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An Overview on Heart failure after myocardial infarction

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Abstract:

Background: Heart failure (HF) is a common and serious complication following myocardial infarction (MI), contributing significantly to morbidity, mortality, and healthcare burden worldwide. Despite improvements in early reperfusion therapies and secondary prevention, a substantial proportion of MI survivors develop acute or chronic heart failure due to myocardial injury and adverse ventricular remodeling. Understanding the mechanisms and predictors of post-MI heart failure is critical for early risk stratification, targeted intervention, and improved patient outcomes.

Keywords: Heart Failure, Myocardial Infarction, Left Ventricular Dysfunction, Reperfusion, Ventricular Remodeling, LVEF, Prognostic Factors, Acute Coronary Syndrome.

Introduction:

Heart failure (HF) is a clinical syndrome, which has been traditionally defined as a condition characterized by the reduced ability of the heart to pump and/or fill with blood, or alternatively as an abnormality of cardiac structure/function leading to an inadequate cardiac output or to an adequate cardiac output secondary to compensatory neurohormonal activation and increased left ventricular filling pressure**(1)**.

The development of HF after MI has a significant impact on outcomes, regardless of the HF type. Among patients with a history of MI, HF development increases total mortality risk threefold and cardiovascular mortality four-fold. The timing of HF development also has an impact on adverse events. HF developing more than 3 days after MI is associated with a 43% higher mortality risk as compared with patients with HF developing in the first 3 days after MI. This may be explained by different risk factors and mechanisms leading to HF at different time points**(2)**.

Heart failure (HF) is widely recognized as the significant prognostic factor for ST-segment elevation myocardial infarction (STEMI), and it can occur in the acute or subacute phase of STEMI . the incidence of new-onset HF after acute STEMI reported in different studies varies considerably, ranging from 10% to 45% and this is affected by factors such as myocardial infarction type, myocardial infarction site and reperfusion mode **(3)**.

Clinical risk factors

- **Age**

The incidence of in-hospital HF is three times higher in patients 75–85 years old as compared with those 25–54 years old. After hospital discharge, HF incidence is six times higher in the older age group. After multivariate adjustment, the in-hospital HF risk increases by approximately 50% and post-discharge HF by 20–50% for every 10 years of age**(2)**.

