



Effect of centre volume on pathological outcomes and postoperative complications after surgery for colorectal cancer: results of a multicentre national study

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Abstract

Background: The association between volume, complications and pathological outcomes is still under debate regarding colorectal cancer surgery. The aim of the study was to assess the association between centre volume and severe complications, mortality, less-than-radical oncologic surgery, and indications for neoadjuvant therapy.

Methods: Retrospective analysis of 16,883 colorectal cancer cases from 80 centres (2018–2021). Outcomes: 30-day mortality; Clavien-Dindo grade >2 complications; removal of ≥ 12 lymph nodes; non-radical resection; neoadjuvant therapy. Quartiles of hospital volumes were classified as LOW, MEDIUM, HIGH, and VERY HIGH. Independent predictors, both overall and for rectal cancer, were evaluated using logistic regression including age, gender, AJCC stage and cancer site.

Results: LOW-volume centres reported a higher rate of severe postoperative complications (OR 1.50, 95% c.i. 1.15–1.096, $P = 0.003$). The rate of ≥ 12 lymph nodes removed in LOW-volume (OR 0.68, 95% c.i. 0.56–0.85, $P < 0.001$) and MEDIUM-volume (OR 0.72, 95% c.i. 0.62–0.83, $P < 0.001$) centres was lower than in VERY HIGH-volume centres. Of the 4676 rectal cancer patients, the rate of ≥ 12 lymph nodes removed was lower in LOW-volume than in VERY HIGH-volume centres (OR 0.57, 95% c.i. 0.41–0.80, $P = 0.001$). A lower rate of neoadjuvant chemoradiation was associated with HIGH (OR 0.66, 95% c.i. 0.56–0.77, $P < 0.001$), MEDIUM (OR 0.75, 95% c.i. 0.60–0.92, $P = 0.006$), and LOW (OR 0.70, 95% c.i. 0.52–0.94, $P = 0.019$) volume centres (vs. VERY HIGH).

Conclusion: Colorectal cancer surgery in low-volume centres is at higher risk of suboptimal management, poor postoperative outcomes, and less-than-adequate oncologic resections. Centralisation of rectal cancer cases should be taken into consideration to optimise the outcomes.

Introduction

A conclusive association between low case volume and poor postoperative and oncological outcomes has yet to be defined in the setting of colorectal cancer surgery. While several studies have suggested that specific perioperative outcomes would improve with increased caseload¹, others have not reported any volume–outcome relationship². Furthermore, identifying these outcomes and the volume thresholds has proven to be unreliable³. The great variations among the different studies are most likely due to different settings and study populations. For instance, the use of administrative data sets, which have the advantage of providing a large number of cases, reduces the possibility of adjusting the analyses for the many confounders that should be taken into account regarding their effect on

outcomes^{4,5}. On the other hand, collaborative research studies often include a limited number of cases per centre and a higher proportion of high-volume centres^{6,7}.

The aim of the present study was to analyse the data from a large collaborative study that included high- and low-volume centres over a four-year period, in order to identify potential correlations between hospital volume, mortality, postoperative complications and oncological outcomes.

Methods

The coronavirus disease 2019 (COVID-19) ColoRectal Cancer (COVID-CRC) Collaborative study data set retrospectively included 17 938 patients undergoing surgery for colorectal cancer between

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Table 1 Selected demographic and clinical characteristics, and outcomes for the whole cohort and stratified by hospital volume

	Overall sample	Patients by hospital volume*				P#
		Low†	Medium‡	High§	Very high¶	
Patients (hospitals), n	16 883 (80)	999 (21)	2644 (19)	4675 (20)	8565 (20)	
Male/female gender, %	44.1/55.9	44.9/55.1	45.4/54.6	44.6/55.4	43.4/56.6	
Mean age in years (s.d.)	70.4 (12.2)	70.4 (12.2)	71.3 (11.8)	70.8 (12.0)	69.8 (12.4)	e, f
Co-morbidities, %						
None	23.5	23.6	22.1	25.8	22.6	c, d, f
1	39.9	36.6	42.9	36.6	41.2	b, c, d, f
2	24.5	24.8	23.8	25.1	24.4	b, c, e
3 or more	12.1	15.0	11.2	12.5	11.8	a
Anatomical location, %						
Right-transverse colon	42.7	42.7	45.3	43.8	41.4	e, f
Left colon	29.0	32.8	28.5	31.1	27.5	a, c, d, f
Rectum	27.7	23.4	25.9	24.6	30.4	c, e, f
Multiple lesions	0.6	1.1	0.3	0.5	0.7	a, e
T4 stage, %	6.0	8.7	6.2	3.8	6.9	a, b, c, d, f
Rectal lesions only, %	(n = 4676)	(n = 233)	(n = 685)	(n = 1153)	(n = 2605)	
N1 stage	40.0	37.8	35.2	33.9	44.2	e, f
T4 stage	6.9	8.2	4.8	6.6	7.5	e
Metastatic lesions, %	9.6	10.9	10.4	6.5	10.8	b, d, f
Stenosing lesions, %	13.1	14.8	11.4	11.0	14.6	a, b, e, f
Urgent surgery, %	8.8	17.5	11.4	7.6	7.6	a, c, d, e
ASA score >2, %	43.5	47.5	40.2	40.9	45.4	a, b, e, f
	(N = 12 722)	(N = 824)	(N = 2241)	(N = 3808)	(N = 5849)	
Anastomosis, %	93.2	89.1	93.4	92.7	93.9	a, b, c, f
Additional surgery, %	10.3	11.4	9.7	6.8	12.3	b, d, e, f
Laparoscopic surgery, %	74.5	58.1	67.7	76.8	77.2	a, b, c, d, e
	(N = 12 572)	(N = 580)	(N = 1789)	(N = 3592)	(N = 6611)	
Conversion to open surgery, %	7.3	8.3	8.1	6.1	7.6	b, d, f
	(N = 14 943)	(N = 868)	(N = 2372)	(N = 4228)	(N = 7475)	
Loop ileostomy, %	16.1	12.3	14.4	12.5	19.1	c, d, e, f
ICU admission, %	15.0	15.7	12.9	15.3	15.5	a, d, e

