Original Article

Eur J Breast Health 2024; 20(1): 38-44
DOI: 10.4274/ejbh.galenos.2023.2023-9-5

Omission of Radiotherapy in Women >60 Years Old After Breast Conserving Surgery for Breast Cancer is Non-Inferior in Terms of Local Recurrence: A Retrospective Cohort Study

Anna Sachoulidou[1], Fani Apostolidou[2], Charalambos Fronis[3], Despoina Misailidou[4], Aichan Bozoglou[1], Themis Anastasia Tataridou[1], Aristomenis Ampatzoglou[1], Ioannis Galanis[1]

[1]Second Department of Propaedeutic Surgery, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Hippokration General Hospital of Thessaloniki, Aristotle University of Thessaloniki, Thessaloniki, Greece
[2]Department of Hygiene, Social-Preventive Medicine and Medical Statistics, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessalonik, Thessalonik, Greece
[3]Cyanous Stavros, Euromedica, Thessaloniki, Greece
[4]Department of Radiation Oncology, St. Luke's Hospital, Thessaloniki, Greece

ABSTRACT

Objective: Local recurrence rate may show no significant differences between women aged 60 and older who receive breast-conserving surgery followed by radiotherapy and those in the same age group who undergo breast-conserving surgery without subsequent radiotherapy.

Materials and Methods: Retrospective cohort study from a single practice with median follow-up time 44 months (interquartile range: 16, 82), comparing women older than 60 years old at diagnosis of breast cancer, treated with breast conserving surgery and either receiving or not receiving radiation therapy postoperatively. The primary endpoint was local recurrence difference between the two groups.

Results: Local recurrence did not differ significantly between the two groups in terms of radiotherapy or not [odds ratio (OR) 0.96, 95% confidence interval (CI) 0.89–1.02, Fisher's exact test p = 0.388], nor between two age groups with cut-off at 65 years of age (OR: 0.99, 95% CI 0.92–1.07, Fisher's Exact test p = 0.6). Local recurrence also did not differ when subgroups of age (60–65 years and >66 years) were considered. All patients received 5 years of hormonal therapy.

Conclusion: Omission of radiotherapy in selected patients is not inferior to radiotherapy after breast conserving surgery in terms of preventing local recurrence.

Keywords: Breast conserving surgery; local recurrence; radiotherapy omission

Cite this article as: Sachoulidou A, Apostolidou F, Fronis C, Misailidou D, Bozoglou A, Tataridou TA, Ampatzoglou A, Galanis I. Omission of Radiotherapy in Women > 60 Years Old After Breast Conserving Surgery for Breast Cancer is Non-Inferior in Terms of Local Recurrence: A Retrospective Cohort Study. Eur J Breast Health 2024; 20(1): 38-44

Key Points

- Local recurrence risk was not significantly different in radiation-receiving and radiation-omitting women older than 60 years at diagnosis.
- This lack of difference was detected among patients who underwent breast conserving surgery with positive estrogen receptor status and had received 5 years of endocrine therapy.
- Radiation therapy may be safely omitted in patients older than 60 years of age at diagnosis in terms of the risk of local recurrence.

Corresponding Author:
Anna Sachoulidou; a.sachoulidou@gmail.com

Received: 13.11.2023
Accepted: 04.12.2023
Available Online Date: 27.12.2024

©Copyright 2024 by the Turkish Federation of Breast Diseases Societies / European Journal of Breast Health published by Galenos Publishing House.

Introduction

Radiotherapy in breast cancer cases was commonplace across clinical guidelines in the past decades (1). Associated morbidity, together with poorer patient-reported quality of life needs to be taken into consideration when planning postoperative treatment with the advance of patient age at diagnosis (2). During the Coronavirus disease 2019 pandemic, the limitation of resources and the need for protection of oncological patients brought up the question of omitting radiation therapy in selected subgroups of patients with breast cancer. A literature review of the available studies (3) concluded that older adults with early-stage breast cancer and favourable prognostic factors should undergo tailored therapeutic strategies, including the omission of radiation therapy. Later studies have demonstrated the lack of benefit concerning local recurrence in patients older than 65 years (4-6). The purpose of this retrospective study was to evaluate whether the omission of radiotherapy after breast conserving surgery was non-inferior to outcomes in patients receiving radiotherapy in terms of local recurrence.

