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The association between hospital and surgeon volume and rectal cancer surgery outcomes in rectal cancer patients treated since 2000: systematic literature review and meta-analysis

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Abstract

Background: Previous reviews and meta-analyses, which predominantly focused on patients treated before 2000, have reported conflicting evidence about the association between hospital/surgeon volume and rectal cancer outcomes. Given advances in rectal cancer resection such as total mesorectal excision, it is essential to determine if volume plays a role in rectal cancer outcomes among patients treated since 2000.

Objective: Determine if there is an association between hospital/surgeon volume and rectal cancer surgery outcomes among patients treated since 2000.

Data sources: We searched PubMed and Embase for articles published between January 2000 and 29 December 2017.

Study selection: Articles published between January 2000 and 29 December 2017 that analyzed the association between hospital/surgeon volume and rectal cancer outcomes.

Study selection: Rectal cancer resection.

Main outcome measures: The outcomes of this study were surgical morbidity, post-operative mortality, surgical margin positivity, permanent colostomy rates, recurrence, and overall survival.

Results: While 2,845 articles were retrieved and assessed by the search strategy, 21 were met the inclusion and exclusion criteria. There was a significant protective association between higher hospital volume and surgical morbidity [Odds Ratio = 0.80 (0.70, 0.93); I^2=35%], permanent

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colostomy [Odds Ratio = 0.51 (0.29, 0.92); I^2=34%] and post-operative mortality [Odds Ratio = 0.67 (0.50, 0.90); I^2=41%]. Stratified analysis showed variation in significance between hospital volume and rectal surgery outcomes by geographic location. Hospital and surgeon volume were not significantly associated with overall survival. The articles included in this analysis were high quality according to the Newcastle Ottawa scale. Funnel plots suggested that the potential for publication bias was low.

Limitations: Variations in volume definitions across the studies limits inference about the appropriate minimum volume threshold value associated with better outcomes.

Conclusion: Among patients diagnosed since 2000, higher hospital volume has a significant protective effect on rectal cancer surgery outcomes.

Introduction

Rectal cancer is expected to account for approximately 43,000 newly diagnosed cancer cases in the United States in 2018[1]. Currently, the advanced rectal cancer standard of care is a multimodal approach which entails neoadjuvant therapy and surgery[2,3]. Surgical excision of the rectum is complex because of its proximity to genitourinary organs, and the bony confines of the pelvis which present challenges to achieving good oncologic outcomes while minimizing morbidity[4,5]. Even though advances in rectal cancer management, such as total mesorectal excision (TME), have improved oncologic and quality of life outcomes for rectal cancer patients[6–10], the average 5-year survival rate is only 66%[11]. Determining factors that affect rectal cancer surgery outcomes is essential to improving morbidity and mortality in rectal cancer patients.

In particular, it has been postulated that surgeons and hospitals that treat a high volume of rectal cancer patients have better rectal cancer surgery outcomes[12,13]. High volume subspecialty trained surgeons have better outcomes based on their training, volume and experience, while high volume hospitals achieve superior outcomes based on available resources and multidisciplinary care[13]. Nevertheless, previous reviews analyzing the association between hospital volume and rectal cancer surgery outcomes have been inconsistent[13–15]. These reviews included studies that had patients treated for rectal cancer from 1990 through the early 2000s[13–15]. Given the widespread use of technically complex TME and advances in rectal cancer management such as sphincter preserving surgery and neoadjuvant therapy since 2000, it is essential to evaluate the effect of surgeon and hospital volume on patient outcomes based on current practice. Hence, the purpose of this meta-analysis is to estimate the strength of the association between hospital/surgeon volume and outcomes in rectal cancer patients who received surgery since 2000.

Materials and Methods

Search strategy

Boolean logic was used to retrieve relevant PubMed and Embase English articles published from 1 January 2000 to 29 December 2017 using the following keywords; (“colorectal cancer” or (“rectal/rectum cancer”) and “surgery” and (hospital volume” or “surgeon volume” or “hospital caseload” or “surgeon caseload” or “hospital workload” or “surgeon workload" or "surgical volume" or "surgical caseload" or "surgical workload") and ("treatment outcomes" or "treatment failure" or "adverse" or "surgical complications" or "intraoperative complications" or "postoperative complications" or "stoma" or "quality of healthcare" or "length of stay" or "recurrence" or "mortality" or "survival"). Relevant articles were retrieved from references found from PubMed and Embase articles.

