

## Impact of hospital volume on breast cancer outcome: a population-based study in the Netherlands

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**Abstract** For low-volume tumours, high surgical hospital volume is associated with better survival. For high-volume tumours like breast cancer, this association is unclear. The aim of this study is to determine to what extent the yearly surgical hospital breast cancer volume is associated with overall survival. All patients, diagnosed with primary invasive non-metastatic breast cancer in the period 2001–2005, were selected from the Netherlands Cancer Registry. Hospitals were grouped by their annual volume of surgery for invasive breast cancer. Cox proportional hazard models were used including patient and tumour characteristics as covariates. Follow-up was completed until the 1st of February 2013. Primary endpoint was 10-year overall survival rate. In total, 58,982 patients with

invasive non-metastatic breast cancer were diagnosed during the period 2001–2005. Hospitals were grouped by their (mean) annual surgical volume: <75 ( $n = 19$ ), 75–99 ( $n = 30$ ), 100–149 ( $n = 29$ ), 150–199 ( $n = 9$ ) and  $\geq 200$  ( $n = 14$ ). The 10-year observed survival rates were 77, 81, 80, 82 and 82 %, respectively. After case-mix adjustment, patients in low-volume hospitals had a HR of 1.09 (<75 vs.  $\geq 200$ ; 95 % CI 1.03–1.15). Survival was significantly higher for lobular carcinoma and for diagnosis in the most recent year (2005). Being a male, having a higher age at diagnosis, a higher tumour grade, a larger tumour size, a higher number of positive lymph nodes, an earlier year of diagnosis and a lower SES resulted in a reduced survival and influenced death, all to a larger extent than surgical volume did. In the Netherlands, surgical hospital volume

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influences 10-year overall survival only marginally and far less than patient and tumour characteristics. No difference in survival was revealed for invasive non-metastatic breast cancer patients in hospitals with 75–99 operations per year compared with hospitals with over 200 operations per year.

**Keywords** Breast cancer · Hospital volume · Survival · Quality of health care

## Introduction

In recent years, there has been an increasing interest in quality of care and the need for reliable parameters to measure quality. One of the parameters that has been investigated frequently is surgical volume and its relation with patient outcome. For several surgical procedures especially in tumours with relative low incidence, like oesophageal and pancreatic cancer, higher postoperative mortality in patients treated in hospitals with a low surgical volume has been reported [1–4]. For breast cancer patients, this volume–outcome relationship is not clear. Contradicting results are described with regard to the relation between surgical volume and long-term outcome [5–7].

The European Society of Breast Cancer Specialists (EUSOMA) has a minimal annual volume standard of 150 breast cancer patients diagnosed per hospital and the minimum number of primary surgical procedures for breast cancer should be at least 50 per year per surgeon. The reason for these recommendations are not based on evidence from literature, though the belief that by implementing these recommendations, the hospital caseload ensures to maintain expertise for each team member and a breast unit can be maximally cost-effective [8].

In the Netherlands, the National Breast Cancer network (NABON) describes how multidisciplinary breast cancer care should be organised from diagnosis, treatment, support and follow-up and defines several criteria for high-quality breast cancer care [9, 10]. The ‘Stichting Oncologische Samenwerking’ (SONCOS), an interdisciplinary platform of professional organisations involved in cancer care: the Dutch Association for Surgical Oncology (NVCO), the Dutch Association for Medical Oncology (NVMO) and the

Dutch Association for Radiotherapy and Oncology (NVRO) stated the standard on at least 50 operations on breast cancer per hospital per year in addition to the NABON. Since 2011, all Dutch hospitals meet this volume standard [11]. In the Netherlands, no standard was set for the minimal number of diagnosis per year per hospital.

The relation between surgical hospital volume and outcome (10-year overall survival) has not been described before in the Netherlands. Based on the data from the population-based Netherlands Cancer Registry (NCR), the relation between surgical hospital volume and survival of patients 10 years after diagnosis can be evaluated. This insight can feed the debate on whether being a low-volume hospital is a risk factor for unfavourable long-term outcomes in breast cancer patients. The aim of this study was to determine to what extent surgical hospital volume determines the 10-year survival rate in breast cancer patients.

