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Chapter

Extracorporeal Membrane Oxygenation for the Support of Adults with Acute Myocarditis

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Abstract

Myocarditis is an inflammatory disease of the myocardium diagnosed through a combination of histological, immunological and immunohistochemical criteria. Its clinical presentation varies from an acute coronary-like symptoms to heart failure. Diagnostic workup includes elevated biomarkers, ECG and echocardiographic findings. Cardiac magnetic resonance is the most important examination providing information on both ventricular function and tissue characterization. However, in the case of critically ill patients, CMR should be replaced with endomyocardial biopsy (EMB) which remains the gold standard in myocarditis diagnosis. EMB provides information on both the etiology and prognosis thus affecting the therapeutic approach to the patient. For example, virus positive myocarditis benefits from antiviral treatment while in virus negative ones, immunosuppression is more appropriate. Mechanical circulatory support (MCS) is often necessary in patients presenting with cardiogenic shock. MCS includes intra-aortic balloon pump, temporary percutaneous or even surgically implanted ventricular assist devices and extracorporeal membrane oxygenation (ECMO). ECMO essentially bypasses the heart and provides adequate oxygenation to peripheral organs. Due to the increased afterload under ECMO support, it seems reasonable to be combined with intra-aortic balloon pump or percutaneous VAD implantation to promote left ventricular unloading and potential recovery.

Keywords: myocarditis, cardiogenic shock, ecmosupport, extracorporeal membrane oxygenation, acute myocarditis

1. Introduction

Myocarditis is defined by the ESC as an inflammatory disease of the myocardium diagnosed by established histological, immunological and immunohistochemical criteria. Histological criteria consist of histological evidence of inflammatory infiltrates within the myocardium associated with myocyte degeneration and necrosis of non-ischemic origin while immunohistochemical criteria consist of ≥14 leucocytes/mm² including up to 4 monocytes/mm² with the presence of CD3 positive T-lymphocytes ≥7 cells/mm² [1].
The clinical presentation of myocarditis varies significantly. It can range from acute coronary syndrome-like to acute or chronic heart failure forms. Specifically, it may present as acute chest pain frequently associated with recent infections, as new-onset heart failure (symptoms within 2 weeks to 3 months), as chronic heart failure (symptoms >3 months) or as a “life-threatening” – fulminant condition (refractory arrhythmias, cardiogenic shock). In general, acute coronary syndrome-like presentation has been associated with a better overall prognosis while heart failure is usually associated with a worse one, resulting in dilated cardiomyopathy or even death.

Diagnosis of acute myocarditis requires a workup consisting of both routine and specialized tests. ECG is usually abnormal in most cases, however, there are no specific signs. The most common findings are sinus tachycardia and repolarization abnormalities (either negative T waves or concave ST-T segment elevation as also seen in acute pericarditis) [1].

Unfortunately, there are no specific biomarkers for the diagnosis of myocarditis. Inflammatory markers are usually raised along with markers of myocardial injury (troponin, creatine kinase and its MB isoenzyme) and brain natriuretic peptides. Viral antibodies in the serum provide no information and may lead to an incorrect diagnosis. In general, only findings in myocardial tissue can be considered reliable with the exception of systemic diseases like hepatitis C, Lyme disease, HIV or rickettsial infections [1].

Echocardiography should always be performed in suspected myocarditis both for ruling out other cardiac diseases and for assessing ventricular function. In acute myocarditis, the findings may include regional wall motion abnormalities (usually beyond the supply area of coronary arteries), global ventricular dysfunction and/or pericardial effusion. Increased wall thickness may be observed most likely as a result of edema. Ventricular dilation is rare in the acute setting. While there are no specific signs seen through echocardiography, newer imaging techniques may provide some additional information since myocardial strain is most commonly affected in the inferolateral wall [2].

The exclusion of coronary artery disease should be performed in all patients suspected of myocarditis. This can be done through either classical or computed tomography coronary angiography.

