Breast-conserving surgery versus mastectomy - what is the current state of knowledge?

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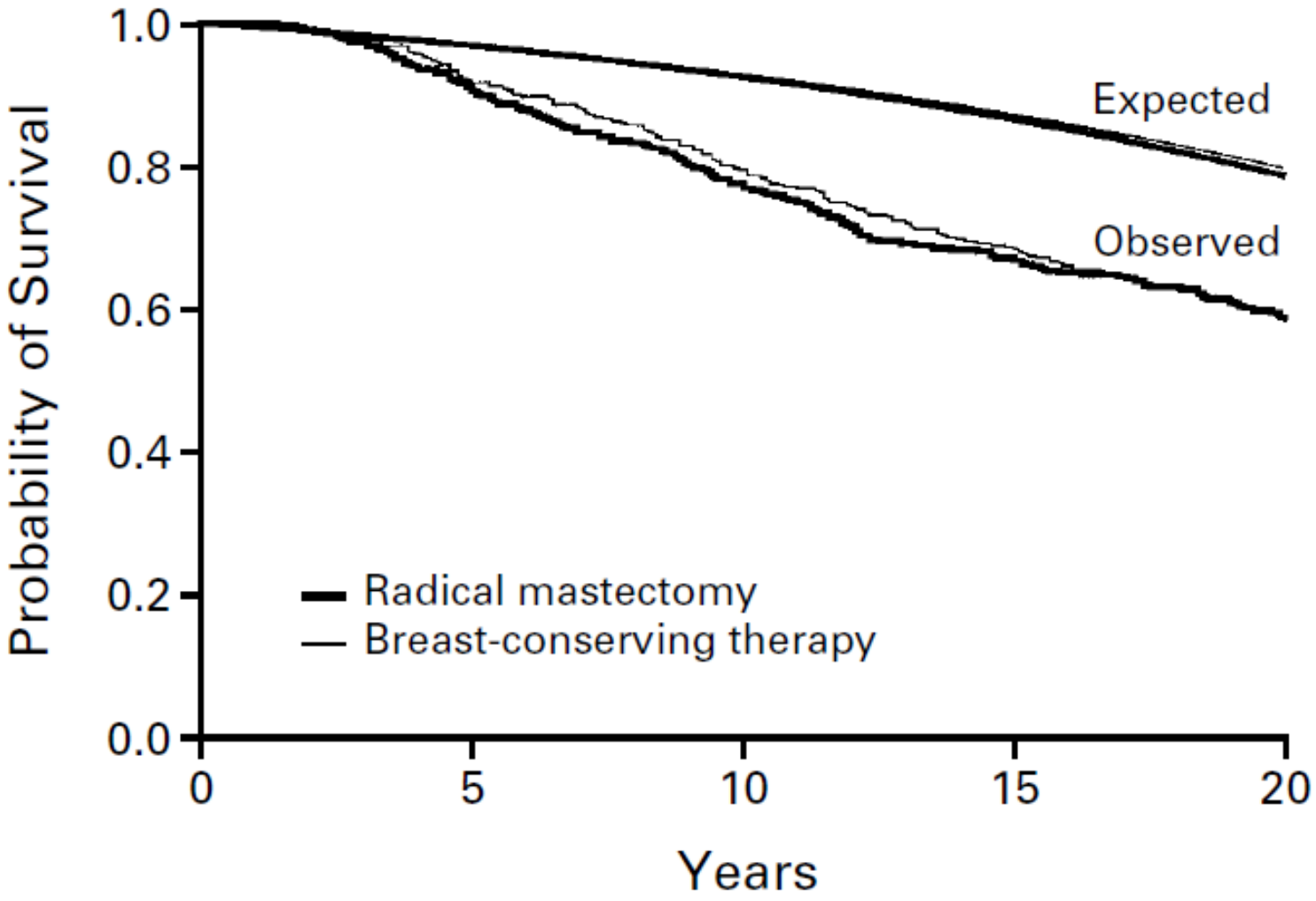
Milano 1 trial – Overall Survival



Veronesi et al. NEJM 2002

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Milano 1 trial – Local recurrences

Veronesi et al. NEJM 2002

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Management of breast cancer has improved

- Diagnostic preoperative assessment
- Adjuvant medical treatment
- Radiation treatment
- Genetic predisposition
- Tailored approach

