The increasing number of cancer survivors in this country can be attributed in part to improvements in cancer treatment as well as to the increasing age of the population and thus higher prevalence of cancer. The recent attention directed toward this phenomenon (1) has largely centered on appropriateness of care for the cancer survivor, who has too often become lost in the system and fallen into the cracks between care providers. Thus, it is critical that cancer survivors be evaluated for clues to the prediction of potential outcomes and, of perhaps greater importance, for clues to management opportunities that might improve these outcomes. The Institute of Medicine and others have called for cancer survivorship plans (1,2). However such plans need to be guided by evidence.

The report by Braithwaite et al. (3) in this issue of the Journal provides important information to inform survivorship plans from both perspectives—prognostication and management. The authors assessed physical functioning using a battery of well-accepted tools in a large cohort of women (for an average of 21 months after diagnosis) who had completed treatment for breast cancer and followed them for survival and the occurrence of new events for an average of 9 years (95% followed for >6 years). Unfortunately, this assessment was not done before initiation of therapy, which would have provided a level of potentially useful additional information. Nevertheless, follow-up was excellent, and very important information has emerged. First, the authors have documented that functional limitations are common in such subjects, with 39% exhibiting at least one limitation. Moreover, the prevalence of functional limitations increased with age so that approximately 50% of those older than 65 had at least one such limitation. Second, the presence of functional limitations was strongly predictive of all-cause mortality. The driver of this outcome was the impact on competing cause (ie, non-breast cancer mortality) and not breast cancer mortality. This impact was seen across all age and body mass index groups, although the hazard ratios were somewhat higher in the older age groups. It is relevant that this was a relatively young cohort of breast cancer patients (median age 57), and one suspects that the relationships between age and functional limitations might have been more striking had there been a more proportionate representation of older subjects. Moreover, although body mass index did not appear to have a differential effect on the impact of functional limitations, almost two-thirds of these subjects were overweight or obese, and three-quarters had at least one comorbidity (greater in those with limitations), suggesting both groups as potential targets for intervention. There is substantial evidence to suggest that increased body mass index, comorbidities, and functional limitations generally predict subsequent functional status decline (4).

This study was only able to assess mortality outcomes, but it is likely that a major additional burden of functional limitations will be seen in such patients as they age (5). Another important contribution is the observation that the impact of functional limitations was seen largely in patients with early-stage disease, not in those with advanced stage, where the effect of the cancer per se appears to override the impact of functional limitations on survival.

This new information fits well into and enhances our broader understanding of the issues surrounding functional status assessment and cancer outcomes. Oncologists have long recognized the importance of functional status, harkening back to the widespread use of first, Karnofsky Performance Status (KPS), and then Eastern Cooperative Oncology Group (ECOG) performance status (6). These have largely been used and have been shown to be important predictors of outcome in the initial treatment of the cancer patient. With the growth of the discipline of geriatrics and more recently of geriatric oncology, a broader assessment of functional status using tools such as those used by Braithwaite et al. (3), has been shown to predict outcomes better than KPS or ECOG alone (6,7). In fact, the assessment of functional status and its consideration in clinical care have been a hallmark of geriatrics practice because it has substantial impact on life expectancy in older people, independent of the effects of multiple morbidities (8). The more expanded evaluation, which has come to be known as Comprehensive Geriatric Assessment (CGA), provides even more useful information because it evaluates such issues as comorbidities, medications, nutritional status, psychosocial functioning, environmental and economic status, as well as function. Geriatric management based on CGA has been shown to have a positive impact on functional outcomes (9), and although application to older cancer patients is still under study, there is evidence that management based on CGA can improve pain control and other aspects of quality of life (10). Unfortunately the CGA, as traditionally performed in geriatrics, is labor intensive and time consuming. However, newer approaches using largely patient self-reported information show promise for broader applicability and use in active cancer patients as well as survivors (11).

It is logical to incorporate such an evaluation in cancer survivorship plans, especially for the older survivor, because in addition to indicating patients with a poor prognosis, as Braithwaite et al. (3) point out, the main impact of functional limitations is on noncancer causes of death. Such an evaluation could guide therapy regarding underlying comorbidities and other reasons for functional decline, such as obesity and decreased physical activity. In that regard, recent studies have demonstrated that practical
approaches to exercise and diet in cancer survivors can improve physical activity, dietary habits, and functional status (12). Such approaches should also become part of the survivorship plan.

It will also be important to improve our understanding of the biological basis for the age- and cancer-related functional decline seen in so many older patients and those with cancer, respectively. A phenotype of age-related immune dysregulation and/or chronic inflammation leading to frailty and functional decline has emerged as a potential candidate (13). As might be expected, these are complex relationships, to which many of the phenomena observed in the Braithwaite study (3) may contribute, such as chronic diseases, obesity, decreased physical activity, as well as age-related dysregulation seen in the immune, coagulation, endocrine, and other systems (14). While it would be nice to imagine focusing on such dysregulated systems as targets for specific interventions to improve functional status, we must proceed with caution to avoid unwanted consequences of “messing with Mother Nature.”

In the meantime, in the context of the broader aspects of assessment and management and survivorship plans, the work of Braithwaite et al. (3) suggests that implementing known interventions such as disease screening, chronic disease management, and diet and exercise programs for cancer survivors can have substantial impact. Unfortunately while we may know what to do, we do not do it often enough (15). We should get on with it.

References


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