

# The influence of hospital volume on long-term oncological outcome after rectal cancer surgery

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## ABSTRACT

### Introduction

The association between hospital volume and outcome in rectal cancer surgery is still subject of debate. The purpose of this study was to assess the impact of hospital volume on rectal cancer surgery in the Netherlands in 2011.

### Methods

In this collaborative research with a cross-sectional study design, patients who underwent rectal cancer resection in 71 Dutch hospitals in 2011 were included. Annual hospital volume was stratified as low ( $< 20$ ), medium (20-50) and high ( $\geq 50$ ).

### Results

Of 2095 patients, 258 patients (12.3%) were treated in 23 low-volume hospitals, 1329 (63.4%) in 40 medium volume hospitals, and 508 (24.2%) in 8 high-volume hospitals. Median length of follow-up was 41 months. Clinical tumour stage, neoadjuvant therapy, extended resections, circumferential resection margin (CRM) positivity, and 30-day or in-hospital mortality did not differ significantly between volume groups. Significantly, more laparoscopic procedures were performed in low-volume hospitals, and more diverting stomas in high-volume hospitals. Three year disease-free survival for low-, medium-, and high volume hospitals was 75.0%, 74.8%, and 76.8% ( $p = 0.682$ ). Corresponding 3-year overall survival rates were 75.9%, 79.1%, and 80.3% ( $p = 0.344$ ). In multivariate analysis, hospital volume was not associated with long-term risk of mortality.

### Conclusions

No significant impact of hospital volume on rectal cancer surgery outcome could be observed among 71 Dutch hospitals after implementation of a national audit, with the majority of patients being treated at medium-volume hospitals.

## INTRODUCTION

The association between hospital volume and outcome in rectal cancer surgery is still subject of debate, because current literature is difficult to interpret given the variety in volume definitions and outcome indicators. Furthermore, studies on this topic come from different health care systems, and hospitals may substantially differ in case mix and specialization level regardless volume. Although not uniformly reported, hospital volume has been associated with operative mortality.<sup>(1)</sup> More sphincter-saving surgery and lower permanent colostomy rates are more consistently reported outcomes for high-volume hospitals.<sup>(2,3)</sup> The association with long-term risk of recurrence or survival has almost never been observed.<sup>(4,5)</sup>

The Dutch Foundation for Oncological Collaboration ([www.soncos.nl](http://www.soncos.nl)) defines standards for cancer treatment and included a minimum volume of 20 rectal cancer resections annually per hospital in their first report in 2012. Until then, rectal cancer surgery was performed in every Dutch hospital with a few specialized centres treating locally advanced and recurrent rectal cancer, to which referral was recommended in the Dutch colorectal cancer guideline. These recommend centralization of care for patients with advanced stages of rectal cancer in specialized colorectal cancer hospitals. Quality of rectal cancer surgery with respect to short-term outcome is being monitored by the Dutch Surgical Colorectal Audit (DSCA) since 2009, and participation by each hospital is mandatory by the National Inspectorate of Health Care.

The purpose of this study was to assess the impact of hospital volume on short- and long-term outcomes of rectal cancer surgery in the Netherlands in 2011.

## METHODS

### Study design and data collection

All 94 hospitals that registered in the Dutch Surgical Colorectal Audit (DSCA) in 2011 were asked to participate in a resident-led collaborative research project in 2015. A total of 71 hospitals agreed to participate. Registered rectal cancer resections that were performed in these hospitals in 2011 were identified from the DSCA.<sup>(6)</sup> In the second half of 2015, additional procedural data and long-term surgical and oncological outcomes were retrospectively added to the perioperative DSCA data using a specifically developed web-based and privacy controlled data-entry tool for this purpose. Data-entry in this cross-sectional study was performed by one or two surgical residents supervised by a consultant surgeon. Medical ethics committee of the Academic Medical Centre, Amsterdam, the Netherlands

decided that approval was not required for this study as all data were anonymized and no there was no additional burden for the patient. Details of this Snapshot study cohort have been published previously.(7)

## Hospital volume

Annual hospital volume was defined as the total number of rectal cancer resections performed in 2011. This volume was classified as low (< 20), medium (20-50) or high (> 50). Patient characteristics, stage distribution, type of treatment, postoperative outcome, and disease-free and overall survival were calculated for the three categories of annual hospital volume.

