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EDITORIAL

Novel biomarkers in heart failure and cardio-oncology

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Article Biegus et al., see p. 355

Heart failure (HF) is one of today's major challenges, already affecting more than 26 million people worldwide [1]. It is associated with high morbidity and mortality rates as well as high treatment costs [2]. The prevalence of HF in the general population is strongly correlated with age. In people aged between 20 and 39 years it is < 1%, whereas in people ≥ 80 years old it exceeds 10% [3]. In the industrialised world, cardiovascular (CV) causes are the most frequent reason for hospital admissions [4]. It is expected that treatment costs for CV disease will continue to increase in the next decades [3]. In the general population CV disease is the most common reason for death. Most frequent causes are coronary heart disease, stroke, high blood pressure, and HF. Especially in the elderly population, CV-related deaths surpass those of cancer by far, being the primary cause of death [5].

In order to gain insight into the complex pathophysiology of HF, many large-scale registries [6–8] have been implemented, and they continue to help better understand this complex disease [9–11]. Contemporary registries are connected with biobanks for cryopreservation of biospecimens, mostly blood samples, but other tissue samples are sometimes also frozen at low temperatures (–80°C). This ensures the possibility of searching for new biomarkers that predict morbidity and mortality. Consequently, a new pathophysiological research hypothesis can be generated. In general, a good biomarker should add clinical information that could affect the treatment of the patient and be universally available. One such new biomarker was found in the current study by Biegus et al. [12]. The authors showed that persistent hyperlactataemia in 222 acute HF (AHF) patients, defined as lactate level ≥ 2 mmol/L on admission and after 24 h, was associated with more intensive HF treatment, worsening of HF and higher one-year all-cause mortality. Other important CV blood biomarkers that have already been established in AHF include natriuretic peptides, troponins, mid-regional pro-adrenomedullin, interleukin-6, ST2, C-reactive protein, galectin-3, semaphorin 4D, and neutrophil gelatinase–associated lipocalin [13–18]. Multimarker strategies have shown even better results in predicting outcomes [19].

Biomarkers are not only important in AHF but are also becoming an essential part of cardio-oncology during treatment with chemo-, immuno-, radio-, and targeted therapy [20, 21]. Cardiotoxicity itself has been defined as a reduction of left ventricular ejection fraction by 10 percentage points below the local lower limit of normality (50%–55%) [22]. Troponin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are the standard parameters for monitoring cancer patients for early signs of cardiotoxicity while receiving potentially cardiotoxic therapies [22]. An increase in these biomarkers is associated with a higher risk of HF or in some cases even severe myocarditis [23]. Therefore, an increase in troponin and NT-proBNP in cancer patients should always trigger further clinical investigations with resting-electrocardiograms and echocardiography [24, 25]. Regarding the initiation of CV drug therapy in these patients, the International CardioOncology Society-one trial (ICOS-ONE), conducted in 273 low-CV-risk adult cancer patients receiving low-dose anthracycline therapy, tested two different treatment strategies. The first group received enalapril only when troponin increased during cardiotoxic chemotherapy, and in the second group all patients received enalapril during the entire chemotherapy regime. The results for prevention of cardiotoxicity were simi-

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lar in both groups. This shows the importance of determining CV biomarkers to identify patients who could benefit from further therapy. However, CV biomarkers not only predict the development of systolic dysfunction but are also good predictors of long-term mortality [26].

Today, there are also other biomarkers available. Metabolic markers can help identify patients with an imbalanced anabolic and catabolic metabolism [27, 28], high risk of weight loss [29], cachexia [30], anorexia [31], fatigue [32], sarcopaenia [33], and muscle wasting [34]. Important metabolic biomarkers include C-reactive protein, interleukin-6, haemoglobin, serum albumin, and microRNAs [35–38]. More research is needed to better understand the pathophysiology of these metabolic diseases. Many studies are currently investigating new treatment strategies because the aforementioned comorbidities are associated with reduced quality of life, dyspnoea, oedema, and depression [39–41]. For the treatment of cachexia in cancer, there is currently no guideline-recommended therapy. Dietary supplements are possible but have not been shown to reverse cachexia [42]. Other therapies that are currently being investigated include leucine [43], megestrol acetate [44], espindolol [45], and small-molecule inhibition of MuRF1 [46]. Likewise, for the treatment of cachexia in chronic HF, dietary supplements are sometimes prescribed, but with limited effect [47]. Patients are furthermore encouraged to engage in physical activity — to prevent the loss of muscle mass [47]. Lately, the COPERNICUS [48] trial in 2289 patients with severe chronic HF has shown promising results for the prevention and partial reversal of cachexia with carvedilol. Other substances that are currently being investigated include omega-3 polyunsaturated fatty acids, amino acids, anabolics, appetite stimulants, and immunomodulators [49].

While extensive research is being done in the field of biomarkers, one should not forget the importance of personal contact with patients. They want to be aware of the risk-benefit ratio of their therapy as well as possible side effects. Treatment decisions should be made together with a patient who received all the information necessary for an informed choice. If patients do not understand the need for a specific therapy, it is likely that they will not adhere to the proposed medications. Likewise, polypharmacy increases the chance of patients forgetting some of their drugs, especially in the case of elderly patients [50]. It can be very helpful if a caregiver or family member helps them by sorting their weekly medication into labelled boxes.

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