*Hospital procedure volume was defined as the number of operations performed during the study period (2018–2021). The unit of analysis was individual patients unless otherwise stated. †Low-volume hospitals performed between 19 and 111 procedures. ‡Medium-volume hospitals performed between 112 and 167 procedures. §High-volume hospitals performed between 168 and 263 procedures. ¶Very high-volume hospitals performed between 264 and 638 procedures. #Chi-squared test for the categorical variables; one-way ANOVA with Bonferroni corrections for continuous ones. a = $P < 0.05$ for the comparison between low- and medium-volume hospitals; b = $P < 0.05$ for the comparison between low- and high-volume hospitals; c = $P < 0.05$ for the comparison between low- and very high-volume hospitals; d = $P < 0.05$ for the comparison between medium- and high-volume hospitals; e = $P < 0.05$ for the comparison between medium- and very high-volume hospitals; f = $P < 0.05$ for the comparison between high- and very high-volume hospitals. All Ps not indicated were >0.05 .

January 2018 and December 2021 in 80 Italian hospitals⁸. No minimum number of cases was required for the centres to register for the study; thus tertiary centres and community hospitals were enrolled regardless of hospital volume.

The variables of interest were identified using institutional databases and entered into a REDCap (Research Electronic Data Capture)⁹ database by a team of clinicians. A proportion of cases (20%) was subsequently validated by an independent investigator in each centre.

The data set reported the details of co-morbidities, preoperative diagnosis, neoadjuvant therapy, surgery (type of operation and intraoperative complications) and postoperative outcome at 30 days from surgery. The histological details included the stage and the biological characteristics of the tumour, as well as the radicality of surgery.

The following inclusion criteria were adopted: patients ≥ 18 years of age; any type of colorectal surgery for cancer (including surgery after non-radical endoscopic excision of a cancer); elective or urgent surgery with curative intent; location of cancer in the colon, rectum or anus; and a minimum follow-up of 30 days from surgery. The exclusion criteria were recurrent cancer and cancer originating from other locations, cancers other than adenocarcinoma or squamous cell carcinoma, benign lesions and palliative surgery (defined as procedures not aiming to radically remove the primary tumour).

The main aim of the study was to assess the correlation among different volumes of procedures and the following five outcomes:

30-day mortality, severe postoperative complications (defined according to the Clavien–Dindo classification $>$ grade 2)¹⁰, adequate lymph node sampling (≥ 12 lymph nodes on the histological specimen), non-radical resection (defined as involvement of any margin from the tumour) and use of neoadjuvant therapy. A subgroup analysis was carried out including only patients undergoing surgery for rectal cancer.

The Ethics Committees of all participating centres approved the study, which was registered on ClinicalTrials.gov (NCT04712292). A written consent form was obtained from all available patients. The study followed the STROBE guidelines¹¹.

Statistical analysis

Hospitals were ranked by volume according to the number of interventions performed between 2018 and 2021. In order to evaluate the association between all variables recorded and hospital procedure volumes, quartiles of hospital volumes based on the number of interventions performed in the four-year study period were identified, namely low (first quartile—between 19 and 111 procedures), medium (second quartile—between 112 and 167 procedures), high (third quartile—168 and 263 procedures) and very high (fourth quartile— ≥ 264 procedures). Potential differences in the distribution of all clinical characteristics recorded across quartiles of hospital volume were then assessed using the chi-squared test for

Table 2 Pathological and postoperative variables and outcomes, overall and by hospital surgical volume