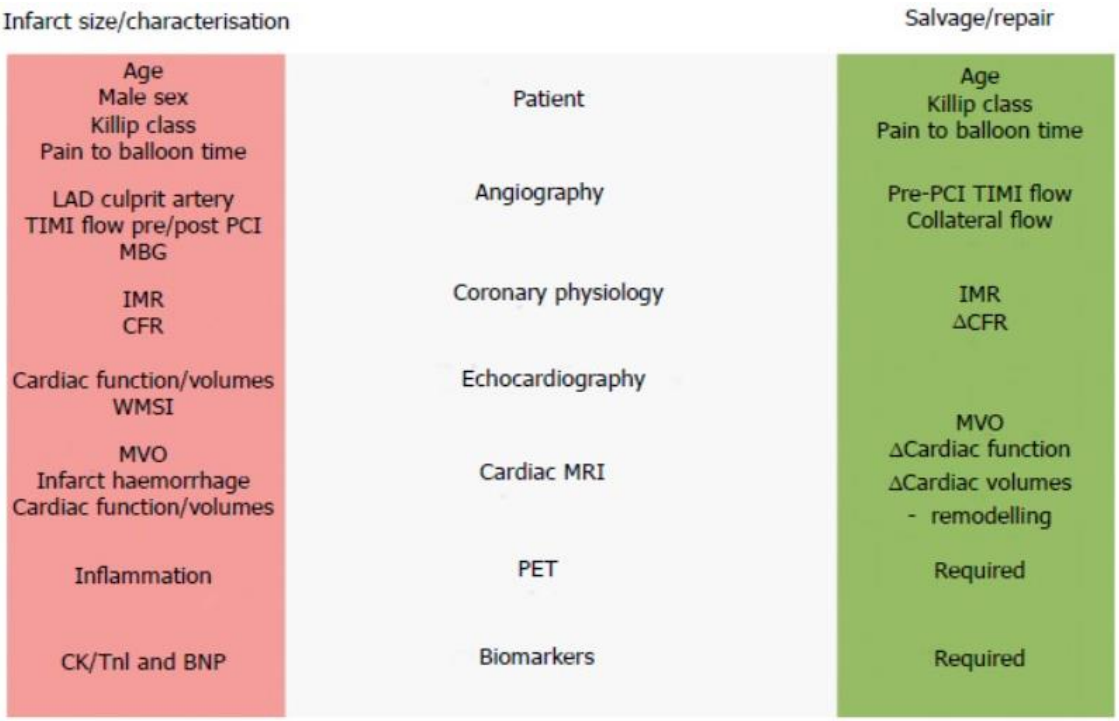

Figure 1: Heart failure after myocardial infarction - strategies for prediction of infarct size and salvage. BNP: B-type natriuretic peptide; CFR: Coronary flow reserve; CK: Creatine kinease; IMR: Index of microcirculatory resistance; LAD: Left anterior descending; MBG: Myocardial blush grade; MVO: Microvascular occlusion; PET: Positron emission tomography; PCI: Percutaneous coronary intervention; TIMI flow: Thrombolysis In Myocardial Infarction flow score; TnI: Troponin I; WMSI: Wall motion score index**(4).**

- **Gender**

Female sex was found to be independently associated with increased HF risk after MI in some studies, but not in others **(5)**. Several reasons may explain higher HF risk in women. Compared with men, female patients presenting with MI are older and have a higher prevalence of co-morbidities and worse functional status. The impact of co-morbidities such as diabetes, hypertriglyceridemia, and metabolic syndrome on cardiovascular risk appears to be higher in women than men. Furthermore, gender disparities in MI presentation and less aggressive hospital care of female patients, including the underuse of revascularization, may further contribute to the higher HF risk in women **(6)**.

- **Number and location of infarct-related artery**

Multi-vessel disease (MVD) reflects the high atherosclerotic burden with more prominent endothelial dysfunction and systemic inflammation. Patients with MVD are generally older and have diabetes and renal impairment as common co-morbidities. MVD is associated with lower ejection fraction and increased risk of major adverse cardiovascular events (MACE), including HF, by 80%. Anterior MI is associated with a higher risk of adverse remodelling and HF. The higher risk of HF associated with anterior MI is caused by the greater magnitude of irreversible LV damage, as compared with other MI locations**(2)**.

- **Prior myocardial infarction**

A history of MI increases the risk of HF by 21–89%. Excess risk may be explained by pre-existing systolic and/or diastolic dysfunction **(7)**.

- **Arterial hypertension**

Many studies reported that arterial hypertension increases the risk of HF. The excess risk associated with arterial hypertension ranged from 7% to 70%. More common microvascular injury and myocardial haemorrhage contribute to the excess HF risk in patients with arterial hypertension. Furthermore, higher neurohormonal activation and more common LV remodelling was described in hypertensive patients after MI **(8)**.

- **Higher heart rate**

A higher heart rate at admission was a risk factor for HF after acute MI **(9)**.

- **Atrial fibrillation**

New-onset atrial fibrillation complicates 2–21% cases of MI and may reflect left atrial pressure increase and atrial fluid overload during MI. Atrial fibrillation increases the risk of HF after MI by 20–51% **(10)**.