Analisys of LR recurrences after BCS

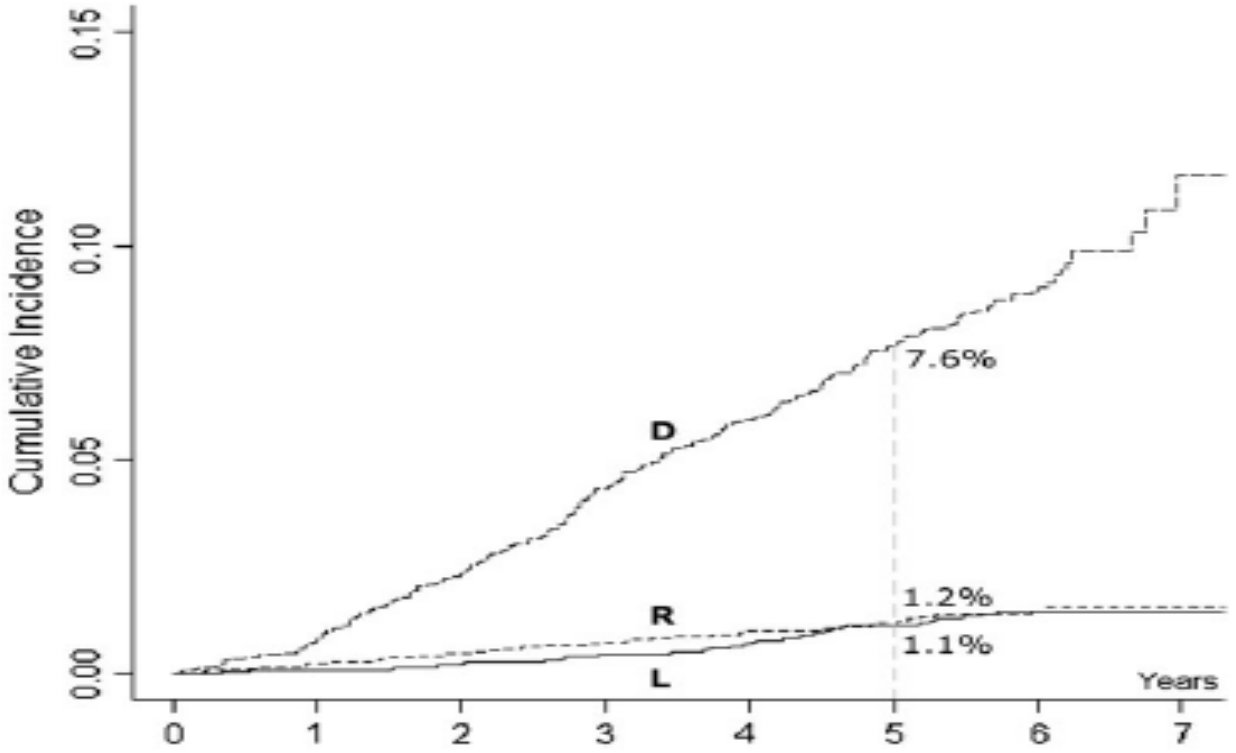

Figure 3. Cumulative incidence of first events. L: local recurrence; R: regional recurrence; and D: distant metastases or death. Percentages are calculated at 5 years.

Botteri et al. Ann Oncol 2010

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ELIOT trial

	External radiotherapy (n=654)		Intraoperative radiotherapy with electrons (n=651)		Log-rank p value
	Number	5-year event rate (95% CI)	Number	5-year event rate (95% CI)	
Ipsilateral breast tumour recurrence	4	0·4% (0·0–1·0)	35	4·4% (2·7–6·1)	<0·0001
Local relapse	4	0·4% (0·0–1·0)	21	2·5% (1·2–3·8)	0·0003
New ipsilateral breast tumour	0	0	14	1·9% (0·8–3·1)	0·0001
Axillary or other regional lymph node metastasis	2	0·3% (0·0–0·8)	9	1·0% (0·2–1·9)	0·03
Locoregional tumour recurrence	6	0·8% (0·0–1·5)	44	5·4% (3·5–7·2)	<0·0001
Contralateral breast tumour	13	1·7% (0·6–2·7)	8	1·1% (0·2–2·1)	0·34
Distant metastasis*	35	4·8% (3·1–6·5)	33	5·1% (3·3–6·9)	0·94
Other primary cancer	22	3·2% (1·8–4·7)	20	2·5% (1·2–3·8)	0·88
Death as first event	7	0·9% (0·1–1·7)	8	1·0% (0·1–2·0)	0·69
Total deaths	31	3·1% (1·7–4·5)	34	3·2% (1·7–4·7)	0·59
Breast cancer	20	2·0% (0·9–3·2)	23	2·1% (0·9–3·3)	0·56
Other cause	11	1·1% (0·2–2·0)	11	1·1% (0·2–2·0)	0·93

Person-years until last visit 3920 for external radiotherapy, 3716 for intraoperative radiotherapy with electrons. Person years until last contact 4107 for external radiotherapy, 3997 for intraoperative radiotherapy with electrons. *As first or secondary event (including four diagnosed at the time of surgery, all in the intraoperative radiotherapy group).

***Table 2:* Events identified during follow-up according to allocated group (intention-to-treat population)**

Veronesi U et al. Lancet Oncol 2013

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Question

If BCT was not inferior to mastectomy in terms of OS despite a statistically significant excess in local events, what happens if LR reaches the lowest conceivable rate?

In the end mastectomy is still better and safer…

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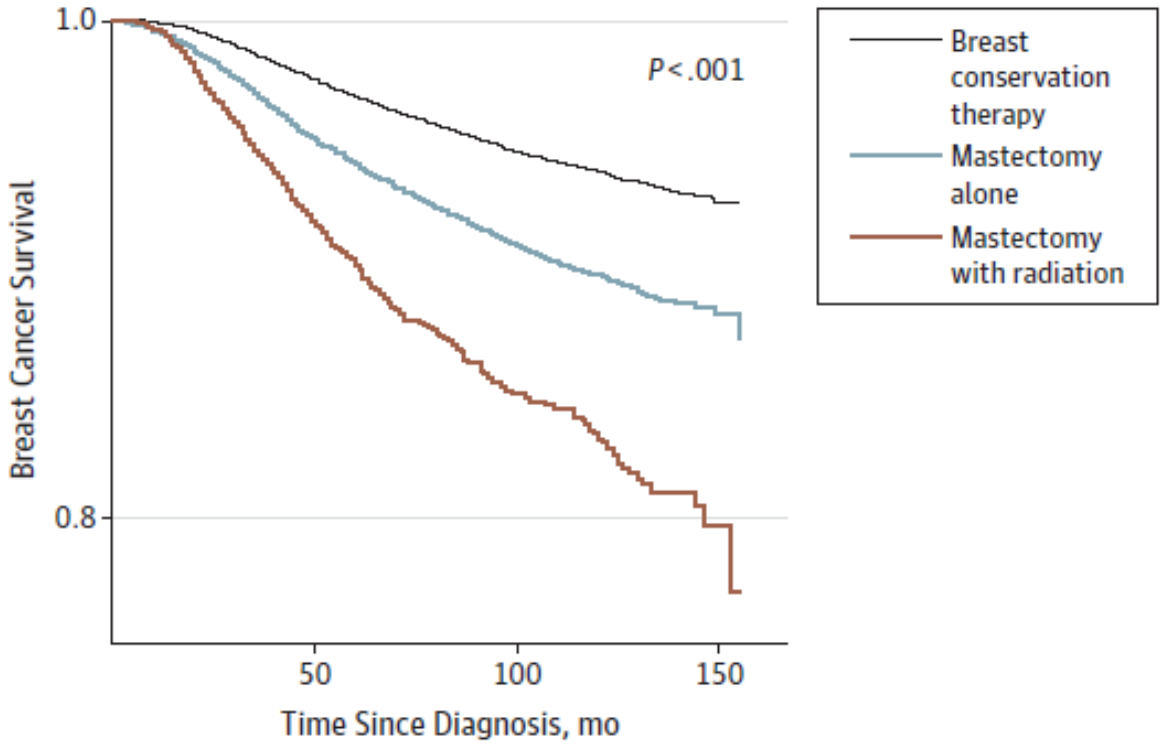
Effect of BCT vs mastectomy on disease-specific survival for early-stage breast cancer