Article titles and abstracts that were identified from the literature using the above search strategy were uploaded to Endnote; no duplicates were found. The eligibility of research articles was assessed by four reviewers (CC, JS, NDV and MC). Two reviewers were involved in the data abstraction process (CC and NDV). Disagreements pertaining to the eligibility of articles or data abstraction was resolved via discussion.

Inclusion and exclusion criteria

This systematic literature review included studies that reported results based on original data analyzing the association between hospital or surgeon volume and rectal cancer outcomes in patients treated since 2000. We included articles that included patients with cancer of the rectum or rectosigmoid junction; this information was based on the International Classification of Diseases, 9th Revision (ICD-9-M) codes or tumor location information. The articles had to have information about rectal cancer surgery, hospital or surgeon volume and patient outcomes after surgery. Studies that delineated between colon and rectal cancers were included in the analysis. Articles that were based on single institutions or had one hospital/surgeon volume level were excluded from the study since they did not compare outcomes across hospital/surgeon volume levels. Only English language peer-reviewed literature found in PubMed or Embase were reviewed to reduce bias since authors were unable to translate the Chinese articles. For further information, some authors were contacted.

Measures and outcomes

Hospital or surgeon volume were the primary exposures of interest. Hospital volume was defined as the mean/number of rectal and/or rectosigmoid resections (i.e. low anterior resection and abdominoperineal resection) per year or over the study period in a specific hospital. Surgeon volume was defined as either the mean/number of resections performed by a surgeon per year or over the study period. Hospital and surgeon volume categorizations were based on the definitions from the original articles. The outcomes of interest in this study were: surgical morbidity, post-operative mortality, surgical margin positivity, permanent colostomy rates, recurrence, and overall survival. Surgical morbidity included conditions such as anastomic leakage, abscess, iatrogenic complications, bleeding, peritonitis, stoma necrosis, stoma fistula, and wound dehiscence; the definition of surgical morbidity varied across the studies. Post-operative mortality was defined as death within 30 days of surgery. Follow-up time after rectal cancer surgery for articles that reported overall survival was defined as 1, 3 or 5 years.

Analysis

An evidence grid (Table 1) was constructed to characterize study population characteristics (age, cancer stage, type of surgery), sample size, study type and study results. Statistical significance from the articles was reported for effect sizes regardless of level of significance; in the presence of both bivariate and multivariate analyses, we reported multivariate effect sizes.

Review Manager 5[16] was used to perform the meta-analysis. A meta-analysis was performed when more than two studies reported on an outcome. A random effects model was used to perform a meta-analysis using statistically adjusted data from the included studies[17]. The meta-analysis used the natural logarithm of adjusted odds ratios that were extracted from the original articles, while the natural logarithm of standard errors was derived from the extracted confidence intervals. We stratified the analyses by the following factors: study location, type of outcome (i.e. surgical morbidity was stratified by articles reporting anastomic leak only versus studies that include anastomic leaks and other type of complications) and low volume definitions (≤ 11/ >11 rectal cancer resections per year). Articles were classified into ≤ 11 low volume definitions if low hospital volume was defined as less than or equal to eleven surgeries per year while the rest were classified into ≥11 rectal surgeries per year; this cutoff was based on the hospital volume distribution of the articles in the paper. Heterogeneity between studies was assessed using the I^2 statistic[18]. Risk of bias was assessed using the Newcastle Ottawa scale for observational studies[19]; this was assessed by 4 reviewers (CC, JS, NDV and MC). Funnel plots were used to evaluate publication bias.

Results

Description of Included Studies

The search strategy yielded 2,845 potentially relevant articles from PubMed (n=2,745) and Embase (n=100) (Figure 1). Of the 2,866 articles that were screened for eligibility based on the title, 2,820 were excluded, and an additional 121 articles were excluded after reading the abstract. There were 21 additional articles that were retrieved from the references of the remaining eligible articles (n=24); hence a total of 35 full articles were read to determine eligibility. Upon reading the full articles, 14 more articles were excluded because they did not meet the inclusion and exclusion criteria. Hence, a total of 21[20–40] articles were included in the meta-analysis.

