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Management of ipsilateral breast tumor recurrence following breast conservation surgery for ductal carcinoma in situ – a data-poor zone

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Abstract

Background: Breast conserving surgery (BCS) is well established for the management of ductal carcinoma in situ (DCIS). A growing body of retrospective data support re-conservation therapy (re-BCS) for ipsilateral breast tumor recurrence (IBTR) following BCS for invasive cancer, but neither randomized trials nor guidelines address management of IBTR after BCS for DCIS. Here we compare the outcomes of mastectomy vs re-BCS for a large series of DCIS patients with IBTR.

Methods: We identified women treated with BCS for DCIS who developed IBTR as a first event. Between those treated with mastectomy vs re-BCS, we compare the clinicopathologic characteristics for the initial and recurrent tumors, the use of adjuvant radiotherapy (RT) both upfront ("primary RT") and post IBTR ("secondary RT"), of tamoxifen, the rate of third events (local, regional, distant), and both breast cancer specific (BCSS) and overall survival (OS).

Results: of 3001 women treated with BCS for DCIS (1978–2010), we identified 383 who developed an IBTR as a first event (1983–2023) and were treated at our institution, 197 (51%) with mastectomy vs 186 (49%) with re-BCS. Re-BCS was more frequent over time, comprising 56% of the most recent patients (2014–2023). Compared to re-BCS, those treated by mastectomy were significantly more likely at initial DCIS presentation to have necrosis (74% vs 59%), high grade (47% vs 28%), comedo histology (38% vs 20%), and to have received primary RT (61% vs 21%). Between mastectomy vs re-BCS, there were no significant differences in disease-free interval (DFI), in the pathologic characteristics of the IBTR, or in the proportion of invasive vs in situ disease. Among re-BCS patients, breast re-recurrence was least frequent among those who received primary *and* secondary RT (9%) and most frequent among those who received primary but not secondary RT (22%). At a median follow up of 7 yrs post-mastectomy and 7.7 years post-re-BCS, third local events in total were more frequent for re-BCS vs mastectomy (16% vs 3%, p=0.001), but there were no differences in breast cancer specific or overall survival.

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Conclusions: Our data show that for women with isolated IBTR following BCS for DCIS and treated by mastectomy vs re-BCS, 1) treatment with mastectomy was associated with less favorable initial pathology and more frequent use of primary RT, 2) re- recurrence was more frequent with re-BCS, and 3) BCSS and OS were comparable. In an era of increasing surgical de-escalation, our data suggest a wider role for re-BCS and – as for patients having re-BCS for IBTR following invasive cancer – further study of the relationship between secondary RT and the rate of third breast events.

Keywords

DCIS; breast conservation surgery; re-conservation surgery; ipsilateral breast tumor recurrence

Introduction

As for invasive cancer[1], breast conserving surgery (BCS) for DCIS is well established[2]. The 10 year results (and 13–20 year follow-up[3–6]) of 4 randomized trials of BCS plus or minus radiotherapy (RT) accrued from 1985–1998 confirm that - compared to BCS alone - BCS/RT was associated with significant absolute and proportional reductions in ipsilateral breast tumor recurrence (IBTR) across all categories of age, extent of surgery, use of tamoxifen, and tumor characteristics. Although RT reduced the 10 year absolute rate of IBTR overall from 28% to 12.9%, breast cancer mortality was comparable with vs without RT (4.1% vs 3.7%). More recently large retrospective studies of DCIS from our own institution have confirmed the efficacy of RT but also observed declining rates of IBTR (with or without RT) over time[7], by increasing patient age[8], and by increasing margin width (in women how elected BCS without RT)[9]. Mastectomy is still considered to be standard treatment for IBTR[10] and although a growing body of data address re-conservation (re-BCS) for IBTR following BCS for invasive cancer[11], it remains counterintuitive that so few studies address re-BCS in DCIS, where breast cancer specific survival is expected to be the highest. Here we aim to compare the outcomes of mastectomy vs re-BCS in our patients with IBTR following BCS for DCIS.