	Overall sample	Patients by hospital volume*				P#
		Low†	Medium‡	High§	Very high¶	
Patients (hospitals), n	16 883 (80)	999 (21)	2644 (19)	4675 (20)	8565 (20)	
AJCC stage, %	(N = 16 273)	(N = 979)	(N = 2526)	(N = 4535)	(N = 8233)	
0	3.2	3.6	3.4	3.3	3.1	
I	24.5	21.6	23.3	24.6	25.2	b, c, e
II	32.3	32.0	31.9	35.0	31.0	c, f
III	30.0	31.7	30.5	30.4	29.4	
IV	10.0	11.1	10.9	6.7	11.3	c, e, f
Median hospital length of stay (i.q.r.)	7.0 (5.0)	8.0 (5.0)	7.0 (4.0)	7.0 (4.0)	7.0 (5.0)	a, b, e, f
Postoperative medical complications, %						
All complications**	16.0	15.4	16.2	13.8	17.2	d, f
Anaemia	4.6	4.7	6.7	4.5	4.0	
Pulmonary complications††	3.1	5.0	2.3	3.3	3.0	
Sepsis	2.0	2.3	1.3	1.4	2.4	
Acute kidney failure	1.2	2.0	1.1	0.8	1.3	
Myocardial infarction	0.3	0.4	0.5	0.3	0.2	
Venous thromboembolism	0.2	0.0	0.2	0.1	0.3	
Pulmonary embolism	0.3	0.5	0.2	0.2	0.3	
Stroke	0.1	0.3	0.1	0.1	0.2	
Postoperative surgical complications, %						
All complications‡‡	17.7	19.5	15.0	14.9	19.9	a, b, e, f
Surgical site infection	4.0	5.8	3.6	3.0	4.4	
Intra-abdominal bleeding	1.1	1.9	1.1	1.1	1.0	
Intraluminal bleeding	1.2	1.1	0.7	1.4	1.2	
Intra-abdominal sepsis§§	7.1	7.6	5.5	6.0	8.1	
Dehiscence	5.0	4.5	4.2	4.6	5.6	
Abdominal abscess	2.6	3.4	1.5	1.7	3.5	
Peritonitis	0.9	1.1	0.3	0.7	1.1	
Paralytic ileus	2.9	1.5	2.3	2.6	3.4	
Bowel occlusion	1.0	1.4	0.8	0.8	1.1	
Outcomes						
30-day mortality, %	1.6	2.5	1.9	1.5	1.5	b, c
	(N = 4840)	(N = 289)	(N = 703)	(N = 1135)	(N = 2713)	
Clavien–Dindo classification ≥3, %	34.5	42.6	34.4	35.3	33.3	a, b, c
≥12 lymph nodes, %	85.2	82.6	83.3	86.7	85.4	b, c, d, e, f
Non-radical surgery (R1/2), %	2.6	2.0	2.2	2.3	2.9	e
Neoadjuvant therapy, %	15.4	11.6	12.3	11.6	18.8	c, e, f

*Hospital procedure volume was defined as the number of operations performed during the study period (2018–2021). The unit of analysis was individual patients unless otherwise stated. †Low-volume hospitals performed between 19 and 111 procedures. ‡Medium-volume hospitals performed between 112 and 167 procedures. §High-volume hospitals performed between 168 and 263 procedures. ¶Very high-volume hospitals performed between 264 and 638 procedures. #Chi-squared test for the categorical variables; one-way ANOVA with Bonferroni corrections for continuous ones. a = $P < 0.05$ for the comparison between low- and medium-volume hospitals; b = $P < 0.05$ for the comparison between low- and high-volume hospitals; c = $P < 0.05$ for the comparison between low- and very high-volume hospitals; d = $P < 0.05$ for the comparison between medium- and high-volume hospitals; e = $P < 0.05$ for the comparison between medium- and very high-volume hospitals; f = $P < 0.05$ for the comparison between high- and very high-volume hospitals. All the Ps not indicated were > 0.05 . **Including: anaemia, myocardial infarction, stroke, pulmonary embolism, venous thromboembolism, acute kidney failure, sepsis, pneumonia, acute respiratory distress syndrome, respiratory failure. ††Pneumonia, and/or acute respiratory distress syndrome, and/or respiratory failure. ‡‡Including intra-abdominal or intraluminal bleeding, dehiscence, surgical site infection, abdominal abscess, peritonitis, paralytic ileus, bowel occlusion. §§Including dehiscence, abdominal abscess, peritonitis.

categorical variables, and one-way ANOVA with Bonferroni correction for continuous variables.

For each of the five outcomes of interest, potential independent predictors were separately evaluated using logistic regression. The covariates were tested for multi-collinearity and selected for inclusion in the final models using a stepwise forward process with the following inclusion criteria: clinical relevance, $P < 0.10$ at univariate analyses, age, gender, AJCC stage, cancer site (rectum versus others), and urgent surgery. As a separate, additional analysis, the same outcomes were evaluated in the subsample of patients undergoing surgery for rectal cancer.

For the latter analyses, hospital volume was categorized both using quartiles and adopting a minimum threshold of ≥ 10 surgical procedures per year, in accordance with the National Institute for Health and Care Excellence (NICE) guidelines¹². Accordingly, all analyses were repeated comparing low-volume (< 10 surgical procedures per year) versus high-volume (≥ 10 per year) centres. Standard diagnostic procedures were adopted to check the validity of all the models, including influential

observation analysis (Dbeta, change in Pearson chi-square), Hosmer–Lemeshow test for the goodness of fit, and C statistic (area under the receiving operator characteristic curve). Statistical significance was defined as a two-sided $P < 0.05$. All analyses were carried out using Stata, version 13.1 (Stata Corp., College Station, Texas, 2014).