Table 1 describes the characteristics of the studies that were included in the meta-analysis. Thirteen were from Europe[21–23,25–30], six studies were from the Northern America[20,31,32,34,36,37] and two were from Asia[33,35]. Only four studies were based on prospective cohort data[21–23,39]; two other studies were based on study populations derived from voluntary inclusion[33,37]. Population based datasets, such as cancer registries or state health records, were used in the remaining 15 studies[20,24–32,34,35,37,38,40]. The mean patient age ranged from 59 to 67 years[33,34,36,37,39] and there were more male versus female rectal cancer patients. Only five articles included rectosigmoid tumors[20,24,29,35,38], while five articles did not report on the inclusion of rectosigmoid tumors[25,28,30,33,34] and 11 articles did not include rectosigmoid tumors[21–23,26,27,31,32,36,37,39,40]. The types of surgeries reported in the decreasing order in the majority of articles were low anterior resection and abdominoperineal resection.

Risk of bias assessment

Based on the Newcastle Ottawa scale, the studies included were generally high quality studies (Figure 2). All the articles had an adequate selection of non-exposed cohorts, demonstrated that the outcome was not present before the beginning of the study and had study populations that were generally representative of rectal cancer patient demographic and disease stage. Of the 21 studies, only three studies did not have adequate follow-up time or had minimal loss to follow-up[27,29,38]. Even though all the studies included in the meta-analysis adjusted for potential confounders, the type of variables that were adjusted for varied across the studies. In particular, three studies did not adjust for cancer stage[31,32,35], 11 studies did not adjust for neoadjuvant treatment[20,24,26,28,30–33,38–40] and nine studies did not adjust for either type of surgery or urgency of surgery[21,27,34–39]. An evaluation of the funnel plots showed symmetry, suggesting that the potential of publication bias was limited (see Appendix).

Quantitative synthesis

Surgical morbidity—Higher hospital volume was significantly associated with decreased surgical morbidity [OR = 0.80; (0.70, 0.93); I^2=35%] in rectal cancer patients who received surgery since 2000 (Figure 3). Similar results were obtained after excluding the Yasunaga et al.[33] article to reduce heterogeneity because there is no standard neoadjuvant chemoradiation for rectal cancer and variation in types of rectal resection in Japan. Stratified analysis revealed a marginally significant association between higher hospital volume and surgical morbidity in five studies from non-USA countries [OR = 0.85 (0.72, 1.00); I^2=18%]. Yeo et al.[20] did a study in the USA that suggested that higher hospital volume is significantly associated with decreased surgical morbidity [OR = 0.71 (0.60, 0.83)]. Furthermore, hospital volume was significantly associated with surgical morbidity in studies that defined low volume as greater than 11 rectal cancer resections [OR = 0.77 (0.62, 0.97); I^2=56%] compared to those that defined low volume as less than or equal to 11 rectal cancer resections [OR = 0.86 (0.70, 1.04); I^2=5%]. Stratified analysis by the nature of the surgical morbidity also showed that studies that incorporated anastomic leakage and other complications, such as peritonitis and bleeding, had a significant association with hospital volume [OR = 0.76 (0.65, 0.90); I^2=36%]. However, Bos et al.[29] and Ortiz et al.[21] who only looked at the association between hospital volume and anastomic leakage did not report significant results (Table 1).

Pathological surgical margins, Permanent colostomy and Recurrence—Among the two studies that assessed pathological margins, Gietelink et al.[30] and Lorimer et al.[34] suggested that lower volume versus higher hospital volume was significantly associated with circumferential resection margins [OR = 1.54 (1.12, 2.11)] and positive surgical margins [OR = 1.45 (1.25, 1.70)], respectively. In addition, higher volume hospitals were 49% less likely to perform surgery with permanent colostomy compared to low volume hospitals [OR = 0.51 (0.29, 0.92); I^2=34%]. Among the two studies that assessed recurrence, higher hospital volume was not significantly associated with recurrence in either study [Ortiz et al.[23]: OR = 0.84 (0.48, 1.45); Ptok et al.[39]: OR = 0.99 (0.51, 1.91)].

Post-operative mortality—Higher hospital volume had a significantly protective association with post-operative mortality, however, these studies were moderately heterogeneous [OR = 0.67 (0.50, 0.90); I^2=41%] (Figure 4). The Leonard et al.[38] study which measured hospital volume continuously was excluded from this analysis because including it in the analysis introduced significant heterogeneity. The Leonard et al.[38] study reported borderline significant associations between hospital volume and post-operative mortality. Higher hospital volume was significantly associated with decreased post-operative mortality in the USA [Baek et al.[32]: OR = 0.45 (0.24, 0.84); Aquina et al.[31]: OR = 0.43 (0.21, 0.88)]. Nevertheless, hospital volume was not associated with post-operative mortality in studies from non-USA countries. Similar to the association between hospital volume and surgical morbidity, hospital volume was significantly associated with post-operative mortality in >11 low volume definitions studies [OR = 0.56 (0.38, 0.83); I^2=38] but not significant in >11 low volume definitions studies [OR = 0.76 (0.39, 1.50); I^2=48%].

