Abstract

Obesity has been associated with reduced survival and increased risk of recurrence among patients with breast cancer. A recent meta-analysis of 82 studies reported that obese breast cancer cases have 41% higher total mortality than normal-weight cases and 35% higher breast cancer mortality. Although fully-dosed women with obesity do not appear to experience more toxicity than fully-dosed normal-weight women, the data are very restricted concerning more severe obesity and in the real-world context of comorbidities. The **long-term goal** is to improve the understanding of optimal dosing of chemotherapeutic agents among patients with obesity and breast cancer. The current steps are to fill in the gaps in knowledge related to chemotherapy dosing in women with obesity and to address the question of whether chemotherapy dose reductions among patients with obesity may explain the association between obesity and breast cancer survival with the rich data of two integrative healthcare delivery systems, Kaiser Permanente Northern California and Group Health, in nearly 34,000 patients. ***Aim 1*** will identify ***predictors of chemotherapy dose intensity***, focusing on whether body size is a principal driver of dose reduction, and whether other predictors of dose reduction vary by body mass index. Factors to be considered include patient-level factors (e.g., age, race/ethnicity, level of obesity, or comorbidities), disease characteristics (e.g., stage, nodal involvement, grade, or hormone receptor status), treatment, and provider-level factors (e.g., practice size, gender, age, or provider-patient racial concordance). ***Aim 2*** will evaluate ***the associations between body size (body mass index) at the time of diagnosis and breast cancer recurrence and survival and the extent*** to which dose reductions in chemotherapy mediate these associations. ***Aim 3*** will evaluate ***the association between body mass index and toxicity*** among women receiving the full body surface area-determined dose of chemotherapy. This will unveil if fully-dosed class I women with obesity (body mass index 30 -< 35) and fully-dosed class II+ women with obesity (body mass index 35+) experience excess toxicity as compared to their fully-dosed non-obese counterparts (body mass index 18.5-<30). The likely impact of this research is to improve care for the estimated 102,000 women with obesity and invasive breast cancer each year in the USA. Specifically, the first cycle dose proportion (the value calculated by dividing the observed dose by the expected dose), the average relative dose intensity (the mean values of the relative dose intensity of all drugs used in a chemotherapy cycle), survival and recurrence, and a composite measure of severe toxicity, including neutropenia, neuropathy, renal impairment, hepatic impairment, and cardiotoxicity, defined as Grade 3+ toxicity will be gathered as the outcomes. The resulting findings will contribute to understanding optimal chemotherapy dosing practices, and likely affect clinical practice and improve health outcomes for women with obesity and breast cancer in the USA.