The Safety and Effectiveness of Intraoperative Radiotherapy with Low-Energy X-Rays for Breast Cancer: a Systematic Review

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OBJECTIVES

Treatment with breast-conserving surgery and adjuvant radiotherapy, rather than total mastectomy, is suitable for most breast cancer patients. Most breast recurrences are limited to the same quadrant of the primary tumor. Intraoperative radiotherapy with low-energy X-rays is a boost-dose radiation therapy that involves irradiating areas surrounding a tumor with low-energy X-rays during breast-conserving surgery (boost IORT), followed by radiotherapy. This treatment is associated with a reduced risk of recurrence.

This systematic review aimed to evaluate the safety and effectiveness of boost IORT for breast cancer patients.

METHODS

Research Question

Patient	▪ Breast cancer undergoing breast-conserving surgery
Intervention	▪ Intraoperative radiotherapy with low-energy X-rays + post-operative radiotherapy (boost IORT)
Comparator	▪ External beam radiotherapy (EBRT) ▪ Interstitial brachytherapy ▪ Intraoperative electron radiotherapy + post-operative radiotherapy (boost IOERT)
Outcomes	▪ Safety • Procedure-related complications ▪ Effectiveness • Recurrence, Mortality, Survival, Quality of Life (QOL), Duration of treatment

Data Sources

Ovid-MEDLINE, Ovid-Embase, Cochrane Library, and five Korean databases, including KoreaMed, were searched using key terms related to the research question on February 19, 2021.

Study Selection

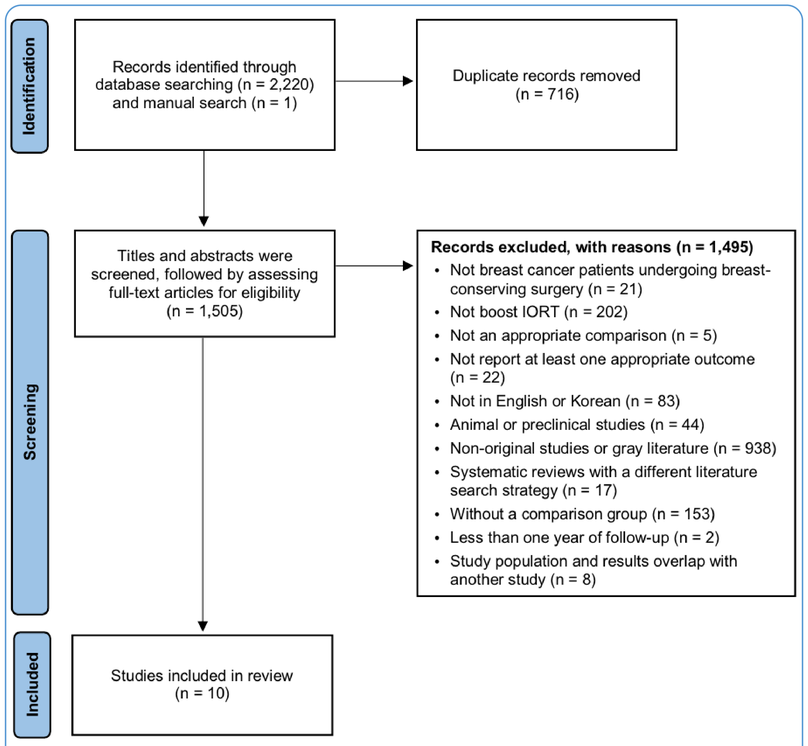
Studies that were eligible for the research question and published in peer reviewed journals in English or Korean were included. Studies without a comparison group, studies with less than one year of follow-up, non-original studies, gray literature, and systematic reviews with a different literature search strategy were excluded.

Data Extraction and Quality Assessment

Data extraction and quality assessment were undertaken by two independent reviewers. Differences in opinion were resolved by discussion at each stage. The quality of each study was assessed using the SIGN methodology checklist, and the assessment results were described based on the quality appraisal results and level of evidence.