Overall survival—Overall, survival appears marginally associated with hospital volume [OR = 0.95 (0.91, 1.00); I^2=92%] (Figure 5); this stratified analysis suggested significant heterogeneity. There was no significant association between hospital volume and overall survival in >11 low volume definition studies [OR = 0.92 (0.80, 1.05); I^2=92%]. Analysis of the association between hospital volume and overall survival by follow-up time differed; hospital volume was significantly associated with overall survival within 5 years [OR = 1.03 (1.01, 1.05); I^2=0%], while this association was not significant and had significant heterogeneity if follow-up time was more than 5 years [OR = 0.87 (0.74, 1.02); I^2=94%].

Similarly, surgeon volume was not significantly associated with overall survival [OR = 0.82 (0.62, 1.08); I^2=63%]; there was significant heterogeneity in this analysis. Richardson et al.[37] [OR = 0.67 (0.43, 1.02)], Comber et al.[40] [OR = 0.97 (0.93, 1.01)] and Gort et al.[28] [OR = 0.70 (0.47, 1.03)] reported no significant association between surgeon volume and overall survival.

Discussion and Conclusion

The results of this study are similar to what has been published by the Consortium for Optimizing the Treatment of Rectal Cancer (OSTRiCh)[4]. The results of this study suggest that high hospital volume is associated with lower odds of surgical morbidity, permanent colostomy and post-operative mortality. Surgeon volume was not significantly associated with overall survival.

Generally, the included studies had low heterogeneity. The similarity of these results to previously published meta-analyses is a strength of this study[13,15]. Furthermore, all the studies were sufficiently powered to analyze the association of interest, the potential for publication bias was low and the patients were representatives of rectal cancer patients. The inclusion of high quality studies with low risk of bias is another strength of the study.

A limitation in this analysis was that the definitions of hospital and surgeon volume were heterogeneous across the studies; some studies used continuous variables[38,40] and the cutoff values in studies with categorical definitions of volume differed[20–37,39] (Table 1). This introduced bias in the meta-analysis; nevertheless, the low heterogeneity in most of the analyses suggest that its impact may be minimal. In addition, there were variations in the studies based on data source, data period, geographic location, tumor location, neoadjuvant treatment and surgical procedures used. However, the use of stratified analysis was able to illuminate the volume-outcome association across some strata. Only eight of the studies accounted for clustering by surgeon or hospital[20–23,31,33,38,40]. Even though most studies adjusted for some potential confounders, most of them did not adjust for all confounders, which is probably due to limitations in data availability.

The significance of these associations differed across strata. In particular, while the volume-outcome relationship remained significant in USA based studies[20,31,32,34], this was not the case in non-USA based studies[21,22,24–29,33,35,36,38,40]. This is not surprising since most non-USA locations, especially in Europe, have centralized rectal cancer management centers while the USA does not; USA based articles generally had ≤11 low volume definitions (annual hospital volume between 5 and 11 surgeries) while non-USA based articles reported >11 low volume definitions (annual hospital volume greater than or equal to 20 surgeries) (Table 1). This suggests that centralization of rectal cancer management could result in better rectal cancer care management and ultimately improve outcomes in the USA. Baek et al.[32] indicated a significant association between non-mandated regionalization and improved outcomes in rectal cancer patients in New York, strengthening the argument for regionalization of rectal cancer surgery, which has also been shown in relation to other high risk procedures like esophagectomy and pancreatic surgery[41].

The association between volume and surgical morbidity, mortality, and overall survival was not significant in studies that had ≤ 11 low volume definitions while the aforementioned associations were significant in studies that had >11 low volume definitions (Table 2). This result suggests that there is a threshold volume that confers better outcomes; this is similar to what has been published previously on other high risk cancer resections[42]. Nevertheless, the variations in defining high versus low volume across the studies makes it difficult to infer the appropriate minimum threshold values that confer better outcomes.