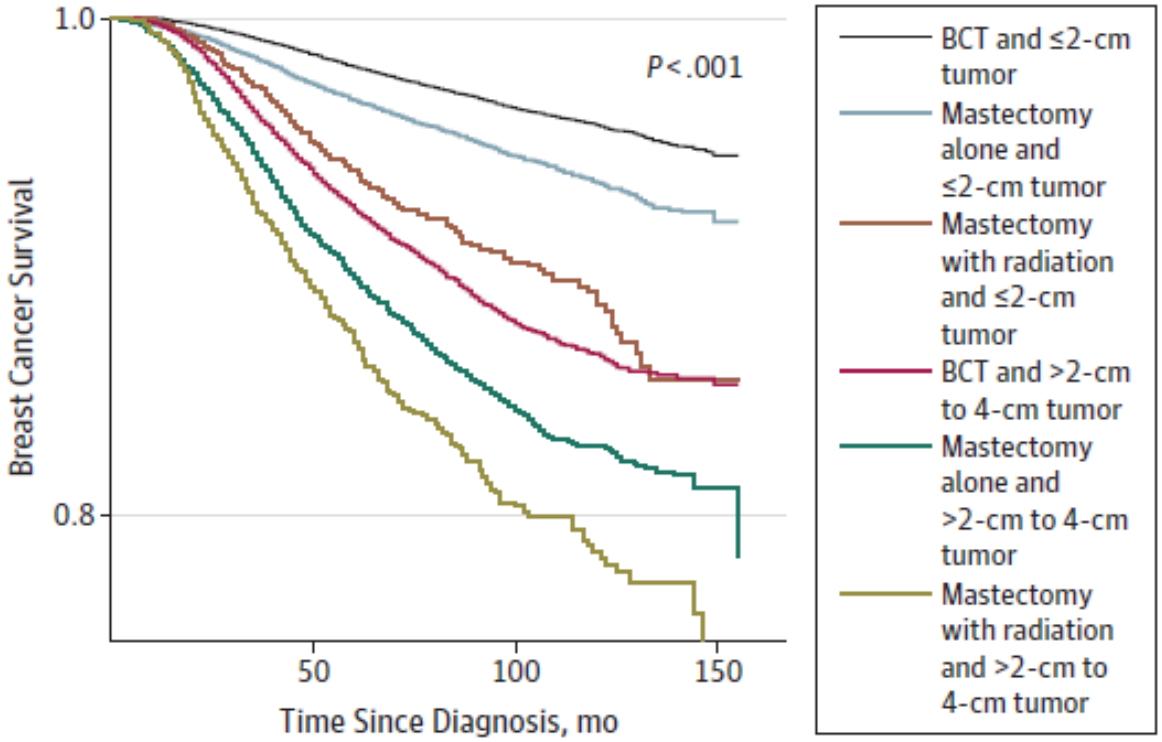
Figure 1. Kaplan-Meier Survival Analysis Stratified by Treatment Type



Agarwal S. et al. JAMA Surgery 2015

Effect of BCT vs mastectomy on disease-specific survival for early-stage breast cancer

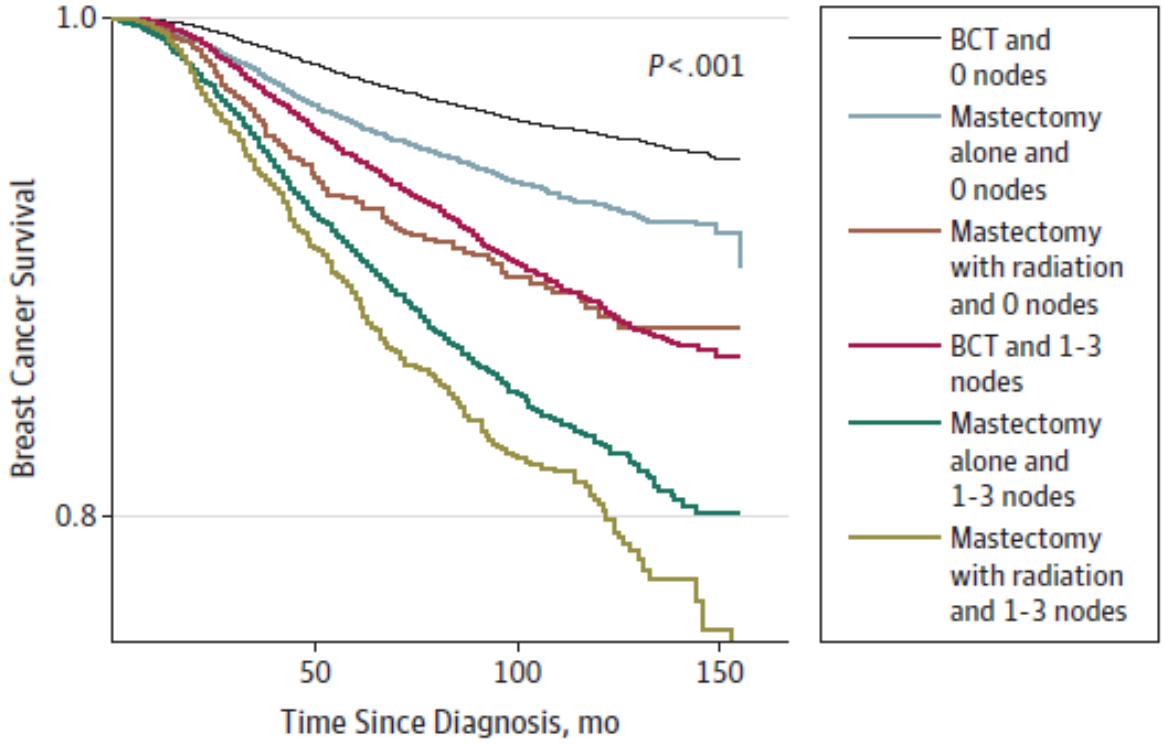
Figure 2. Kaplan-Meier Survival Analysis Stratified by Treatment Type and Tumor Size



Agarwal S. et al. JAMA Surgery 2015

Effect of BCT vs mastectomy on disease-specific survival for early-stage breast cancer

Figure 3. Kaplan-Meier Survival Analysis Stratified by Treatment Type and Lymph Node Status



Agarwal S. et al. JAMA Surgery 2015

She’s so young… it’s better to go for mastectomy!