Results

A total of 16 883 patients treated in 80 centres were included in the final analysis. Tables 1, 2 show the distribution of the demographic and clinical characteristics, as well as the five outcomes using the quartiles of hospital volume (low volume: 21 centres, 999 patients; medium volume: 19 centres, 2644 patients; high volume: 20 centres, 4675 patients; very high volume: 20 centres, 8565 patients). Tables 1, 2 also report the univariate comparisons among the quartiles. A significantly higher rate of cancer located in the rectum was reported in the very high-volume centres (30.4%) as compared to the high- (24.6%), medium- (25.9%)

Table 3 Multivariate analyses evaluating the association between hospital volume and each postoperative outcome recorded*

Hospital volume†	30-day mortality (n = 266)		P	Severe complications (n = 1670)		P
	%	OR (95% c.i.)		%	OR (95% c.i.)	
Very high	1.5	1 (ref. cat.)	–	33.3	1 (ref. cat.)	–
High	1.5	0.93 (0.67–1.28)	0.6	35.3	1.10 (0.94–1.29)	0.2
Medium	1.9	0.84 (0.53–1.33)	0.5	34.4	0.97 (0.78–1.20)	0.8
Low	2.5	1.29 (0.80–2.07)	0.3	42.6	1.50 (1.15–1.96)	0.003
Hospital volume†	Removal of ≥12 nodes (n = 13 497)		P	Non-radical resection (R1/2) (n = 429)		P
	%	OR (95% c.i.)		%	OR (95% c.i.)	
Very high	85.4	1 (ref. cat.)	–	2.9	1 (ref. cat.)	–
High	86.7	1.12 (0.99–1.27)	0.070	2.3	0.92 (0.71–1.19)	0.6
Medium	83.3	0.72 (0.62–0.83)	<0.001	2.2	0.69 (0.48–0.99)	0.045
Low	82.6	0.68 (0.56–0.85)	<0.001	2.0	0.65 (0.40–1.06)	0.09
Hospital volume†	Neoadjuvant therapy (n = 2595)		P			
	%	OR (95% c.i.)				
Very high	18.8	1 (ref. cat.)	–			
High	11.6	0.56 (0.48–0.65)	<0.001			
Medium	12.3	0.66 (0.54–0.80)	<0.001			
Low	11.6	0.66 (0.50–0.87)	0.003			

ref. cat.: reference category. *Hospital procedure volume was defined as the number of operations performed during the study period (2017–2022). Low-volume hospitals performed between 19 and 111 procedures; medium-volume hospitals performed between 112 and 167 procedures; high-volume hospitals performed between 168 and 263 procedures; very high-volume hospitals performed between 264 and 638 procedures. †All final models were adjusted for: age, gender, lesion site (rectum versus others), aggressive biology, AJCC stage, urgent surgery, history of previous colorectal cancer, history of inflammatory bowel disease, presence of other co-morbidities and familial history of colorectal cancer. Severe complications were classified as Clavien–Dindo grade 3 and higher.

Table 4 Multivariate analyses evaluating the association between hospital volume and each postoperative outcome recorded for patients undergoing surgery for rectal cancer†

Hospital volume†	30-day mortality** (n = 51)		P	Severe complications (n = 569)		P
	%	OR (95% c.i.)		%	OR (95% c.i.)	
Very high	0.8	1 (ref. cat.)	–	37.7	1 (ref. cat.)	–
High	1.1	1.18 (0.56–2.49)	0.7	34.5	0.89 (0.66–1.19)	–
Medium	1.6	1.67 (0.89–3.96)	0.09	43.4	1.27 (0.87–1.87)	0.4
Low	2.2	1.21 (0.86–6.43)	0.09	48.7	1.47 (0.90–2.42)	0.2
Hospital volume†	Removal of ≥ 12 nodes (n = 3042)		P	Non-radical resection (R1/2) (n = 214)		P
	%	OR (95% c.i.)		%	OR (95% c.i.)	
Very high	72.3	1 (ref. cat.)	–	5.1	1 (ref. cat.)	–
High	73.3	1.12 (0.93–1.35)	0.2	4.2	0.77 (0.53–1.12)	0.2
Medium	72.9	0.90 (0.71–1.14)	0.4	3.8	0.54 (0.31–0.94)	0.028
Low	63.5	0.57 (0.41–0.80)	0.001	4.4	0.70 (0.34–1.42)	0.3
Hospital volume†	Neoadjuvant therapy (n = 2331)		P			
	%	OR (95% c.i.)				
Very high	54.7	1 (ref. cat.)	–			
High	44.2	0.66 (0.56–0.77)	<0.001			
Medium	43.2	0.75 (0.60–0.92)	0.006			
Low	43.4	0.70 (0.52–0.94)	0.019			

ref. cat.: reference category. *Hospital procedure volume was defined as the number of surgical procedures performed during the study period (2018–2021). Low-volume hospitals performed between 19 and 111 procedures; medium-volume hospitals performed between 112 and 167 procedures; high-volume hospitals performed between 168 and 263 procedures and very high-volume hospitals performed between 264 and 638 procedures. †All final models were adjusted for age, gender, aggressive biology, AJCC stage, urgent surgery, history of previous colorectal cancer, history of inflammatory bowel disease, presence of other co-morbidities and familial history of colorectal cancer. Severe complications were classified as Clavien–Dindo grade 3 and higher. ‡Due to the scarce number of successes (n = 51), the final model was adjusted for age, gender, AJCC stage, history of previous colorectal cancer.

and low-volume (23.4%) centres. Further detail of centre volume is shown in [Table S1](#).

The rate of urgent surgery (defined as the need for surgery within 48 h of hospital admission) was significantly higher in the low-volume centres (17.5%) than in the medium- (11.4%), high- (7.6%) and very high-volume (7.6%) centres, while the use of a minimally invasive approach was significantly lower (58.1% versus 67.7%, 76.8% and 77.2%, respectively).

A significantly higher risk of mortality was found in the low-volume centres (2.5%) as compared to the other centres (1.9%, 1.5% and 1.5%, respectively). The risk of severe postoperative complications was also significantly higher in the low-volume centres (42.6%) than in the medium- (34.4%), high- (35.3%) and very high-volume (33.3%) centres.