Materials and Methods

This was a retrospective cohort study to assess the impact of postoperative radiotherapy following breast conserving surgery on local recurrence. The records of a single practice were the source of data. Patients older than 60 years at the time of initial surgical consultation, candidate for breast conserving excision, hormonally dependent tumour biology and histologic grade up to III were assessed for inclusion. Patients with hormonally dependent tumours and histological grade up to III were considered low risk patients and thus included in the cohort. The age limit was chosen in accordance with recent publications (2, 5, 6). Breast conserving excision was defined as lumpectomy or partial mastectomy with clear margins combined with sentinel lymph node biopsy. A minimum of six months follow up was required to be assessed for local recurrence. Local recurrence was defined as any abnormal clinical or ultrasonographic finding at the site of initial excision undergoing biopsy (fine needle or open) and proving to be malignant. Patients with lymph node involvement confirmed either intra-operatively or post-operatively were not included. The radiation therapy protocol was whole breast irradiation with approximately 45–50.4 Gy (1.8–2 Gy/fraction, 25–28 fractions) with or without boost dose to the tumour bed (external radiotherapy of 10–16 Gy at 2 Gy/fraction). All included patients were eligible for a five-year hormonal treatment protocol. Systemic chemotherapy was administered only to patients with histologic grade III.

Written consent was not obtained since all patient records were anonymized. The study was approved by the Ethics Committee of the Department of Medicine of the Aristotle University of Thessaloniki (approval number: 6/2023, date: 07.11.2023).

Statistical Analysis

Descriptive statistics, dictated by normality assessment where appropriate, were used to summarise the raw data. Pairwise comparisons between the two groups were done with either Wilcoxon rank-sum test (non-normally distributed, continuous data) or chi-square test and Fisher's Exact test (categorical data). Significance level was set to 5%. Kaplan-Meier curves were used to investigate the time to local recurrence and the log-rank test was used to formally assess the difference in curves. Due to the nature of the initial database (single private practice records) a proportion of patients were followed up in tertiary centres after receiving radiotherapy and their data on local recurrence were not available. To account for this loss of patients we decided to run subgroup analysis including only patients followed up for more than 21 months after surgery (roughly up to the sixth follow-up visit) and compare the results with the initial estimation. Starting point was defined as the date of surgery to ensure all patients had similar initiation of follow-up.

Sample Size Calculation

Based on the natural history of the disease, specifically the local recurrence rate (7), and published data from large, randomized trials we can estimate that 125 observations should suffice to detect an effect (w = 0.25) with level of significance 5% and 80% power using Pearson's chi-squared test.

This study is reported in accordance with STROBE guidelines (8) for cohort studies.

Data were collected using an Access database (Microsoft Office 365©) and calculations were done with R Statistical Software (v4.2.3; R Core Team) (9–13) for Windows (Microsoft Corporation©) using the RStudio IDE (14).

Results

A hundred and twenty-nine patients were identified but only 127 were included in this analysis since the last two patients underwent breast-conserving surgery less than six months ago (Table 1). All patients were positive for estrogen and progesterone receptors. Median age was 67 years old [interquartile range (IQR) 63, 72], and did not differ significantly between the two groups (Wilcoxon rank-sum test p = 0.2). Similarly, median follow-up time (no radiotherapy median: 46 months, IQR: 18–73 and radiotherapy median: 44 months, IQR: 16–88 respectively, Wilcoxon rank-sum test p = 0.7), tumour size (no radiotherapy median: 1.50, IQR: 1.00–2.00 and radiotherapy median: 1.50, IQR: 1.05–2.00, Wilcoxon rank-sum test p = 0.2), histologic grade (Figure 1 and Table 1), sentinel lymph node status (100% negative in both groups), five-year hormonal therapy adherence (one non-adherent patient in the no radiotherapy group and none in the radiotherapy group) and Ki-67 status (no radiotherapy median: 14, IQR: 8–17 and radiotherapy median: 15, IQR: 15–30, Wilcoxon rank-sum test p = 0.093) were comparable between groups. Local recurrence rate was not statistically different between the groups [odds ratio (OR) 0.96, 95% confidence interval (CI) 0.89–1.02, Fisher's Exact test p = 0.388; see Figure 1]. All patients had negative resection