The variation in significance between hospital volume and surgical morbidity type (anastomic leakage versus other surgical morbidity) suggests that high volume may be beneficial in preventing specific complications. Similar to what has been previously published[13,15,43], the significant association between hospital volume and <5 year overall survival suggests that volume does have a significant impact on short-term outcomes. However, this is in contrast to what was published in another review. A systemic literature review concluded that volume was not associated with rectal cancer outcomes[14] while two meta-analyses[13,15] reported the opposite, study types may also explain this variation. The differences in results may also be due to variations in factors, such as the populations of the studies, study period and types of rectal cancer resections received in those populations. Given that most rectal cancer recurrences occur within 5 years of diagnosis, it is not surprising that volume is not significantly associated with overall survival ≥5 years. The high heterogeneity between studies analyzing hospital volume and 5-year survival limit the inferences that can be made about this association, hence there is a need for further research in this area of inquiry.

The results of this study contribute to the body of knowledge that indicate that high hospital volume is associated with better outcomes among rectal cancer patients treated since 2000. Future research should determine how hospital and surgeon characteristics contribute to better outcomes in rectal cancer patients who receive surgery. In conclusion, as rectal cancer treatment becomes more complex, initiatives to reduce variation in outcomes by hospital and surgeon volume in countries such as the US are essential.

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Appendix

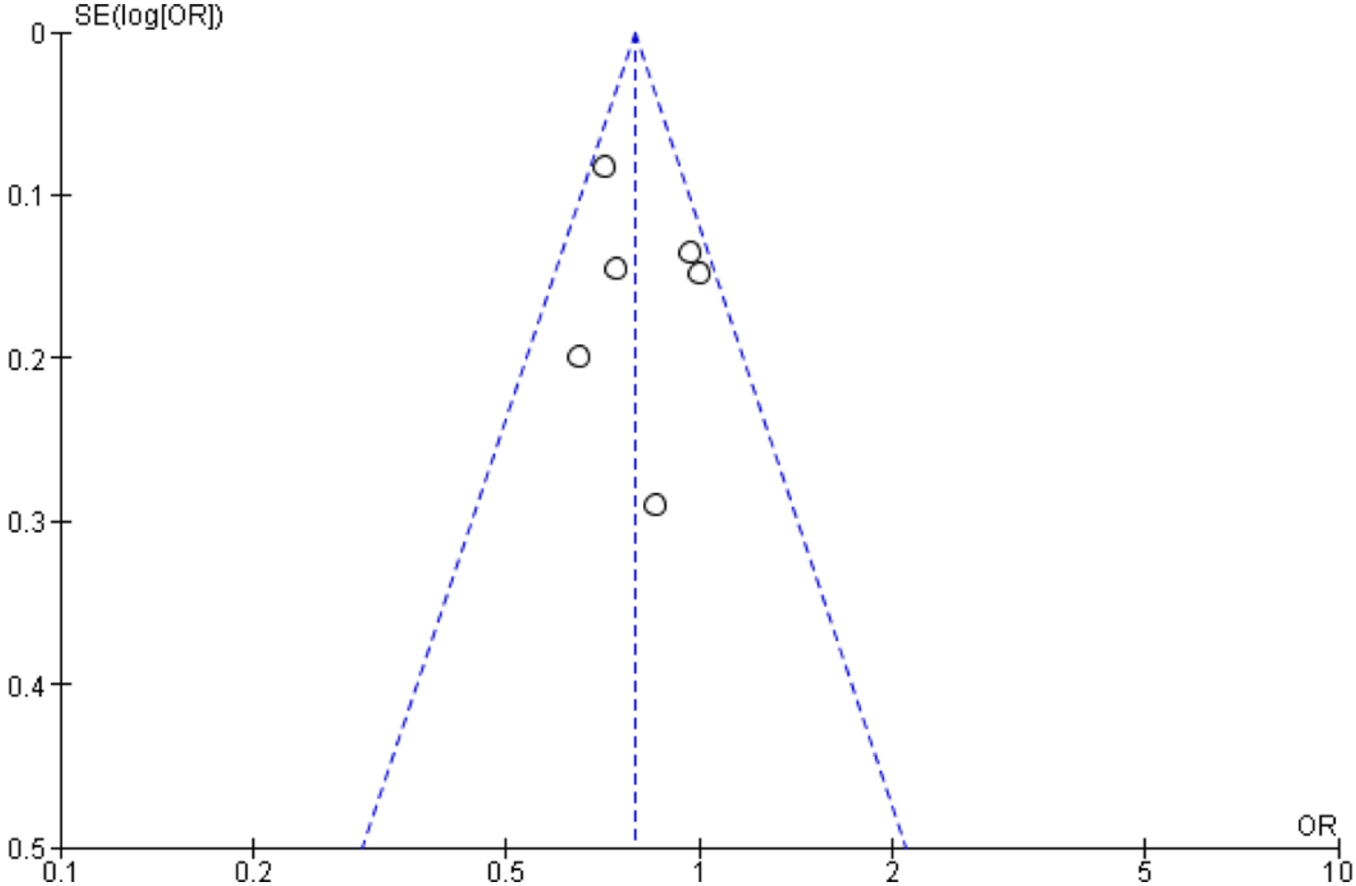

Figure A1:
Funnel plot of association between hospital volume and surgical morbidity