The probability of a final AJCC stage I increased progressively from low-volume centres (21.6%) to very high-volume centres (25.2%). The proportion of cases with ≥ 12 lymph nodes removed during surgery was 82.6% in the low-volume centres, and significantly lower than that in the high- (86.7%) and very high-volume (85.4%) centres.

[Table 3](#) shows the multivariate analyses assessing the association between the quartile of case-volume and the five outcomes in the overall population, adjusted for age, gender, AJCC stage, cancer site (rectum versus others) and urgent surgery. The low-volume centres were significantly associated with a higher risk of severe complications (OR 1.5, 95% c.i. 1.15–1.96) than the very high-volume centres. A significantly higher risk of mortality associated with low- versus very high-volume centres was found in the model before the introduction of the variable ‘urgent surgery’ (before: OR 1.62, 95% c.i. 1.02–2.58, $P=0.40$; after: OR 1.29, 95% c.i. 0.80–2.07, $P=0.3$), as shown in [Tables S2, S3](#).

The probability of adequate lymph node sampling was significantly lower in the low-volume (OR 0.68, 95 per cent c.i. 0.56–0.85, $P<0.001$) and in the medium-volume (OR 0.72, 95 per cent c.i. 0.62–0.83, $P<0.001$) centres than in the very high-volume centres.

When only cases of rectal cancer were considered ([Table 4](#)), low-volume centres reported a significantly lower rate of adequate lymph node removal (OR 0.57, 95% c.i. 0.41–0.80, $P=0.001$) than the very high-volume centres. In the latter centres, patients affected by rectal cancer were more likely to undergo neoadjuvant therapy than those who were treated in high- (OR 0.65, 95% c.i. 0.56–0.77, $P<0.001$), medium- (OR 0.75, 95% c.i. 0.60–0.92, $P=0.006$) and low-volume (OR 0.70, 95% c.i. 0.52–0.94, $P=0.019$) centres, even after adjustment for confounders.

The results of the additional analysis of the same outcomes evaluated in the subsample of patients undergoing surgery for rectal cancer when hospital volume was categorized adopting a minimum threshold of ≥ 10 surgical procedures per year are shown in [Tables S4, S6](#).

Discussion

In this national multicentre study, patients who underwent surgery in a very high-volume centre had a higher chance of adequate lymph node resection. In addition, more frequent utilization of neoadjuvant therapy was observed in the very high-volume centres as compared to all others. Comparing these results to those in the current literature is challenging, as it is unclear¹³ whether low volumes are associated with more frequent postoperative complications and mortality as well as worse pathological/oncological outcomes. A recent

meta-analysis showed significant heterogeneity of study populations, location of the cancer and definition of high and low volume³. Most studies simply dichotomized the volume based on the median, and the thresholds varied greatly in both the ‘low-’ and ‘high-’ volume centres. In addition, only one study reported the outcomes separately for the colon and the rectum¹⁴. Of the 47 studies included in the meta-analysis, only 21 reported a statistical adjustment for potential confounders, confirming that the lack of standardization of the methodological quality was a major limitation in many surgical studies¹⁵.

In the present study, age, gender, AJCC stage and urgent surgery were included in the multivariate analysis *a priori* in order to reduce the bias represented by the expected differences among the centres. Urgent surgery in particular was included because a greater percentage of patients underwent urgent surgery in the low-volume centres (17.5% versus 7.6% in the high and very high-volume centres). Interestingly, this resulted in the difference in the rate of mortality between low- and very high-volume centres no longer being statistically significant (from OR 1.62, 95% c.i. 1.02–2.58, to OR 1.29, 95% c.i. 0.80–2.07), indicating the prevailing effect of the timing of surgery on the risk of mortality. Previous studies have shown that perioperative mortality could increase up to 34% when emergency surgery for colorectal cancer was carried out¹⁶. In the present series, however, urgent surgery was defined as any operation that was performed in the first 48 h after admission. This definition did not strictly refer only to emergency cases, and likely also included those cases that might have been initially treated conservatively, for example by stenting¹⁷. Moreover, the lack of a dedicated colorectal cancer pathway might have increased the utilization of urgent surgical care and, therefore, increased the risks of suboptimal preoperative assessment of these complex patients. Other significant findings among cases treated in low-volume centres were the inadequate lymph node sampling in both overall (OR 0.68, 95% c.i. 0.56–0.85) and rectal cancer (OR 0.57, 95% c.i. 0.41–0.80) cohorts, as well as the use of neoadjuvant therapy in cases of rectal cancer (OR 0.70, 95% c.i. 0.52–0.94). A similar difference was found when centres were grouped into high- (≥ 10 cases per year) and low-volume (<10 cases per year) hospitals. While similar findings regarding the association between suboptimal lymph node removal and surgery performed in low-volume centres have been extensively noted in lung, pancreatic and gastric cancer surgery^{18–21}, similarly clear evidence regarding colorectal cancer has been lacking^{6,22,23}. Although the significance of the number ‘12’ as a threshold has been criticised over the years²⁴, it remains one of the most important markers of oncologic adequacy and could reflect not only the expertise of the surgeon but also that of the pathologist^{25,26}. This might also explain the reduced rate of neoadjuvant therapy in rectal cancer that was observed in all centres when compared to the very high-volume centres. Similar findings have also been reported by other authors^{27,28}.

