Long-term incidence of venous thromboembolism (VTE) among survivors of childhood cancer: A report from the Childhood Cancer Survivor Study (CCSS).

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Abstract Text:

**Background:** This study aimed to estimate the incidence of late-occurring VTE among survivors of childhood cancer, and to identify associated demographic and clinical factors that define high-risk subgroups for potential screening and prevention.

**Methods:** Using data from CCSS, a multi-institutional, longitudinal cohort of 5-year survivors of childhood cancer (diagnosed 1970-1999) and their siblings, the primary endpoint of self-reported late VTE (occurring ≥5 years after diagnosis) was estimated using multivariable piecewise exponential models adjusted for age, sex, and race. Generalized estimating equations accounted for potential within-family correlation where applicable. **Results:** Among 23,601 survivors and 5051 siblings, the incidence of VTE was 1.15 and 0.48 events per 1000 person-years, respectively. For survivors, median age at last follow-up was 28.6 years (range 5.6-58.3) and median follow-up time from diagnosis was 21.2 years (range 5.0-39.3). The adjusted rate ratio (RR) for survivors compared to siblings was 2.2 (95% confidence interval [CI] = 1.7-2.8, \( P < 0.01 \)). Among survivors, risk factors for VTE included BMI≥30kg/m\(^2\) (ref. BMI 18.5-24.5; RR = 1.5, CI = 1.2-2.0, \( P < 0.01 \)), increasing number of severe or life-threatening (i.e. CTCAE grades 3 or 4) non-VTE chronic conditions (ref. 0 conditions; 1-2 conditions: RR = 2.5, CI = 2.0-3.1, \( P < 0.01 \); ≥3 conditions: RR = 3.5, CI = 2.5-4.9, \( P < 0.01 \)), and cancer recurrence or second malignant neoplasm (RR = 3.5, CI = 2.7-4.6, \( P < 0.01 \)). Incidence of late VTE was associated with increased subsequent mortality, independent of non-VTE chronic conditions (RR 2.2, 95% CI = 1.7-2.8, \( P < 0.01 \)). **Conclusions:** Survivors of childhood cancer remain at increased risk for VTE across their lifespan. While typically not causal, late VTE was associated with subsequent mortality. Care providers should be aware of this increased risk and consider interventions that target modifiable co-morbidities such as obesity. Surveillance and education should be directed toward high-risk survivors.

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