## Method

### Patients grouping

Patients with invasive breast cancer were selected from the NCR ([www.cancerregistry.nl](http://www.cancerregistry.nl)). This nationwide population-based registry gathers data on all newly diagnosed malignancies and is hosted by the Comprehensive Cancer Centre the Netherlands (IKNL). The main notification sources are the National Automated Pathology Archive (PALGA) and the National hospital discharge register.

Patients with metastasis at the time of diagnosis were excluded. To determine the survival, all patients in whom invasive breast cancer was diagnosed for the first time during the period January 1st 2001 and 31 December 2005 were selected from the NCR. Patients with a second primary invasive breast cancer diagnosed in the period 2001–2005 but with a first breast cancer before the year 2001 were excluded from the analysis. Specially trained registrars gathered data on patient and tumour characteristics directly from the patient files in all hospitals. Stage was classified according to the TNM seventh version and both clinical as well as postoperative stage were gathered. Patient vital status was obtained from the municipality register (GBA). Follow-up was completed until February 1st, 2013. For patients who were still alive, this date was taken as last date alive; unless the patient emigrated, the date of emigration was taken as last date. Patients were grouped by hospital of surgery or hospital of diagnosis for non-surgical patients.

### Hospital grouping

To determine the number of surgical procedures per hospital, the number of operations on newly diagnosed

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**Table 1** Mean number of operated invasive breast cancer patients per hospital per year (incl. M1), 2001–2005

Number of operated invasive breast cancers per year	Number of hospitals	Mean number of patients per year (range)	Total number of operated invasive breast cancers	Total number of invasive breast cancers
Less than 75	19 <sup>a</sup>	57 (26–74)	4,819	5,304
75–99	30	86 (75–98)	11,708	12,825
100–149	29	124 (100–144)	15,772	17,211
150–199	9	173 (154–197)	6,581	7,282
200 or more	14	237 (202–298)	15,021	16,360
Total	101	120 (26–298)	53,901	58,982

<sup>a</sup> Four hospitals less than 50 per year with 860 cancers and 777 operations

invasive breast cancers was determined over the period 2001–2005, irrespective of their stage. Surgery performed on non-invasive breast cancer (DCIS, LCIS) and non-epithelial tumours, like sarcoma and lymphoma, were not included. Surgery followed by another surgical procedure in the same breast was counted as one surgical treated breast cancer. In case of two surgeries as in bilateral breast cancer, this was counted as two surgeries.

For hospitals that merged in the period 2001–2005, the hospitals were counted as separate until the date of the merge and as one after the merge or the subsequent year if this was during the year.

In total, 101 hospitals were included in the analyses (Table 1). Nineteen hospitals performed less than 75 surgeries on invasive breast cancer per year of which four hospitals had less than 50 surgeries per year, 30 hospitals performed 75–100 surgeries, 29 hospitals 100–150, nine hospitals between 151 and 199 and 14 hospitals more than 200.

#### Statistical analysis

Observed relative survival was calculated to determine survival standardized for age. This was not corrected for other factors like stage. Relative survival is a proxy for disease-specific survival since it presents the survival related to the age-specific survival in the general population.

Survival corrected for factors influencing survival was determined using Cox proportional hazard models. Patient and tumour characteristics like age at time of diagnoses (grouped in five age groups: 15–29, 30–44, 45–59, 60–74 and 75 year or older), morphology, tumour grade, tumour size (pT), lymph node status, year of diagnosis and socioeconomic status (SES) were taken as covariates in the model. SES determined by the postal code at the time of diagnosis was included and grouped in conformity with Statistics Netherlands [12]. No information was available for co-morbid conditions. Proportional hazard assumption

was assessed by graphical-based (log–log survival plots) and residual-based methods. Log–log and residual plots showed that the proportional hazards assumption was violated for various variables (age group, morphology, tumour grade, pT and lymph node status). These variables were entered in a model with an interaction with time (three-year interval). No further violations of proportional hazard assumptions were observed.

