Deadline: February 17, 2020, at 11:59 PM (EST)

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Efficacy of clinical breast examination (CBE) in chest-irradiated female survivors of childhood Hodgkin lymphoma (HL)

Background: Female survivors of childhood HL treated with ≥10 Gy of chest radiation are at high risk for breast cancer (BC). The Children's Oncology Group (COG) guidelines recommend CBE annually starting at puberty and then semiannually from age 25, plus lifetime annual mammography (MAM) and breast Magnetic Resonance Imaging (MRI) starting 8y after chest radiation or age 25, whichever is later. While imaging-based screening recommendations are largely consistent with US guidelines for women at high BC risk, only the COG guidelines recommend CBE. The benefits of lifetime CBE starting from puberty for life in chest-irradiated HL survivors is unknown.

Methods: Life-years (LYs) and lifetime BC mortality risk were estimated from a simulated cohort of 5-million HL survivors using the data from 5y female survivors of HL in the Childhood Cancer Survivor Study (CCSS) treated with ≥10 Gy of chest radiation. The simulated cohort underwent annual MAM+MRI from age 25 for life, with and without annual CBE from age 11 (presumed age of puberty) to age 24 and with and without semiannual CBE from age 25 for life with 100% adherence. BC included in-situ and invasive BC. Treatment-related BC incidence and non-BC mortality risks were estimated from the CCSS data. Risks at age <25 were extrapolated from the CCSS estimates while risks beyond age 50 were extrapolated additionally using the US population rates. CBE sensitivity (17.8%, in-situ and invasive BC) and specificity (98%) and MAM+MRI sensitivity (84.2-86.0%, in-situ; 96.7-97.1%, invasive) and specificity (75.3%) were obtained from the medical literature.

Results: The CCSS cohort included 1057 female HL survivors. BC (all invasive) developed in three patients at age <25 (ages: 23, 24, 24). In the simulated cohort receiving no screening, lifetime BC risk was 40.8% and BC mortality was 17.5%. HL survivors around age 50 were at a 7.4-fold higher risk of developing BC and a 5.2-fold higher risk of non-BC mortality when compared with the general population. Compared to no annual CBE for ages 11-24y, undergoing annual CBE did not increase gains in LYs or reduce lifetime BC mortality relative to no screening (**Table**). Among those who survived to age ≥25, undergoing semiannual CBE from age 25 for life compared to no semiannual CBE also resulted in little gain in LYs or reduction in lifetime BC mortality relative to no screening.

Conclusion: Lifetime CBE starting at puberty in conjunction with MAM+MRI appears to add little survival benefits compared with no CBE, suggesting that COG guidelines may be revised without adverse effect on long-term outcomes for chest-irradiated female survivors of childhood HL.

Strategy	Annual CBE 11-24y	Semiannual CBE 25y-life	LY gained	BC mortality reduced (%)
No screening	NA	NA	REF	REF
Entire HL cohort undergoing MAM+MRI from age 25 for life	No	Yes	0.47	10.6
	Yes	Yes	0.47	10.6
HL cohort age≥25y undergoing MAM+MRI from age 25 for life	NA	No	0.47	9.9
	NA	Yes	0.49	10.3

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