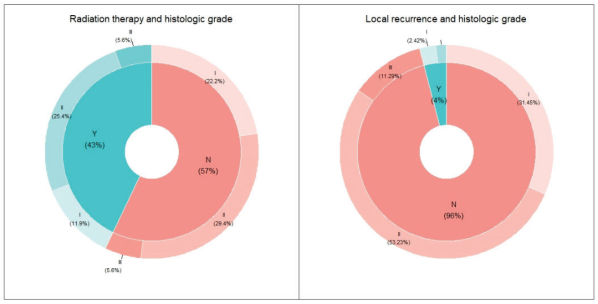

Figure 1. Donut-pie charts depicting the analogy of histological grade (I: grade I, II: grade II, III: grade III, along with relative frequencies) between the two radiation groups (Y: Receiving postoperative radiation, N: Not receiving postoperative radiation) on the left side, and the analogy of histological grade (I: grade I, II: grade II, III: grade III, along with relative frequencies) between those with local recurrence (Y) and those without (N) on the right side

margins. Seven patients in each group received systemic chemotherapy (Fisher's Exact test p = 0.78).

There were 55 patients in the radiotherapy group. Median total radiotherapy dose was 4082 (IQR: 4005–5000) and ten patients were treated with boost radiotherapy (29%), though there were many missing data on the boost protocol (n = 20). Interestingly, in the subgroup analysis of patients receiving radiotherapy, a difference in the radiotherapy dose was detected regarding the radiotherapy protocol (with or without boost doses). The initial dose was higher in the group in the boost protocol compared to the dose in the no boost protocol (Boost group: 4256 (4005, 5000), no Boost group: 4005 (2951, 4121), Wilcoxon rank-sum test p = 0.022).

Table 1. Sample baseline characteristics

Characteristic	Overall, n = 127[1]	No radiotherapy, n = 72[1]	Radiotherapy, n = 55[1]	p^2
Age	67 (63, 72)	67 (63, 74)	65 (63, 70)	0.2
Tumour size	1.50 (1.00, 2.00)	1.50 (1.00, 2.00)	1.50 (1.05, 2.00)	0.2
Histologic grade				0.4
I	43 (34%)	28 (39%)	15 (28%)	
II	69 (55%)	37 (51%)	32 (59%)	
III	14 (11%)	7 (9.7%)	7 (13%)	
Unknown	1	0	1	
Chemotherapy				0.78
No	113 (89%)	65 (90%)	48 (87%)	
Yes	14 (11%)	7 (10%)	7 (13%)	
Sentinel lymph node status				
Negative	127 (100%)	72 (100%)	55 (100%)	
Hormonal therapy				>0.9
No	1 (0.8%)	1 (1.4%)	0 (0%)	
Yes	126 (99%)	71 (99%)	55 (100%)	
Ki-67 status	15 (10, 24)	14 (8, 17)	15 (14, 30)	0.093
Unknown	80	42	38	
Radiotherapy				-
No	72 (57%)	-	-	
Yes	55 (43%)	-	-	
Radiotherapy dose (cGy)	4082 (4005, 5000)	-	4082 (4005, 5000)	
Unknown	19	72	19	
Boost radiotherapy protocol				>0.9
No	10 (29%)	-	10 (29%)	
Yes	25 (71%)	-	25 (71%)	
Unknown	92	72	20	
Local recurrence				0.4
No	120 (96%)	67 (94%)	53 (98%)	
Yes	5 (4.0%)	4 (5.6%)	1 (1.9%)	
Unknown	2	1	1	
Surgery date	1994-03-01 to 2023-02-22	1994-03-01 to 2023-03-28	1998-05-01 to 2023-02-22	0.3
Last follow-up	2003-06-01 to 2023-08-02	2003-06-01 to 2023-08-02	2010-05-01 to 2023-08-02	0.13
Follow-up (months)	44 (16, 82)	46 (18, 73)	44 (16, 88)	0.7
Follow-up (years)	4.0 (1.0, 7.0)	4.0 (1.8, 6.0)	4.0 (1.0, 7.0)	0.7

[1]Median (IQR); n (%); range
[2]Wilcoxon rank-sum test; Pearson's chi-squared test; Fisher's Exact test