The most important examination in myocarditis workup is the cardiac magnetic resonance (CMR) which provides information on both ventricular function and tissue characterization. In clinically stable patients, CMR can almost single-handsedly confirm the diagnosis through the use of the updated Lake Louise criteria. These criteria require finding evidence of both myocardial edema (as seen through T2 mapping or T2-weighted images) and non-ischemic myocardial injury (as seen through T1 imaging, extracellular volume or late gadolinium enhancement) while supportive criteria include the presence of concomitant pericarditis or systolic left ventricular dysfunction [3]. For many years, the most commonly used criterion was the pattern of late gadolinium enhancement (LGE) which represent myocardial necrosis and fibrosis. In myocarditis, LGE is usually seen in the subepicardial and midmyocardial layers [4] and in the inferolateral wall [5]. Its presence in the anteroseptal wall is associated with a worse prognosis [6].

Despite the important role of CMR, diagnosis of myocarditis is confirmed through proposed criteria by a position statement of the European Society of Cardiology. A combination of at least 1 clinical and 1 para-clinical criteria is necessary or at least 2 para-clinical criteria in the case of asymptomatic patients. Clinical
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criteria include: (i) acute chest pain; (ii) new-onset or chronic heart failure symptoms; (iii) palpitation, unexplained arrhythmias or syncope and (iv) unexplained cardiogenic shock. Para-clinical criteria include: (i) ECG findings such as repolarization abnormalities, atrio-ventricular block, sinus tachycardia, frequent premature ventricular complexes etc.; (ii) elevated levels of troponin; (iii) functional and structural abnormalities on cardiac imaging and (iv) consistent findings through tissue characterization by CMR [1].

Treatment of myocarditis is consistent with heart failure treatment in hemodynamically stable patients. B-blockers and ACE inhibitors have been the mainstay of therapy for many decades with good results. The addition of mineralocorticoid receptor antagonists (MRAs) can be considered in cases of persistent left ventricular dysfunction. Newer treatments such as angiotensin receptor neprilysin inhibitors (ARNIs) or sodium-glucose co-transporter 2 inhibitors (SGLT2-i) have not been examined in myocarditis patients apart from animal studies [7, 8] but may prove useful in the future. Finally, device treatment such as ICD implantation is important in case of recurrent ventricular arrhythmias, aborted sudden cardiac death (as secondary prevention) or persistent ventricular dysfunction (as primary prevention). However, ICD implantation should be avoided in the acute setting, since arrhythmias may be ameliorated. In the above-mentioned cases of secondary prevention, wearable ICDs may be of use and the decision for permanent ICD implantation can take place during the follow-up [9]. More specialized myocarditis treatment (immunosuppressive treatment and mechanical circulatory support) will be further analyzed below.

This chapter will be mostly focused on fulminant variations since those generally have an indication for extracorporeal life support. Fulminant myocarditis requires urgent management and a quick referral to tertiary expert centers for advanced heart failure therapies. Due to its urgency, the diagnostic work-up should happen simultaneously with management. As a result, the first step usually includes imaging of the coronary arteries to exclude the possibility of the acute coronary syndrome. Management should include support of the respiratory system – usually requiring the use of either non-invasive or invasive ventilation – and circulatory support – requiring the use of inotropes or mechanical circulatory support in later stages [10].

While in less severe forms, diagnosis of myocarditis is often made through CMR, patients presenting with fulminant myocarditis are in a too critical condition to undergo this examination [11]. The “gold standard” for myocarditis diagnosis has long been the endomyocardial biopsy (EMB) which can also provide information on the specific etiology of myocarditis in each patient. From a pathological standpoint, there are three main types of myocarditis: lymphocytic, eosinophilic and giant-cell while, as far as etiology is of concern, it can be viral or non-viral. The differentiation of which type of myocarditis one deals with, is necessary for providing etiology-specific treatment. Specifically, viral forms of myocarditis may benefit from virus-specific treatment [12] (e.g. acyclovir for HHV-6, interferon for enteroviruses, etc.) while non-viral forms may benefit from immunosuppression. Eosinophilic myocarditis benefits from corticosteroid administration while also treating the underlying cause of eosinophilia (parasitic infections, hematologic syndromes, etc.). Finally, giant cell myocarditis is the variation with the worse prognosis requiring combination immunosuppressive treatment and consideration for urgent ventricular assist device implantation or heart transplantation [13–15]. As a result, it comes as no surprise that the performance of EMB in fulminant myocarditis patients is associated with a better
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prognosis [16, 17]. It should be noted that EMB may not necessarily reveal the proper etiology due to the absence of pathological findings from the sample site. In high clinical suspicion (especially in the case of giant-cell myocarditis), EMB should be repeated in order to acquire samples from different sites.