Methods

Under a Waiver of Authorization from our Institutional Review Board we reviewed our prospectively maintained service database and identified 3001 women treated for DCIS with BCS (1978–2010), of whom 383 developed IBTR as a first event (1983–2023). We excluded patients with contralateral breast cancer, BRCA mutations, and concurrent regional node or distant metastasis. Our standard post-BCS follow up comprised physical examination 1–2 times a year, annual mammography, with annual ultrasound for women with dense breasts, and MRI done selectively for problem-solving. Between 197 treated by mastectomy and 186 by re-BCS we compare the clinicopathologic characteristics for the initial and recurrent tumors, the use of adjuvant RT both upfront (“primary RT”) and post IBTR (“secondary RT”), the use of endocrine therapy, the rate of re-recurrence (local, regional, distant), breast cancer specific (BCSS) and overall survival (OS). Unless documented in the chart, secondary RT was assumed not to have been given.

Categorical variables were compared between the two surgical groups using Chi-square test or Fisher's exact test and continuous variables were compared using Wilcoxon rank sum test or t-test. Kaplan Meier curves were constructed to assess BCSS and OS in the two surgical groups using a log-rank test to determine statistical significance. All analysis was conducted using R 4.2.

Results

Re-BCS was more frequent over time, increasing from 47% (1983–2013) to 56% (2014–2023) of patients. Compared to re-BCS (Table 1) mastectomy patients were significantly younger, with initial tumors more likely to contain necrosis and comedo histology, and more likely to be treated initially with RT and endocrine therapy. Regarding clinical characteristics of the IBTR, there were no significant differences between mastectomy and re-BCS in disease-free interval (DFI), the proportion of invasive vs in situ cancer, and the use of hormonal therapy. Secondary RT was more frequent for re-BCS than mastectomy, 44% vs 9%, $p<0.001$).

Compared to re-BCS (Table 2), patients treated by mastectomy were significantly more likely to have received primary RT (62% vs 21%) and less likely to have received secondary RT (9% vs 44%). A comparable proportion of mastectomy vs re-BCS patients had neither primary RT nor secondary RT (34% vs 41%).

Among those treated by re-BCS, local re-recurrence (Table 3) developed in 30 patients, was least frequent among those who received both primary and secondary RT (9%) and most frequent among those who received primary but not secondary RT (22%). Local re-recurrence overall was more frequent for those treated by re-BCS than by mastectomy (16% vs 3%, $p=0.001$) but at a median follow up post-IBTR of 7 years for mastectomy and 7.7 years for re-BCS (Table 4), there were no differences between mastectomy and re-BCS in either breast cancer specific (Fig 1, $p=0.59$) or overall survival (Fig 2, $p=0.27$). Three patients died of breast cancer, 2 after mastectomy and 1 after re-BCS.

Discussion

Mastectomy is still considered to be standard treatment for patients with IBTR after BCS/RT for both invasive and in-situ breast cancer, based largely on concerns about a) the risk of re-RT ("you can't radiate the breast a second time") and b) an incremental risk of distant disease posed by local re-recurrence. In fact, a growing body of data support re-BCS and re-RT following IBTR.

Regarding re-BCS, a recent systematic review and meta-analysis by Tollan et.al.[11] comprising 42 observational studies (1988–2021) of re-BCS following BCS - 24 for invasive cancer, 17 for both invasive and DCIS, and 1 for DCIS only - observes summary rates of re-recurrence for mastectomy vs re-BCS/RT vs re-BCS alone of 10%, 10% and 16% respectively, suggesting a benefit for adjuvant RT following re-BCS. OS at 5 years favored re-BCS (87% vs 80%), almost certainly reflecting more favorable biology and case selection. In a separate meta-analysis by Mo et.al.[12] of 15 studies (1988–2019) local recurrence was more frequent for re-BCT vs mastectomy and more frequent for re-BCS

vs re-BCS/RT. Of note, the included studies are limited by retrospective design and small size, with variation in tumor characteristics, case selection and treatment, all evolving over time. The most persuasive is the large multicenter study of Hannoun-Levi et.al.[13]; among 1327 patients with IBTR (1995–2007), they observed comparable outcomes for mastectomy (n=377) vs re-BCS/interstitial brachytherapy (n=377), propensity matched on age, DFI and tumor characteristics. In our own study of re-BCS vs mastectomy for IBTR[14] we observed higher rates of re-recurrence for re-BCS vs mastectomy (13% vs 2%) but comparable BCSS and OS at a median of 10.7 yrs after initial treatment and 6.4 years after IBTR. The most significant limitations of that study included selection for re-BCS of patients with older age (66 vs 53) and longer DFI (5.8 vs 2.7 years), as well as the inclusion of patients initially treated for DCIS *or* invasive cancer. In the present study we aimed to focus on those initially treated for DCIS, a group a) in which survival following IBTR should be excellent and b) for whom there are very few reports of management or outcome following IBTR.