The study population was also assessed based on age, with a cut-off at 65 years on surgery. There were no systematic differences detected on local recurrence rates (OR: 0.99, 95% CI 0.92–1.07, Fisher's Exact test p = 0.6, Table 2). Local recurrence did not differ among radiotherapy groups either in the 60–65 years old group, nor the >65 years old group (OR: 0.21, 95% CI 0.01–4.13, p = 0.49 for the 60–65 years group and OR: 0.79, 95% CI 0.08–8.4, p = 0.89 for the >65 years group). Median follow-up time was similarly distributed between groups (median 62 months, IQR 15–93 in the 60–65 years old group and median 38 months, IQR 16–74 in the 66–88 years old group, Wilcoxon rank-sum test p = 0.11). Patients' characteristics were not found to differ systematically between the two groups. Tumour size was not different between the two groups (median 1.50, IQR: 1.00–2.00 in both groups, Wilcoxon rank-sum test p = 0.9), neither was the relative frequencies of histologic grade (chi-squared test p = 0.5). Sentinel lymph node status was 100% negative in both groups and ki-67 status was similarly distributed (median: 14, IQR: 14–20 in the 60–65 years old group and median: 15, IQR: 8–25 in the 66–88 years old group, Wilcoxon rank-sum test p = 0.6). Adherence to hormonal therapy demonstrated no difference with one non-adherent patient in the 60–65 years old group and none in the 66–88 years old (Fisher's Exact test p = 0.4). The proportion of patients undergoing radiotherapy was similar between the two groups (OR: 0.81, 95% CI: 0.59–1.11, Fisher's Exact test p = 0.2) as was the proportion of patients receiving boost doses (OR: 0.79, 95% CI: 0.27–2.32, Fisher's Exact test p = 0.7). Radiotherapy doses were comparable between groups (median: 4160, IQR: 4005–5000 in the 60–65 years old group and median: 4240, IQR: 4005–4428 in the 66–88 years old group, Wilcoxon rank-sum test p = 0.3). Eight patients in the 60–65 years old group and six in the 66–88 years old group received systematic chemotherapy (Fisher's Exact test p = 0.39).

Table 2. Sample characteristics between age groups

Characteristic	60–65 years old n = 56[1]	66–88 years old n = 71[1]	p^2
Tumour size	1.50 (1.00, 2.00)	1.50 (1.00, 2.00)	0.9
Histologic grade			0.5
I	17 (31%)	26 (37%)	
II	30 (55%)	39 (55%)	
III	8 (15%)	6 (8.5%)	
Unknown	1	0	
Chemotherapy			0.39
No	48 (85.8%)	65 (91.6%)	
Yes	8 (14.2%)	6 (8.4%)	
Sentinel lymph node status			
Negative	56 (100%)	71 (100%)	
Hormonal therapy			0.4
No	1 (1.8%)	0 (0%)	
Yes	55 (98%)	71 (100%)	
Ki-67 status	14 (14, 20)	15 (8, 25)	0.6
Unknown	33	41	
Radiotherapy			0.2
No	28 (50%)	44 (62%)	
Yes	28 (50%)	27 (38%)	
Radiotherapy dose (cGy)	4160 (4005, 5000)	4240 (4005, 4428)	0.3
Unknown	35	52	
Boost radiotherapy protocol			0.7
No	4 (25%)	6 (32%)	
Yes	12 (75%)	13 (68%)	
Unknown	40	53	
Local recurrence			0.9
No	53 (96%)	67 (96%)	
Yes	2 (3.6%)	3 (4.3%)	
Unknown	1	1	
Surgery date	1994-03-01 to 2023-02-21	2000-11-01 to 2023-02-22	0.9
Last follow-up	2005-02-01 to 2023-08-02	2003-06-01 to 2023-08-02	0.2
Follow-up (months)	62 (15, 93)	38 (16, 74)	0.11
Follow-up (years)	5.0 (1.0, 8.2)	3.0 (1.0, 6.0)	0.076

[1]Median (IQR); n (%); range

[2]Wilcoxon rank-sum test; Pearson's chi-squared test; Fisher's Exact test

Kaplan-Meier curves were used to assess the time to local recurrence and compare the two radiotherapy groups. In this sample, median survival time could not be determined for either group since less than half of the patients were diagnosed with local recurrence until the end of observation. The log-rank test did not detect any systematic difference between the two survival curves (Figure 2). When comparing Kaplan-Meier curves in the two age groups, the absence of statistically significant difference between radiation groups remained (Figure 3).