The present study has a few limitations. Concerning the study design, no long-term follow-up was recorded, and therefore the impact of hospital volume on survival could not be analysed. In addition, the study period partially covered the COVID-19 pandemic, which could represent a source of deviation from the usual outcomes. Moreover, for cases to be included, centres had to voluntarily enrol in the study. This probably excluded many of the smallest centres that are usually included in population-based studies. On the other hand, as proven by the

present and other authors' analyses, the pandemic did not affect the outcomes of colorectal cancer surgery in terms of postoperative complications and adequacy of treatment^{8,29}. The voluntary enrolment of the 80 centres provided validated data of a large population of patients treated all over the country in different types of hospitals and collected over a 4-year period, thus counterbalancing the potential variations of volumes and outcomes between years.

A call for the centralization of at least rectal cancer would be a rational answer to these findings. However, drastic variation has been observed regarding the correlation between case volume and outcomes in individual hospitals, as shown by Becerra *et al.* in their study analysing rectal cancer cases from the United States National Cancer Database²⁷. Other points should be taken into consideration, namely the possibility of improving colorectal cancer pathways in low-volume centres by implementing multidisciplinary case discussion and audit of outcomes. Moreover, rural or community hospitals with low case volumes could concentrate their colorectal cancer cases at a dedicated local surgical centre in order to increase the volume and improve the outcome.

Although its limitations should be acknowledged, the present study confirmed that hospital volume is strongly associated with the risk of postoperative complications and oncologic adequacy of surgery for colorectal cancer.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at BJS online.

Data availability

The data will be made available upon request to the corresponding author.

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Title: Effect of centre volume on pathological outcomes and postoperative complications after surgery for colorectal cancer: results of a multicentre national study

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Supplementary Table 1.

Centres grouped according to hospital volume quartiles within the 4-years of the study (2018-2021)

Group	Number of procedures (4 years)	Overall number of patients	Number of centers
LOW	19-111	999	21
MEDIUM	112-167	2644	19
HIGH	168-263	4675	20
VERY-HIGH	≥264	8565	20

Supplementary Table 2 - Results of the multivariate analysis evaluating the association between hospital volume with postoperative outcomes (2A) and pathological and oncological outcomes (2B) in the overall cohort when not adjusted for urgent surgery

Supplementary Table 2A.

Hospital volume ‡	%	30-day mortality (n=266)		Severe complications (n=1670)		
		OR (95% CI)	p	%	OR (95% CI)	p
Very high	1.5	1 (ref. cat.)	--	33.3	1 (ref. cat.)	--
High	1.5	0.94 (0.68-1.30)	0.7	35.3	1.10 (0.94-1.29)	0.2
Medium	1.9	0.87 (0.55-1.37)	0.5	34.4	0.97 (0.78-1.20)	0.8
Low	2.5	1.62 (1.02-2.58)	0.040	42.6	3.28 (1.19-2.02)	0.001

Supplementary Table 2B. Overall - Multivariate analyses evaluating the association between hospital volume, and each pathological and oncologic outcome recorded *.

Hospital volume ‡	%	Removal of ≥12 nodes (n=13,497)		Non-radical resection (n=429)		
		OR (95% CI)	p	%	OR (95% CI)	p
Very high	85.4	1 (ref. cat.)	--	2.9	1 (ref. cat.)	--
High	86.7	1.12 (0.99-1.27)	0.070	2.3	0.94 (0.73-1.21)	0.6
Medium	83.3	0.72 (0.62-0.83)	<0.001	2.2	0.71 (0.49-1.01)	0.06
Low	82.6	0.68 (0.56-0.84)	<0.001	2.0	0.74 (0.46-1.20)	0.2

‡ Hospital procedure volume was defined as the number of surgical procedures performed during the study period (2018-2021). Low-volume hospitals performed between 19 and 111 procedures; medium-volume hospitals performed between 112 and 167 procedures; high-volume hospitals performed between 168 and 263 procedures; very high-volume hospitals performed between 264 and 638 procedures.

* All final models were adjusted for: age, gender, lesion site (rectum vs. others), aggressive biology, AJCC stage, history of previous colorectal cancer, history of inflammatory bowel disease, presence of other comorbidities and familial history of colorectal cancer. Severe complications were classified as Clavien-Dindo grade 3 and higher.

OR: odds ratio; CI: confidence interval; ref. cat.: reference category; AJCC: American Joint Committee on Cancer

Supplementary Table 3 - Results of the multivariate analysis evaluating the association between hospital volume with postoperative outcomes (3A) and pathological and oncological outcomes (3B) in the rectal cancer cohort when not adjusted for urgent surgery

Supplementary Table 3A.

Hospital volume ‡	30-day mortality** (n=51)			Severe complications (n=569)		
	%	OR (95% CI)	p	%	OR (95% CI)	p
Very high	0.8	1 (ref. cat.)	--	37.7	1 (ref. cat.)	--
High	1.1	1.31 (0.65-2.63)	0.5	34.5	0.89 (0.66-1.19)	0.4
Medium	1.6	1.67 (0.89-3.96)	0.09	43.4	1.28 (0.87-1.87)	0.2
Low	2.2	1.21 (0.86-6.43)	0.09	48.7	1.48 (0.91-2.83)	0.12

Supplementary Table 3B.

