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Cardio-oncology, novel biomarkers, and advances in structural heart disease and arrhythmia management

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ABSTRACT

Cardiovascular medicine continues to move towards precision-based, individualised patient care, supported by novel biomarkers, refined imaging protocols, and multidisciplinary risk assessment. The studies featured in this issue of Acta Cardiologica span cardio-oncology, structural heart disease, immune and proteomic biomarkers, sepsis-related cardiac dysfunction, arrhythmia management, and vascular disease. Collectively, they underscore the growing importance of individualised diagnostic and therapeutic strategies across the cardiovascular spectrum, from cancer-related heart failure to conduction system pacing and cardiac arrest prevention.

KEYWORDS

Cardio-oncology; heart failure; biomarkers; structural heart disease; arrhythmia; risk stratification

Since 2022, this editorial series in Acta Cardiologica has tracked the rapid evolution of cardiovascular medicine, from an initial overview of the journal's highlights [1], through recent advances in cardiovascular pathophysiology, biomarkers, and therapeutic strategies [2], to a discussion of precision and pragmatism in contemporary cardiology [3] and, most recently, heart failure, structural heart disease, and emerging cardiovascular risk markers [4]. The articles presented in this issue extend these developments across cardio-oncology, structural imaging, novel biomarkers, arrhythmia management, and vascular disease, further reinforcing the shift towards precision-based, individualised cardiovascular care.

Cancer therapy-related heart failure remains an important challenge in cardio-oncology, with limited evidence regarding the implementation of guideline-recommended medical therapy. Bozduman Habip et al. examined 71 patients with *de novo* heart failure after cancer diagnosis, in whom the median time to heart failure onset was 14 months [5]. Heart failure with preserved ejection fraction was the most common phenotype (42.3%), followed by reduced (29.8%) and mildly reduced (28.2%) ejection fraction (Figure 1). While guideline-recommended therapy was consistently prescribed in patients with reduced or mildly reduced ejection fraction, it remained underused in those with preserved ejection fraction, particularly mineralocorticoid receptor antagonists and SGLT2 inhibitors. Left ventricular recovery occurred in 71.4% of patients with reduced ejection fraction, and all-cause mortality

reached 25.4% during follow-up, with older age and male sex independently predicting death. These findings support broader implementation of guideline-directed therapies in cancer-related heart failure while awaiting prospective validation.

Accurate imaging assessment remains essential in structural heart disease. Guler et al. evaluated 331 mechanical prosthetic heart valves in 262 patients undergoing cinefluoroscopy and found optimal imaging in 94.8% of aortic valves compared with only 66.7% of mitral valves [6]. The supine position provided the best visualisation for both valve locations, with left anterior oblique-cranial and right anterior oblique-cranial projections proving most effective for aortic and mitral prostheses, respectively. These results highlight the value of standardised acquisition protocols to improve diagnostic accuracy while minimising radiation exposure.

Novel molecular pathways continue to be explored in coronary artery disease. Using proteomic profiling, Agnihotri et al. identified 197 differentially expressed plasma proteins in patients with coronary artery disease, among which serotransferrin was significantly downregulated and correlated inversely with cardiac troponin I [7]. The authors hypothesised that reduced serotransferrin availability may result from phosphorylation mediated by calcium/calmodulin-dependent protein kinase kinase 2, suggesting a role for altered iron homeostasis in coronary artery disease pathophysiology that warrants further mechanistic investigation.



Figure 1. (Up) The distribution of the use of guideline-recommended medical therapy in cancer patients with *de novo* heart failure; (bottom) Sankey diagram illustrates the changes in left ventricular ejection fraction during follow-up. BB: beta-blockers; LVEF: left ventricular ejection fraction; MRA: mineralocorticoid receptor antagonist; RASi: renin-angiotensin system inhibitors; SGLT2: sodium-glucose co-transporter-2 (from reference [5]).