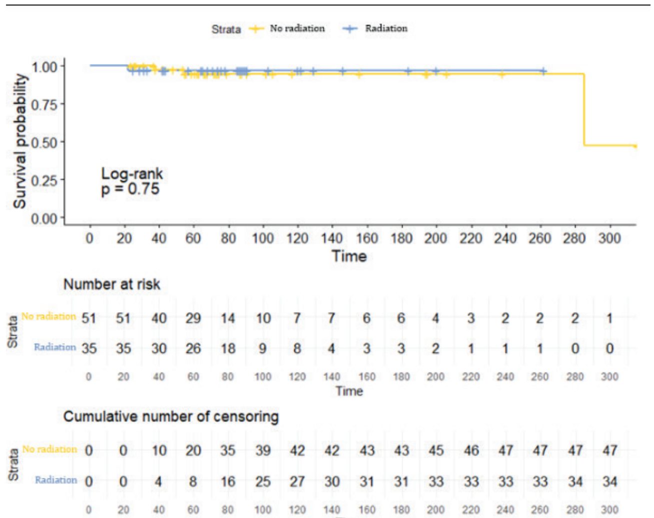

Figure 2. Kaplan-Meier curves for local recurrence between the two radiation groups, along with tables with number remaining at risk and cumulative censoring at each time interval. No statistically significant difference is detected, either from inspection of the curves or with the log-rank test

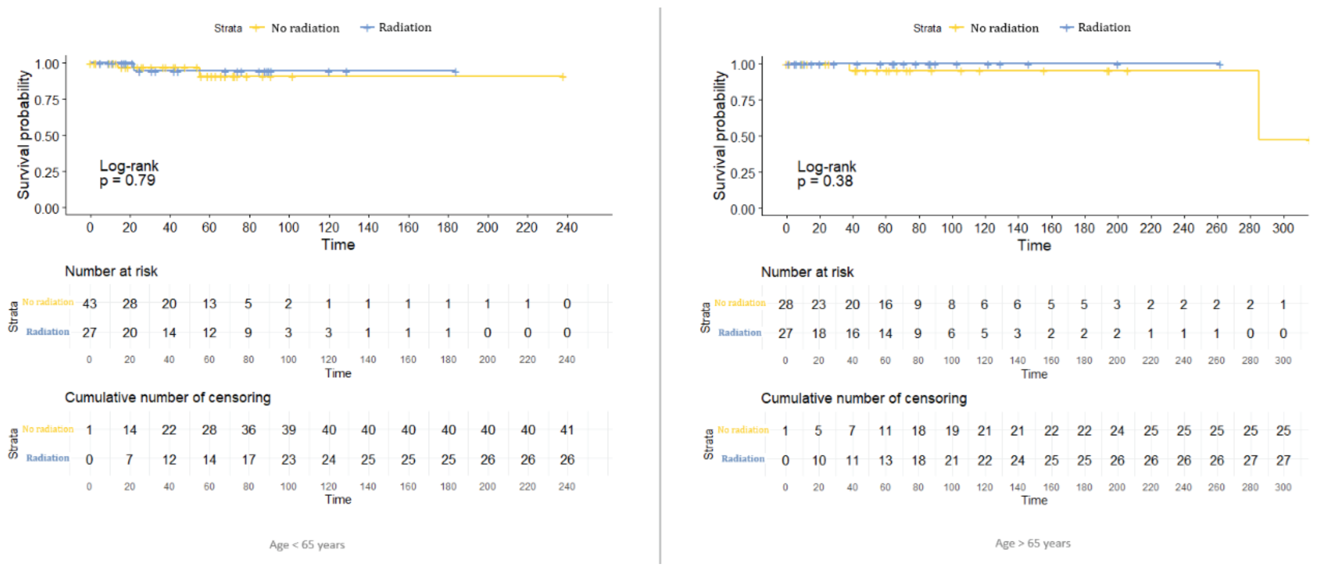

Figure 3. Kaplan-Meier curves for local recurrence between the two radiation groups, along with tables with number remaining at risk and cumulative censoring at each time interval and for each age group (left: age <65 years old, right: age >65 years old). No statistically significant difference is detected, either from inspection of the curves or with the log-rank test

Discussion and Conclusion

The main finding of this retrospective analysis was the lack of difference in survival rates for local recurrence between those receiving radiation therapy and those who did not in patients older than 60 years old, over a follow-up period of around 45 months.

In this cohort, patients with T1 or T2 breast tumours and node-negative status were found to have no significant difference in local recurrence survival time whether they had radiotherapy or not. Stueber et al. (15) conducted an analysis of 2384 patients from the BRENDA registry and concluded that patients aged older than 70 years old with low-risk early breast cancer (luminal A, T1 or T2 and node-negative) receiving GA-BCS were a suitable group to forego postoperative radiation as there was no significant benefit for either local recurrence or for tumour-associated death. In the same study, higher-risk (G3 or T3/T4 or node-positive or other than luminal A tumours) patients were found to have benefit and should undergo irradiation. Subsequent reports were in accordance with these findings (16).

