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Editorial

Targeting precipitants to prevent heart failure hospitalization. Does season matter?

Heart failure (HF) decompensation commonly results from a gradual increase in cardiac filling pressures, often precipitated by intervening factors. Precipitants are specific extrinsic factors triggering an acute event in patients with a pre-existing cardiac structural disease [1,2], summarized, with a few differences, by HF Guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association/Heart Failure Society of America (ACC/AHA/HFSA) (**Table 1**). Both guidelines emphasize the importance of acute coronary syndromes, dysrhythmias, uncontrolled hypertension, infections, nonadherence with medications or dietary intake, adverse effects of drugs, metabolic/hormonal derangements, anaemia [1,2]. Different precipitant factors impact on hospital stay length and outcome, and influence the therapeutic choices [3]. Though the ACC/AHA/HFSA guideline statement "the common precipitating factors and the overall patient trajectory should be assessed to guide appropriate therapy" holds a class of recommendation 1, the supporting literature is still restricted to a few observational studies (level of evidence C-LD) [2].

In this issue of the Journal, Wang et al. [4] expand our knowledge on the HF hospitalization precipitants by conducting a large observational study including 6918 patients admitted for HF over a 20-year period between 1998 and 2018 from the Management of Cardiac Failure (MACARF) program in Sydney, Australia. At least one precipitant factor among 5 prespecified (infection, ischemia, arrhythmia, medication-related and diet noncompliance) could be identified in 78% of patients, with infection, ischaemia, arrhythmia being by far the most common. Among patients with a single identifiable factor (53%), those with arrhythmias or infections had a lower risk of one-year rehospitalization. This variability was mainly driven by differences in HF rather than non-HF readmissions [4]. This might be explained by the fact that both arrhythmias and infections are usually transient triggers, less likely to leave long-term sequelae once adequately addressed. Conversely, an ischaemic precipitant inducing cardiac damage can worsen cardiac dysfunction, which might lower the clinical threshold for subsequent HF decompensations.

Apart from a single study demonstrating that patients with an HF hospitalization precipitated by a cardiovascular factor are at higher risk of subsequent readmissions [5], to date little is known about the impact of antecedent precipitants of HF decompensation on subsequent triggers of rehospitalization. Wang et al. [4] should be congratulated for addressing this gap in knowledge, by demonstrating that HF readmissions tend to be precipitated by the same factor that triggered the initial HF hospitalization. These results provide a solid basis for the ACC/AHA/HFSA recommendations on the routine assessment of HF precipitants and suggest the possibility of adopting preventive strategies, which should be tailored to the specific precipitant. For example, patients with an ischaemic trigger might benefit from either revascularization, when needed, or by optimization of treatments aimed at controlling hypertension, dyslipidaemia, and diabetes [1,2]. As for atrial fibrillation, a few randomized controlled trials have shown that left atrial catheter ablation seems more effective than either rhythm or rate drug control strategy in reducing symptoms, and possibly even morbidity and mortality [1,2]. Further, vaccination against influenza and pneumococcal pneumonia could represent an effective tool to prevent respiratory infections, being recommended by both Guidelines to reduce either HF hospitalizations [1] or mortality [2]. Even COVID-19 vaccination should also be considered, given that SARS-CoV 2 infection has been associated with HF decompensation and poor outcomes [1,2]. Finally, patients non-compliant with medications or diet should be directed to education programs, which have already been demonstrated to be effective in improving prognosis [6].

Wang et al. [4] also reported that all precipitants of HF hospitalization, especially infections, were more common in winter. This is in accordance with prior studies demonstrating "winter peaks" in morbidity and mortality in HF patients [7]. Apart from a higher susceptibility to respiratory infections several, physiological, behavioural, and environmental factors might contribute to the seasonality of HF morbidity and mortality. Physiological response to cold mainly consists of peripheral vasoconstriction and shivering, which are largely mediated by the sympathetic nervous system, a major pathophysiological determinant of HF. In winter, subjects tend to reduce physical activity and shift toward unhealthier dietary patterns, which can promote clinical decompensation. Higher levels of some air pollutants have been reported in winter, with an associated increased likelihood of developing respiratory illnesses, as well as cardiovascular diseases [7].