Immune mechanisms following myocardial injury are also gaining attention. González-Rojas et al. evaluated anti-cardiac troponin I antibodies in 23 patients with acute myocardial infarction and detected them in 73.9% of patients at presentation, with most seronegative patients becoming antibody-positive during six-month

follow-up [8]. Higher antibody titres at admission were significantly associated with greater left ventricular end-diastolic and end-systolic volumes at six months, suggesting that these autoantibodies may provide prognostic information beyond conventional biomarkers, pending confirmation in larger prospective cohorts.

Simple, widely available biomarkers continue to demonstrate prognostic value. In a large MIMIC-IV cohort of 10,879 critically ill patients with congestive heart failure and atrial fibrillation, Li et al. showed that higher red cell distribution width was independently associated with increased in-hospital mortality, following a non-linear relationship with a threshold effect below 16.565% [9]. These findings support red cell distribution width as a readily available marker for early risk stratification in this high-risk population.

Sepsis-related cardiac dysfunction is increasingly recognised as a heterogeneous syndrome with

important prognostic implications. Iqbal et al. reviewed current mechanistic insights, highlighting mitochondrial dysfunction, dysregulated immune-cardiac interactions, and programmed cell death as key contributors to myocardial injury, and emphasised the limitations of ejection fraction-based assessment in favour of multimodal phenotyping incorporating strain, tissue characterisation, and emerging biomarkers (Figure 2) [10]. In an accompanying editorial, Houben and Hans underscored the heterogeneity and temporal dynamics of this condition, supporting the integration of multi-omics and machine learning approaches to