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Breast cancer in young women

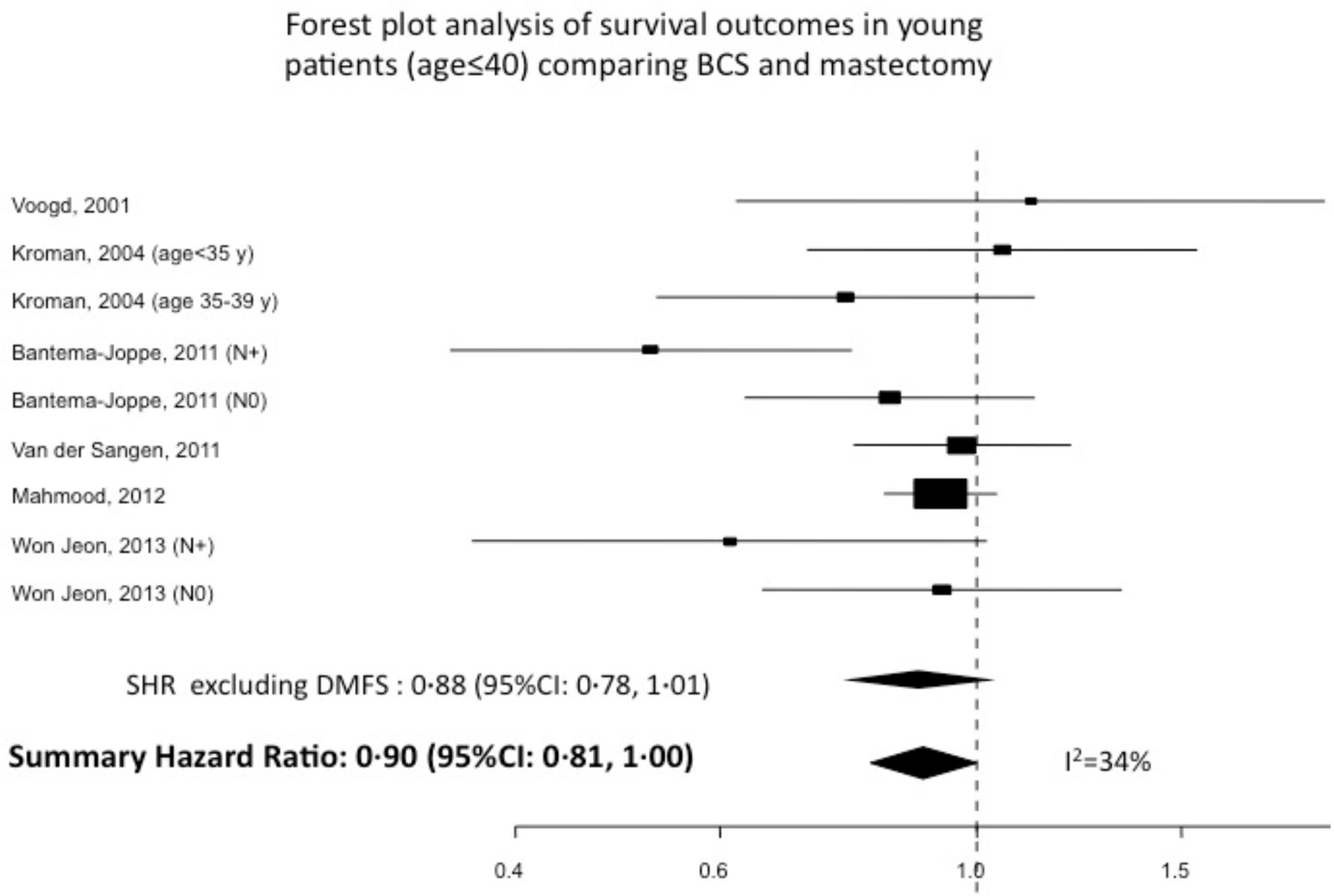
- Breast cancer occurring in young age has worse biological features if compared to older counterparts leading to higher risk of recurrence
- Young age is an independent factor of increased risk of recurrence after BCS and WBRT
- Young women with breast cancer are more frequently at increased genetic risk
- Long life expectancy

OSPEDALE SAN RAFFAELE

Overall survival according to type of surgery in young (≤40 years) early breast cancer patients: a systematic meta-analysis comparing breast-conserving surgery versus mastectomy.