In cases where the patient’s clinical condition rapidly deteriorates despite hemodynamic support, corticosteroids and even immunosuppression should be administered while awaiting biopsy results. Studies on both animal and human subjects have shown that corticosteroid administration has not been associated with exacerbation in the case of possible viral disease or worse overall prognosis in the case of fulminant myocarditis [18].

In critically ill patients with significantly reduced ejection fraction, inotrope administration may stabilize their clinical condition. However, the treating team should be ready to use mechanical circulatory support devices (intra-aortic balloon pump, percutaneous ventricular assist devices or extracorporeal membrane oxygenation).

2. Extracorporeal life support (ELS) or extracorporeal membrane oxygenation (ECMO)

Extracorporeal membrane oxygenation (ECMO) is a device that allows temporary support in pulmonary and/or cardiac failure refractory to conventional medical management [19]. It mainly consists of a blood pump, oxygenator, drainage and returns cannulae and arterial and venous access points (Figure 1). The blood pump propels the blood to the oxygenator membrane where the gas exchange between the patient’s blood and the gas mixture of the device happens.

The ECMO has three main configurations depending on the access sites used: veno-venous (VV) ECMO, peripheral veno-arterial (VA) ECMO and central VA

![Figure 1. A diagram demonstrating the components of an extracorporeal membrane oxygenation device [19]. (The figure is shared through the CC BY 4.0 according to the original article).](image_url)
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ECMO. In VV ECMO, veins are used as both access sites with the purpose of supporting mainly the respiratory system. In this chapter, we will not focus on this configuration.

In VA ECMO, an artery and a vein are used as access sites. In central VA ECMO, the drainage cannula can be inserted directly into the right atrium, and the return cannula into the ascending aorta. On the other hand, in the peripheral VA ECMO, the drainage cannula is usually inserted into the femoral vein and the return cannula into the femoral artery (Figure 2). In this configuration, the patient’s respiratory and circulatory systems are both supported essentially bypassing the heart and lungs providing oxygenated blood to peripheral organs. The heart still pumps blood up to the descending aorta depending on its systolic function.

The main complications of ECMO consist of device thrombosis, bleeding (access site, gastrointestinal or intracranial due to anticoagulation), acute kidney injury, limb ischemia (in peripheral configuration) and infection.

3. The role of extracorporeal membrane oxygenation in the management of acute myocarditis

Despite its complications, mechanical circulatory support is the most crucial and effective option in the management of fulminant myocarditis refractory to medical treatment providing valuable time for recovery either spontaneously or through the specific treatment described above.

Intra-aortic balloon pump (IABP) is usually the first option acting through afterload reduction and a small increase in cardiac output (around 0.5 L) [20]. Though its
complication rate is relatively low compared to more invasive options, IABP cannot support worsening patients exactly due to its limitations of provided flow.

The next option is the percutaneous ventricular assist devices (pLVAD) which consist of Impella and TandemHeart – temporary LVADs implanted through the femoral artery. Their main advantage is the significant increase of cardiac output providing a flow of up to 5 L (depending on which model is used) along with a less invasive approach of surgically implanted VADs. Despite the small series of patients treated with this option, the reported results are generally satisfactory [21]. Their main disadvantages include the support of one ventricle only – usually the left one. As a consequence, this option is limited to patients with adequate right ventricular function to prevent the post-implantation development of right ventricular failure, unless two such devices are implanted simultaneously (one for each ventricle), thus, significantly increasing the odds of adverse effects.