Our cohort study included women aged 60 to 88 years old. Further cohort (5, 17) studies as well as RCTs (4) suggested that the age cut-off for radiation omission in low-risk breast cancer could be at 65 years of age at diagnosis. These concluded that the omission of radiation should be considered based on comorbidities considering that lack of apparent benefit in overall survival. In our subgroup analysis with a cut-off at 65 years of age, local recurrence rate did not differ significantly between those receiving radiation and those not in either group.

Our cohort consisted entirely of ER+ tumours undergoing endocrine therapy for five years. Previous studies (4, 18) found evidence of the protective role of endocrine therapy for local recurrence. Additionally, it has been a decade since the establishment of the similarity of reduction of local recurrence between radiotherapy and endocrine therapy (19). A common conclusion was that the decision for radiation omission in patients can be safely considered given that they will adhere to five-year endocrine therapy. This decision should take into consideration the patient's preference and potential markers of radiation sensitivity (20) since an analysis of cost-effectiveness comparing treatment options did not reveal systematic differences (21) to rely upon.

Radiation therapy has been a close adjunct to breast cancer treatment for many decades. There are several (22, 23) registry reports that advocate the benefits of radiation therapy in elderly patients with low-risk breast cancer undergoing either breast conserving surgery or mastectomy. However, even these studies that found statistically significant differences in tumour-specific survival, concluded that individual counselling in elder patients is the preferred decision-making process regarding radiation therapy. It is noteworthy that prospective, randomised trials of the same period (6) had already begun to suggest the omission of radiotherapy in selected patients without greater hazard for death or local recurrence.

One of the most notable systematic reviews on the subject is an extensive meta-analysis of individual patient data (1). This comprehensive analysis demonstrated a clear advantage after receiving radiotherapy, significantly reducing the risk of recurrence and moderately lowering the overall risk of death. Another recent systematic review and meta-analysis (24) specifically focused on elderly patients, evaluating both the omission of radiation therapy and endocrine therapy. Interestingly, the endpoint related to the omission of radiotherapy showed a significant impact on local recurrence but not on overall survival. Despite their data supporting the omission of radiotherapy, it should be noted that their literature search concluded before the publication of subsequent large cohorts and randomized controlled trials. This gap in the existing literature calls for a fresh synthesis that incorporates various study types as methodologically appropriate. To address this, a protocol has been registered in the Cochrane database. The aim is to assess the omission of radiation in postmenopausal women, with planned subgroup analyses based on age, receipt of adjuvant chemotherapy, and receipt of adjuvant hormonal treatment, providing a more up-to-date and comprehensive understanding of the topic.

Several ongoing studies aim to address the question of personalizing radiation therapy omission. The expansion of patient age (25, 26) and the incorporation of new genetic markers (25, 26), in conjunction with standard histopathological tumour evaluation, are being explored to identify patients who can safely omit radiotherapy. Additionally, research is underway to investigate the effect of human epidermal growth factor receptor 2 status (27) and explore the feasibility of omitting radiation therapy in favour of partial irradiation instead of whole breast irradiation (28). The diversity in study protocols and modalities used for identifying at-risk patients underscores the ongoing necessity for more individualized treatments based on evidence-derived recommendations (29).

Study Limitations

The limitations of this study are the sample size and the rarity of the local recurrence. We believe that this is due to the fact that a proportion of the sample continued their follow-up in the referral centre where they underwent oncological consultation. This loss from follow-up resulted in high censoring and thus the inability to determine median survival times. The retrospective nature of the collected data cannot allow for generalization, but the aim of this study was to provide a motive for tailoring radiation therapy rather than provide broad recommendations. Several additional sources of bias should be taken into consideration when interpreting these results. These include that no confounding factors could be investigated due to the few local recurrences, the cohort may suffer sampling bias due to its source from a single practice and possibly, immortal time bias since the starting time is the surgery date and not the treatment completion day, which is the final radiotherapy session for the patients in the radiotherapy group.

In conclusion, our findings support the existing evidence on personalized omission of radiation therapy with primary focus on the patient's age, given they present with low-risk breast tumours and estrogen receptor positive status. A systematic review of the existing literature should determine whether more RCTs and registry analyses are needed to address this question.