Regarding RT, any IBTR patient *initially treated with BCS alone*, a group which comprised 46% of our DCIS patients (typically those with older age and small low-grade lesions)[7] can be treated conventionally with whole- or partial-breast RT following re-BCS. Regarding re-RT in IBTR patients *initially treated with BCS/whole breast RT (WBRT*), a comprehensive review of 10 studies[15] (largely using interstitial brachytherapy) observed re-recurrence in 0–26%, grade III/IV toxicity in 0–11%, and good/excellent results in 53–100% of patients. The results of the more recent prospective NRG/RTOG 1014 trial are particularly promising[16]: among 58 IBTR patients initially treated with BCS/WBRT and having partial breast RT (PBI) after re-BCS, the rate of 5 year local recurrence was 5%, and toxicity was minimal (grade III in 4 patients and grade IV in none), results which open the way to wider use of re-RT, and have paralleled our own favorable experience with re-RT[17].

Few studies have reported on management of IBTR following BCS for DCIS. In the 1998 report of the randomized NSABP B-17 trial[18], for the 28% of patients with IBTR after BCS alone and for the 12% with IBTR after BCS/RT, about half were treated with re-BCS and among a total of 72 IBTR patients treated by re-BCT there was a single breast cancer death (in a patient initially treated with BCS/RT). In a non-randomized 2002 multicenter study of BCS vs BCS/RT for DCIS[19], IBTR occurred in 48% of patients after BCS and 17% after BCS/RT, of which 42% and 26% respectively had re-BCS. Among a total of 39 IBTR patients treated by re-BCS, 18 (46%) developed re-recurrence. In 2005 Solin et.al.[20] reported on 90 patients with IBTR following BCT/RT for DCIS; 10 year cause-specific survival - unrelated to the operation performed – was 95%. Finally, Li et.al.[21] using SEER data, identified 5344 patients with IBTR following BCS for DCIS, 66% treated with mastectomy and 34% with re-BCS, and after adjustment for confounders found no differences in survival.

The results of our own study are consistent with all of the above. Our earlier studies have confirmed lower rates of IBTR for BCS/RT vs BCS alone *as initial treatment* for DCIS, but suggest that there is a low-risk group for whom RT may not be required, in that 46% of our DCIS patients initially treated with BCS did not receive RT[7]. Our current data confirm that for IBTR treated by re-BCS vs mastectomy the rate of subsequent re-recurrence was higher, 16% vs 3%, but that BCSS and OS at 5 years were unaffected. Our results also

suggest a benefit from re-RT in IBTR patients treated with re-BCS (Table 3) and confirm excellent survival despite many patients having had *neither primary nor secondary RT* (34% of mastectomy and 41% of re-BCS patients, Table 2). A trend toward greater all-cause mortality with re-BCS (Table 4) is consistent with preferential selection for re-BCS of older patients (Table 1), and a trend toward more distant recurrences following mastectomy suggests less favorable biology (Table 4).

Our study has some limitations. First, isolated IBTR at a first event represents a favorable subset of all patients with local recurrence - by excluding those with regional node or distant metastases, good outcomes are not surprising. Second, the number of re-BCS patients developing re-recurrence (Table 3) is small, suggesting but not proving a benefit from re-BCS/RT. Third, the 7.4 year median follow up post-IBTR is relatively short - for invasive cancer 15 years of follow up were required to establish a modest survival benefit from a reduction in local recurrence at 5 years[22]. It is reassuring that for DCIS the 13–20 year results of the 4 RCTs[3–6] confirm a very low rate of breast-cancer specific mortality. Fourth, despite a favorable experience with re-RT[17], we lack validated surgeon and patient-reported comparative outcome data. Finally, lacking fixed criteria, the choice of mastectomy vs re-BCS represents a composite of surgeons' and patients' values and preferences, taking into account age, disease-free interval, size and biologic characteristics of the IBTR; individual thresholds for surgeons recommending and for patients choosing between mastectomy and re-BCS may have varied.