## Data analysis

Missing data were not defaulted to negative and denominators reflect only actual reported cases. Nominal variables were compared between the three groups using the Chi-square test, and continuous variables using the Student's *t* test. Kaplan Meier survival analysis with log rank test was used to compare disease-free and overall survival rates at 3 years between volume groups. Multivariable Cox regression analysis was performed to determine independent predictors of long-term mortality. Hospital volume was included in this model besides all variables that were significant in univariable analysis ( $p < 0.05$ ). SPSS 22 was utilized for the analyses, and a  $p$  value  $< 0.05$  was considered significant. The STROBE guidelines were used to ensure the reporting of this observational study.(8)

## RESULTS

### Baseline characteristics

A total of 2095 patients with rectal cancer were included, of which 258 patients (12.3%) were treated in 23 low-volume hospitals, 1329 (63.4%) in 40 medium-volume hospitals, and 508 (24.2%) in 8 high-volume hospitals. Baseline characteristics are displayed in Table 1, stratified for annual hospital volume. Demographics, medical history, clinical tumour stage, distance of the tumour to the anorectal junction, type of surgical procedure, and extended resection for cT4 did not differ significantly between different volume groups. Overall, approximately 90% of patients underwent neoadjuvant therapy, while there were small differences in neoadjuvant regimes between different volume groups (Table 1). High volume hospitals diagnosed significantly more often a clinical node-positive status compared to low and medium volume hospitals ( $p < 0.001$ ), mainly as cN2-stage. A laparoscopic approach was more frequently used in low-volume hospitals compared to medium and high volume (59.8% vs. 44.8% and 45.7,  $p < 0.001$ ). In patients undergoing low

anterior resection, the anastomosis was more frequently diverted in high-volume hospitals compared to low and medium-volume hospitals (80.3% vs. 65.5% and 68.5%,  $p = 0.001$ ).

**Table 1.** Baseline and operative characteristics of rectal cancer patients stratified for hospital volume

	Low volume (<20) N= 258 (12.3%)	Medium volume (20-50) N= 1329 (63.4%)	High volume (>50) N=508 (24.2%)	P value
Age (year)	66.0 $\pm$ 12.3	66.9 $\pm$ 11.1	66.7 $\pm$ 11.2	0.448
Male gender	153 (59.3%)	855 (64.4%)	309 (60.8%)	0.164
Medical history				
Cardiac	58 (31.4%)	295 (33.4%)	107 (30.2%)	0.380
Vascular	91 (49.5%)	441 (49.9%)	174 (49.2%)	0.862
Pulmonal	36 (19.5%)	147 (16.6%)	59 (16.7%)	0.790
Diabetes	37 (20.0%)	170 (19.2%)	66 (18.6%)	0.960
Neurologic	24 (13.0%)	153 (17.3%)	60 (16.9%)	0.622
ASA class 3/4	39 (15.7%)	223 (17.2%)	81 (16.3%)	0.796
Multidisciplinary tumour board meeting	241 (98.4%)	1243 (95.8%)	481 (96.6%)	0.130
Neoadjuvant therapy	232 (89.9%)	1187 (89.3%)	457 (90.0%)	0.901
Short-course (5x5 Gy)	116 (45.0%)	620 (46.7%)	219 (43.1%)	
Long-course	8 (3.1%)	53 (4.0%)	8 (1.6%)	
Chemoradiotherapy	91 (35.3%)	465 (35.0%)	155 (30.5%)	
Different regimen	17 (6.6%)	49 (3.7%)	75 (14.8%)	<0.001
cT stage				
cT1	6 (2.8%)	56 (4.8%)	18 (4.2%)	
cT2	55 (25.9%)	289 (25.0%)	129 (30.0%)	
cT3	128 (60.4%)	709 (61.2%)	230 (53.5%)	
cT4	23 (10.8%)	104 (9.0%)	53 (12.3%)	0.070
cN stage				
cN0	89 (45.4%)	517 (45.9%)	146 (35.3%)	
cN1	76 (38.8%)	440 (39.1%)	167 (40.3%)	
cN2	31 (15.8%)	169 (15.0%)	101 (24.4%)	<0.001
cM1	19 (8.3%)	90 (7.1%)	30 (6.8%)	0.777
Distance to anal verge (cm)	5.6 $\pm$ 3.6	5.9 $\pm$ 3.9	6.2 $\pm$ 4.0	0.152
Operative characteristics				
LAR	113 (43.8%)	635 (47.8%)	250 (49.2%)	
APR	79 (30.6%)	401 (30.2%)	159 (31.3%)	
Low Hartmann	53 (20.5%)	261 (19.6%)	88 (17.3%)	
Different	13 (5.0%)	32 (2.4%)	11 (2.2%)	0.142
Deviating stoma (in LAR)	76 (65.5%)	440 (68.5%)	204 (80.3%)	0.001
Laparoscopic	149 (59.8%)	582 (44.8%)	227 (45.7%)	<0.001