Vila J, Gandini S, Gentilini O. The Breast 2015

OSPEDALE SAN RAFFAELE



Vila J, Gandini S, Gentilini O. The Breast 2015

She is young, the risk of local recurrence is high…

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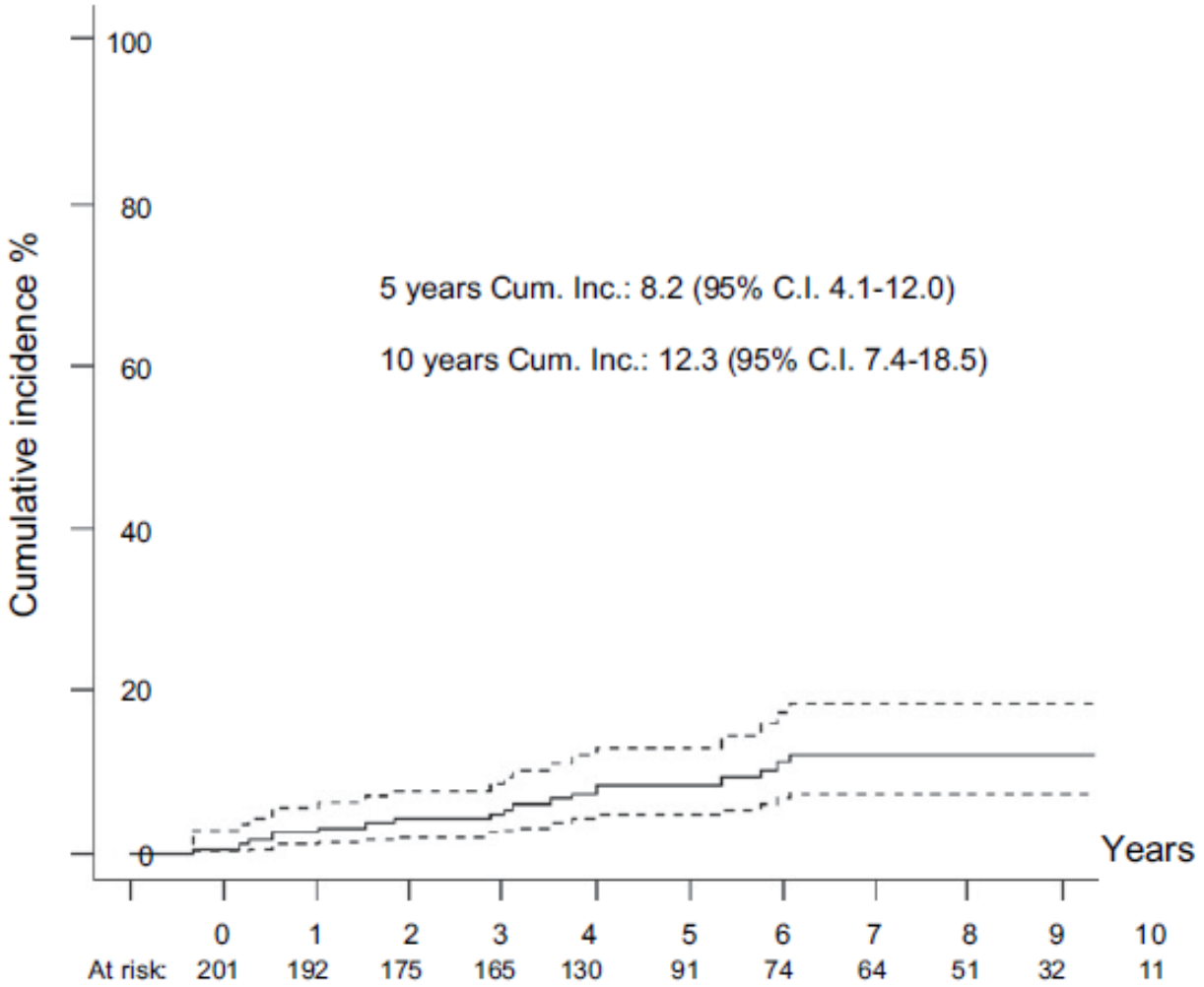
Local recurrence after BCT in 201 very young women



Gentilini et al. Breast 2010

Original article

Improved prognosis of young patients with breast cancer undergoing breast-conserving surgery

E. Botteri[1,8,9], P. Veronesi[2,6], J. Vila[4,10], N. Rotmensz[1], V. Galimberti[2], M. V. Thomazini[2], G. Viale[3,6], R. Orecchia[4,7], A. Goldhirsch[5] and O. Gentilini[2]

- 1331 patients younger than 40 years who had BCS and whole-breast radiotherapy in a single cancer centre between 1997 and 2010
- The patients were followed until 2016. Median follow-up of 9·3 years.
- Women were divided into three groups of similar size based on tertiles of the date of diagnosis: 1997–2002 (524 patients), 2003–2005 (350) and 2006–2010 (457).
- The risk of local recurrence was 1·42 per 100 person-years in women diagnosed in the first interval, 0·85 per 100 person-years in the second and 0·48 per 100 person-years in the third (P for trend=0·028).
- The respective values were 3·01, 2·52 and 2·07 per 100 person-years for any breast cancer-related event (P =0·004), and 1·59, 1·22 and 0·64 per 100 person-years for death (P =0·003).
- Each passing year was associated with a decreasing risk of local recurrence (hazard ratio (HR) 0·93, 95 per cent c.i. 0·87 to 1·00), any breast cancer-related event (HR 0·94, 0·91 to 0·98) and death (HR 0·89, 0·83 to 0·94).

Botteri et al. Br J Surg 2017

Risk of recurrence and death over time

Date of surgery	At risk No. (%)	Local events No. (annual rate %)	P	Breast cancer related events No. (annual rate %)	P	Deaths No. (annual rate %)	P
	1,331	114 (1.05)		289 (2.66)		138 (1.27)	
≤ 2002	524	77 (1.42)	0.03	163 (3.01)	<0.01	86 (1.59)	<0.01
2003 - 2005	350	25 (0.85)		74 (2.52)		36 (1.22)	
> 2005	457	12 (0.48)		52 (2.07)		16 (0.64)	

Number of events per 100 person-years

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Multivariate analysis

		Local events HR (95% CI)	Breast cancer related events HR (95% CI)	Deaths HR (95% CI)
Age	**One year increase**	0.99 (0.94-1.04)	0.99 (0.96-1.02)	0.98 (0.94-1.02)
Date of diagnosis (from 1997 to 2010)	**One year increase**	0.93 (0.87-1.00)	0.94 (0.91-0.98)	0.89 (0.83-0.94)
Histotype	**Ductal *vs.* others**	1.53 (0.78-3.02)	1.45 (0.91-2.33)	1.09 (0.55-2.16)
Tumor size (cm)	**> 2 vs ≤ 2**	1.31 (0.88-1.94)	1.62 (1.27-2.06)	1.87 (1.33-2.64)
Multifocality/centricity	**Present vs Absent**	1.33 (0.79-2.25)	1.18 (0.85-1.65)	0.75 (0.44-1.29)
Positive LNs	**1-3 vs 0**	0.88 (0.56-1.39)	1.08 (0.81-1.44)	1.05 (0.67-1.64)
	> 3 vs 0	1.19 (0.65-2.17)	1.56 (1.10-2.20)	2.36 (1.46-3.8)
Molecular subtype	**Lum B (High Ki67) vs. Lum A**	0.86 (0.46-1.58)	1.62 (0.98-2.68)	1.86 (0.79-4.37)
	Lum B (HER2+) vs. Lum A	0.91 (0.42-1.97)	1.19 (0.65-2.18)	1.35 (0.50-3.69)
	HER2+ vs. Lum A	1.98 (0.78-5.02)	3.83 (2.03-7.23)	3.71 (1.33-10.4)
	Triple Negative vs. Lum A	0.76 (0.35-1.63)	1.51 (0.85-2.67)	3.62 (1.47-8.9)
Peritumoral vascular invasion	**Focal *vs* absent**	1.23 (0.78-1.94)	1.40 (1.04-1.88)	1.81 (1.17-2.81)
	Extensive *vs* absent	0.86 (0.44-1.66)	1.58 (1.12-2.23)	2.53 (1.56-4.09)

