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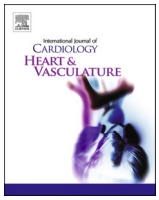

Editorial

Arrhythmic risk in acute myocarditis: Early threats, late events, and clinical uncertainty

Acute myocarditis is an inflammatory heart muscle disease with an heterogenous presentation ranging from infarct-like presentations with chest pain, heart failure, or arrhythmic syndromes. A small subset of patients shows malignant ventricular arrhythmias or even sudden cardiac death (SCD) during the acute phase [1]. Clinicians thus face a dilemma: how intensively and for how long to monitor myocarditis patients for life-threatening arrhythmias, and how to stratify those at risk. Krempke et al. investigate this issue in their study of patients with suspected acute myocarditis, focusing on the incidence, timing, and predictors of life-threatening ventricular arrhythmias [2]. In this editorial, we summarise the key findings of Krempke et al. paper, discuss the study's strengths and limitations, and place the results in context with emerging evidence. We also consider the clinical implications of these findings, including current gaps in risk stratification and priorities for future research in myocarditis care.

Krempke et al. [2] report that life-threatening ventricular arrhythmias (sustained ventricular tachycardia, ventricular fibrillation, or cardiac arrest) are uncommon in acute myocarditis, occurring in approximately 1 out of 30 patients (3.3 %). Among 304 patients with suspected myocarditis (mean age ~ 41 years), only 10 patients experienced such arrhythmic events. Crucially, when arrhythmias did occur, they clustered early in the clinical course: over half (8/13 events) took place within the first 24 h of hospitalisation, and 10/13 within 48 h. Nonetheless, a notable minority (~23 %) of these events arose late, i. e. beyond 72 h after admission (3 events). This finding indicates that while the highest-risk period is the first day or two of illness, delayed malignant arrhythmias can occasionally happen even after several days, an issue that complicates decisions about the duration of monitoring. Patients who suffered life-threatening arrhythmias had markedly worse outcomes. Krempke et al. found a ~ 40 % in-hospital mortality in the arrhythmic group versus only 0.3 % in those without arrhythmia. In other words, experiencing a ventricular tachyarrhythmia in acute myocarditis is associated with higher risk of early death, underscoring that such arrhythmias often coincide with fulminant myocarditis or severe haemodynamic compromise. Krempke et al. also identified clinical differences in those who developed arrhythmias: these patients tended to have higher peak cardiac troponin levels and lower left ventricular ejection fraction (LVEF) – indicators of more extensive myocardial injury – and were more likely to present with acute heart failure features (cardiogenic shock or significant LV dysfunction). These observations are consistent with previous observations on complicated myocarditis: more severe myocardial inflammation or necrosis predisposes to electrical instability. Interestingly, probably due to sample size limitations, the authors could not determine a single parameter that reliably ruled out risk. There was substantial overlap in peak high-sensitivity troponin-T values and LVEF between those who did and did not develop arrhythmias. In practical terms, even patients with only moderate enzyme rise or preserved ejection fraction were not entirely exempt from arrhythmic events, although risk was clearly higher with greater injury. Furthermore, Krempke et al. examined the timing of arrhythmias relative to the biochemical course of myocarditis. They noted that arrhythmias did not consistently occur only at the peak of troponin release: this finding is clinically important – it means one cannot assume a patient is "out of the woods" simply because their enzymes have peaked or begun to decline. Arrhythmia risk may persist even as acute inflammation markers wane, so decisions on monitoring should not rely solely on troponin trends. To improve risk stratification, Krempke et al. derived a simple multivariable model using three early variables: LVEF, peak troponin, and patient sex. Notably, female sex emerged in the model with an odds ratio < 1 (suggesting male sex may confer higher arrhythmic risk). The model achieved a high area under the curve (~0.98) for predicting patients without life-threatening arrhythmia, with 99 % sensitivity and 75 % specificity in the study cohort. In essence, if a patient had a combination of factors (e. g. higher LVEF and lower troponin, and possibly female) indicating low risk, the model could rule out serious arrhythmias with high confidence. This enabled classification of patients into strata: a large low-risk majority versus a small high-risk minority. While these results are promising – pointing towards an "early rule-out" tool to identify patients who might not require prolonged telemetry – the model needs external validation. It was derived from a limited number of arrhythmic events (10 patients), so there is risk of overfitting. Nonetheless, the concept is valuable: integrating simple clinical parameters might allow clinicians to safely shorten monitoring in low-risk myocarditis patients, while flagging those who warrant closer observation or prophylactic measures.

Krempke et al. should be commended for assembling a sizeable cohort (over 300 patients) in a clinical scenario that is relatively uncommon. All patients underwent continuous rhythm monitoring in an intensive or intermediate care setting, which is a strength – it ensured that arrhythmic events were likely to be detected and accurately recorded. The study's focus on suspected myocarditis (defined by clinical presentation, biomarker elevation and exclusion of acute coronary syndromes) reflects real-world practice, where a definitive endomyocardial biopsy is often unavailable. This enhances generalisability, since clinicians frequently manage myocarditis empirically based on clinical diagnosis. The authors' analysis of arrhythmia timing in relation to