- **Diabetes**

After MI, the incidence of HF among diabetic patients is 60–70% higher than in patients without diabetes. After accounting for other co-morbidities associated with diabetes, its presence still results in 30–42% higher risk of HF after MI. Compared with non-diabetic patients with similar infarct size, similar systolic function, and infarct-related coronary artery patency rate, diabetic patients develop more often adverse LV remodelling and HF. This may be explained by a more common microvascular obstruction and diastolic dysfunction in those with diabetes. The excess risk seems to be similar in patients with pre-existing diabetes and diabetes diagnosed at the time of MI **(11)**

- **Chronic kidney disease**

Chronic kidney disease increases the risk of HF development after MI approximately two-fold. Excess HF risk in CKD can be explained by accelerated atherosclerosis, more common MVD, atypical MI presentation, and lower odds of revascularization, which results in larger infarct size and more severe ventricular dysfunction. Moreover, CKD leads to fluid overload, secondary hypertension, anaemia, chronic inflammation, and alterations of the renin–angiotensin–aldosterone system. Lower prescription of evidence-based medications in CKD patients has also been reported**(2)**.

- **Ischaemic preconditioning and heart failure after myocardial infarction**

Preconditioning is the process by which brief, repetitive episodes of ischaemia reduce the size of a subsequent MI. Compared with those without antecedent angina, patients with angina have a decreased risk of HF development during MI, lower risk of mortality or adverse LV remodelling after MI, and enhanced recovery of cardiac contractile function after MI. The protective effect of angina has been described up to 3 months prior to MI. The difference in outcomes in patients with and without angina preceding MI may be explained by ischaemic preconditioning or a larger extent of collateral circulation in patients with antecedent angina **(12)**.

HF after MI Mechanism

MI remains the most common cause of heart failure (HF). According to the time sequence of MI occurrence and HF development, three clinical presentations differing in pathophysiology, clinical characteristics, and outcomes can be identified: (i) HF onset at the time of MI presentation, (ii) HF developing during hospitalization for MI, and (iii) HF onset after discharge from the index hospitalization **(2)**

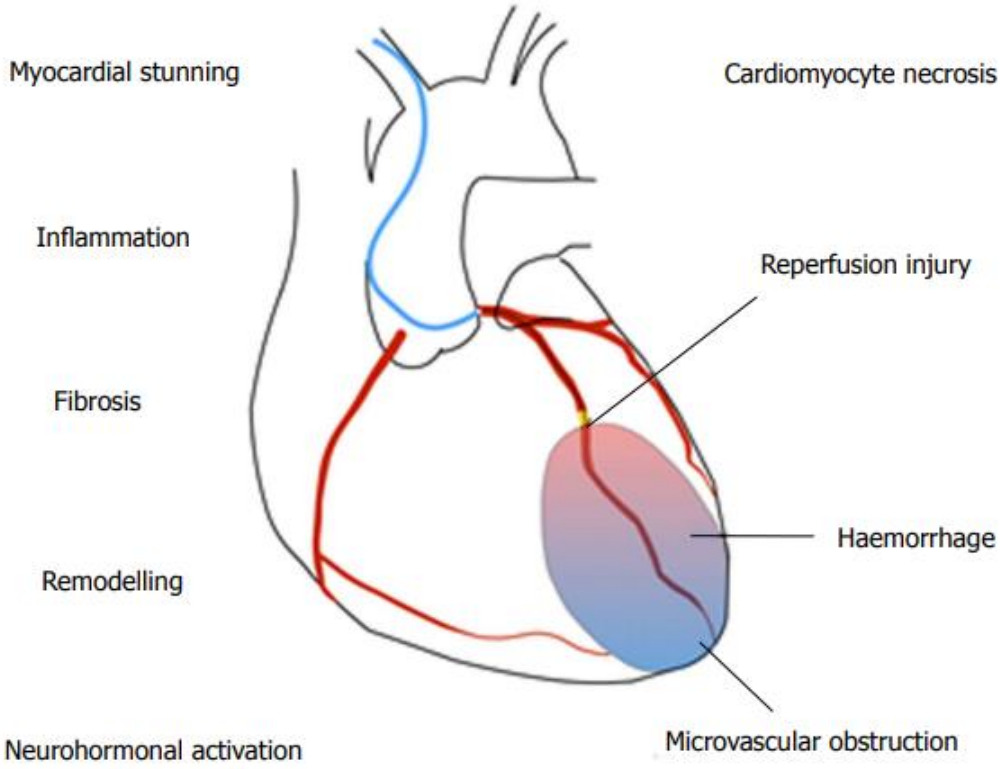

Figure 2: Mechanisms of heart failure after myocardial infarction(4).