Analysis was performed in STATA (version 12.0, Statacorp LP, College Station, TX).

## Results

### Baseline patient characteristics

Over the period 2001–2005, 55,554 women and 335 men were diagnosed with in total 55,889 non-metastatic invasive breast cancers (Table 2). Of this total number of 55,889 primary breast cancers, 9 % was surgically treated in a low-volume hospital (<75 operations), 22 % in low-medium volume hospitals (75–99 operations), 29 % in medium volume hospitals (100–149 operations), 12 % in high-medium volume hospitals (150–199 operations) and 28 % in high-volume hospitals (>200 operations per year) in average over the five-year period (table 1). There were only small differences with respect to the distribution of patient and tumour characteristics between the various hospital categories, and compliance to adjuvant treatment was comparable (Table 2).

The uncorrected 10-year relative survival rates were 77, 81, 80, 82 and 82 %, respectively (Fig. 1).

### Multivariable analysis on survival

Median follow-up was 114 months. No difference in survival could be found between hospitals with more than 200, 150–199, 100–149 and 75–99 surgically treated invasive breast cancers per year. The mortality in hospitals with less

**Table 2** Patient characteristics and adjuvant treatment of patients with invasive non-metastatic breast cancer according to hospital categories in the Netherlands, 2001–2005

Variable	Total		Hospital operation volume				
			<75	75–99	100–149	150–199	200 or more
Number of invasive non-metastatic breast cancer per year		55,889	5,000	12,130	16,291	6,548	15,620
	N	%	%	%	%	%	%
<b>Gender</b>							
Female	55,554	99.4	99.4	99.3	99.4	99.4	99.4
Male	335	0.6	0.6	0.7	0.6	0.6	0.6
<b>Age at diagnosis</b>							
Median age		59	60	59	59	59	59
<b>Morphology</b>							
Ductal	41,380	74	74	74	75	76	73
Lobular	8,460	15	16	16	14	14	16
Other	6,049	11	10	10	11	10	11
<b>Grade</b>							
I	9,537	17	19	18	16	19	16
II	21,180	38	36	37	37	39	40
III or undifferentiated	16,082	29	26	30	30	25	29
Unknown	9,090	16	18	15	17	17	15
<b>Size/pT</b>							
T1mic (<=0.1 cm)	227	0.4	0.5	0.5	0.3	0.3	0.4
T1a (0.1–0.5 cm)	1,595	3	3	3	3	3	3
T1b (0.5–1 cm)	7,007	13	12	12	12	13	13
T1c (1–2 cm)	21,548	39	38	38	38	41	38
T2 (2–5 cm)	18,788	34	35	34	34	31	33
T3 (>5 cm)	1,749	3	4	4	3	2	3
T4	1,101	2	2	2	2	2	2
Unknown	3,874	7	7	6	7	7	7
<b>Number of positive lymph nodes</b>							
0	30,254	54	54	53	54	55	55
Only micrometastasis	3,028	5	5	6	6	6	5
1–3	11,850	21	22	21	21	21	21
4–9	4,417	8	8	8	8	8	8
10 or more	2,200	4	4	4	4	4	4
Unknown	4,140	7	8	7	(8	7	7
<b>Year of diagnosis</b>							
2001	11,015	20	22	20	21	19	17
2002	10,934	20	19	19	20	20	20
2003	11,169	20	19	20	20	19	21
2004	11,397	20	22	20	20	19	21
2005	11,374	20	19	20	19	23	21
<b>Socioeconomic status</b>							
High	14,290	26	18	28	27	28	24
High-middle	14,114	25	20	25	26	26	26
Low-middle	11,602	21	26	20	18	19	23
Low	15,883	28	36	27	29	27	26