Hospital volume ‡	Removal of ≥12 nodes (n=3042)			Non-radical resection (n=214)		
	%	OR (95% CI)	p	%	OR (95% CI)	p
Very high	72.3	1 (ref. cat.)	--	5.1	1 (ref. cat.)	--
High	73.3	1.13 (0.93-1.36)	0.2	4.2	0.79 (0.54-1.15)	0.2
Medium	72.9	0.90 (0.71-1.15)	0.4	3.8	0.56 (0.32-0.98)	0.01
Low	63.5	0.58 (0.42-0.81)	0.01	4.4	0.78 (0.39-1.57)	0.5

‡ Hospital procedure volume was defined as the number of operations performed during the study period (2018-2021). Low-volume hospitals performed between 19 and 111 procedures; medium-volume hospitals performed between 112 and 167 procedures; high-volume hospitals performed between 168 and 263 procedures and very high-volume hospitals performed between 264 and 638 procedures.

* All final models were adjusted for age, gender, aggressive biology, AJCC stage, history of previous colorectal cancer, history of inflammatory bowel disease, presence of other comorbidities and familial history of colorectal cancer. Severe complications were classified as Clavien-Dindo grade 3 and higher.

** Due to the scarce number of successes (n=51), the final model was adjusted for age, gender, AJCC stage, history of previous colorectal cancer.

OR: odds ratio; CI: confidence interval; ref. cat.: reference category.

Supplementary Table 4. Selected demographic and clinical characteristics and outcomes, overall and by hospital surgical volume ([‡] high volume: ≥10 surgery cases per year; low volume: <10 surgery cases per year) in the sub-sample of patients with rectal cancer.

	Overall sample	Low volume[‡]	High volume[‡]	p **
Patients (hospitals), n	4676 (79)*	869 (39)	3807 (40)	
Male gender, %	39.1	40.6	38.8	0.3
Mean age at diagnosis in years (SD)	67.8 (12.3)	69.6 (11.7)	67.4 (12.4)	<0.001
Mean BMI (SD)	25.3 (4.3)	25.3 (4.0)	25.3 (4.0)	0.9
Current or past smoker, %	44.9	42.8	45.4	0.2
Surgery performed during the pandemic period, %	42.6	47.4	41.6	0.02
<i>Comorbidities:</i>				
Family history of colorectal cancer, %	11.7	9.4	12.2	0.04
Previous history of colorectal cancer, %	2.3	0.8	2.7	0.001
Previous history of cancer (others), %	10.4	8.6	10.5	0.06
Inflammatory bowel disease, %	1.15	1.15	1.16	0.9
Other comorbidities, %				0.6
- None	26.9	27.5	26.8	
- 1	41.0	42.0	41.0	
- 2	22.8	22.2	22.9	
- 3 or more	9.3	8.3	9.6	
Previous polypectomy, %	1.5	1.3	1.5	0.6
Asymptomatic disease, %	15.2	14.5	15.3	0.5
Fecal occult blood test performed, %	(n=4510) 20.8	(n=782) 20.6	(n=3728) 20.3	0.9
T4 stage, %	6.9	6.9	6.9	0.9
Synchronous adenomas, %	(n=4326) 19.8	(n=740) 16.8	(n=3586) 20.4	0.03
Synchronous cancers, %	(n=4330) 3.7	(n=771) 3.5	(n=3559) 3.7	0.8
Metastatic lesions, %	10.9	11.4	10.8	0.6
Stenosing lesions, %	8.6	9.6	8.3	0.2
Urgent surgery, %	4.2	7.9	3.3	<0.001
Mean serum Hb, g/dL (SD)	(N=4257) 128.2 (18.5)	(N=783) 123.4 (19.0)	(N=3474) 129.3 (18.2)	<0.001
Mean blood glucose, mg/dL (SD)	(N=4057) 105.5 (29.0)	(N=687) 108.8 (33.8)	(N=3370) 104.9 (27.9)	0.001
Median CEA, ng/mL (IQR)	(N=3021) 2.8 (4.8)	(N=459) 3.0 (6.0)	(N=2562) 2.4 (5.0)	<0.001
ASA score >2, %	37.9	42.1	37.0	0.005
	(N=2976)	(N=663)	(N=2313)	

Anastomosis, %	88.3	86.4	88.9	0.09
Additional surgery, %	10.5	10.1	10.5	0.7
Laparoscopic surgery, %	74.0	64.0	76.2	<0.001
Conversion to open surgery, %	(N=3442) 6.7	(N=554) 7.6	(N=2888) 6.5	0.3
Loop ileostomy, %	(N=3560) 56.9	(N=672) 49.1	(N=2888) 58.7	<0.001
ICU admission, %	14.2	13.7	14.3	0.7

* 1 Unit reported zero cases of rectal cancer surgery. ** Chi-squared test for categorical variables; t-test and Kruskal-Wallis test for parametric and non-parametric continuous variables, respectively.

SD: standard deviation; IQR: interquartile range; BMI: Body Mass Index; CEA: carcinoembryonic antigen; ASA: American Society of Anesthesiologists; ICU: Intensive Care Unit.

Supplementary Table 5. Pathological and postoperative variables and outcomes, overall and by hospital surgical volume ([†] high volume: ≥10 surgery cases per year; low volume: <10 surgery cases per year) in the sub-sample of patients with rectal cancer.