**Table 1.** Baseline and operative characteristics of rectal cancer patients stratified for hospital volume (continued)

	Low volume (<20) N= 258 (12.3%)	Medium volume (20-50) N= 1329 (63.4%)	High volume (>50) N=508 (24.2%)	P value
Additional resection	18 (7.2%)	94 (7.2%)	42 (8.4%)	0.676
Partial vaginectomy	13 (5.0%)	29 (2.2%)	12 (2.4%)	0.028
Uterus resection	2 (0.8%)	20 (1.5%)	7 (1.4%)	0.656
Ovariectomy	1 (0.4%)	18 (1.4%)	11 (2.2%)	0.136
Vesicula seminalis resection	2 (0.8%)	10 (0.8%)	10 (2.0%)	0.066
Partial prostatectomy	2 (0.8%)	18 (1.4%)	5 (1.0%)	0.649
Partial bladder resection	1 (0.4%)	9 (0.7%)	4 (0.8%)	0.812
Total exenteration	2 (0.8%)	12 (0.9%)	4 (0.8%)	0.960

ASA: American Society of Anaesthesiologists

LAR: low anterior resection; APR: abdominoperineal resection; low Hartmann: total mesorectal excision with end-colostomy.

Different included proctocolectomy or local excision followed by rectal resection.

**Table 2.** Pathologic and short-term outcome of rectal cancer patients stratified for hospital volume

	Low volume (<20) N= 258 (12.3%)	Medium volume (20-50) N= 1329 (63.4%)	High volume (>50) N=508 (24.2%)	P value
Pathologic tumour stage				
(y)pT0	28 (11.3%)	86 (6.8%)	19 (4.0%)	
(y)pT1	21 (8.5%)	94 (7.4%)	41 (8.6%)	
(y)pT2	81 (32.8%)	413 (32.7%)	164 (34.3%)	
(y)pT3	103 (41.7%)	610 (48.3%)	225 (47.1%)	
(y)pT4	14 (5.7%)	61 (4.8%)	29 (6.1%)	0.027
Pathologic lymph node stage				
(y)pN0	163 (66.8%)	787 (62.5%)	328 (66.3%)	
(y)pN1	63 (25.8%)	331 (26.3%)	126 (25.5%)	
(y)pN2	18 (7.4%)	142 (11.3%)	41 (8.3%)	0.172
CRM involvement <sup>a</sup>	17 (8.9%)	96 (9.2%)	35 (9.2%)	0.993
Postoperative outcomes				
Overall complication	81 (32.5%)	506 (39.2%)	186 (37.7%)	0.004
Reintervention	30 (14.1%)	186 (17.2%)	53 (13.6%)	0.184
30-day or in-hospital mortality	7 (2.8%)	34 (2.6%)	14 (2.8%)	0.970

