


SHORT COMMUNICATION

An actualised population-based study on the use of radiotherapy in breast cancer patients in the Netherlands

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Abstract

The utilization rate of RT increased from 64.4% in 2011 to 70.3% in 2015. After BCS and mastectomy, 97.3% and 26.1% of the patients received RT, respectively. For patients undergoing BCS and mastectomy, lower age and ER + tumours were associated with higher RT utilisation rates. After mastectomy, also larger tumour sizes, lymph node involvement, grade-2 and 3 tumours and diagnosis in more recent years were associated with higher RT use.

1 | INTRODUCTION

Substantial variation in the use of RT in breast cancer patients and underutilization of RT is observed worldwide.¹⁻⁸ Between 1997 and 2008 the use of RT for breast cancer in the Netherlands increased, which was associated with an increased use of BCS.⁹ We investigated the use and trends over time (focussing on age effects) of RT for all invasive breast cancer patients.

2 | MATERIALS AND METHODS

2.1 | Patients

Patients with primary invasive breast cancer were selected from the Netherlands Cancer Registry, covering all hospitals (N = 92) and all

radiotherapy departments. All female patients diagnosed with first primary non-metastatic invasive breast cancer between January 1st, 2011 and December 31st, 2015 were included.

2.2 | Statistics

Factors associated with RT use were assessed using chi-square tests with a *P*-value of <0.025 being considered to be statistically significant (a *P*-value of < 0.025 was chosen, as this is in agreement with the large number of patients included). Trends over time in the use of different treatment combinations were analysed separately for all ages combined and those aged >75 years. The cut-off of 75 years was chosen, since patients aged 50-75 are invited for the nationwide breast cancer screening programme. Utilisation rates of RT over time were stratified by tumour stage and assessed for

four different groups of patients; patients treated with BCS (with and without primary systemic therapy [PST]) and those treated with mastectomy (with and without PST). Logistic regression analyses were performed separately for BCS and mastectomy. Patients who were treated with chemotherapy prior to surgical treatment were excluded from logistic regression analysis as PST influences the pathologically assessed tumour characteristics. Variables that were tested were; age, screen-detected tumours, pathological tumour size, number of positive lymph nodes, tumour grade according to Bloom Richardson, Her2, oestrogen (ER), progesterone (PR) receptor status and year of diagnosis. Factors that were significantly associated with the use of RT in univariable analyses were included in the multivariable model. Analyses were performed in STATA (version 13.1 2013).

3 | RESULTS

3.1 | Patients

The annual number of patients (mean age 61.2 years) diagnosed with non-metastatic breast cancer was 13 500 (total N = 68 271, Table 1). The utilization rate of RT increased from 64.4% to 70.3% for all patients and from 26.6% to 34.9% for patients aged >75 years. After BCS and mastectomy, 97.3% and 26.1% received RT, respectively. The use of RT was associated with a lower mean age (59.1 years) compared to those who received no RT (65.6 years). PST was given to 18.7% of the patients. Surgery, RT and systemic therapy was used in 46.7% of all patients (Table 1).

3.2 | Breast conserving surgery and mastectomy (with and without PST)

The utilization rate of RT increased from 64.4% in 2011 to 70.3% in 2015 (Figure 1). This increase consisted of 2.3% more patients receiving surgery in combination with RT and 3.6% more patients receiving surgery, RT and systemic therapy. The utilization rate of RT increased in patients >75 years with 8.3%. This increase was composed by 3.6% more patients undergoing surgery and RT and 4.2% undergoing surgery, RT and systemic therapy (Figure 2). From 2011 till 2015, an increase of 8.4% for patients treated with mastectomy (with or without PST) was observed. For patients >75 years, an increase in the utilization rate of RT of 3.4% was observed after BCS (with or without PST) and of 7.7% after mastectomy (with or without PST). After BCS, comparable utilization rates were observed for patients who did or did not receive PST. For patients treated with mastectomy without PST an overall increase in the use of RT was observed from 23.5% in 2011 to 29.1% in 2015. For patients with post-surgically assessed stage-2 disease, an increase in the use of RT of 17.5% was observed ($P < 0.025$). For patients who received PST prior to mastectomy, a decrease in the use of RT was observed from 80.0% in 2011 to 67.1% in 2015.

3.3 | Breast conserving surgery without primary systemic therapy

In total 34 286 patients underwent BCS (without PST) and a mean utilization rate of 97.3% RT was observed. Multivariable logistic regression demonstrated that elderly were significantly less likely to undergo RT than patients aged <50 years. Patients bearing screen-detected breast cancers were more likely to be treated with RT compared to those diagnosed with non-screen-detected breast cancers. Those with ER + tumours were associated with higher utilization rates compared to those with ER- tumours.

