

Supplementary Methods

Study Population

Patients were enrolled in the Platinum Study that includes nine sites in the U.S., Canada, and the United Kingdom: Memorial Sloan Kettering Cancer Center, Indiana University, University of Pennsylvania, University of Rochester, Dana-Farber Institute, M.D. Anderson Cancer Center, Princess Margaret Hospital, British Columbia Cancer Agency, and the Royal Marsden Hospital. Participants were age ≥ 18 years at study consent, and could not have received subsequent salvage chemotherapy, radiotherapy, or antecedent chemotherapy for another primary cancer. None of the participants received carboplatin-based regimens. All participants were disease-free at clinical evaluation and are referred to as TCS.

Clinical Characteristics and Treatment Information

As described previously (Frisina et al. 2016), standard forms were used by trained personnel to abstract cancer diagnosis and treatment information from medical records. Chemotherapy regimens and dates of administration, number of cycles, and cumulative cisplatin dose (later grouped into ≤ 300 , >300 mg/m²) were collected. This cut-point was selected since the most common chemotherapy regimen was bleomycin, etoposide, and cisplatin (BEP) (median cumulative dose=300 mg/m²).

Sociodemographic Characteristics, Health Behaviors, and Patient-reported

Adverse Health Outcomes (AHOs)

Sociodemographic characteristics (race, education, and employment status at the time of study enrollment), health behaviors (smoking status, alcohol consumption, and physical activity during the past year), and adverse health outcomes (AHOs) were

assessed though validated questionnaires (Ainsworth et al. 2011; Chasan-Taber et al. 1996; Oldenburg et al. 2006; Postma et al. 2005; Taylor et al. 1978; Ware and Sherbourne 1992).

Physical activity. For physical activity, participants were asked about the type of physical activity (walking; jogging (>10 min/mile); running (\leq 10 min/mile); bicycling; aerobic exercise; lower intensity exercise such as yoga, stretching, or toning; tennis, squash, or racquetball; lap swimming; weight lifting or stretch swimming) and average time per week (during the past year) spent at each of these activities. Participants were also asked about the number of flights of stairs they climb daily. A metabolic equivalent task (MET) value was assigned to each physical activity based on its energy cost. One MET is defined as the amount of energy expended for sitting quietly (Ainsworth et al. 1993). Walking pace was used to calculate MET-hours/week from walking (Ainsworth et al. 1993). Physical activity (total MET-hours/week) was derived from reported hours per week of each physical activity plus the reported number of climbed flights of stairs per day (Curhan et al. 2013). Vigorous physical activity was defined based on activities with MET value \geq 6 (Ainsworth et al. 2011).

Hypertension. “Hypertension and on prescription medication” was defined if the patient answered “yes” to (1) have you ever been diagnosed with high blood pressure and “yes, current” to (2) have you ever taken prescription medications for high blood pressure (including current use) (Chunkit Fung et al. 2017).

Hypercholesterolemia. “Hypercholesterolemia and on prescription medication” was defined if the patient answered “yes, current” to the following question: have you ever taken prescription medications for high cholesterol (Chunkit Fung et al. 2017).

Diabetes. Diabetes and on prescription medication was defined if the patient answered “yes” to either of the following questions: (1) diabetes requiring insulin or (2) diabetes requiring tablets or pills (Chunkit Fung et al. 2017).

Cardiovascular disease. Cardiovascular disease (CVD) was defined if the patient was told by physician that he had any of the following conditions (angina, coronary artery disease, heart attack or myocardial infarction, heart failure, stroke, or mini stroke (transient ischemic attack) or had any of the following procedures (angioplasty or stent placement, coronary bypass surgery, or carotid artery surgery).

