

Editorial

Beyond the storm: rethinking recovery in fulminant myocarditis



Fulminant myocarditis, once thought to confer better long-term outcomes than non-fulminant forms after acute recovery [1], is now shown to be associated with persistently impaired left ventricular ejection fraction [2,3], challenging a long-held clinical belief [1]. In the published Chinese multicentre retrospective study by Li et al. [2], the authors examined long-term left ventricular ejection fraction (LVEF) outcomes in fulminant myocarditis (FM) versus non-fulminant myocarditis (NFM). The cohort included 324 acute myocarditis patients (163 FM, 161 NFM) confirmed by endomyocardial biopsy or cardiac MRI. The primary endpoint was a binary outcome of LVEF < 55 % at the final two follow-up visits. A secondary endpoint tracked LVEF as a continuous measure over time. Over a standardized follow-up, the investigators employed rigorous statistical methods to adjust for confounders and differentiate treatment effects from disease effects. FM patients had significantly higher odds of long-term LV dysfunction than NFM patients. Early aggressive therapies in FM—specifically intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO) support—were associated with better LVEF recovery [2].

The study has several clinical implications. First of all, a long-term prognostic insight. FM patients retain significantly worse LVEF than NFM even in the post-acute phase, challenging prior assumptions of full recovery [1] and in agreement with previous Italian and International experiences [3,4]. Second, the study highlights the need for a long-term monitoring of these patients with persistent LVEF < 55 %. In FM patients the early use of IABP and ECMO correlates with better long-term LVEF. These findings support the current approach, also consistent with the AHA scientific statement on FM, that recommends early recognition and rapid initiation of MCS (e.g. IABP, VA-ECMO) in these patients. Early hemodynamic support can stabilise end-organ perfusion, reduce myocardial workload, and potentially allow myocardial recovery, improving survival [5].

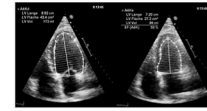
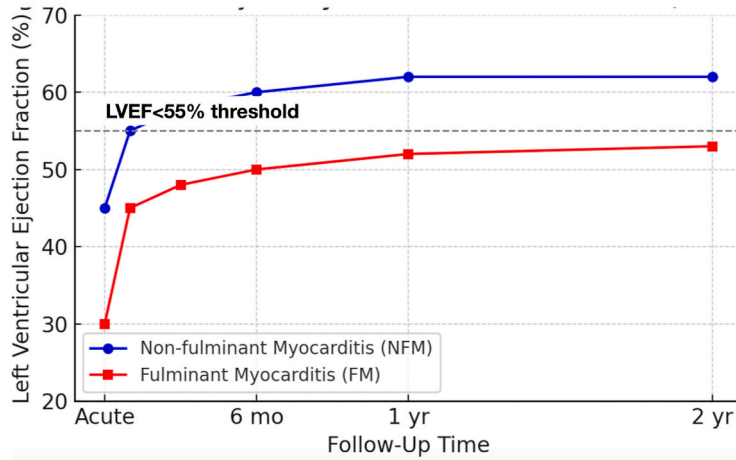
Stratified models show FM increases risk across sexes, highlighting the need for sex-independent vigilance [2]. On the contrary, a recently

published Italian study showed that fulminant onset and female sex are both associated with worse long-term cardiac outcomes, although LVEF remains a key prognostic indicator [6].

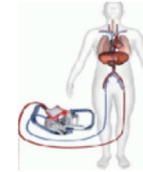
The present study is one of the first large-scale multicentre study in China and provides critical insight into FM/NFM outcomes in an Asian cohort. In this study, combining binary and longitudinal LVEF measures strengthens result reliability. Nevertheless, the study has some limitations and weaknesses. First of all, the retrospective design. Second, only patients who survived the acute hospitalisation were included in the analysis. This excludes the most severe FM cases that resulted in early death, potentially underestimating the overall severity, and long-term burden of FM. Moreover, pathological subtype data are missing, since the study lacks immunohistochemical or viral PCR subclassification of myocarditis (e.g., lymphocytic, eosinophilic, giant cell), which limits insights into aetiology-specific outcomes. There is some heterogeneity in follow-up timing. While a standardised protocol was in place, there was still variability in the exact follow-up intervals, which could affect the precision of longitudinal LVEF comparisons. The study also presents some gender imbalance: there was a notable gender disparity between FM and NFM groups. Although sex-stratified analyses were performed, residual confounding related to sex-specific biology cannot be fully excluded. Moreover, the “Chinese regimen” involving early EMB, steroids, and immunoglobulin may not reflect practice in Western health-care systems. This limits external validity to centres, that use similar immunomodulatory strategies. Despite use of DAG-informed modelling, some potential confounders—such as socioeconomic status, adherence to medication post-discharge, or detailed viral testing—were not accounted for. Some subgroup analyses, particularly in females, had insufficient event rates to support full multivariate modelling, limiting interpretation in these strata.

