ejection fracion on date of admission*

Among the 75 cases collected from hospital the 31 patients were observed with 20%-30% Ejection Fraction (EF) which is preent upto (41.30%) and 38 patients were observed with 31%-40% Ejection Fraction (EF) which ispresent up to (50.60%) and 6 patients were observed with 41%-50% Ejection Fraction (EF) which is present upto (8.10%).These resuls were represented in bar graph and pie chart.

### *Range of ejection fraction after adminstrating drug Milrinone (AT THE TIME OF DISCHARGE)*

Among these 75 cases collected from hospital , 46 cases incresed which is present upto (61.00%) the Ejection Fraction (EF) at the time of discharge after administration of drug milrinone and the other 29 cases no change in Ejection Fraction (EF) at the time of discharge. The 31 patients who are admitted with Ejection Fraction (EF) (20%-30%), The Ejection Fraction (EF) was incresed in 29 patients which is present upto (38.00%), and the 38 patients who are admitted with EF (31%-40%) The Ejection Fraction (EF) was incresed in 15 patients which is present up to (20.00%) and the 6 patients who are admitted with Ejection Fraction (EF) 41%-50%, The ef was incresed in 2 patients which is present upto (2.60%) These results were represented in bar graphs and pie charts.

### Range of ejection fraction after 11 days of administring drug milrinone

Among these 75 cases collected from hospital the Ejection Fraction (EF) of 46 cases were increased at the time of discharge, on these 46 patients after 11 days 18 paients Ejection Fraction (EF) has be increased which is present upto (24.00%). the 29 patients with Ejection Fraction (EF) (20%-30%) the Ejection Fraction (EF) was increased in 12 patients which is present upto (16.00%). and the 15 patients with EF (31%-40%) the Ejection Fraction (EF) is increased in 6 patients which is present upto (8.00%). and the 2 patients with Ejection Fraction (EF) (41%-50%) there is no change in Ejection Fraction (EF).

***ON MITRIAL REGURGITATION (MR)***

**Range of MR at the time of admission**

Among the 75 cases collected from the hospital the MR is observed Among these cases 12 cases have severe MR which is present upto 16.00% and the 31 cases have moderate MR which is present upto 41.30% and the 24 cases have mild MR which is present upto 32.00% and the 8 cases have trivial MR which is present upto 10.70.

**Range of MR at the time of discharge**

Among these 75 cases (100%) collected from the hospital 43 cases (56.59%) MR was increased at the time discharge. Among these 43 cases the 12 cases has change in MR from severe to moderate which is present upto (15.90%) and the 13 cases has change in MR from moderate to mild which is present upto (17.50%) and the 10 cases has change in MR from mild to trivial which is present upto (23.19%).

**CONCLUSION**

A short-term prospective study on drug milrinone in heart failure patients with reduced ejection fraction by a group of four students in hospital with in the time period of 6 months.

A clinicalstudy conducted on heart failure patients with reduced ejection fraction. During the study process conducted on 75 in patients the people of age group between 51-65 years are more prone to get the heart failure with low ejectionfraction. which accounts upto 45.30% when compared with age groups 35-50 years (which varies upto 28.00%) and 66-80 years (which varies upto 26.70%)

The data collected from 75 cases were divided accounting to ejection fraction. the 31 patients were observed with 20%-30% Ejection Fraction (EF) which is present upto (41.30%) and 38 patients were observed with 31%-40% Ejection Fraction (EF) which ispresent up to (50.60%) and 6 patients were observed with 41%-50% Ejection Fraction (EF) which is present upto (8.10%).

**Range of ejection fraction after administrating drug Milrinone (AT THE TIME OF DISCHARGE):** Among these 75 cases collected from hospital, 46 cases increased which is present upto (61.00%) the Ejection Fraction (EF) at the time of discharge after administration of drug milrinone and the other 29 cases no change in Ejection Fraction (EF) at the time of discharge. The 31 patients who are admitted with Ejection Fraction (EF) (20%-30%), The

Ejection Fraction (EF) was increased in 29 patients which is present upto (38.00%), and the 38 patients who are admitted with EF (31%-40%) The Ejection Fraction (EF) was increased in 15 patients which is present up to (20.00%) and the 6 patients who are admitted with Ejection Fraction (EF) 41%-50%, The EF was increased in 2 patients which is present upto (2.60%) These results were represented in bar graphs and pie charts.

**Range of ejection fraction after 11 days of administrating drug milrinone:** Among these 75 cases collected from hospital the Ejection Fraction (EF) of 46 cases were increased at the time of discharge, on these 46 patients after 11 days 18 patients Ejection Fraction (EF) has be increased which is present upto (24.00%). the 29 patients with Ejection Fraction (EF) (20%-30%) the Ejection Fraction (EF) was increased in 12 patients which is present upto (16.00%). and the 15 patients with EF (31%-40%) the Ejection Fraction (EF) is increased in 6 patients which is present upto (8.00%). and the 2 patients with Ejection Fraction (EF) (41%-50%) there is no change in Ejection Fraction (EF).

Out of 75 cases 22 cases (29.3%) are diagnosed as ICMP, 26 cases are diagnosed as 26 (34.6%) DCMP and 27 (36.0%) cases are diagnosed as MI Hence this study proves that drug milrinone is mostly effectively acting on heart failure patients to increase the ejection fraction in short duration.

## REFERENCES

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