Ethics Committee Approval: study was approved by the Ethics Committee of the Department of Medicine of the Aristotle University of Thessaloniki (approval number: 6/2023, date: 07.11.2023).

Informed Consent: Written consent was not obtained since all patient records were anonymized.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.S., F.A., C.F., D.M., A.B., T.A.T., A.A., I.G.; Concept: A.S., F.A., C.F., A.A., I.G.; Design: A.S., F.A., C.F., A.A., I.G.; Data Collection and/or Processing: A.S., C.F.; Analysis and/or Interpretation: A.S., F.A.; Literature Search: F.A., D.M., A.B., T.A.T.; Writing: D.M., A.B., T.A.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG); Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet 2011; 378 : 1707-1716. (PMID: 22019144) [Crossref]
2. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM; PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol 2015; 16: e105. (PMID: 25752559) [Crossref]
3. Palumbo I, Borghesi S, Gregucci F, Falivene S, Fontana A, Aristei C, et al. Omission of adjuvant radiotherapy for older adults with early-stage breast cancer particularly in the COVID era: A literature review (on the behalf of Italian Association of Radiotherapy and Clinical Oncology). J Geriatr Oncol 2021; 12: 1130-1135. (PMID: 34020908) [Crossref]
4. Kunkler IH, Williams LJ, Jack WJL, Cameron DA, Dixon JM. Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer. N Engl J Med 2023; 16; 388: 585-594. (PMID: 36791159) [Crossref]
5. Lai X, Han W, Zhang H, Hou J, Wang G, Luo X, et al. Prognostic role of radiotherapy in low-risk elderly breast cancer patients after breast-conserving surgery: a cohort study. Gland Surg 2022; 11: 847-859. (PMID: 35694094) [Crossref]
6. Tinterri C, Gatzemeier W, Costa A, Gentilini MA, Zanini V, Regolo L, et al. Breast-conservative surgery with and without radiotherapy in patients aged 55-75 years with early-stage breast cancer: a prospective, randomized, multicenter trial analysis after 108 months of median follow-up. Ann Surg Oncol 2014; 21: 408-415. (PMID: 24197757) [Crossref]
7. Kaidar-Person O, Giasafaki P, Boersma L, De Brouwer P, Weltens C, Kirkove C, et al. Mapping the location of local and regional recurrences according to breast cancer surgery and radiation therapy: Results from EORTC 22922/10925. Radiother Oncol 2023; 185: 109698. (PMID: 37211281) [Crossref]
8. Cuschieri S. The STROBE guidelines. Saudi J Anaesth 2019; 13(Suppl 1): 31. (PMID: 30930717) [Crossref]
9. Wickham H. ggplot2: Elegant Graphics for Data Analysis. New York: Springer-Verlag; 2016. https://link.springer.com/book/10.1007/978-3-319-24277-4?utm_medium=email&utm_source=transaction [Crossref]
10. Sjoberg DD, Whiting K, Curry M, Lavery JA, Larmarange J. Reproducible Summary Tables with the gtsummary Package. The R Journal 2021; 13: 570-580. https://journal.r-project.org/archive/2021/RJ-2021-053/RJ-2021-053.pdf [Crossref]
11. Kassambara A, Kosinski M, Biecek P, Fabian S. survminer: Drawing Survival Curves using "ggplot2." 2021. https://cran.r-project.org/web/packages/survminer/survminer.pdf [Crossref]
12. Therneau T. A Package for Survival Analysis in R. 2023. https://cran.r-project.org/web/packages/survival/vignettes/survival.pdf [Crossref]
13. Core Team R. A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2023. https://www.bibsonomy.org/bibtex/7469ffee3b07f9167cf47e7555041ee7 [Crossref]
14. RStudio Team. RStudio: Integrated Development Environment for R. Boston, MA: RStudio, PBC; 2020. (https://www.r-project.org/conferences/useR-2011/abstracts/180111-allairejj.pdf) [Crossref]
15. Stueber TN, Diessner J, Bartmann C, Leinert E, Janni W, Herr D, et al. Effect of adjuvant radiotherapy in elderly patients with breast cancer. PLoS One 2020; 15: e0229518. (PMID: 32434215) [Crossref]
16. Zhong Y, Xu Y, Zhou Y, Mao F, Lin Y, Guan J, et al. Omitting radiotherapy is safe in breast cancer patients ≥ 70 years old after breast-conserving surgery without axillary lymph node operation. Sci Rep 2020; 10: 19481. (PMID: 33173112) [Crossref]
17. Polgár C, Fodor J, Major T, Sulyok Z, Kásler M. Breast-conserving therapy with partial or whole breast irradiation: ten-year results of the Budapest randomized trial. Radiother Oncol 2013; 108: 197-202. (PMID: 23742961) [Crossref]
18. Wickberg Å, Liljegren G, Killander F, Lindman H, Bjöhle J, Carlberg M, et al. Omitting radiotherapy in women ≥ 65 years with low-risk early breast cancer after breast-conserving surgery and adjuvant endocrine therapy is safe. Eur J Surg Oncol 2018; 44: 951-956. (PMID: 29709338) [Crossref]