A) Heart failure developing at the time of myocardial infarction hospitalization

The factors that contribute to the pathogenesis of HF development at the time of the MI hospitalization include myocardial compromise due to myocardial necrosis, myocardial stunning, and mechanical complications such as papillary muscle rupture, ventricular septal defect, and ventricular free wall rupture. Within 30 min of ischaemia, cardiomyocyte structural changes and oedema develop, leading to progressive myocyte death after 3 h of ischaemia **(13, 14).**

Reperfusion itself causes a second wave of injury through the production of reactive oxygen species. Despite successful epicardial reperfusion, the embolization of thrombotic debris leads to ongoing microvascular dysfunction and myocardial ischaemia. The inflammatory response to myocyte death also contributes to HF development. Furthermore, HF at this stage can be also triggered by exacerbation of pre-existing HF and co-morbidities, for example, anaemia, chronic kidney disease (CKD), or chronic obstructive pulmonary disease **(15)**.

B) Heart failure developing after myocardial infarction hospitalization

Heart failure developing after MI hospitalization is a consequence of cardiomyocyte death and scar formation, which triggers chronic neurohumoral activation (renin–angiotensin–aldosterone and sympathetic nervous system up-regulation) and ventricular remodelling. Left ventricular (LV) remodelling is more pronounced in men, patients with larger infarct size, and late or unsuccessful reperfusion of epicardial or microvascular bed. Ventricular remodelling changes ventricular geometry and leads to wall thinning, ischaemic mitral regurgitation, and further cardiomyocyte loss **(16)**.

Myocardial injury leads to activation of a stereotyped inflammatory cascade, comprised of early neutrophil ingress followed by monocyte-macrophage infiltration. Between days 3-5 following MI there is a transition from inflammation to repair, with activation of fibroblasts and progressive scar deposition. Over time there is compensatory activation of the renin-angiotensin and sympathetic nervous systems and pathological remodelling, with changes to the ventricular geometry, wall thinning, ischaemic mitral regurgitation and further cardiomyocyte loss. The precise contribution of the different pathophysiological components (*e.g.*, microvascular

dysfunction, inflammation) to injury is likely to be heterogeneous, and understanding mechanistic pathways in specific patient subgroups will be key to identifying novel therapeutic strategies **(17)**.

C) Heart failure development after hospital discharge

Heart failure development after hospital discharge is very prevalent. It is diagnosed in approximately 13% of patients at 30 days and 20–30% at 1 year after discharge for MI. The incidence of HF after MI discharge is highest in the first months, and then it drops and remains stable at a rate of 1.3–2.2% per year afterwards **(18)**.

Assessment of Heart Failure After MI

The priority is the identification of the mechanisms involved in HF after MI, because this step can determine the treatment. Regardless the mechanism, an adequate history and clinical examination remain the most important tools in the evaluation of ventricular dysfunction after MI **(19)**.

The simplest and most widely used method of assessing the severity of heart failure after MI is the Killip classification: class 1, patients have no evidence of heart failure; class 2, patients have rales present in up to one half of the lung fields or a third heart sound and systolic blood pressure >90 mm Hg; class 3, patients have frank pulmonary edema and systolic blood pressure >90 mm Hg; class 4, patients have cardiogenic shock with rales and systolic blood pressure >90 mm Hg. Importantly, recent studies have demonstrated that the Killip classification system is a strong predictor of long-term mortality after MI **(20)**.