3.4 | Mastectomy without primary systemic therapy

In total 21 048 patients underwent mastectomy without PST and 26.1% (N = 5498) underwent RT. Multivariable analyses demonstrated that patients aged ≥ 50 years were less likely to receive RT compared to those aged <50 years. Increasing tumour size, number of positive lymph nodes and higher grade were associated with increasing odds of receiving RT. Over the years, RT utilization rates significantly increased.

4 | DISCUSSION

4.1 | Breast conserving surgery and mastectomy

The increased utilization rate of RT was associated with more patients undergoing RT after mastectomy. In a recent study an optimal utilisation proportion of 87% was calculated for the Netherlands.¹⁰ This is considerably higher than the observed actual utilisation rate as observed in the current study. Part of this dissimilarity could be explained by the following considerations. In the present study we included only the primary use of RT, whereas Borrás and colleagues calculated the optimal utilization proportion, based on the use of RT during the entire course of the disease. The latter includes (amongst others) the use of RT after recurrent disease as well. Furthermore, taking account of patient's preferences and their performance status may have led to a lower use of RT.

Since women diagnosed with breast cancer at young age have more often aggressive disease the higher utilization rates of RT for younger patients was anticipated.¹¹ Besides, also differences in variables influencing the use of RT between patients treated with BCS and mastectomy were observed.

4.2 | Breast conserving surgery

For patients treated with BCS, no further increase in RT use was expected, since almost all already received RT after BCS. No decrease of RT use in patients aged over 75 years with stage 1 breast cancer was observed. This is not in line with recent reports suggesting that endocrine therapy alone after BCS should replace the use of radiotherapy in elderly patients.^{12,13} We want to stress that in the Netherlands in this specific group of patients the use of adjuvant endocrine therapy was limited to approximately 30%.

TABLE 1 Patient, tumour and treatment characteristics (N = 68 271)

	Radiotherapy (N = 46 140)		Total (N = 68 271)		P-value*
	N	%	N	%	
Primary systemic therapy					
No	38 950	84.4	55 486	81.3	<0.025
Yes	7020	15.2	8538	12.5	
No surgery	170	0.4	4247	6.2	
Age (in y)					
Mean	59.1		61.2		<0.025
0-49	10 067	21.8	14 379	21.1	
50-65	21 194	45.9	27 758	40.7	
66-75	11 787	25.5	15 851	23.2	
76-85	2785	6.0	6961	10.2	
>85	307	0.7	3322	4.9	
Diagnosed after screening					
No	12 341	26.7	17 710	25.9	<0.025
Yes	20 180	43.7	25 179	36.9	
Not applicable	13 159	28.5	24 662	36.1	
Unknown	460	1.0	720	1.1	
Tumour size (in mm)					
0-10	14 056	30.5	19 771	29.0	<0.025
11-20	18 927	41.0	25 343	37.1	
21-30	7389	16.0	11 851	17.4	
>30	4308	9.3	7231	10.6	
Unknown	1415	3.1	4075	6.0	
Number of positive lymph nodes					
0	28 869	62.6	41 865	61.3	<0.025
1-3	12 570	27.2	18 034	26.4	
>3	4205	9.1	4690	6.9	
Unknown	496	1.1	3682	5.4	
Grade					
1	10 954	23.7	14 579	21.4	<0.025
2	18 672	40.5	27 199	39.8	
3	11 284	24.5	16 210	23.7	
Unknown	5230	11.3	10 283	15.1	
Her2					
Her2-	39 027	84.6	56 030	82.1	<0.025
Her2+	5683	12.3	8507	12.5	
Doubtful	145	0.3	273	0.4	
Unknown	1285	2.8	3461	5.1	
Oestrogen receptor					
ER-	7092	15.4	10 324	15.1	<0.025
ER+	38 294	83.0	56 528	82.8	
Unknown	754	1.6	1419	2.1	
Progesterone receptor					
PR-	13 931	30.2	20 697	30.3	<0.025
PR+	31 387	68.0	46 014	67.4	
Unknown	822	1.8	1560	2.3	

(Continues)

TABLE 1 (Continued)

	Radiotherapy (N = 46 140)		Total (N = 68 271)		P-value*
	N	%	N	%	
Year of diagnosis					
2011	8662	18.8	13 443	19.7	<0.025
2012	9050	19.6	13 650	20.0	
2013	9253	20.1	13 671	20.0	
2014	9564	20.7	13 836	20.3	
2015	9611	20.8	13 671	20.0	
Therapy					
S	na	na	5471	8.0	<0.025
S + RT	14 085	30.5	14 085	20.6	
S + SYSTM	na	na	12 583	18.4	
S + RT+SYSTM	31 884	69.1	31 884	46.7	
SYSTM	na	na	3952	5.8	
Other	171	0.4	296	0.4	

Abbreviations: na, Not applicable; RT, Radiation therapy; S, Surgery; SYSTM, Systemic therapy.

*P value < 0.025 is considered as statistically significant.