In conclusion, our comparison of mastectomy vs re-BCS as treatment for IBTR following BCS for DCIS demonstrates a higher rate of local re-recurrence following re-BCS (16% vs 3%) but very low breast cancer mortality and no differences in BCSS and OS. Our results support wider consideration of re-BCS in this setting, and suggest further study of the relationship between secondary RT and the rate of third breast events.

Acknowledgments

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References

1. Effects of radiotherapy and surgery in early breast cancer. An overview of the randomized trials. N Engl J Med 1995; 333(22):1444–55. [PubMed: 7477144]
2. Correa C, McGale P, Taylor C, et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. J Natl Cancer Inst Monogr 2010; 2010(41):162–77. [PubMed: 20956824]
3. Wapnir IL, Dignam JJ, Fisher B, et al. Long-term outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS. J Natl Cancer Inst 2011; 103(6):478–88. [PubMed: 21398619]
4. Donker M, Litière S, Werutsky G, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma In Situ: 15-year recurrence rates and outcome after a recurrence, from the EORTC 10853 randomized phase III trial. J Clin Oncol 2013; 31(32):4054–9. [PubMed: 24043739]
5. Wärnberg F, Garmo H, Emdin S, et al. Effect of radiotherapy after breast-conserving surgery for ductal carcinoma in situ: 20 years follow-up in the randomized SweDCIS Trial. J Clin Oncol 2014; 32(32):3613–8. [PubMed: 25311220]

6. Cuzick J, Sestak I, Pinder SE, et al. Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. Lancet Oncol 2011; 12(1):21–9. [PubMed: 21145284]
7. Subhedar P, Olcese C, Patil S, et al. Decreasing Recurrence Rates for Ductal Carcinoma In Situ: Analysis of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years. Ann Surg Oncol 2015; 22(10):3273–81. [PubMed: 26215193]
8. Cronin PA, Olcese C, Patil S, et al. Impact of Age on Risk of Recurrence of Ductal Carcinoma In Situ: Outcomes of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years. Ann Surg Oncol 2016; 23(9):2816–24. [PubMed: 27198513]
9. Van Zee KJ, Subhedar P, Olcese C, et al. Relationship Between Margin Width and Recurrence of Ductal Carcinoma In Situ: Analysis of 2996 Women Treated With Breast-conserving Surgery for 30 Years. Ann Surg 2015; 262(4):623–31. [PubMed: 26366541]
10. NCCN Guidelines 2024. Breast Cancer version 2.2024 www.nccn.org/professionals/physician_gls/pdf/breast
11. Tollan CJ, Pantiora E, Valachis A, et al. A Systematic Review and Meta-Analysis on the Role of Repeat Breast-Conserving Surgery for the Management of Ipsilateral Breast Cancer Recurrence. Ann Surg Oncol 2022; 29(10):6440–6453. [PubMed: 35849299]
12. Mo C, Ruan W, Lin J, et al. Repeat Breast-Conserving Surgery Versus Salvage Mastectomy for Ipsilateral Breast Tumour Recurrence After Breast-Conserving Surgery in Breast Cancer Patients: A Meta-Analysis. Front Oncol 2021; 11:734719. [PubMed: 34888233]
13. Hannoun-Levi JM, Gal J, Van Limbergen E, et al. Salvage Mastectomy Versus Second Conservative Treatment for Second Ipsilateral Breast Tumor Event: A Propensity Score-Matched Cohort Analysis of the GEC-ESTRO Breast Cancer Working Group Database. Int J Radiat Oncol Biol Phys 2021; 110(2):452–461. [PubMed: 33383125]
14. Van den Bruele AB, Chen I, Sevilimedu V, et al. Management of ipsilateral breast tumor recurrence following breast conservation surgery: a comparative study of re-conservation vs mastectomy. Breast Cancer Res Treat 2021; 187(1):105–112. [PubMed: 33433775]
15. Hannoun-Levi JM, Ihrai T, Courdi A. Local treatment options for ipsilateral breast tumour recurrence. Cancer Treat Rev 2013; 39(7):737–41. [PubMed: 23465859]
16. Arthur DW, Winter KA, Kuerer HM, et al. Effectiveness of Breast-Conserving Surgery and 3-Dimensional Conformal Partial Breast Reirradiation for Recurrence of Breast Cancer in the Ipsilateral Breast: The NRG Oncology/RTOG 1014 Phase 2 Clinical Trial. JAMA Oncol 2020; 6(1):75–82. [PubMed: 31750868]
17. Chen I, Botty Van den Bruele AM, Gillespie EF, et al. Salvage of locally recurrent breast cancer with repeat breast conservation using 45 Gy hyperfractionated partial breast re-irradiation. Breast Cancer Res Treat 2021; 188(2):409–414. [PubMed: 33770311]
18. Fisher B, Dignam J, Wolmark N, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-17. J Clin Oncol 1998; 16(2):441–52. [PubMed: 9469327]
19. Cutuli B, Cohen-Solal-le Nir C, de Lafontan B, et al. Breast-conserving therapy for ductal carcinoma in situ of the breast: the French Cancer Centers' experience. Int J Radiat Oncol Biol Phys 2002; 53(4):868–79. [PubMed: 12095552]
20. Solin LJ, Fourquet A, Vicini FA, et al. Salvage treatment for local or local-regional recurrence after initial breast conservation treatment with radiation for ductal carcinoma in situ. Eur J Cancer 2005; 41(12):1715–23. [PubMed: 16043350]
21. Li Q, Wang K, Yang L, et al. Long-term Survival Comparison of Repeated Breast-conserving Surgery Versus Mastectomy for Patients with DCIS with Ipsilateral Breast Tumor Recurrence: A Real-world Longitudinal Study. Clin Breast Cancer 2021; 21(4):360–372. [PubMed: 33846099]
22. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005; 366(9503):2087–106. [PubMed: 16360786]