	Overall sample 4676 (79)*	Low volume* 869 (39)	High volume* 3807 (40)	p **
Patients (hospitals), n				
Multiple lesions, %	4.2	3.9	4.2	0.7
	(N=4235)	(N=826)	(N=3409)	
Aggressive biology, %	60.9	59.2	60.3	0.3
Histology, %				
- Adenocarcinoma	96.3	96.4	96.3	0.9
AJCC stage, %	(N=4235)	(N=826)	(N=3409)	
- 0	3.4	3.2	3.5	0.3
- I	32.5	26.4	34.0	<0.001
- II	24.0	28.0	23.0	0.003
- III	28.0	30.4	27.4	0.02
- IV	12.1	12.0	12.1	0.9
Median in-hospital length of stay (IQR)	8.0 (6.0)	8.0 (6.0)	8.0 (6.0)	0.9
<i>Postoperative medical complications, %:</i>				
All complications ^E	16.2	18.2	15.7	0.07
Anemia	3.7	6.1	3.2	<0.001
Pulmonary complications ^F	2.7	3.3	2.6	0.2
Sepsis	2.1	2.3	2.1	0.3
Acute kidney failure	1.3	1.6	1.2	0.4
Myocardial infarction	0.36	0.81	0.26	0.02
Venous thromboembolism	0.32	0.23	0.34	0.6
Pulmonary embolism	0.21	0.12	0.24	0.5
Stroke	0.11	0.12	0.11	0.9
<i>Postoperative surgical complications, %:</i>				
All complications ^G	21.1	19.5	21.4	0.2
Surgical site infection	4.2	4.7	4.0	0.4
Intra-abdominal bleeding	1.1	1.4	1.1	0.4
Intra-luminal bleeding	0.66	0.69	0.66	0.9
Intra-abdominal sepsis ^H	9.2	8.6	9.3	0.5
Dehiscence	7.6	7.7	7.6	0.9
Abdominal abscess	3.9	2.3	4.3	0.007
Peritonitis	0.81	0.46	0.89	0.2
Paralytic ileus	2.9	2.2	3.1	0.2
Bowel occlusion	1.5	1.0	1.7	0.2
<i>Outcomes:</i>				
30-day mortality, %	1.1	2.1	0.87	0.002
	(N=1484)	(N=274)	(N=1210)	
Clavien-Dindo classification ≥3, %	38.3	39.8	38.0	0.6
<i>Number of resected lymph nodes:</i>				
- Median (IQR)	(N=4213) 15.0 (10.0)	(N=804) 14.0 (10.0)	(N=3409) 15.0 (11.0)	<0.001
- ≥12 lymph nodes, %	72.2	67.9	73.2	0.033
Non- radical surgery, %	4.7	4.8	4.6	0.8
Neoadjuvant therapy, %	49.9	40.6	52.0	<0.001

* 1 Unit reported zero cases of rectal cancer surgery. ** Chi-squared test for categorical variables; t-test and Kruskal-Wallis test for parametric and non-parametric continuous variables, respectively.

^E Including: anemia, myocardial infarction, stroke, pulmonary embolism, venous thromboembolism, acute kidney failure, sepsis, pneumonia, acute respiratory distress syndrome, respiratory failure.

^F Pneumonia, and/or acute respiratory distress syndrome, and/or respiratory failure.

^G Including intra-abdominal or intra-luminal bleeding, dehiscence, surgical site infection, abdominal abscess, peritonitis, paralytic ileus, bowel occlusion.

^H Including dehiscence, abdominal abscess, and peritonitis.

SD: standard deviation; IQR: interquartile range; AJCC: American Joint Committee on Cancer.

Supplementary Table 6 - Results of the multivariate analysis evaluating the association between hospital volume with postoperative outcomes (6A) and pathological and oncological outcomes (6B) in the rectal cancer cohort

Supplementary Table 6A.

Hospital volume ‡	30-day mortality** (n=51)			Severe complications (n=569)		
	%	OR (95% CI)	p	%	OR (95% CI)	p
High	0.87	1 (ref. cat.)	--	38.0	1 (ref. cat.)	--
Low	2.07	1.73 (0.84-3.55)	0.13	39.8	1.15 (0.84-1.56)	0.4

Supplementary Table 6B.

Hospital volume ‡	Removal of ≥12 nodes (n=3042)			Non-radical resections (n=214)			Neoadjuvant therapy (n=2331)		
	%	OR (95% CI)	p	%	OR (95% CI)	p	%	OR (95% CI)	p
High	73.2	1 (ref. cat.)	--	4.6	1 (ref. cat.)	--	52.0	1 (ref. cat.)	--
Low	67.9	0.65 (0.54-0.80)	<0.001	4.8	0.77 (0.50-1.18)	0.2	40.6	0.64 (0.54-0.77)	<0.001

‡ Hospital procedure volume was defined as the number of surgical procedures performed during the study period (2018-2021). High volume: ≥10 surgery cases per year; low volume: <10 surgery cases per year.

* All final models were adjusted for age, gender, aggressive biology, AJCC stage, urgent surgery, history of previous colorectal cancer, history of inflammatory bowel disease, presence of other comorbidities and familial history of colorectal cancer. Severe complications were classified as Clavien-Dindo grade 3 and higher.

** Due to the scarce number of successes (n=51), the final model was adjusted for age, gender, AJCC stage, history of previous colorectal cancer.

OR: odds ratio; CI: confidence interval; ref. cat.: reference category.