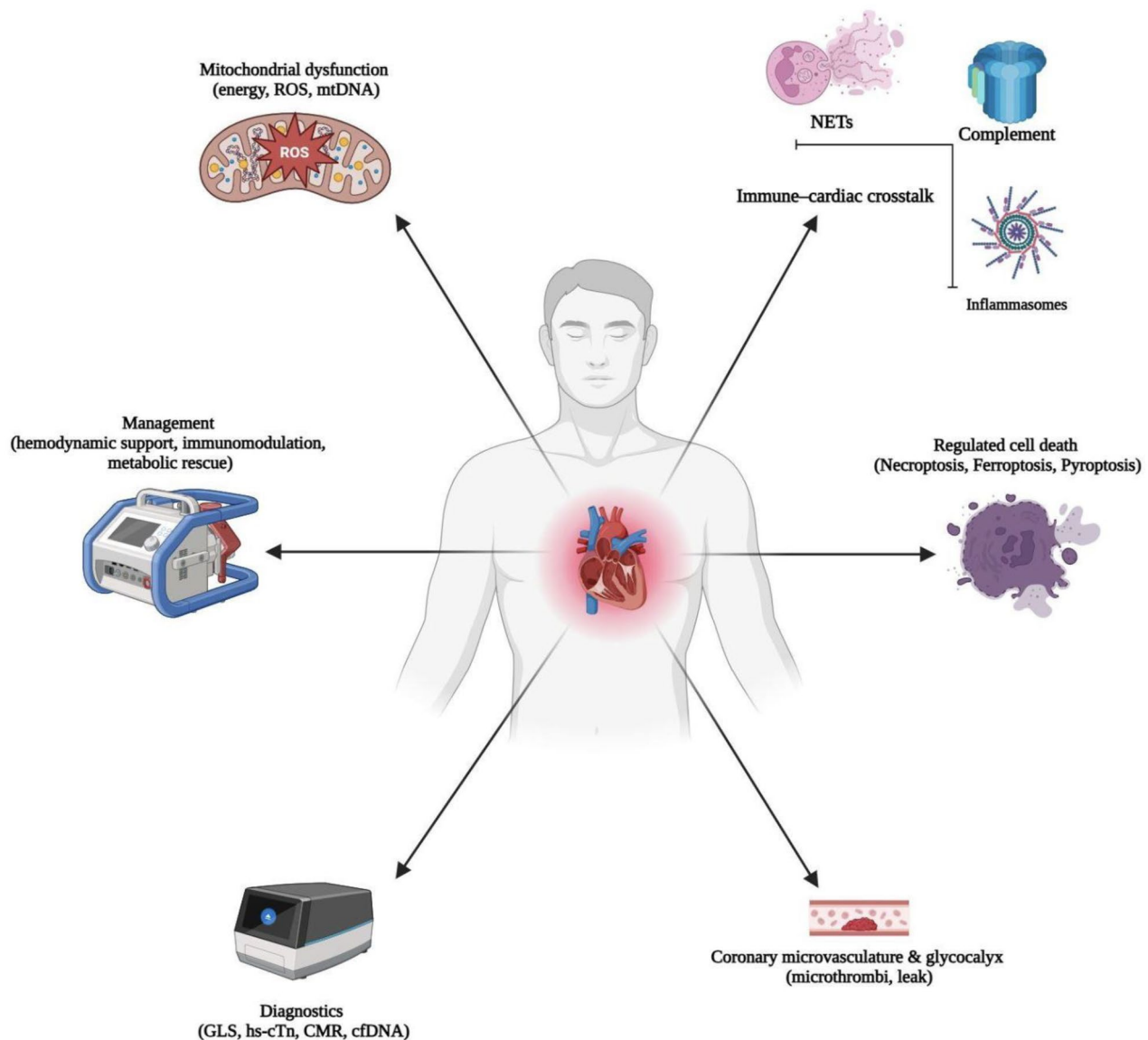


Figure 2. This figure synthesises key mechanistic drivers of sepsis-related cardiac dysfunction, mitochondrial energetic collapse, dysregulated immune-cardiac signalling (neutrophil extracellular traps (NETs), complement, inflammasomes), programmed cardiomyocyte death (necroptosis/ferroptosis/pyroptosis), and coronary microvascular/glycocalyx injury, and links them to translational levers for diagnosis and treatment. Multimodal phenotyping (strain imaging, high-sensitivity troponin, cardiac MRI, cardiomyocyte cfDNA (cell-free DNA)) combined with mechanism-targeted interventions (precision hemodynamic support, immunomodulation, metabolic/mitochondrial rescue, and cell-death inhibitors) forms a roadmap to endotype-guided trials and personalised care (from reference [10]).

identify biologically distinct endotypes and enable more personalised therapeutic strategies [11].

Rare but clinically important cardiac manifestations of systemic disease are illustrated by Rioux et al. who reported a case of cardiac involvement in Whipple's disease and reviewed the associated literature [12]. Although *Tropheryma whipplei* is a recognised cause of blood culture-negative endocarditis, accounting for approximately 4% of cases, other forms of cardiac involvement remain underrecognised. This report emphasises the diagnostic challenges encountered when classical clinical features are absent and the importance of early recognition to avoid progressive multisystem disease.

Postoperative atrial fibrillation remains a frequent and burdensome complication after cardiac surgery. In a systematic review and meta-analysis of 207 studies including 180,223 patients undergoing coronary artery bypass graft surgery, Farzaneh et al. confirmed an overall incidence of 24% [13]. Advanced age, male sex, heart failure, hypertension, chronic obstructive pulmonary disease, and renal dysfunction were independently associated with higher risk, while perioperative factors such as on-pump surgery, prolonged cross-clamp time, and larger left atrial size further increased susceptibility. Preoperative statin therapy and higher left ventricular ejection fraction were protective, underscoring the multifactorial nature of this complication and the value of comprehensive preoperative risk assessment.

Vascular imaging is also evolving beyond simple anatomical measurement. Bruls et al. followed 197 patients with abdominal aortic aneurysms undergoing baseline [18F]FDG PET/CT, with 121 patients undergoing serial imaging over up to nine years [14]. While baseline PET positivity was not independently associated with rapid growth or mortality, its emergence or persistence during follow-up was associated with accelerated aneurysm growth and symptomatic presentation. Female patients were more likely to exhibit PET positivity, rapid expansion, and higher mortality, and histological analyses demonstrated reduced elastin content in PET-positive segments, supporting a link between metabolic activity and structural wall weakening that may guide future PET-based surveillance strategies.