Synopsis:

For women with ipsilateral breast tumor recurrence following breast conserving surgery (BCS) for ductal carcinoma in situ (DCIS) we found a higher rate of local re-recurrence with re-BCS compared to mastectomy but no difference in other oncologic outcomes.

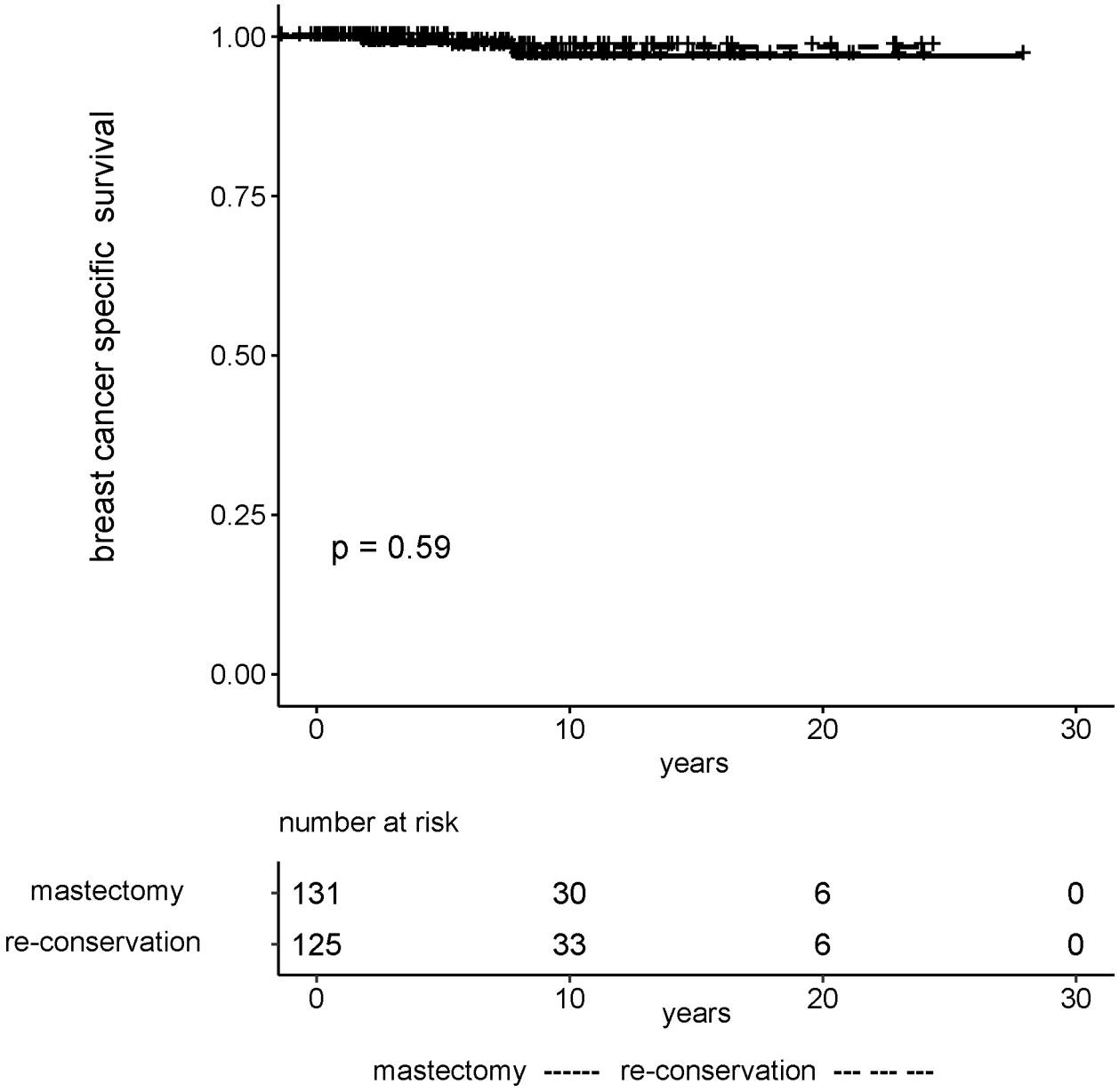

Figure 1.
Comparison of breast cancer specific survival for mastectomy vs re-conservation