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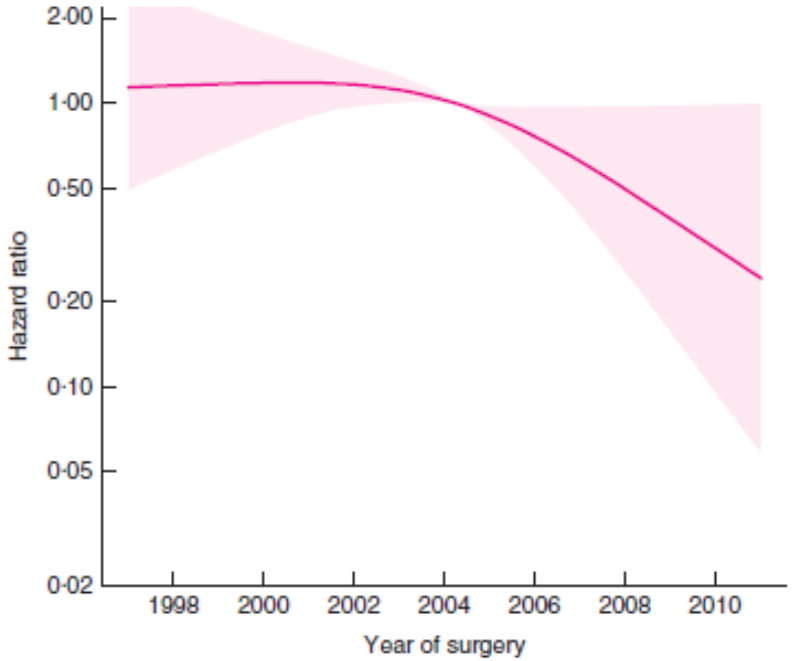
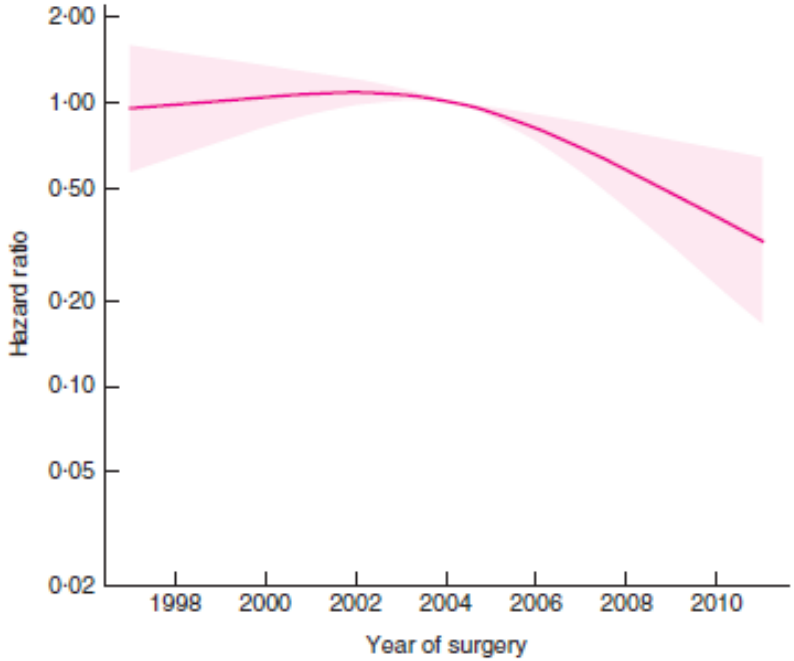
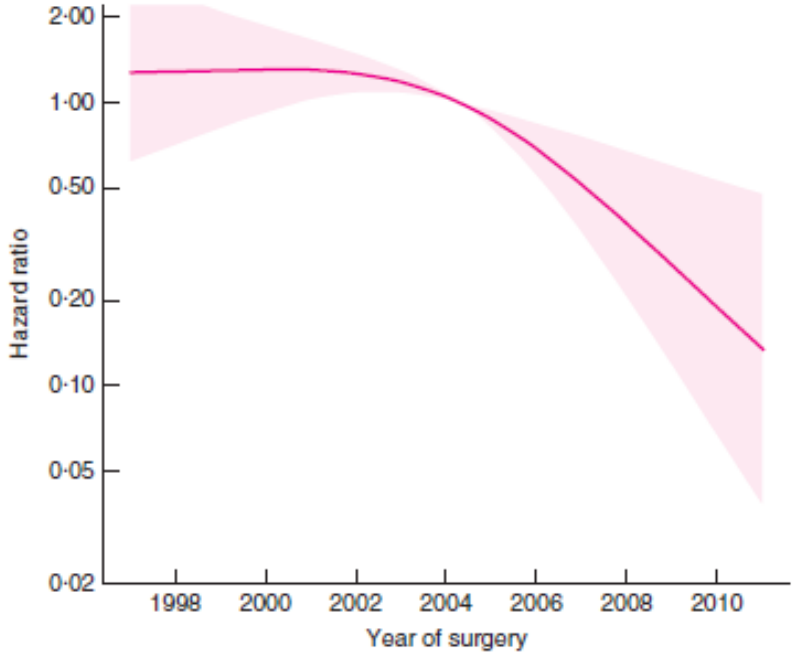


a Local recurrence



b Any breast cancer-related event



c Death from any cause

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By mastectomy we avoid radiotherapy…