The timing of guideline-directed medical therapy is receiving renewed attention. Velibey et al. discuss the concept of chronotherapy in heart failure, questioning whether the timing of drug administration may influence therapeutic efficacy and tolerability, an area that merits further dedicated investigation [15].

Building on earlier work in this journal regarding body composition in heart failure, Prokopidis et al. analysed data from 73 adults with heart failure and found

that higher C-reactive protein levels were independently associated with lower appendicular lean soft tissue index, a relationship observed in men but not in women [16]. In an accompanying comment, Murat and Murat discussed the implications of these sex-specific findings, reinforcing the concept that inflammation may contribute differentially to sarcopenia according to sex and supporting consideration of inflammatory status when evaluating body composition in heart failure [17].

Optimal perioperative management strategies in acute aortic dissection also remain an area of active investigation. Wan et al. evaluated 443 patients with acute aortic dissection and found that higher platelet transfusion rates were associated with significantly lower in-hospital and long-term mortality, identifying 144.75 mL/h as a threshold beyond which mortality declined, with the lowest estimated risk near 282.5 mL/h [18]. In a methodological comment, Bakhriansyah et al. raised important considerations regarding the interpretation of these thresholds derived from the MIMIC-IV database, highlighting the need for prospective validation before incorporation into transfusion protocols [19].

Device-based therapy was also addressed by Ozkaya et al. who compared long-term outcomes following upgrade to cardiac resynchronisation therapy between patients with ischaemic and non-ischaemic heart disease, contributing to the ongoing effort to refine patient selection for resynchronisation strategies [20].

Conduction system pacing continues to gain traction as a physiological alternative to conventional right ventricular pacing. In a nationwide survey of 136 Italian cardiac pacing centres, Palmisano et al. found that 86% were performing conduction system pacing, with left bundle branch area pacing the preferred strategy and atrioventricular block the leading indication, although limited operator training and procedural experience remained important barriers to wider adoption [21]. In an accompanying editorial, Gerra et al. situated these findings within the broader evolution from guidelines to real-world practice, emphasising the need for dedicated training programs to support the physiological pacing paradigm [22].

Age-related differences in acute myocardial infarction presentation continue to inform risk assessment. Among 117 patients with acute myocardial infarction, Sierra-Castillo et al. found that younger patients had higher body weight and significantly elevated total cholesterol, while older patients had higher glycated haemoglobin and comorbidity burden, despite a similar distribution of culprit lesions dominated by the left anterior descending artery [23]. In a methodological comment, Çelik and Kalçık raised concerns regarding age stratification approaches in this population,