In conclusion, despite some limitations, this study shows that we must rethink recovery in FM beyond the storm of the acute phase. FM is a high-risk entity requiring, not only acute intervention, but long-term

Fulminant Myocarditis Vs. Non-Fulminant Myocarditis



1. EF values: FM patients consistently demonstrate inferior LVEF compared with NFM patients



2. MCS: Early application of IABP and ECMO can enhance long-term LVEF and outcome in FM

Fig. 1. Conceptual illustration of LVEF recovery trajectories in fulminant vs non-fulminant myocarditis.

cardiac monitoring, and tailored therapy to optimise recovery (see Fig. 1).

References

[1] R.E. McCarthy 3rd, J.P. Boehmer, R.H. Hruban, G.M. Hutchins, E.K. Kasper, J. M. Hare, K.L. Baughman, Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis, *N. Engl. J. Med.* 342 (10) (2000 Mar 9) 690–695, <https://doi.org/10.1056/NEJM200003093421003>. PMID: 10706898.

[2] G. Li, J. Zhang, Z. Xu, et al., Long-Term Left Ventricular Ejection Fraction changes in Fulminant and Non-Fulminant Myocarditis: a Multicenter Study in China, *IJC Heart Vasc.* (2025) in press.


[3] E. Ammirati, M. Cipriani, M. Lilliu, P. Sormani, M. Varrenti, C. Raineri, D. Petrella, A. Garascia, P. Pedrotti, A. Roghi, E. Bonacina, A. Moreo, M. Bottirotti, M. P. Gagliardone, M. Mondino, S. Ghio, R. Totaro, F.M. Turazza, C.F. Russo, F. Oliva, P.G. Camici, M. Frigerio, Survival and Left Ventricular Function changes in Fulminant Versus Nonfulminant Acute Myocarditis, *Circulation* 136 (6) (2017 Aug 8) 529–545, <https://doi.org/10.1161/CIRCULATIONAHA.117.026386>. Epub 2017 Jun 2 PMID: 28576783.

[4] E. Ammirati, G. Veronese, M. Brambatti, M. Merlo, M. Cipriani, L. Potena, P. Sormani, T. Aoki, K. Sugimura, A. Sawamura, T. Okumura, S. Pinney, K. Hong, P. Shah, Ö. Braun, C.M. Van de Heyning, S. Montero, D. Petrella, F. Huang, M. Schmidt, C. Raineri, A. Lala, M. Varrenti, A. Foà, O. Leone, P. Gentile, J. Artico, V. Agostini, R. Patel, A. Garascia, E.M. Van Craenenbroeck, K. Hirose, A. Isotani, T. Murohara, Y. Arita, A. Sionis, E. Fabris, S. Hashem, V. Garcia-Hernando, F. Oliva, B. Greenberg, H. Shimokawa, G. Sinagra, E.D. Adler, M. Frigerio, P.G. Camici, Fulminant Versus Acute Nonfulminant Myocarditis in patients with Left Ventricular

Systolic Dysfunction, *J. Am. Coll. Cardiol.* 74 (3) (2019 Jul 23) 299–311, <https://doi.org/10.1016/j.jacc.2019.04.063>. PMID: 31319912.

[5] Kociol RD, Cooper LT, Fang JC, Moslehi JJ, Pang PS, Sabe MA, Shah RV, Sims DB, Thiene G, Vardeny O; American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. Recognition and Initial Management of Fulminant Myocarditis: A Scientific Statement From the American Heart Association. *Circulation.* 2020 Feb 11;141(6):e69-e92. doi: 10.1161/CIR.0000000000000745. Epub 2020 Jan 6. PMID: 31902242.

[6] A. Baritussio, A. Schiavo, C. Basso, A.S. Giordani, C.Y. Cheng, E. Pontara, M. G. Cattini, E. Bison, N. Gallo, M. De Gaspari, E. Carturan, G. Thiene, G. Tarantini, M. Plebani, S. Rizzo, D. Gregori, S. Iliceto, R. Marcolongo, A.L.P. Caforio, Predictors of relapse, death or heart transplantation in myocarditis before the introduction of immunosuppression: negative prognostic impact of female gender, fulminant onset, lower ejection fraction and serum autoantibodies, *Eur. J. Heart Fail.* 24 (6) (2022 Jun) 1033–1044, <https://doi.org/10.1002/ehfj.2496>. Epub 2022 Apr 19 PMID: 35377503.

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