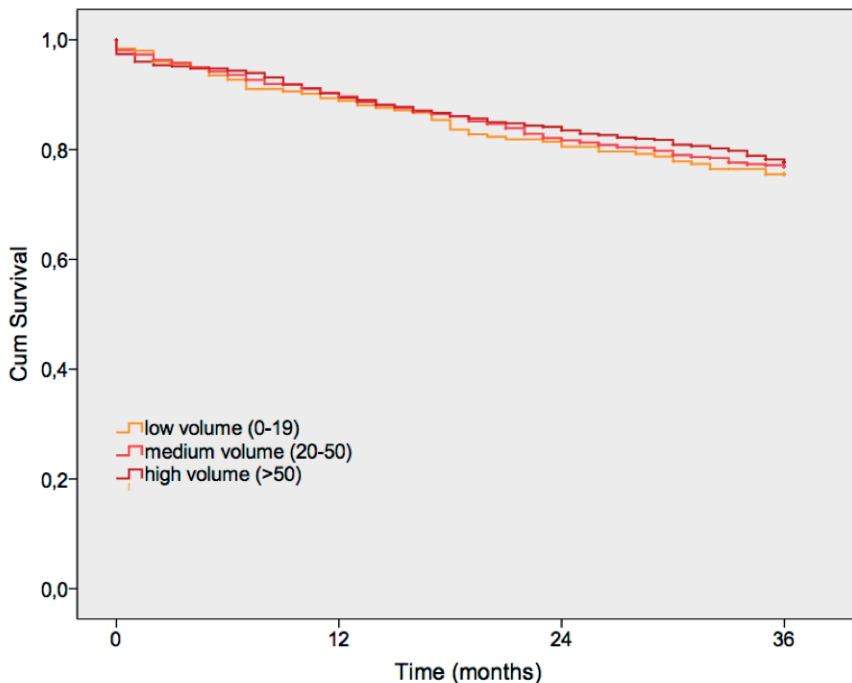
<sup>a</sup> CRM (circumferential resection margin) involvement: if the smallest non-peritoneal resection margin to the tumour was ≤ 1mm at pathologic examination.

## Postoperative outcomes

Pathological tumour stage slightly differed among the volume groups with more complete response (y) pT0 (11.3% vs. 6.8% and 4.0%) and less (y) pT3 stage (41.7% vs. 48.1% and 47.3%,  $p = 0.027$ ) in low-volume compared to medium and high-volume hospitals. The overall higher cN stage in high-volume hospitals did not translate into high (y)pN stage ( $p = 0.172$ ). Circumferential resection margin involvement was found in approximately 9% and did not differ among volume groups (Table 2;  $p = 0.993$ ). Overall complication rate was lower in low-volume hospitals compared to medium and high-volume hospitals, with non-significantly different reintervention rates. The 30-day or in-hospital mortality rate was 2.8% in low volume hospitals as compared to 2.6% and 2.8% in medium and high-volume hospitals, respectively ( $p = 0.970$ ).

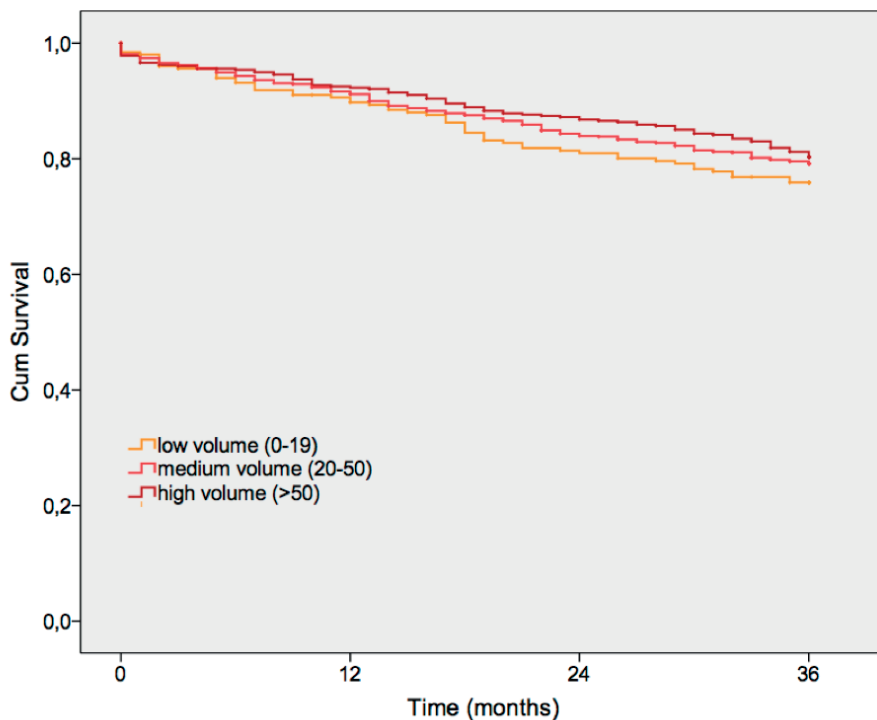
## Long-term oncological outcomes

Median length of follow-up was 41 months (interquartile range 30 - 52 months). Disease-free survival at 3 years was 75.0% for patients operated in low-volume hospitals, compared to 74.8% and 76.8% in medium and high-volume hospitals (Figure 1,  $p = 0.682$ ).