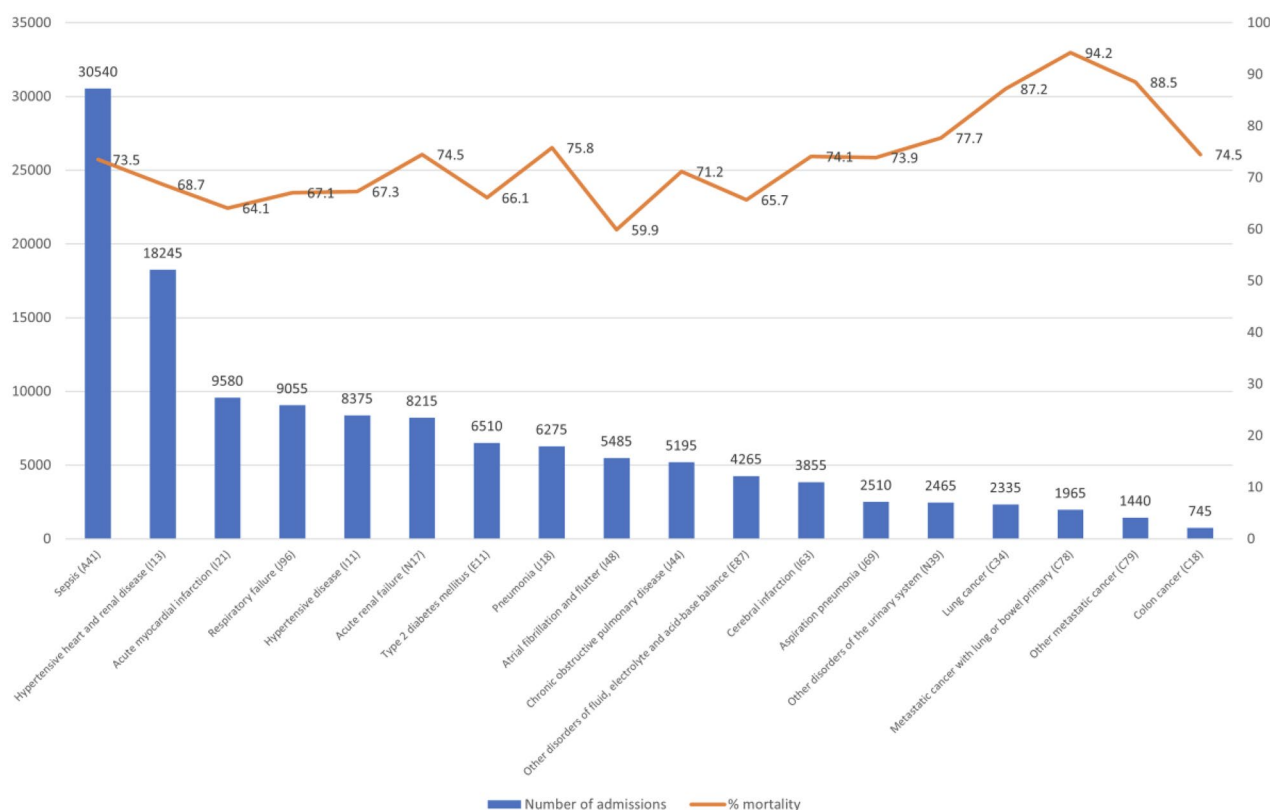


Figure 3. Significant independent predictors of preceding hospitalisation during the 30-day period. Multiple logistic regression to identify factors associated with previous admission in the 30-day period before hospitalisation with cardiac arrest (from reference [25]).

underscoring the importance of early detection and treatment of dyslipidaemia across age groups [24].

Finally, the identification of high-risk patients before cardiac arrest represents an important opportunity for prevention. Among more than 1.6 million hospitalisations for cardiac arrest, Kwok et al. found that 15.6% were preceded by a hospital admission within the previous 30 days, most commonly for cardiovascular, infectious, or respiratory conditions, with cancer, chronic kidney disease, and chronic lung disease as the strongest predictors of recent hospitalisation (Figure 3) [25]. A preceding admission was independently associated with significantly higher in-hospital mortality following cardiac arrest. This theme is further illustrated by the case reported by Castillo-Rodriguez et al. describing cardiac arrest in a young woman attributed to the potentially fatal synergy of selective serotonin reuptake inhibitors and recreational marijuana use [26]. In an accompanying editorial, Gerra et al. discussed how such hospitalisation patterns may help predict the unpredictable, supporting improved surveillance and targeted preventive strategies in vulnerable populations [27].

This issue also includes several educational focus images illustrating noteworthy cardiovascular cases,

spanning three-dimensional printing of a mitral valve cleft, left atrial appendage myxoma, mycotic femoral artery aneurysm, aortic arch and descending aorta stenosis, retrieval of an embolised patent foramen ovale occluder, thrombus aspiration from an ectatic coronary artery, anomalous pulmonary venous drainage, cardiac cavernous haemangioma, intracardiac extension of intravenous leiomyomatosis, and a complex anomalous course of the right coronary artery [28–37]. Collectively, the studies presented in this issue illustrate the breadth of contemporary cardiovascular research, from cardio-oncology and novel biomarkers to structural imaging, arrhythmia management, and vascular disease, reinforcing the continued shift towards precision-based, individualised cardiovascular care.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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