Another method to evaluate the severity of HF is the New York Heart Association (NYHA) class. Patients in class I have no limitation of physical activity. Patients in class II present slight limitation of physical activity. Patients in class III refer marked limitation of physical activity. Finally, patients in class IV are unable to carry on any physical activity without discomfort **(21)**.

Biochemical markers can be useful to evaluate patients after MI. Indeed, elevated plasma natriuretic peptides (BNP and NT-proBNP) are usually associated with abnormal ventricular function **(22)**.

Considering images methods, chest radiography is also useful for detecting signs of ventricular dysfunction. However, some patients with normal chest x-rays may have hemodynamic cardiogenic disorders. Echocardiography is the most widespread method for determining the degree of ventricular dysfunction following MI and to exclude mechanical complications **(23)**.

Other less common modalities to assess cardiac morphology and function after MI include nuclear imaging (SPECT), computed tomography, and magnetic resonance imaging **(24)**

Treatment of Heart Failure After MI

A) Acute Treatment

The benefit from myocardial reperfusion with reduced infarct size and associated improvement in later regional and global ventricular function is well established. Patients with mild post-MI heart failure (Killip class 2) could have hypoxemia. In this setting, oxygen supplementation with nasal catheter or facial mask is necessary for the resolution of hypoxemia. If wheezing is present, indicating bronchial hyperreactivity, β_2-agonist inhalation should be used with careful monitoring of the patient's heart rate. Corticosteroid use in the acute phase of MI remains controversial due to concerns about increases in infarct expansion, the development of aneurysms, and left ventricular rupture **(25)**.

Diuretics treatments are essential in cases where there is dyspnea and signs of water and sodium retention. Intravenous loop diuretics are widely used given their effects on sodium and water excretion, as well as a possible vasodilator effect. However, if signs and symptoms do not improve with this management, nitrates may be used, mainly nitroglycerin. Intravenous nitrates are useful in reducing preload and relieving symptoms of heart failure after MI **(26)**.

In addition, angiotensin-converting enzyme (ACE) inhibitors should also be used during this phase. Close monitoring of arterial blood pressure, potassium, and creatinine levels are important in the management of

ACE inhibitors. Patients with severe post-MI heart failure (Killip class 3) whose hypoxemia does not improve with a nasal catheter or facial mask may require the use of noninvasive ventilation **(27)**.

In situations where tissue hypoperfusion occurs without cardiogenic shock, inotropic agents could be an option. However, some inotropes, such as digitalis and dobutamine, have contradictory effects, and others, like milrinone, could worsen prognosis. Patients with Killip class 4 have cardiogenic shock. The incidence of cardiogenic shock post-MI is about 7%, and despite therapeutic advances, it continues to have mortality rates over 50%.With regard to medical treatment, the use of inotropic agents in these patients is of special interest. However, it is important to note that despite hemodynamic improvement with dopamine, dobutamine, and levosimendan use, no increase in survival was observed **(28)**.

The use of intra-aortic balloon counterpulsation (IABP) in cardiogenic shock, when not quickly reversed by pharmacologic therapy, is recommended. IABP reduces systolic overload, increases diastolic pressure, and therefore, coronary perfusion, improving left systolic function. The primary limitations of IABP include the lack of active cardiac support, the need for accurate synchronization with the cardiac cycle, and the requirement for a certain level of left ventricular function **(29)**.

Usually percutaneous left ventricular assist devices (LVAD) are used as a bridge to recovery and are designed for a maximum use of 14 days. In general there are 3 types of devices, which are as follows: percutaneous cardiopulmonary bypass, axial flow pumps, and left atrial-to-femoral arterial LVAD **(30)**.

