Late-onset Anorectal Disease and Psychosocial Impact in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

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Background: The prevalence of late-onset anorectal disease after childhood cancer treatment and associated psychosocial morbidity is not known.

Methods: 25,530 survivors diagnosed between 1970-1999 (median age at cancer diagnosis 6.1 years, interquartile range 3.0-12.4; age at survey 30.2, 23.8-37.7) and 5036 siblings self-reported the presence or absence of late-onset anorectal disease, defined as fistula-in-ano, anorectal stricture, or anorectal subsequent malignant neoplasm (SMN) >5 years from primary cancer diagnosis. Psychosocial outcomes were evaluated using the Brief Symptom Inventory-18 (BSI-18) and the 36-Item Short Form Health Survey (SF-36), and dichotomized into impaired vs. not
impaired using thresholds set at the population norm highest 10th percentile (T-score ≥63) values for the BSI and the lowest 16th percentile (T-score <40) for the SF-36. Piecewise exponential models compared the rate of late-onset anorectal disease between survivors and siblings, and evaluated the associations between cancer treatments and late-onset anorectal disease among survivors. Multivariable logistic regression with generalized estimating equations examined associations between late-onset anorectal disease and emotional distress, as defined by the Brief Symptom Inventory-18 (BSI-18), and Health Related Quality of Life, using the 36-Item Short Form Health Survey (SF-36).

**Results:** By 45 years after diagnosis, 394 survivors (fistula, n=291; stricture, n=116; anorectal SMN, n=26) and 84 siblings (fistula, n=73; stricture, n=23; anorectal SMN, n=1) had developed late-onset anorectal disease (adjusted RR=1.2 for survivors vs. siblings, 95% CI=1.0-1.5). Among survivors, pelvic radiotherapy ≥30 Gy within 5 years of cancer diagnosis was associated with late-onset anorectal disease (30-49.9 Gy vs. none, adjusted rate ratio=1.6, 95% CI=1.1-2.3; ≥50 Gy vs. none, adjusted rate ratio=5.4, 95% CI=3.1-9.2). The 40-year post-diagnosis cumulative incidence (95% CI) of late-onset anorectal disease was 3.9% for 30-49.9 Gy and 9.7% for ≥50 Gy, compared with 2.7% for no radiation). Late-onset anorectal disease was associated with psychosocial impairment in all BSI-18 and SF-36 domains (Table).

**Conclusion:** Late-onset anorectal disease is uncommon among childhood cancer survivors but associated with previous history of higher dose directed pelvic radiotherapy. For survivors who experience late-onset anorectal disease, there is substantial psychosocial morbidity.