**Table 2** continued

Variable			Total	Hospital operation volume				
				<75	75–99	100–149	150–199	200 or more
Number of invasive non-metastatic breast cancer per year			55,889	5,000	12,130	16,291	6,548	15,620
	N	%	%	%	%	%	%	%
<b>Radiotherapy</b>								
Yes	33,748	60	58	59	59	63	62	62
No	22,128	40	42	41	41	38	38	38
<b>Chemotherapy</b>								
Yes	18,728	34	33	33	33	32	35	35
No	37,148	66	67	67	67	68	65	65
<b>Endocrine therapy</b>								
Yes	24,211	43	45	44	43	42	43	43
No	31,665	57	55	56	57	58	57	57

than 75 surgically treated invasive breast cancers per year was relatively 9 % higher than in a hospital with >200 breast operations on average per year (HR 1.09, 95 % CI 1.03–1.15; Table 3). This was adjusted for age group, sex, morphology, tumour grade, T-stage, N-stage, year of diagnosis and socio-economic status, whereby age group, morphology, tumour grade, T-stage and N-stage were entered in a model with an interaction with time (3-year interval) due to violation of the proportional hazard assumption. Survival was significantly higher for lobular carcinoma and for diagnosis in the most recent year (2005). Being a male, having a higher age at diagnosis, a higher tumour grade, a larger tumour size, a higher number of positive lymph nodes, an earlier year of diagnosis and a lower SES resulted in a reduced survival. Including the adjuvant treatment in the model did not change the results with regard to risks associated with patient, tumour and hospital characteristics (data not shown).

Analysing survival for the individual hospital level according to the mean number of operations per year, survival was significantly higher in nine hospitals (HR varying between 0.71 and 0.89), and seven hospitals had a significant lower survival (HR varying between 1.16 and 1.28). These extremes were seen in both low- as well as in high-volume hospitals. No differences were seen in the type of hospital (academic, teaching or general).

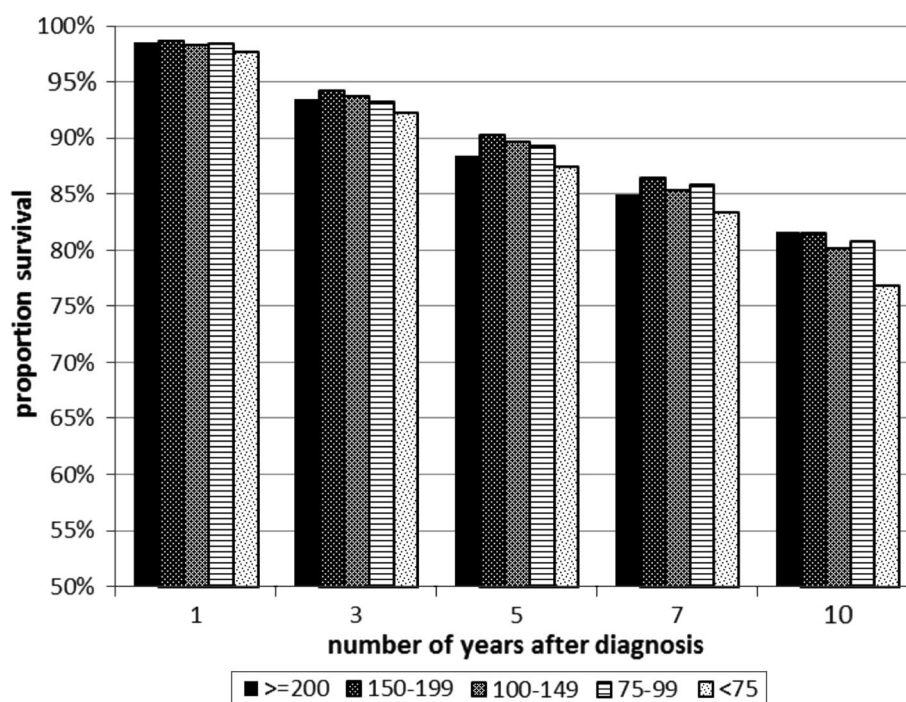
## Discussion

For breast cancer, the impact of surgical volume on patient outcome is not clear [5–7]. In the Netherlands, there is a tendency towards proclaiming that the number of breast cancer patients per hospital has to increase, though, there is