**Figure 1.** Disease-free survival after rectal cancer surgery, stratified for hospital volume. Disease-free survival at 3 years was 75.0% for patients operated in low-volume hospitals, compared to 74.8% in and 76.8% in medium and high-volume hospitals ( $p = 0.682$ ).

Three-year overall survival was 75.9% for patients operated in low-volume hospitals, compared to 79.1% in and 80.3% in medium and high-volume hospitals (Figure 2,  $p = 0.344$ ).



**Figure 2.** Overall survival after rectal cancer surgery, stratified for hospital volume. The overall survival rate at 3 years was 75.9% for patients operated in low-volume hospitals, compared to 79.1% in and 80.3% in medium and high-volume hospitals ( $p = 0.344$ ).

Independent predictors of long-term mortality in Cox regression analysis were age above 70 years, ASA class 3 or 4, pathological tumour and nodal stage, synchronous metastasis, extended resection because of suspected tumour involvement, and circumferential resection margin (CRM) involvement (Table 3). After adjustment for these factors, annual hospital volume was not significantly associated with a long-term risk of mortality.



**Table 3.** Multivariate cox regression analysis of predictors of long-term mortality after rectal cancer surgery

Variable	Odds ratio	95% CI	p value
Age > 70	2.28	1.84-2.82	<0.001
Female gender	0.84	0.67-1.04	0.114
ASA class 3/4	2.08	1.65-2.63	<0.001
Neoadjuvant therapy	0.85	0.62-1.17	0.320
Laparoscopic	1.02	0.82-1.26	0.883
Pathologic tumour stage			
pT0	1.00	-	-
pT1	0.37	0.16-0.83	0.016
pT2	0.60	0.33-1.08	0.089
pT3	1.07	0.61-1.88	0.815
pT4	1.01	0.52-1.94	0.979
Pathologic nodal stage			
N1/N2	1.15	1.05-1.26	0.003
Synchronous metastasis	2.71	2.08-3.52	<0.001
Additional resection	2.07	1.49-2.89	<0.001
CRM involvement	1.78	1.34-2.34	<0.001
Hospital volume <sup>a</sup>			
Low volume (0-19)	1.00	-	-
Medium volume (20-50)	0.93	0.68-1.27	0.635
High volume (>50)	0.93	0.65-1.32	0.676

<sup>a</sup> Low volume was used as reference category

## DISCUSSION

In this Snapshot study, including 2095 patients treated in 71 Dutch hospitals, annual hospital volume was not significantly associated with any outcome measure after rectal cancer surgery. The only differences that were observed among volume groups were related to clinical nodal staging and the surgical treatment, regarding the use of minimally invasive surgery and diverting stoma. Treatment of locally advanced disease did not seem to be related to annual hospital volume.

This cross-sectional study design enabled evaluation of a much debated volume-outcome relationship within the context of most recently provided rectal cancer care in the Netherlands. Since the TME trial in the late 1990s, rectal cancer care has increasingly been provided by dedicated multidisciplinary teams in the Netherlands, with rectal resections almost exclusively performed by specialized surgeons in recent years. The Association of

Surgeons of the Netherlands initiated a colorectal audit in 2009. The first report revealed substantial inter-hospital variability in process and outcome indicators. Regularly updated feedback and quality improvement projects led to substantial improvements in the next few years.(6) This probably explains the overall high performance independent of hospital volume as observed in the present snapshot of 2011.