The main limitation of the present study relies on its generalizability to populations other than Eastern Australia one. Indeed, a study on 18,553 patients from 44 countries found significant regional differences regarding the most common HF hospitalization precipitants [8]. The socio-economic status might another source of variability, particularly impacting on the lack of adherence to medications and dietary regimens [9]. Moreover, the population described in the present paper seems not to adequately reflect current HF cohorts because of a suboptimal implementation of guideline-directed medical therapy. Further, the MACARF registry was built over a long period of time (1998–2018), during which therapeutic options for HF have dramatically changed; obviously no patient in this study was prescribed with most

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Table 1
Common precipitants of heart failure hospitalization.

2021 ESC	2022 ACC/AHA/HFSA
Acute coronary syndrome	Acute coronary syndrome
Tachyarrhythmia (e.g. atrial fibrillation, ventricular tachycardia)	Atrial fibrillation and other arrhythmias
Bradyarrhythmia	
Excessive rise in blood pressure	Uncontrolled hypertension
–	Additional cardiac disease (e.g., endocarditis)
Infection (e.g. pneumonia, infective endocarditis, sepsis)	Acute infections (e.g., pneumonia, urinary tract)
Non-adherence with salt/fluid intake or medications	Nonadherence with medication regimen or dietary intake
Toxic substances (alcohol, recreational drugs)	–
Drugs (e.g. NSAIDs, corticosteroids, negative inotropic substances, cardiotoxic chemotherapeutics)	Medications that increase sodium retention (e.g., NSAID)
	Medications with negative inotropic effect (e.g., verapamil)
Exacerbation of COPD	–
Pulmonary embolism	–
Surgery and perioperative complications	–
Increased sympathetic drive, stress-related cardiomyopathy	–
Metabolic/hormonal derangements (e.g. thyroid dysfunction, diabetic ketosis, adrenal dysfunction)	Hyper- or hypothyroidism
Severe anaemia	Anaemia
Pregnancy and peripartum related abnormalities	–
Cerebrovascular insult	–
Acute mechanical cause: myocardial rupture complicating acute coronary syndrome (free wall rupture, ventricular septal defect, acute mitral regurgitation), chest trauma or cardiac intervention, acute native or prosthetic valve incompetence secondary to endocarditis, aortic dissection or thrombosis	–

ACC/AHA/HFSA, American College of Cardiology/American Heart Association/Heart Failure Society of America; COPD, chronic obstructive pulmonary disease; ESC, European Society of Cardiology; NSAIDs, nonsteroidal anti-inflammatory drug.

contemporary drugs, such as angiotensin receptor-neprilysin or sodium-glucose cotransporter 2 inhibitors.

Another limitation is that, besides the 5 prespecified HF precipitating factors, this study does not provide any information on other epidemiologically relevant HF triggers, such as worsening renal function, uncontrolled hypertension, and anaemia [3,5,8]. In addition, we cannot exclude that the restricted choice among only 5 precipitant factors might have generated an attribution bias, hiding the true trigger of HF decompensation. For example, diet noncompliance in the present study consisted of non-adherence to a restricted fluid and salt diet. However, although non-adherence to a low-sodium diet is reported as a possible precipitating factor for HF in several studies and even guidelines, the true impact of this trigger seems overestimated after the recently published SODIUM-HF trial, demonstrating that dietary interventions to decrease sodium intake do not reduce clinical events in ambulatory HF patients [10].

Despite these limitations, this study strongly supports the identification of HF precipitant factors for risk stratification. The fact that HF hospitalizations tend to be precipitated by the same factor responsible for the first HF decompensation calls for the adoption of tailored preventive strategies targeting the specific precipitant factor.

Declaration of Competing Interest

none.

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