no convincing evidence available in literature to support this policy. Therefore, our study aimed to determine to what extent the yearly surgical hospital breast cancer volume was associated with 10-year overall survival in a large population-based cohort of patients diagnosed with primary non-metastatic invasive breast cancer in the years 2001–2005 in the Netherlands. We observed that surgical hospital volume did not affect 10-year survival rate of breast cancer patients to a great extent. The 10-year survival probability did not differ significantly between hospitals with an annual surgical volume of more than 200 on the one hand and hospitals with 150–199, 100–149 and 75–99 surgically treated invasive breast cancers per year on the other. However, for patients who were operated in hospitals with less than 75 surgeries per year, a lower 10-year survival probability (a relative lower survival of 9 %) was noted. We also investigated the effect on survival in case the standard was 50 operations per year, which was set by the professionals as norm. Hospitals with an average less than 50 operations per year had a HR of 1.04 (<50 vs. >200, 95 % CI 0.92–1.16, data not shown). This group consisted of four hospitals with only 860 cancers and 777 operations.

Several studies on the relation of operative volume and outcome in breast cancer have been performed in other countries. In Belgium, Vijens et al. [6] revealed, after case-mix adjustment, that patients treated in very low- (<50) or low-volume (50–99) hospitals compared with high-volume hospitals had a hazard ratio for death of 1.26 (95 % CI 1.12–1.42) and 1.15 (95 % CI 1.01–1.30), respectively. This was based on Cox and logistic regression models on 5-year survival and in achievement of process indicators across volume categories, adjusting for age, tumour grade and stage. In other breast cancer studies in the UK, US and

**Fig. 1** 1-, 3-, 5-, 7- and 10-year relative survival of patients with invasive non-metastatic breast cancer according to hospital categories in the Netherlands, 2001–2005



**Table 3** Cox regression analysis for the relation of the number of surgical treated invasive breast cancer patients per hospital per year and the risk of death of patients with non-metastatic breast cancer in the Netherlands, 2001–2005

Number of operated invasive breast cancers per year	Crude		Adjusted <sup>a</sup>	
	HR	95 % CI	HR	95 % CI
200 or more	Reference		Reference	
150–199	1.04	0.99–1.10	1.04	0.99–1.09
100–149	1.05	1.01–1.09	1.01	0.97–1.05
75–99	1.07	1.03–1.12	1.04	0.99–1.08
<75	1.15	1.08–1.21	1.09	1.03–1.15

HR Hazard ratio, CI Confidence interval

<sup>a</sup> adjusted for age group, sex, morphology, tumour grade, T-stage, N-stage, year of diagnosis and socio-economic status, whereby age group, morphology, tumour grade, T-stage and N-stage were entered in a model with an interaction with time (3 year interval) due to violation of the proportional hazard assumption

Canada with a low [13, 14] to very low [15, 16] number of operated patients per year, an increased risk of reduced survival was revealed in low-volume hospitals. Simunovic et al. found an increased risk of death in hospitals with less than 30 surgeries per year when compared with hospitals with more than 88 surgeries per year (HR 1.2, 95 % CI 1.0–1.4,  $p < 0.05$ ) [14]. In a breast cancer population in Taiwan, Chen et al. [17]. revealed a lower 5-year survival in low-volume hospitals ( $\leq 258$  operated patients in three years) compared to high-volume hospitals ( $> 585$  in 3 years) of 72 % and 77 %, respectively. Comparing low

with high-volume hospitals, the hazard ratio was 1.4 (not corrected for stage). Based on simulation models, Tanke et al. [19]. stated that the gain in quality of care by centralisation of breast cancer care from 94 to between 15 or 44 locations in the Netherlands would outweigh the higher travel costs of patients. In this study, gain of quality was expressed in QALY's, and survival gain was estimated on 5 % increase in survival based on comparison of literature. In five regions in Canada in a cohort of 1,727 breast cancer patients, a reduced survival was seen in hospitals operating less than 100 patients per year [19]. The HR was 1.80 (95 % CI 1.23–2.63), 1.44 (95 % CI 1.03–2.02) and 1.30 (95 % CI 0.96–1.76) in hospitals with respectively  $< 25$  new cases, 25–49 and 50–99 new cases per year compared to  $\geq 100$  new cases. This effect disappeared, however, after case-mix adjustment. Their final conclusion was that women who were treated in centres with on-site radiotherapy, research activity or teaching status had better outcomes irrespective of the volume of the hospital. In a study performed in the US, teaching status of a hospital influenced survival to a greater extent than volume of HR of teaching vs non teaching hospitals being 0.76 versus the HR of 0.9 of high versus low-volume hospitals [20].