Limitations of the present study are related to potential incompleteness and validity of the data. The hospital volume was based on the number of cases originally registered in the DSCA and data are self-reported. However, validation of the DSCA against the Dutch National Cancer Registry showed high accuracy and completeness of the data.(9) Furthermore, it should be noted that participation in this snapshot study was voluntary, while registration in the DSCA is mandatory. Some small non-teaching regional hospitals that did not participate in this resident-led research project could have influenced the results. In contrast to a similar CRM positivity among volume groups in the current study, a significant higher CRM positivity was found among volume groups in the current study, a significant higher CRM positivity was found in low-volume hospitals in 2011 and 2012 using DSCA data of all 94 Dutch hospitals.(10) This underlines the difficulty in interpretation of hospital volume as a single discriminator, while some low-volume hospitals might be high-performing hospitals.(11)

Treatment of rectal cancer has become more and more complicated considering several clinically relevant subgroups of patients regarding clinical condition, clinical staging, and types of neoadjuvant therapy, different surgical approaches, pathological and molecular assessment, and an increasing number of systemic therapy options. It seems likely that a certain volume is needed to manage this increasing complexity of care. In the Netherlands, centralization of rectal cancer has been recently initiated through a minimum volume of 20 rectal resections annually, with involvement of patient societies and insurance companies besides the relevant national medical societies. Hospitals that did not reach the minimum of 20 resections a year were encouraged to stop performing rectal surgery since 2012, which resulted in collaboration initiatives with concentration of specific patient groups. It may well be that specific subgroups do benefit from centralized care in high-volume centres. However, our patient cohort might not be able to show this because of already implemented quality improvement measures, and because the sample size is still relatively small to show subtle differences between subgroups.

Data from previous studies regarding hospital volume and rectal cancer care are conflicting, and definitions of high and low volume vary considerably. According to the Californian Office of State-wide Health planning and Development database(12) and the Swedish Rectal Cancer Registry(13), short-term mortality rates after rectal cancer surgery were

significantly lower in medium and high-volume hospitals (0.9% - 2.2%) as compared to low-volume centres (2.1% - 3.6%). Noteworthy is the definition of low volume in the Californian study, being 30 procedures or less during a six-year study period, corresponding to an annual volume of 5 or less. A recent analysis from the Rectal Cancer Project of the Spanish Society of Surgeons of 9809 consecutive patients showed an overall postoperative mortality rate of 1.8%, which varied significantly among hospitals, but this could not be attributed to the hospital volume.(14) The same authors could not demonstrate a significant influence of hospital volume on the anastomotic leakage rate after LAR in another study.(15) PROCARE investigators recently found some volume effects in the quality of care in the treatment of rectal cancer, but concluded that their effect size was limited.(4) The authors underline that PROCARE is a voluntary registry, which cannot be extrapolated to the Belgian population.

Regarding the effects of hospital volume on long-term survival after rectal cancer surgery, data is limited. Overall survival rates after 5 years appear not to be associated with hospital volume.(3,13,16,17) Only two studies including patients treated between 1992 and 1997 found a slightly better survival rate after 2 years for high-volume hospitals.(2,18) However, the validity of these historical data for modern rectal cancer management are questionable. In the present study, overall survival rates slightly differed with higher probabilities in high-volume hospitals. However, this did not reach statistical significance and multivariate analysis confirmed that there was no impact of hospital volume on survival. Combining these findings and the previously reported results in the literature, the influence of overall hospital volume on long-term outcomes after rectal cancer resection appears to be limited, if it exists at all.

Care for patients with locally advanced tumours was already centralized in the Netherlands before 2011. If exenterative procedures, sacral resection or intraoperative radiotherapy are indicated, the previous Dutch guideline from 2008 already recommended referral to specialized centres.(19) The similar percentages of extended resections and ypT4 stage among the different volume groups suggest that treatment of locally advanced disease is not related to volume, but more related to availability of expertise and treatment modalities. Patients with cT4 tumours are potentially more accurately assessed in experienced multidisciplinary tumour board meetings and treated by specialized surgeons for 'beyond TME' surgery in centres for locally advanced disease. These centres may not necessarily be high-volume, because of their focus on referred patients with less use of their capacity for patients with cT1-3 tumours.

In conclusion, no impact of hospital volume on outcome after rectal cancer surgery could be demonstrated among 71 Dutch hospitals at the time already significant improvements in rectal cancer care were achieved. Hospital volume as a single discriminator should be used with caution, although a certain unspecified volume is likely needed to gain and retain expertise in rectal cancer care with increasing complexity.

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