For patients undergoing BCS, younger age, screen detection and ER + tumours were positively associated with RT. In a previous study performed by Struikmans et al, a similar increase in the use of RT over the years of approximately 5.5% was observed.⁹ No significant association was found between year of diagnosis and RT compliance after BCS, due the fact that almost all patients already received RT after BCS over all these years (mean 97.3%).

4.3 | Mastectomy

For patients treated with mastectomy, significantly reduced recurrence rates, improved disease-specific survival and improved overall

survival notably in high-risk¹⁴ as well as in intermediate-risk breast cancer patients were reported in previously performed studies.¹⁵⁻¹⁸ Hence, higher utilization rates of post-mastectomy RT were expected. We observed that patients with >3 positive lymph nodes were much more likely to receive RT. Moreover, from 2011 till 2015 an increasing use of RT was noted also for patients with intermediate-risk breast cancer.

The observed differences in the use of RT may be attributed to variables we could not retrieve. Departmental or hospital related factors (eg, policy/personal preference of radiation oncologist concerning RT prescription, weighing the relevance of treatment efficacy vs worsening of the cosmetic result and co-morbidity of the

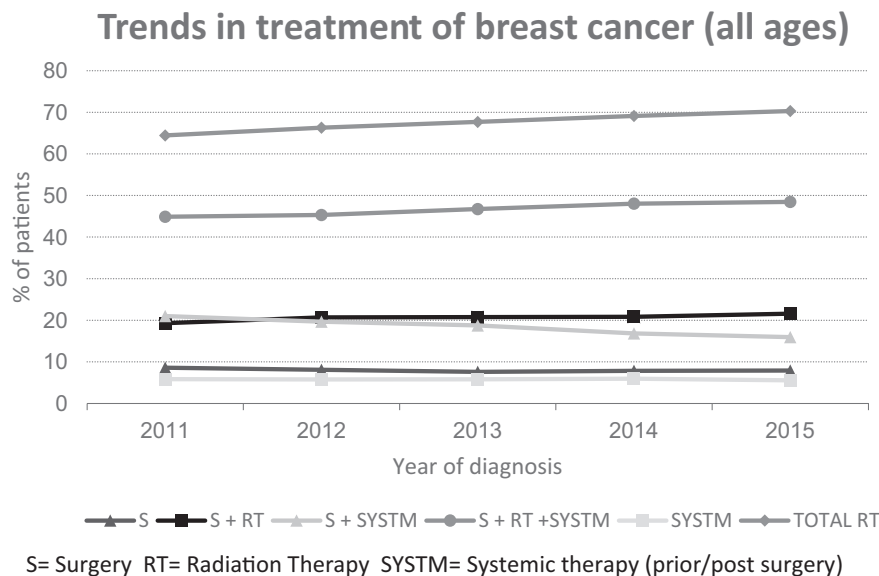


FIGURE 1 Trends in treatment of breast cancer in the Netherlands for all ages over the period 2011-2015 (N = 68 271)

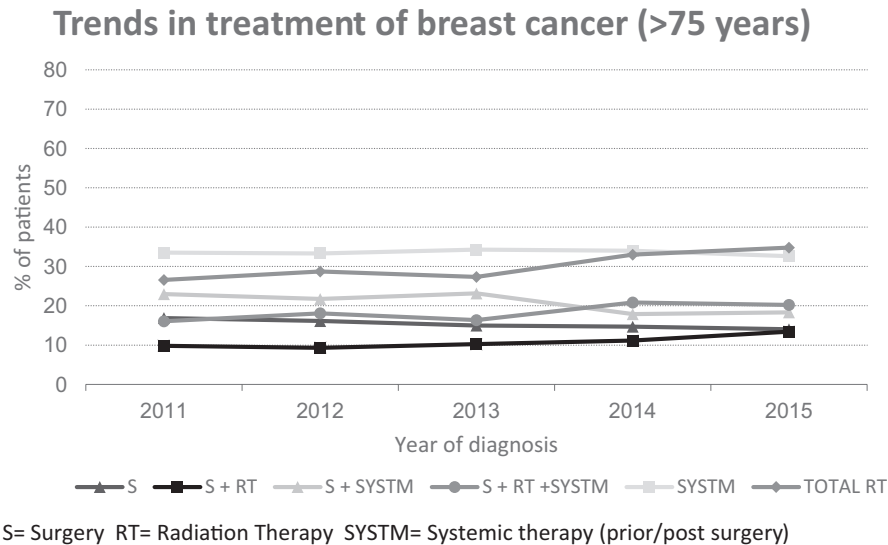


FIGURE 2 Trends in treatment of breast cancer in the Netherlands for patients aged over 75 y over the period 2011-2015 (N = 10 283)

patient or patient preferences) may also have influenced the use of RT.

The population-based character of the present study is unique and does provide insight in the overall use of RT in all 21 departments of radiotherapy in the Netherlands.

5 | CONCLUSIONS

A substantial increase in the use of RT was observed over the years, particularly for patients aged >75 years. Different factors were associated with the utilization rate of RT, differing between BCS and mastectomy.

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