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INCIDENCE AND PREDICTORS OF MAJOR ARRHYTHMIAS EVENTS AFTER MYOCARDITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The long-term arrhythmic risk after myocarditis remain unclear. Recent data indicate that ventricular arrhythmias may be frequently observed both in the acute phase and years after the initial event, making sudden cardiac death (SCD) a prominent cause of death in these patients. The latest European and American guidelines support implantable cardioverter-defibrillator (ICD) implantation as secondary prevention independently on the underlying substrate and evolution. The optimal management of myocarditis patients remains debated.

Purpose: To assess the incidence and predictors of major arrhythmic events (MAEs) after myocarditis.

Methods: We conducted a systematic literature review and meta-analysis including 19 observational studies on myocarditis and MAEs during follow-up. MAEs were defined as a composite of SCD, aborted cardiac arrest (ACA), sustained ventricular tachycardia (sVT) and appropriate ICD or wearable-cardioverter defibrillator (WCD) intervention. The primary outcome was the incidence of MAEs; secondary outcomes included the occurrence of each component of MAEs and the composite of all-cause mortality and heart transplantation (HTx).

Results: 3954 patients with prior myocarditis irrespective from clinical and arrhythmic presentation were included. Among overall population, the majority were male (70,7%) with a median age of 46 (IQR 43-51). Most patients (56%) suffered lymphocytic myocarditis, followed by giant cell myocarditis (7%). At presentation, 38% (IQR 21-64%) experienced ventricular fibrillation or sVT, with a mean left ventricular ejection fraction (LVEF) of 47% (IQR 38-50%). Late gadolinium enhancement on cardiac magnetic resonance (CMR) was found in 89% of cases. Notably, most patients (67%; IQR 36-100%) belonged to the acute myocarditis group, the rest had chronic myocarditis. At discharge, 61% (IQR 36-92%) required ICD implantation, and 88% (IQR 84-94%) were prescribed beta-blocker therapy. At a median follow-up time of 24 months (IQR 19-57), the incidence of MAE was 28% (95% CI 17%-41%), with a median time of presentation of 12 months. The incidence of sVT, ACA, appropriate ICD/WCD intervention and SCD during the same follow-up were 22%, 6%, 20% and 1% respectively. The combined rate of all-cause mortality/HTx was 11% (95% CI 6%-18%). Meta-regression analysis identified advanced atrioventricular block ($p = 0.002$) and life-threatening arrhythmias at presentation ($p = 0.022$) as significant variables associated with higher risk of MAEs during follow-up, while male gender resulted as a protective factor ($p = 0.042$). Due to the high statistical heterogeneity of the studies, we performed a sensitivity analysis limited only to studies in which the population had 100% ICD. This analysis showed the same incidence of MAE over a 30-month follow-up but no SCD and lower incidence of all-cause death/HTx (5% vs. 11%).

Conclusion: The incidence of MAEs after myocarditis remains high over time, especially in patients with life-threatening arrhythmias and high-grade atrioventricular block at presentation. Further prospective studies are needed to better stratify high-risk patients and guide decisions regarding early ICD implantation or other antiarrhythmic strategies.