Patterns and risk of first and subsequent recurrences in women within ten years after primary invasive breast cancer

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Aim

The aim of this study was to analyse the occurrence, timing and predictive factors of first and subsequent local (LR), regional (RR) or distant (DM) recurrence during the first 10 years after treatment for primary invasive breast cancer in women.

Methods

Patients were selected from the Netherlands Cancer Registry (N=9,342)

- Women diagnosed in 2003
- Stage I-III invasive breast cancer without metastasis at diagnosis
- Treated with curative intent
- No previous or synchronous tumours

Recurrences <3 months after diagnosis of the primary tumour were considered synchronous with the primary tumour. Therefore, follow-up time started three months after diagnosis of the primary tumour. In patients with concurrent recurrences, the most serious site of recurrence was taken as endpoint.
Multivariable Cox proportional hazards regression was used to model the hazard of recurrence over time for site-specific first recurrence and for subsequent recurrences after LR or RR. Missing values were multiple imputed using a chained equation approach.

Results

After previous first LR or RR and second LR or RR, a third subsequent recurrence occurred in 18 patients (54.5%).
The risk of first recurrence was highest around 2 years post-diagnosis (HR 0.040 95%CI 0.035-0.043) with a similar pattern for LR, RR and DM.

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Table: Incidence of consecutive events according to recurrence site

	First recurrence (n=9,342)		Subsequent recurrence after LR (n=362)		Subsequent recurrence after RR (n=148)	
	n	%	n	%	n	%
Local (LR)	362	3.9	10	2.8	8	5.4
Regional (RR)	148	1.6	12	3.3	3	2.0
Distant (DM)	1343	14.4	80	22.0	63	42.6
Total	1853	19.8	102	28.2	74	50.0
Median time to recurrence	3.3 years (IQR 1.6-5.8)		1.1 years (IQR 0.3-2.5)		1.1 years (IQR 0.6-2.2)	

LR = local recurrence, RR = regional recurrence, DM = distant recurrence, n=number; IQR = interquartile range.

In multivariable analysis, only hormone status was a significant predictive factor for a second recurrence after RR (HR 0.55 95%CI 0.31-0.98). For a second recurrence after LR both hormone status (HR 0.56 95%CI 0.35-0.88) and 1-3 positive nodes compared to no positive nodes (HR 2.03 95%CI 1.29-3.18) were of significant influence. No significant predictors could be identified for a third recurrence after a LR or RR.
For both recurrences after a first LR, as well as recurrences after a first RR, the hazard of a subsequent second recurrence was highest around one year after the first recurrence.

Conclusions

The pattern of first recurrence was similar for LR, RR and DM. To get towards personalized follow-up, predictive factors could be taken into account. Besides hormone status for second recurrence after a RR and both hormone status and nodal involvement for second recurrence after a first LR, no other predictive factors were of significant influence.

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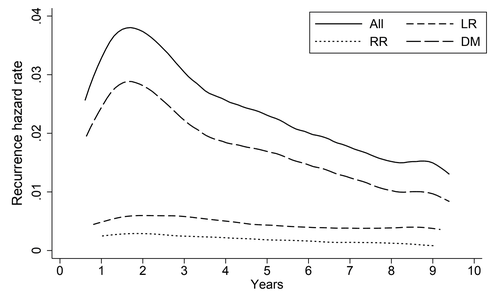
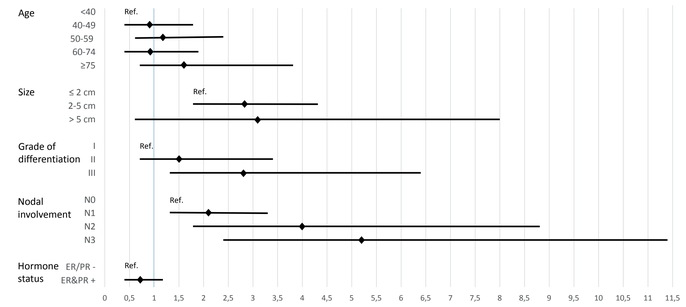
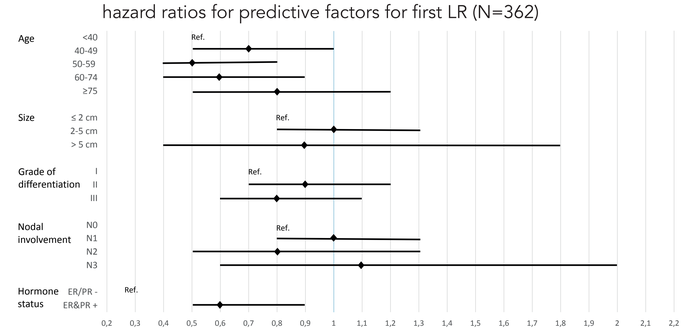
hazard rate of first recurrence during ten years of follow-up



hazard ratios for predictive factors first LR/RR/DM (N=1853)'



hazard ratios for predictive factors for first LR (N=362)



hazard ratios for predictive factors for first RR (N=148)