Interestingly, a recent study compared Tandem Heart (Cardiac Assist, Inc., Pittsburgh, PA) (left atrial-to-femoral arterial LVAD) with IABP in patients with revascularized MI and cardiogenic shock. The LVAD improved hemodynamic status better than IABP. Therefore, the use of percutaneous left ventricular assist devices (LVAD) remains an appealing treatment strategy for cardiogenic shock after MI. However, these devices are currently not supported by randomized controlled trials. Another potential strategy is the use of extracorporeal membrane oxygenator (ECMO). In fact, some evidences suggest that ECMO can offer additional benefits in improving outcomes in patients with acute ST-segment elevation myocardial infarction complicated with cardiogenic shock **(31)**.

B) Chronic Treatment

1) Ace Inhibitors:

It is well established that angiotensin-converting enzyme inhibitors (ACEIs) should be administered to patients with impaired EFs (≤40%) or those who have experienced HF in the early phase of MI **(32)**.

2) Angiotensin-II Receptor Blockers:

In the Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan (OPTIMAAL) study, losartan was compared to captopril in patients after MI with heart failure, left ventricular dysfunction, and other high-risk factors. After 2.7 years, there were no differences in heart failure hospitalization, reinfarction, sudden cardiac death, and all-cause mortality **(33)**.

The Valsartan in Acute Myocardial Infarction (VALIANT) study has compared the effects of captopril and valsartan, alone or in combination, in patients with MI and HF or ventricular dysfunction. After 24.7 months, there were no differences in morbidity and mortality among the groups. These results suggest that there is no difference between ACE inhibitors and ARBs in the treatment of HF after MI. In addition, VALIANT results are consistent with the lack of additional outcome benefits by the dual blockade of the renin-angiotensin system early after MI. Thus, ARBs could be used as an alternative to ACE inhibitors **(34)**.

3) β-Blockers:

The effects of β blockade in patients with left ventricular dysfunction after MI were addressed by the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) trial. In this trial, carvedilol treatment was associated with a 23% decrease in all-case mortality and a 40% reduction in reinfarction after 1.3 years. Other large trials in patients with all-cause systolic heart failure demonstrated that bisoprolol,

metoprolol, and nebivolol reduced the rate of hospital admissions and mortality when they were added to standard therapy **(35)**.

4) Aldosterone Antagonists:

The most important trial of aldosterone antagonists in patients with left ventricular dysfunction and MI was the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS). In this trial, eplerenone, a selective aldosterone antagonist, was given to post-MI patients with left systolic dysfunction for 16 months. It was shown to reduce all-cause mortality by 15%, sudden death by 21%, and hospitalization for heart failure by 15%. Likewise, Hayashi et al have shown that patients with a first anterior myocardial infarction treated with spironolactone for 1 month had a significant improvement in left ventricular remodeling and in ejection fraction **(36)**.

5) Hydralazine and Isosorbide Dinitrate:

There are no studies that specifically evaluate hydralazine and isosorbide dinitrate in patients with left ventricular dysfunction due to MI. However, in all-cause systolic heart failure, this association could be used in self-identified African Americans **(37)**.

6) Lipid Lowering Therapy:

Statins have an antiinflammatory action, and inflammation is thought to play a role in the pathophysiology of heart failure. In fact, 10 mg rosuvastatin daily, in patients with ischemic systolic heart failure, reduced cardiovascular death, myocardial infarction, and stroke mainly in patients with high sensitivity-C reactive protein ≥2.0 mg/L. However, further studies are required to recommend routine use of statins in HF after MI **(38)**.

7) Implantable Cardioverter Defibrillators:

Patients with left ventricular dysfunction after myocardial infarction have an increased risk of sudden death due to lethal arrhythmias. As a result, implantable cardioverter defibrillators are recommended for primary prevention of sudden cardiac death in patients with ischemic heart disease at least 40 days after MI, with an ejection fraction lower than 35%, with an NYHA class of II or III while receiving chronic optimal medical therapy, and with an expectation of survival with good functional status for more than 1 year **(39)**.

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