We should be cautious in comparing our results on hospital volume and outcome in breast cancer with the above-mentioned studies. Our data was based on the total population of the Netherlands, and the low-volume hospitals had a high volume compared to several studies. Moreover, patient selection varied between studies. For instance, in our study, only patients with invasive cancer



were included. Others have included patients with in situ carcinoma, obviously resulting in a more favourable outcome for all subgroups.

Moreover, definitions on hospital volume varies; the definition of ‘low volume’ ranges from less than 10 to less than 50 operations on average per year and the definition of high volume ranges from more than 100 to more than 200, which makes comparisons between studies difficult. In the Netherlands, only four hospitals had less than 50 operations per year, compared to, for instance, Belgium where almost half of all Belgium hospitals ( $n = 57$ ) performed less than 50 surgeries each year. In our study, we revealed a possible 10-year survival benefit of 9 % only by comparing the lowest volume (<75) to the highest volume category (>200), which was comparable to the gain found in the simulation study of Tanke et al. [18]. In our study, hospitals with more than 75 patients per year had similar survival rates as those found in the highest volume group. As in our study, the results found by Hebert et al. [19]. were independent of the primary treatment (adjuvant radiotherapy, chemotherapy or endocrine therapy) or with the type of hospital (data not shown). This could be explained by the fact that the national guideline on diagnosis and treatment in the Netherlands is implemented through a network of consultants of the IKNL, who implement the guideline through regional multidisciplinary breast cancer networks.

Some drawbacks of our study are noted. We cannot exclude the fact that other factors, like variation in comorbidities between patients treated in different hospitals, may have influenced survival as well. Patients with unknown or missing data in the model performed somewhat worse (data not shown). This could be an expression of increased co-morbidities, limited diagnostic work-up, under-staging and under-treatment resulting in a worse survival. Moreover, no information on the hormone receptor status of the patients was available. Although we expect the hormone status to be randomly distributed throughout the hospitals and will not alter our results, we should keep in mind that 10-year survival might be short to evaluate ER negative patients. We did not take into account the small part of patients that received first surgical treatment in another hospital than the one in which definitive surgery or adjuvant radiotherapy and/or chemotherapy took place. We determined the hospital volume on the volume of surgery, taking this as a proxy for the overall organisation of breast cancer care. The compliance of adjuvant treatment did not differ in the different hospital volume groups. Moreover, taking the adjuvant treatment in the regression model did not alter the results. And finally, the cohort described here was treated in the period 2001–2005. More recently, many hospitals have merged. In 2011, only one hospital and in 2012, no hospital has performed less than 75 breast cancer surgeries.

## Conclusions

We conclude that in the Netherlands, surgical hospital volume influences 10-year overall survival only marginally, far less than patient and tumour characteristics do. No differences in survival between hospitals with a surgical volume of 75–99 per year were revealed for invasive non-metastatic breast cancer patients compared to hospitals with over 200 operations. Taking the fluctuations due to the biannual national screening, activities revealed that only three hospitals had a surgical volume of less than 75 patients on average in the period 2007–2012. This implies that for the current situation in the Netherlands, surgical hospital volume is not a critical factor to be taken into account for future breast cancer survival outcome and should not be used as an indicator reflecting the quality of breast cancer care. Due to the development in molecular testing and new treatment modalities treatment, the treatment of breast cancer patients will become increasingly complex and individualized, demanding a multidisciplinary approach in quality of care monitoring.

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