Extracorporeal membrane oxygenation essentially bypasses the heart and provides adequate oxygenation to peripheral organs. Their main use in fulminant myocarditis is as bridge-to-recovery, bridge-to-transplant or bridge-to-bridge (bridge to a more permanent solution such as a durable VAD) in irreversible conditions often as a result of giant cell myocarditis. ECMO efficacy in fulminant myocarditis has been well described with survival rates of around 75% and VAD-free survival rates of around 61% [22, 23].

Even though ECMO supports the peripheral organs, it does not contribute to the unloading of the left ventricle. On the contrary, regardless of central or peripheral configuration, ECMO significantly increases the left ventricular afterload due to the retrograde flow to the aorta. In moderately reduced left ventricular systolic function with peripheral VA ECMO, this results in separate oxygenation of the upper and lower part of the body; the upper body is oxygenated by blood provided by the native flow through the heart while the lower body is oxygenated by blood provided by the device with the “splash” zone lying at some point in the descending aorta [24]. In cases of inadequate lung function, this phenomenon may cause the Harlequin syndrome characterized by hypoxia and cyanosis of the upper body and normal saturation and color of the lower body. The syndrome can be resolved by changing the configuration to a central one whereas the device provides oxygenated blood directly to the ascending aorta. This complication is rare when dealing with fulminant myocarditis due to the generally adequate lung function and the significantly reduced left ventricular function resulting in device blood supply to the whole body since the retrograde flow reaches the ascending aorta.

The above-described increased afterload combined with the significantly reduced ventricular function result in a perpetually loaded left ventricle potentially hindering recovery. In some cases, the aortic valve may remain closed during the cardiac cycle due to the inability of the cardiac muscle fibers to generate enough force/pressure to overcome the increased afterload. This phenomenon is nicely demonstrated by pressure-volume loops (PV loops) (Figure 3) which show a significant reduction of stroke volume with increasing ECMO flows. Potential solutions include the concurrent use of IABP, pVADs or direct transaortic left ventricular venting. All of these options provide some amount of left ventricular unloading thus promoting cardiac recovery [25].

Another main ECMO disadvantage is its temporary nature. In general, ECMO support cannot last the past 14 days due to a significant increase in adverse effects with prolonged support. Bleeding due to continuous heparin administration,
infections and limb ischemia are common in these cases. Specifically for patients with myocarditis, it has been reported that prolonged ECMO support >7 days is associated with a worse prognosis [26]. However, this association could also be explained by the patients’ worse clinical conditions resulting to prolonged ECMO support.

Reported predictors of myocarditis patient outcomes supported with ECMO include clinical characteristics, biomarkers and echocardiographic characteristics. The most important clinical predictor is the prolonged prevalence of arrhythmias be they atrioventricular block or ventricular arrhythmias [27]. SOFA score has also been associated with the patient outcome with scores >12 shown to be predictive of death or established heart failure [28]. CK-MB is the most well-reported biomarker with two independent studies agreeing to its prognostic value with levels >95 ng/mL [28] or >185 IU/L [27] predicting a lower chance of successful weaning. Finally, the only echocardiographic parameter shown to have some prognostic value is the left ventricular posterior wall thickness with better results when >11 mm [27]. Unfortunately, all of the referenced studies are based on a small series due to the low incidence of myocarditis and even lower of its fulminant presentation.

4. Conclusion

Fulminant myocarditis is a rare yet significantly dangerous syndrome that needs urgent referral to tertiary centers for endomyocardial biopsy, advanced heart failure treatments and etiology-specific treatment. Mechanical circulatory support is the cornerstone of its management with extracorporeal membrane oxygenation devices.
being the last resort in conditions refractory to medical and less invasive mechanical circulatory support measures. The outcomes with ECMO devices are more than acceptable with a 75% survival rate especially when combined with solutions for adequate left ventricular unloading.
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References


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