19. Blamey RW, Bates T, Chetty U, Duffy SW, Ellis IO, George D, et al. Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial. Eur J Cancer 2013; 49: 2294-2302. (PMID: 23523089) [Crossref]

20. Killander F, Karlsson P, Anderson H, Mattsson J, Holmberg E, Lundstedt D, et al. No breast cancer subgroup can be spared postoperative radiotherapy after breast-conserving surgery. Fifteen-year results from the Swedish Breast Cancer Group randomised trial, SweBCG 91 RT. Eur J Cancer 2016; 67: 57-65. (PMID: 27614164) [Crossref]

21. Ward MC, Vicini F, Al-Hilli Z, Chadha M, Pierce L, Recht A, et al. Cost-effectiveness analysis of endocrine therapy alone versus partial-breast irradiation alone versus combined treatment for low-risk hormone-positive early-stage breast cancer in women aged 70 years or older. Breast Cancer Res Treat 2020; 182: 355-365. (PMID: 32468336) [Crossref]

22. Wöckel A, Wolters R, Wiegel T, Novopashenny I, Janni W, Kreienberg R, et al. The impact of adjuvant radiotherapy on the survival of primary breast cancer patients: a retrospective multicenter cohort study of 8935 subjects. Ann Oncol 2014; 25: 628-632. (PMID: 24515935) [Crossref]

23. Yang SP, Tan LL, Zhou P, Lian CL, Wu SG, He ZY. The addition of radiotherapy to breast-conserving surgery improves survival for elderly patients with early breast cancer. Front Oncol 2022; 12: 917054. (PMID: 36505844) [Crossref]

24. Savard MF, Clemons M, Hutton B, Jemaan Alzahrani M, Caudrelier JM, Vandermeer L, et al. De-escalating adjuvant therapies in older patients with lower risk estrogen receptor-positive breast cancer treated with breast-conserving surgery: A systematic review and meta-analysis. Cancer Treat Rev 2021; 99: 102254. (PMID: 34242928) [Crossref]

25. The PRECISION Trial (Profiling Early Breast Cancer for Radiotherapy Omission): A Phase II Study of Breast-Conserving Surgery Without Adjuvant Radiotherapy for Favorable-Risk Breast Cancer. NCT02653755. U.S. National Library of Medicine, 2016. https://clinicaltrials.gov/study/NCT02653755 (accessed 2023-12-02) [Crossref]

26. A Randomised Phase III Trial of Adjuvant Radiation Therapy Versus Observation Following Breast Conserving Surgery and Endocrine Therapy in Patients With Molecularly Characterised Luminal A Early Breast Cancer. NCT02889874. U.S. National Library of Medicine, 2017. https://clinicaltrials.gov/study/NCT02889874 (accessed 2023-12-02) [Crossref]

27. Selective Use of Observation After Lumpectomy and Sentinel Lymph Node Biopsy in Her-2 Positive Patients With Pathologic Complete Response to Neoadjuvant Chemotherapy. NCT03460067. U.S. National Library of Medicine, 2018. https://clinicaltrials.gov/study/NCT03460067 (accessed 2023-12-02) [Crossref]

28. The DBCG RT Natural Trial: Partial Breast Versus no Irradiation for Women >=60 Years Operated With Breast Conservation for an Early Breast Cancer: a Clinically Controlled Randomized Phase III Trial. NCT03646955. U.S. National Library of Medicine, 2018. https://clinicaltrials.gov/study/NCT03646955 (accessed 2023-12-02) [Crossref]

29. Lakhanpal R, Jensen K, Shadbolt B, Sullivan L. Omission of whole breast irradiation for postmenopausal women with early breast cancer. Cochrane Database Syst Rev 2017; 2017: CD012469. [Crossref]