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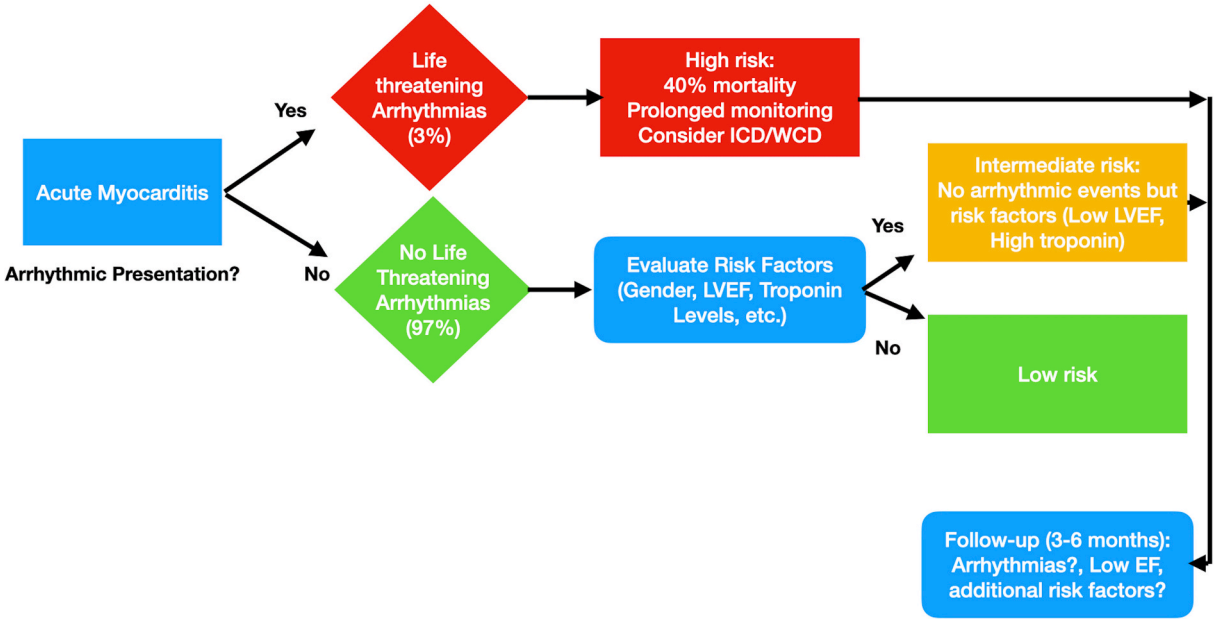

Fig. 1. A practical algorithm for clinical guidance is presented based on the findings of Krempke's study [2] and other systematic or observation data [3,4].

troponin kinetics, and their attempt to derive a predictive model, are innovative aspects that address practical questions (i. e. "how long must we monitor, and can we know who is safe to transfer or discharge earlier?"). However, there are significant limitations including the study's retrospective observational design, limited sample size, and lack of long-term follow-up. The analysis was largely in-hospital; we do not know what proportion of patients later had arrhythmic recurrences or late SCD after discharge. Additionally, by limiting inclusion to ICU/IMC admissions, the study may have preferentially captured more severe myocarditis cases – patients well enough for the general ward or outpatient management were not represented. This could inflate the observed arrhythmia incidence compared to all-comers with myocarditis. Conversely, it means the "low-risk" group in this study were still those deemed sick enough for monitored care, so truly mild cases (who likely have near-zero arrhythmic risk) were not studied. Another consideration is that not all patients had definitive myocarditis confirmation via biopsy or cardiac MRI findings (gadolinum enhancement, edema, etc.). Thus, the sample may have included some diagnostic uncertainty or heterogeneity in aetiology (e. g. some cases might have been ischemic mimics or other cardiomyopathies). The proposed risk model, while showing excellent performance within this dataset, must be interpreted cautiously. With only 10 events, including three variables risks statistical overfitting – the extremely high AUC (0. 98) suggests it may not perform as perfectly in new larger cohorts. Prospective validation in an independent dataset will be needed to confirm the model's utility for guiding clinical decisions. Finally, Krempke et al. did not incorporate cardiac MRI features or specific aetiologies into their risk analysis. There is evidence that certain MRI findings, such as mid-wall septal or extensive late gadolinium enhancement (LGE), are associated with worse prognosis in myocarditis [5]. The absence of LGE data in this study leaves an open question as to whether imaging could further refine risk stratification beyond the basic clinical variables used.

Krempke et al.'s findings are consistent with previous literature on myocarditis-related arrhythmias. Prior studies have established that ventricular arrhythmias tend to occur early in the course of acute myocarditis, especially in fulminant cases. A Danish registry of over 2,500 myocarditis patients, for example, reported a 90-day ventricular arrhythmia incidence of ~ 1.9 %, with the highest hazard in the initial hospitalization period. The same registry found myocarditis patients had a 16-fold higher short-term risk of SCD or malignant arrhythmia than the general population, underscoring the clinical need for vigilance [6]. Krempke et al. quantify this early risk in a monitored setting and importantly show that while most events occur in the first 24–48 h, a non-negligible fraction can arise later [1]. This aligns with clinical experience that delayed arrhythmias, though uncommon, may occur especially if myocardial inflammation remains active or if there is evolving scar-related reentry. The risk factors identified by Krempke et al. parallel those reported elsewhere. Narducci et al. (2024) performed a systematic review of 322 patients from 5 studies, all of whom had acute myocarditis with initial ventricular arrhythmic presentation [3]. They observed that during long-term follow-up, 41 % of these patients experienced major arrhythmic events (recurrent sustained VT/VF, SCD or appropriate ICD shock). On this basis a careful monitoring and clinical decision making is needed in patients with myocarditis and arrhythmic presentation to prevent fatal arrhythmic events during follow- up [4]. A practical algorithm for clinical guidance is presented in the Fig. 1 based on the findings of Krempke's study [2] and other systematic or observation data [3,4].

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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