RESULTS

10 studies, including 5 randomized controlled trials (RCTs) and 5 cohort studies, were selected. Of these 10 studies, 9 used EBRT as the comparator, while one study used EBRT and IOERT + whole breast EBRT (boost IOERT) as the comparators.



Safety

Procedure-related complications were reported in four studies (2 RCTs and 2 cohort studies). Hematoma/seroma, calcification, fat necrosis, circumscribed changes, architectural distortion, fibrosis, retraction, and pain also tended to be more common in the boost IORT group than in the comparison group. Conversely, edema and hyperpigmentation tended to be more common in the comparison group than in the boost IORT group. Scars, toxicity, telangiectasia, ulceration, and acute radiodermatitis occurred at similar rates in both groups.

Effectiveness

Recurrence

Local recurrence (four studies)
▪ In one study, the local recurrence rates was 1.24% in the boost IORT group and 0.95% in the comparison group; however, a statistically significant difference was not reported. ▪ In the three other studies, there were no significant differences between the boost IORT group (1.2–9.9%) and the comparison group (0.7–8.3%).
Distant recurrence (three studies)
▪ The distance recurrence rates were lower in the boost IORT group (4.7–10.3%) than in the comparison group (6.2–23.1%), but the difference between the two groups was not significant.
Any recurrence (two studies)
▪ Any recurrence rates tended to be lower in the boost IORT group (5.9–11.5%) than in the comparison group (6.9–22.5%), but the difference between the two groups was not significant.

Mortality

Breast cancer-related mortality (two studies)
▪ The breast cancer-related mortality rates did not significantly differ between the boost IORT group (3.3–7.7%) and the comparison group (3.2–9.1%).
Non-breast cancer-related mortality (three studies)
▪ In one study, the non-breast cancer-related mortality rate was 0%, significantly lower in the boost IORT group (0–2.5%) than in the comparison group (6.4–10.1%) in the other two studies.
All-cause mortality (two studies)
▪ The all-cause mortality rates were 3.1–5.8% in the boost IORT group and 3.1–4.8% in the comparison group. The difference was not significant in one study, and a statistically significant difference was not reported in the other study.

Survival

Local recurrence-free survival (two studies)
▪ The local recurrence-free survival rates did not significantly differ between the boost IORT and comparison groups (HR 0.61–1.19).
Disease-free survival (three studies)
▪ Five-year DFS rates did not significantly differ between the boost IORT group (85.1%) and the comparison group (86.0%) in one study. However, it tended to be higher, though statistically insignificant, between the boost IORT group (81.0–88.5%) and the comparison group (68.0–75.0%) in the other two studies.
Distant metastasis-free survival (one study)
▪ The distant metastasis-free survival rate was significantly higher in the boost IORT group (95.1%) than in the comparison group (69.0%).

Quality of Life

The QOL was reported in one RCT and was estimated using the QLQ-C30/ QLQ-BR23. the QOL was more improved in the boost IORT group than in the comparison group. However, the boost IORT group experienced more breast-associated symptoms (e.g., pain, swelling, hypersensitivity, and skin problems) than the comparison group.

Duration of treatment

The boost IORT group underwent one session of IORT and 23 to 25 fractions of whole breast EBRT postoperatively in all of the selected studies. The EBRT group underwent 3 to 6 weeks or 25 to 28 fractions of whole breast EBRT. In 6 out of 10 studies, 5 to 8 additional fractions (10–16 Gy) of boost EBRT were performed following whole breast EBRT in some or all of the included patients. In one study, the boost IOERT group underwent one session of IOERT and 25 fractions of postoperative whole breast EBRT.

CONCLUSION

Most procedure-related complications, such as hematoma/seroma, fat necrosis, and edema, occurred early after surgery and were not severe. Therefore, the boost IORT has been found to have an acceptable level of safety.

Despite the fact that most of the included studies assessing effectiveness were retrospective cohort studies, the outcomes were not clinically different from those of the group that received EBRT and IOERT as boost therapy. Hence, IORT is safe and effective as a boost therapy for breast cancer patients undergoing breast-conserving surgery and whole breast EBRT (Level of evidence C).

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