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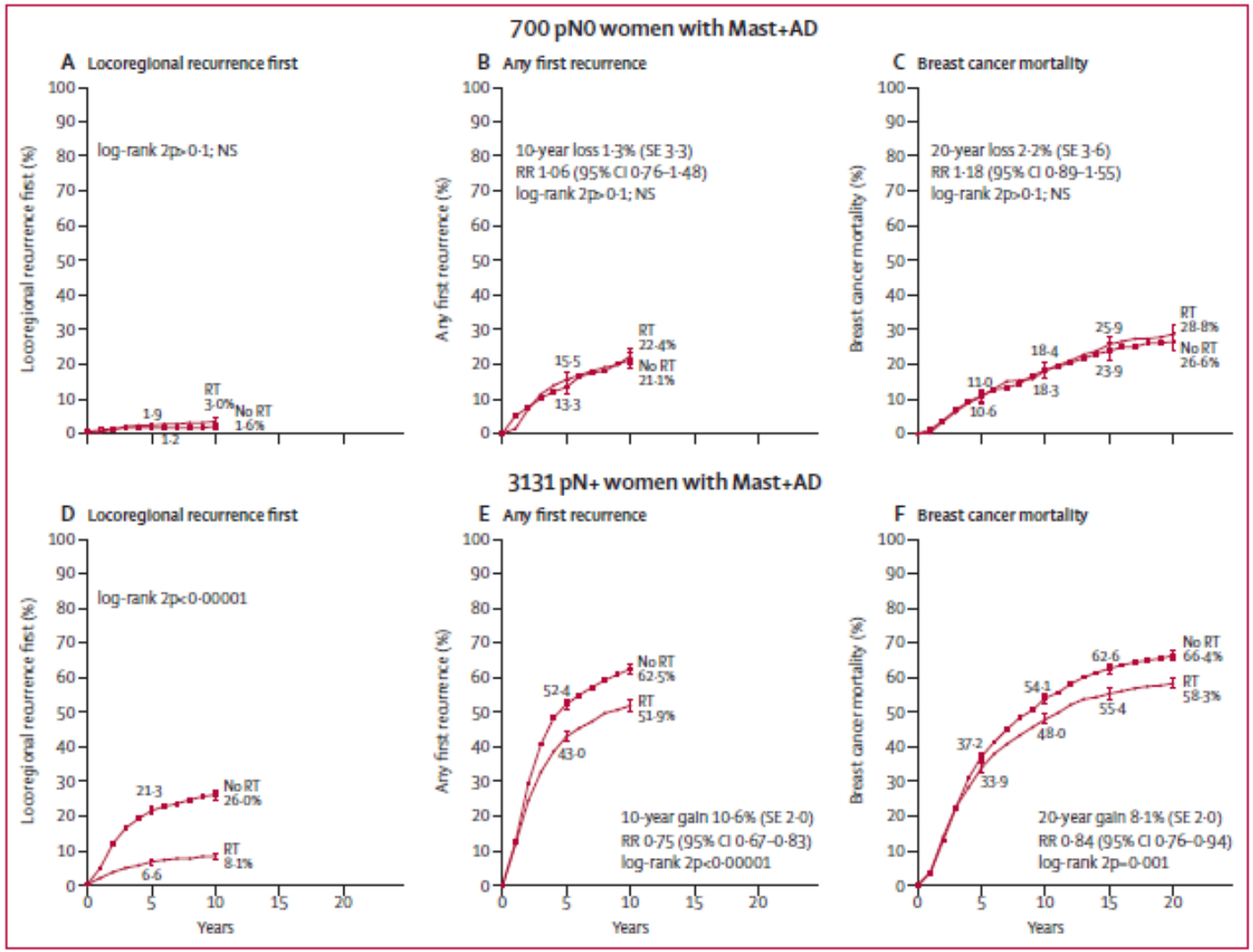
Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials



EBCTCG Lancet 2014

The Breast 35 (2017) 32–33

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Viewpoints and debate

Less is more. Breast conservation might be even better than mastectomy in early breast cancer patients

Oreste D. Gentilini [a, *], Maria-Joao Cardoso [b], Philip Poortmans [c]

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[b] Breast Unit, Champalimaud Foundation, Lisbon, Portugal
[c] Department of Radiation Oncology, Institut Curie, Paris, France

"Sometimes patients demand a mastectomy, driven by fear and the desire of getting rid of the disease while ignoring all this new information. It is important to inform them properly that, in most cases, breast cancer can be cured maybe even better without the need to be separated from of their breasts."

Recent data comparing BCT vs mastectomy

Recent data comparing BCS + RT to Mastectomy.

Author (ref number), year	Study Period	Data source	Inclusion criteria	N. of patients	Outcome Measure	Results		
						BCS+RT	M	M+RT
Agarwal [5], 2014	1998–2008	SEER database	T≤4cm N0-1	132.149	5y BCSS	97	94	90%
					10y BCSS	94	90	83%
Hartman-Johnsen [5], 2015	1998–2008	Norway Cancer Registry	T1-2 N0-1	13.015	5yOS	95	80	–
					10yOS	86	84	
					5y BCSS	97	88	
					10yBCSS	93	82	
Chen [6], 2015	2004–2011	National Cancer Database	T1-2 N1-3	160.880	5y OS	93.2	83.5	83
					8y OS	86.5	72.3	70.4
Lagendijk, Van Maaren [9,10], 2016, 2017	1999–2012	Netherlands Cancer Registry	T1-2 N0-2	129.692	11.7y OS and BCSS (1999-2005 cohort)	OS:HR 0.74 BCSS: HR 0.72	HR 1	–
					6y OS and BCSS (2006-2012 cohort)	OS: HR 0.67 BCSS: HR 0.75	HR 1	

BCSS=Breast Cancer-Specific Survival M = Mastectomy.