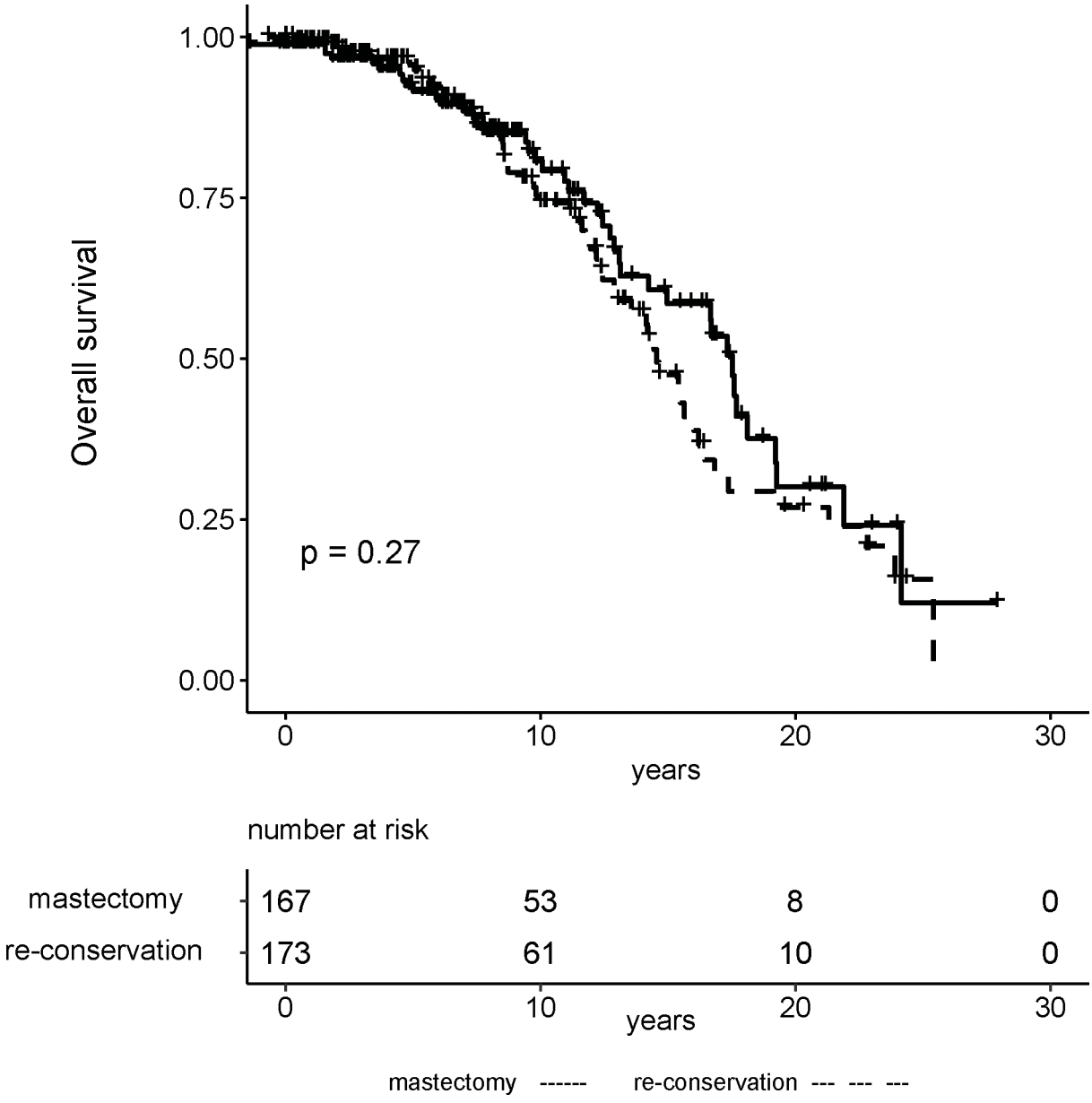

Figure 2.
Comparison of overall survival for mastectomy vs re-conservation

Table 1

Clinical characteristics

Clinical characteristics by treatment of initial DCIS			
	Mastectomy n = 197 # (%)	**Re-conservation n = 186 # (%)**	**p value**
Age	51 (45–61)	59 (48–68)	<0.001
Necrosis	132 (74%)	105 (59%)	0.004
Comedo	68 (38%)	36 (20%)	<0.001
RT	121 (61%)	39 (21%)	<0.001
ET	22 (11%)	9 (5%)	0.023
Clinical characteristics by treatment of IBTR			
DFI	4.5 (2.2–8.0)	4.9 (2.5–10.2)	0.3
Invasive	97 (51%)	80 (43%)	p=0.2
In situ	94 (49%)	104 (57%)	
RT for IBTR	17 (9%)	82 (44%)	<0.001
ET for IBTR	65 (43%)	61 (39%)	0.5

RT = radiotherapy, ET = endocrine therapy, IBTR = ipsilateral breast tumor recurrence, DFI = disease free interval

Table 2

Usage of primary and secondary RT for mastectomy vs re-conservation

Usage of RT	Mastectomy n = 197	Re-conservation n = 186	p value
Primary RT only	112 (57%)	28 (15%)	p<0.001
Secondary RT only	8 (4%)	71 (38%)	
Primary and Secondary RT	9 (5%)	11 (6%)	
Neither	68 (34%)	76 (41%)	

RT = radiotherapy

Table 3

Local re-recurrence after re-conservation by usage of RT

Primary RT X Secondary RT		Secondary RT	
		Yes	No
Primary RT	Yes	1/11 (9%)	6/27 (22%)
	No	12/71 (17%)	11/77 (14%)

RT = radiotherapy

Table 4

Third events post treatment for local-only IBTR

Event	Mastectomy n=197	Re-conservation n=186
Median follow up post-IBTR	7 years	7.7 years
DFI from IBTR to re-recurrence	3.1 yrs	4.7 yrs (p=0.5)
Local re-recurrence	6/197 (3%)	30/186 (16%) (p=0.001)
Regional recurrence	0	0
Distant recurrence	7/197 (3.5%)	2/186 (1%)
Death from any cause	43/197 (22%)	57/186 (31%)
Death from breast cancer	2/197 (1%)	1/186 (0.5%)

IBTR = ipsilateral breast tumor recurrence, DFI = disease free interval