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Omission of adjuvant radiotherapy after breast-conserving surgery in systemically untreated older patients with early-stage estrogen receptor positive breast cancer: 5-year results of the TOP-1 study (BOOG 2016-01)

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Background

Adjuvant radiotherapy (RT) following breast-conserving surgery (BCS) is standard of care in women with early-stage estrogen-receptor positive (ER+) breast cancer (BC). Previous studies on RT omission involved older patients treated with BCS and endocrine therapy (ET), showing low local recurrence (LR) risks. According to Dutch guidelines, ET is not advised in T1, low-grade early-stage BC. This study assessed 5-year LR risk after BCS without RT, in older patients with ER+ BC without ET.

Methods

The prospective, multicenter, observational, single-arm TOP-1 study included women aged ≥ 70 years with low-risk BC (ER+ $\geq 50\%$, HER2-negative, ≤ 1 cm and grade 1/2, or ≤ 2 cm grade 1 with free surgical margins). Primary endpoint was 5-year LR risk, defined as a histologically confirmed invasive ipsilateral event. Secondary endpoints included contralateral BC, overall and BC specific survival. Cumulative incidence analysis was performed with death as competing event. With a 1.3% (99%CI 0.6-2.5%; national registry) 5-year LR risk with RT, and the upper CI limit tripled without RT (7.5%), 800 patients (power 80%) were needed to exclude a 10% 5-year LR risk, acceptable to patient advocates.

Results

Between January 2017 and September 2021, 792 patients were included. Median age was 73.6 years (IQR 71.9-75.5). Median follow-up was 5.1 years (IQR 4.9-5.2). In total, 123 patients developed a LR, resulting in a 5-year LR risk of 14.8% (95%CI 12.3-17.5). Treatment of LR was surgical in 114 (92.7%) patients, of whom 86 (75.4%) BCS, 70 (56.7%) patients received RT and 43 (35.0%) ET. Contralateral BC was diagnosed in 32 (4.0%) patients. Death occurred in 81 (10.2%) patients, of whom 2 (2.5%) BC related.

Conclusions

Omission of adjuvant RT resulted in a 5-year LR risk of 14.8% after BCS without ET, in women aged ≥ 70 with low-grade T1, ER+ BC. Although the LR risk exceeded prior estimates, BCS was possible in most patients and BC specific survival was excellent. Therefore, in a shared decision setting, RT omission is an option for a subgroup of older patients. Follow-up is needed to assess longer-term survival and other secondary endpoints.

Clinical trial identification

National Trial Register: 6147 (however, nowadays outdated). Also registered in the CCMO Research Portal as NL-008797.

Legal entity responsible for the study

TOP-1 steering committee (led by Prof. dr. Gerrit-Jan Liefers) and Clinical Research Centre (department of surgery), Coordinating center: Leiden University Medical Centre, the Netherlands.

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Disclosure

All authors have declared no conflicts of interest.

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