Medication for anxiety and/or depression. Patient-reported medication use included current medications at the time of study enrollment if taken consistently for >1 month. Medications were categorized to anxiety and/or depression according to pharmacological class defined by the National Center for Health Statistics (NCHS) (Centers for Disease Control and Prevention National Center for Health Statistics 2019; Kantor et al. 2015). The following pharmacological classes were considered for anxiety and/or depression: benzodiazepines, tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, phenylpiperazine antidepressants, tetracyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, and miscellaneous antidepressants or anxiolytics (Buspirone) (Centers for Disease Control and Prevention National Center for Health Statistics 2019). Patients also were asked to provide the indication for medication use. If patients specified that they used the medication for indications other than anxiety and/or depression disorders (defined as anxiety, depression, obsessive compulsive disorder, panic attacks, or post-traumatic

stress disorder), they were not considered as users of medications for anxiety and/or depression.

Noise exposure. Noise exposure was defined if patients answered “yes” to either of the following questions: (1) “Have you ever had a job where you were exposed to loud noise for 5 or more hours a week? (Loud noise means noise so loud that you had to speak in a raised voice to be heard)” or (2) “Outside of a job, have you ever been exposed to steady loud noise or music for 5 or more hours a week? (This is noise so loud that you have to raise your voice to be heard. Examples are noise from power tools, lawn mowers, farm machinery, cars, trucks, motorcycles, or loud music).”

Problems hearing speech-in-background-noise. Problems hearing speech-in-background-noise was defined if patients answered “yes” to the following question “Do you have problems hearing words, sounds, or language in crowds?”

Physical Exam Assessments

TCS underwent physical exam assessments to collect information on body mass index (BMI) and waist circumference. BMI was defined as weight in kilograms divided by square of height in meters and grouped to normal, overweight and obese (<25, 25-30, and ≥ 30 kg/m², respectively) (Centers for Disease Control and Prevention 2017). Waist circumference was grouped into two classes (<120 and ≥ 120 cm), since a waist circumference of 120 cm or more in men is considered abdominal obesity (D. Kim et al. 2019).

Audiometric Assessments

Asymmetry assessment between ears. We evaluated asymmetry between ears as described previously (Frisina et al. 2016). Briefly, to evaluate asymmetry between

right and left ears for each patient, we used the geometric mean of hearing thresholds (0.25-12 kHz) for each ear and defined asymmetry when the difference was greater than 20 dB (Frisina et al. 2016). In this study, for eight patients with asymmetric hearing, thresholds were averaged.

Type of HL and middle ear dysfunction. To assess middle ear dysfunction, hearing loss was grouped into three classes: pure sensorineural hearing loss, pure conductive hearing loss, and mixed hearing loss (Frisina et al. 2016). Sensorineural hearing loss was defined as hearing thresholds at any frequency (0.25–12 kHz) >20 dB; except those with air conduction hearing threshold >5 dB relative to the bone conduction hearing threshold for frequencies of 0.25, 0.5, 1, 2, or 4 kHz.

Pure conductive hearing loss was defined as hearing thresholds at 6-12 kHz \leq 20 dB; and air conduction hearing thresholds at 0.25, 0.5, 1, 2, or 4 kHz >20 dB; and air conduction hearing threshold >5 dB relative to bone conduction threshold for frequencies of 0.25, 0.5, 1, 2, or 4 kHz.

Mixed hearing loss was defined as hearing thresholds at 0.25, 0.5, 1, 2 or 4 kHz >20 dB; and at 6, 8, 10 or 12 kHz >20 dB; and those with air conduction threshold >5 dB relative to bone conduction threshold, for frequencies of 0.25, 0.5, 1, 2 or 4 kHz.

Statistical Analysis

Among cancer survivors who self-reported any degree of difficulty hearing, those with hearing loss at only EHF were compared to the survivors with no audiometrically-defined hearing loss in terms of age at audiometry (continuous), cumulative dose of cisplatin, middle ear deficits, noise exposure, and time since completion of chemotherapy. Distributions of continuous variables (age at audiometry, cumulative

dose of cisplatin, and time since completion of chemotherapy) were assessed for normality using the Kolmogorov-Smirnov test. Since these variables were not normally distributed, a non-parametric test (Kruskal-Wallis Test) was used to compare the two groups. Categorical variables were compared using Pearson's chi-square test (**Table 4**).