Reply to: Beyond precision therapy: the need for precision clinical decision-making in recurrent pericarditis

Dear Editors,

We thank Bečić *et al.* for their thoughtful comment on our review, highlighting a relevant gap in the management of recurrent pericarditis: the lack of a structured, phenotype-based algorithm to guide escalation from corticosteroids to interleukin-1 (IL-1) inhibition.

First, we reiterate the central aim of our review: how to use corticosteroids in recurrent pericarditis to avoid common misunderstandings. Per European Society of Cardiology (ESC) guidelines (1), corticosteroids should be considered second-line treatment, reserved for incomplete response or contraindications to NSAIDs and colchicine, and administered at low-to-moderate doses (prednisone 0.2–0.5 mg/kg/day) with a very slow taper guided by clinical remission and C-reactive protein (CRP) normalisation. This therapy is inevitably chronic, similarly to polymyalgia rheumatica: starting from 25 mg/day, tapering should last at least 7 months to reduce recurrences. This prolonged exposure requires early prevention of glucocorticoid-induced osteoporosis, including bisphosphonates, whereas proton-pump inhibitors should be used only with concomitant NSAIDs or aspirin.

The correspondents rightly identify the timing of IL-1 inhibitor initiation as challenging. The 2025 ESC Guidelines support anti-IL-1 agents (anakinra or rilonacept) in corticosteroid dependence, colchicine resistance, and an inflammatory phenotype with elevated CRP. In patients achieving stable remission with low-dose corticosteroids, switching to an IL-1 inhibitor should be individualised according to tolerability, age, sex, and patient preference (1). Children are an exception, in whom earlier IL-1 blockade is preferable due to corticosteroid-related adverse effects (2). The 2025 American College of Cardiology (ACC) Expert Consensus differs, emphasising minimising corticosteroid exposure and earlier IL-1 blockade after failure of colchicine plus NSAIDs (3). Thus, European and US recommendations reflect ongoing debate regarding the optimal timing of IL-1 inhibition rather than an established sequence. The ESC guidelines also consider pharmacoeconomic and drug availability.

At present, we believe the evidence is not sufficiently mature to support an algorithm defining the exact timing of IL-1 inhibition. Rather than a rigid sequence, current evidence supports a phenotype- and patient-centred approach, in which the variables highlighted by the authors – inflammatory phenotype, recurrence burden, previous corticosteroid therapy, colchicine response, contraindications, anticipated treatment duration, age, pregnancy, access to biologics, and patient preference – should contribute to this decision.

In our clinical practice, we consider escalation to anakinra (the only anti-IL1 alpha/beta available in Europe) in four scenarios. First, rare corticosteroid-dependent adult correctly treated from the first attack with colchicine and NSAIDs, in whom corticosteroids (prednisone up to 25 mg) were added and tapering below 10–15 mg/day is difficult or impossible (4). Second, probably more common scenario, patients with a very high disease burden (3–4 hospitalisations in the last 2 years), often not initially treated per guidelines, substantially limited in daily activities and 'exhausted' by the disease, needing rapid and sustained disease control. Third, paediatric patient in whom colchicine and NSAIDs are insufficient to control disease, for whom we use anakinra instead of corticosteroids. Fourth, young patient who wants/needs to practice agonistic sport, in whom anakinra is usually the only treatment allowing full return to competitive activity.

A further challenging subgroup has persistent or recurrent symptoms despite normal CRP. The 2025 ESC Guidelines recognise this as a distinct non-inflammatory phenotype, accounting for 10–20% of recurrent pericarditis cases (5). In selected patients with a well-established diagnosis, evidence of pericardial inflammation on cardiovascular magnetic resonance (CMR) may support treatment escalation irrespective of CRP (1). Mascolo *et al.* reported that in their cohort of 112 patients with recurrent pericarditis and normal CRP, 10 received anakinra and among these 5 discontinued NSAIDs and corticosteroids, suggesting a role for IL-1 blockade in selected CRP-negative patients (6).

Looking ahead, we agree the next step should be prospective, phenotype-stratified studies providing a more solid foundation for treatment decisions, incorporating biomarkers beyond CRP and genetic predisposition to the autoinflammatory phenotype.

In conclusion, we welcome this correspondence as a valuable complement to our review. Corticosteroids remain an important option when used at low doses and tapered slowly, while IL-1 inhibitors have expanded the armamentarium, particularly for paediatric, corticosteroid-dependent, difficult-to-control, and competitive athlete patients. Precision medicine in recurrent pericarditis should ultimately identify the most appropriate strategy for each patient according to phenotype, disease burden, risks and preferences.

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References

1. SCHULZ-MENGER J, COLLINI V, GRÖSCHEL J *et al.*: 2025 ESC Guidelines for the management of myocarditis and pericarditis. *Eur Heart J* 2025; 46: 3952-4041. https://doi.org/10.1093/eurheartj/ehaf192
2. CAORSI R, INSALACO A, BOVIS F *et al.*: Pediatric recurrent pericarditis: appropriateness of the standard of care and response to IL-1 blockade. *J Pediatr* 2023; 256: 18-26.e8. https://10.1016/j.jpeds.2022.11.034
3. WANG TKM, KLEIN AL, CREMER PC *et al.*: 2025 Concise Clinical Guidance: an ACC Expert Consensus Statement on the Diagnosis and Management of Pericarditis: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol* 2025; 86(25): 2691-719. https://10.1016/j.jacc.2025.05.023
4. CERIANI E, AGOZZINO F, BERRA S *et al.*: Duration of disease and long-term outcomes in patients with difficult-to-treat recurrent pericarditis: a chronic condition treated with nonsteroidal anti-inflammatory drugs, colchicine, corticosteroids, and anti-interleukin-1 agents. *ACR Open Rheumatol* 2025; 7(1). https://doi.org/10.1002/acr2.11776
5. IMAZIO M, BRUCATO A, MAESTRONI S *et al.*: Prevalence of C-reactive protein elevation and time course of normalization in acute pericarditis: implications for the diagnosis, therapy, and prognosis of pericarditis. *Circulation* 2011; 123(10): 1092-97. https://10.1161/circulationaha.110.986372
6. MASCOLO R, WU MA, BERRA S *et al.*: Recurrent pericarditis with normal C-reactive protein: clinical and laboratory features, biomarkers and outcome in a non-inflammatory phenotype. *Eur J Intern Med* 2025; 135: 108-17. https://10.1016/j.ejim.2025.03.011