The use of statins to manage hyperlipidemia and to optimally treat patients with established cardiovascular disease, hopefully preventing the progression of a host of vascular conditions, is clearly a major focus of cardiologists worldwide (1). The polypill concept uses a statin in a combination pill to deliver the most broad administration of critically important medications. From the vantage point of a cardiology-centered world, it makes sense to have as complete a distribution of statins to the entire population as possible, although not all eligible patients can tolerate these medications.

In this issue of the Journal, researchers from the Cleveland Clinic and Case Western Reserve University use a case-control observational database to describe the effect of taking statins during cardiotoxic chemotherapy in patients with breast cancer (2). Compared with a matched group of patients who also received similar chemotherapy and did not take statins, it was clearly demonstrated that patients with statin use were protected from the development of heart failure (HF) and had potentially reduced mortality. The differences between the groups were significant and consistent using a variety of models to understand which patients may benefit the most. A careful analysis of cardiovascular risk factors, social determinants of health, number of visits to both oncologists and cardiologists, other comorbidities, and cancer treatment details generally indicated that statin use was connected to improved outcomes. It was also evident that the presence of cardiac risk factors in patients undergoing cardiotoxic chemotherapy was associated with the highest hazard ratio for the development of HF, even higher than the cancer treatment choices. The one area of detailed treatment information that may have also been associated with improved outcomes was whether patients were treated with angiotensin-converting enzyme inhibitors or beta-blockers. Interestingly, the cancer treatment risks for the development of HF included trastuzumab administration, not surprisingly, but also higher doses of cyclophosphamide, a common chemotherapy agent that is not highly associated with cardiotoxicity. Perhaps these data suggest that cyclophosphamide is not an innocent bystander.

The strengths of these data include their thorough observational nature, similar to a practical registry, with an excellent description of cardiovascular risk factors. Previously, there has not been a detailed assessment of cardiac risk factors and comorbidities in a cancer population, and this information enriches our understanding of how to prevent and manage cardiac disease in patients being treated for cancer. Most, if not all, prospective oncology trials do not have careful cardiovascular risk factor assessment or typical cardiac treatments delineated throughout the study, primarily because that is not the focus of these clinical trials. Additionally, cardiotoxicity in oncology treatment trials is historically defined by serial reductions in left ventricular ejection fraction, which limits the definition of cardiotoxicity, and by extension HF, to only those patients who have systolic dysfunction (3). This study, in contrast, uses International Classification of Diseases-Ninth Revision codes for HF that are more inclusive than just measurements of left ventricular ejection fraction for the detection of HF and cardiotoxicity. The limitations of this in-depth analysis indicating a benefit for statin use during chemotherapy are obviously that it was not a randomized, prospectively blinded study. The possibility that the benefit of statins demonstrated in this study could be in part related to additional use of angiotensin-converting enzyme inhibitors or beta-blockers does add a little uncertainty to determining the critical element or elements for optimal cardioprotection during cancer treatment. It would make clinical sense that angiotensin-converting enzyme inhibitors or beta-blockers may prevent the development of HF during cardiotoxic chemotherapy (4), although which therapy is truly cardioprotective on its own would require a prospective randomized study to convincingly establish the recommendation. Furthermore, using International Classification of Diseases-Ninth Revision codes to define cardiac conditions may be the best that can be done in retrospective studies but is not as accurate or complete as prospectively defining HF by acceptable criteria.

Nevertheless, these data are a notable addition to the published research and illustrate a valuable principle that cardiology and oncology clinicians should keep in mind. This principle is that chemotherapy, especially potentially cardiotoxic chemotherapy such as that based on anthracy-
cline and trastuzumab, is a major cardiovascular stressor, and all reasonable efforts to enhance cardiovascular reserve should be undertaken (5). It is also imperative to remember that patients being treated for cancer are likely to have many cardiovascular risk factors and/or asymptomatic cardiac disease that could be exacerbated during aggressive therapy. As a result, proactive attention is required to give patients their best chance for excellent outcomes with cancer treatment.

It is well established that statins reduce mortality in patients with cardiac disease and that cardiovascular disease is a common condition even in patients with cancer. It stands to reason that statins would be beneficial in this population, but it is uncertain how important statins are to add to any chemotherapy regimen. Clearly, chemotherapy is stressful, and certain types are especially challenging to the cardiac system. An enhanced cardiac reserve is beneficial during cancer therapy, and many potential mechanisms to improve reserve can be recruited. This report strongly indicates that statins may be an identifiable and critical element in recruitable cardiac reserve. The idea that statins improve cancer outcomes is becoming accepted knowledge (6). In a manner similar to athletes training to become “fit for battle” and perform at their peak, statins appear to be a necessary component for patients with cancer to ready themselves for their cancer war (7).

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