Research paper

Biomarkers for monitoring and prevention in cancer/heart disease: Traditional and innovative perspectives☆

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Identifying individuals at risk for cardiovascular toxicities of cancer therapy and how to monitor them is challenging, given the heterogeneous and idiosyncratic nature of these toxicities. Measuring blood-based biomarkers has been proposed as a strategy to enhance the prevention, treatment, and management of acute and long-term cardiovascular toxicities (Table 1). Biomarker use can be broadly classified according to the stage of treatment: 1) pre-treatment for risk stratification, 2) during treatment to monitor for and treat cardiotoxicity, and 3) in survivorship to assess the long-term risk of cardiovascular events (Fig. 1).

Most of the data regarding the use of pre-treatment risk stratification biomarkers are based on observational data, with troponin and BNP receiving the most attention. While troponin and BNP levels are associated with the risk of developing cardiotoxicity, their risk discrimination ability was modest at best [1,2]. Currently, there is insufficient evidence to support the systematic measurement of pre-treatment biomarkers given the limited sample sizes in most studies. Nevertheless, elevated levels of cardiac biomarkers should prompt further evaluation by a cardiovascular specialist to optimize cardiovascular co-morbidities prior to potentially cardiotoxic therapies. Pre-treatment cardiac biomarkers may also provide valuable baseline data to assist in interpreting subsequent values in these patients. Larger, prospective studies are needed to adequately evaluate the clinical utility of pre-treatment biomarker risk stratification.

More evidence supports the use of troponin in the monitoring of anthracycline and trastuzumab-related cardiotoxicity [2,3]. Acute and persistent rises in troponin levels after anthracyclines have been associated with incident left ventricular dysfunction and other cardiac events [3,4]. A number of other biomarkers have been investigated in small studies, such as high-sensitivity c-reactive protein and myeloperoxidase. Their clinical utility in patients with cancer is not yet established and warrants large multi-marker studies to assess their predictive value and compare them to traditional cardiovascular biomarkers [5–9]. Combining biomarkers has been proposed for predicting cardiotoxicity – an approach examined in only one study of small sample size that warrants replication [5].

Limited evidence exists for the use of biomarkers in the surveillance of long-term cardiovascular effects in cancer survivors. BNP and GDF-15 correlate with cardiac function in childhood cancer survivors of anthracyclines [10–12]. Other studies have shown no link between traditional biomarkers and long-term effects [13].

Overall, biomarker studies in Cardio-Oncology have been limited by small sample sizes and heterogeneity of the studied population. Despite the limited evidence, biomarkers can be useful in managing patients with cancer. For example, cardiovascular biomarkers such as BNP or high-sensitivity troponin could be checked to detect subclinical cardiac dysfunction in patients with no risk factors referred for evaluation of a mild decrease in ejection fraction in the setting of trastuzumab use. Interruption of treatment should be the last resort, and negative cardiovascular biomarkers can provide reassurance and argue for the continuation of treatment while the LVEF is re-evaluated. However, levels of cardiovascular biomarkers should be interpreted with caution in patients with cancer. BNP levels are highly impacted by renal clearance and adipose tissue – both physiologic parameters that can vary rapidly in patients with cancer. Large changes in BNP levels can be noted in the short- to intermediate-term in the setting of rapid weight loss, especially if concomitant with kidney dysfunction. Thus, a thorough clinical evaluation and cardiac imaging as indicated, should always accompany the interpretation of cardiovascular biomarkers in patients with cancer prior to attributing changes to the cardiotoxicity of treatment and altering the course of care.

Table 1

Characteristics and principles of biomarkers for use in cardio-oncology.

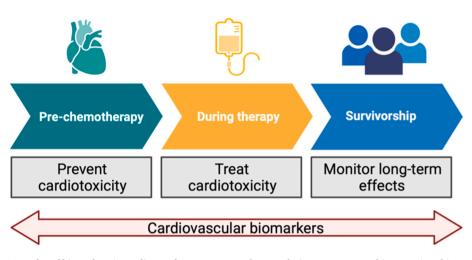| Characteristics of the ideal biomarker	Principles of biomarker use in cardio-oncology
• Pathophysiology connection to disease • Non-invasive • Easily measured • Inexpensive • Clear demarcation between health and disease states • Correlates with clinical response to treatment • Contributes to prognostication and risk stratification	• Compare to baseline biomarker concentrations • Never interpret in isolation • Always confirm if result is inconsistent with clinical picture • Always rule out secondary causes of biomarker elevation • Adjust for relevant confounders • Interruption of treatment is last resort

Fig. 1. Roles of biomarkers in cardio-oncology. Pre-cancer therapy, during treatment, and into survivorship years.

Declaration of competing interest

References

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