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Reasons to explain this strange phenomenon

- Impact of radiotherapy (local treatment having a systemic effect)
- Depression of immune system after more extensive surgery?
- Complex relationship between surgical trauma, radiotherapy, medical treatment and immune response is largely unknown
- Surgery is aimed at removing macroscopic disease and not microscopic foci

Larger surgery does not necessarily equals better outcome

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The protective effect of WBRT on axillary node recurrence

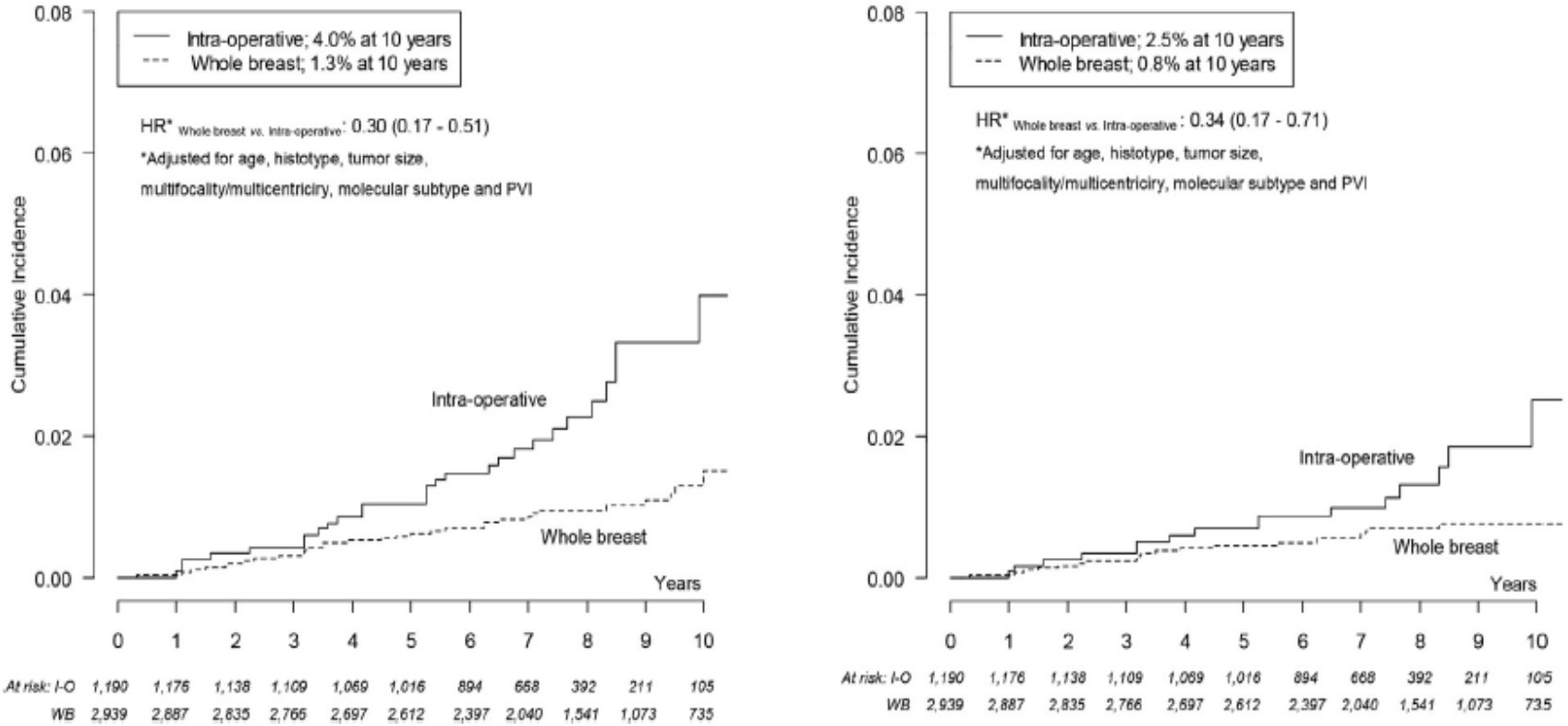

Fig. 1. (A) Axillary recurrences with or without ipsilateral breast recurrence by type of radiotherapy. (B) Axillary recurrences without ipsilateral breast recurrence by type of radiotherapy.

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The protective effect of WBRT on axillary node recurrence

Multivariable analysis.

		Axillary recurrence ± ipsilateral breast recurrence HR (95% CI)	Axillary recurrence without ipsilateral breast recurrence HR (95% CI)
Age (years)	One unit increase	0.98 (0.95–1.00)	0.99 (0.96–1.02)
Histotype	Ductal *vs.* others	2.53 (1.07–5.97)	1.89 (0.65–5.48)
Tumour size (cm)	>1 vs ⩽1	1.42 (0.83–2.45)	1.85 (0.86–4.01)
Multifocality/multicentricity	Present vs Absent	2.56 (1.26–5.18)	2.70 (1.08–6.76)
Molecular subtype	Lum B (High Ki67) vs. Lum A	4.38 (1.58–12.2)	5.42 (1.03–28.5)
	Lum B (HER2+) vs. Lum A	2.49 (1.03–5.99)	5.89 (1.73–20.1)
	HER2+ vs. Lum A	1.64 (0.89–3.04)	3.35 (1.24–9.05)
	Triple Negative vs. Lum A	0.66 (0.15–2.90)	2.04 (0.39–10.8)
Peritumoural vascular invasion	Present *vs* absent	1.69 (0.89–3.19)	1.66 (0.74–3.77)
Type of radiotherapy	Whole breast vs. Intra-operative	0.30 (0.17–0.51)	0.34 (0.17–0.71)

Abbreviations: Lum, luminal; HR, hazard ratio; CI, confidence interval.

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The patient prefers mastectomy!

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The number of patients receiving mastectomy is increasing

General considerations

1. Mastectomy is a permanent and severe mutilation always leading to troublesome consequences from the psychological, sexual, and relational point of view
2. The cosmetic outcome of a mastectomy with reconstruction is very often worse than expected (by both the patient and the surgeon)
3. The risk of complications is higher after mastectomy with reconstruction, with a possible delay in medical treatments
4. The number of patients receiving post-mastectomy RT is increasing making immediate reconstruction more difficult
5. Think about it before recommending mastectomy