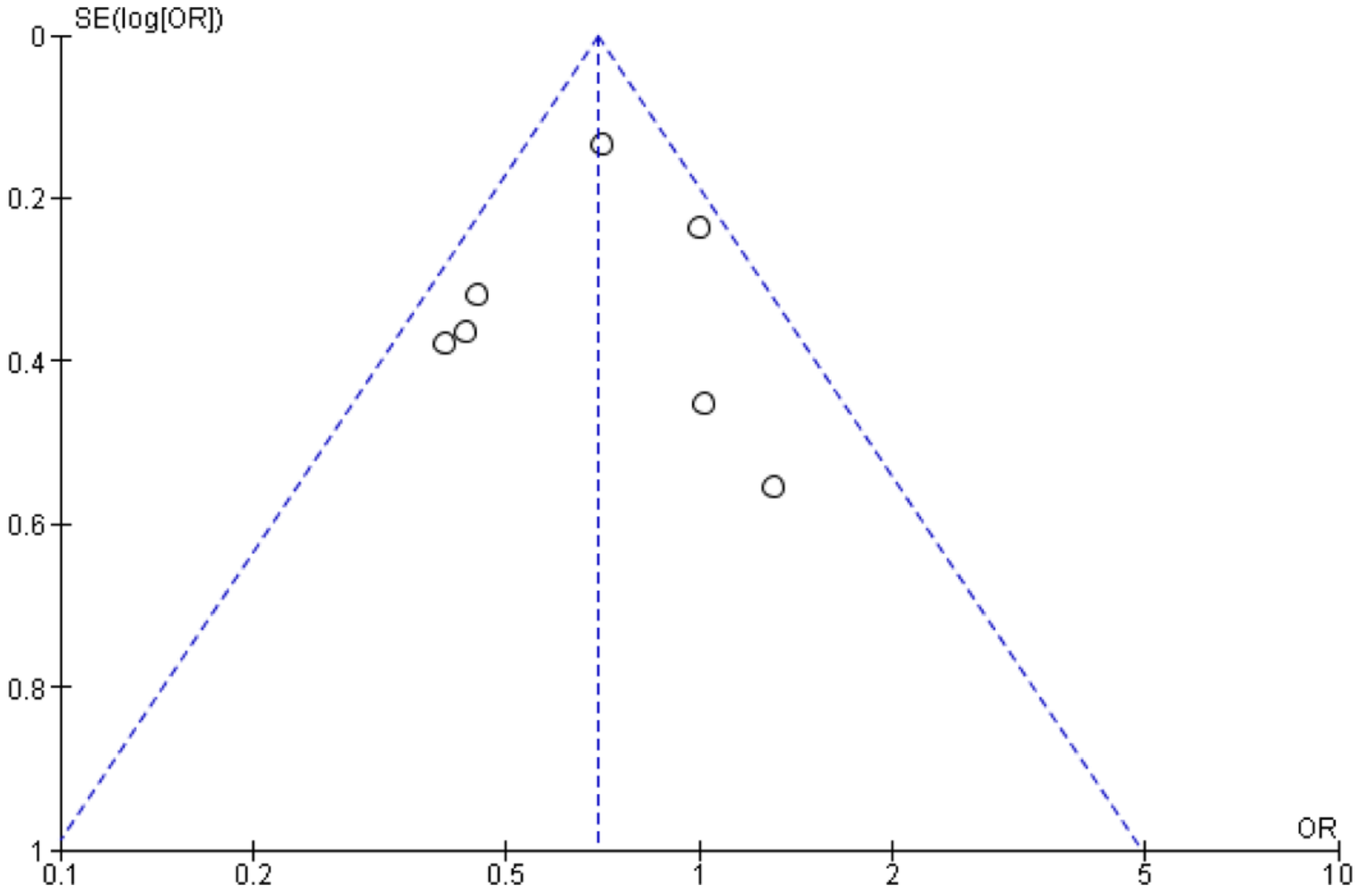

Figure A2:
Funnel plot of association between hospital volume and postoperative mortality

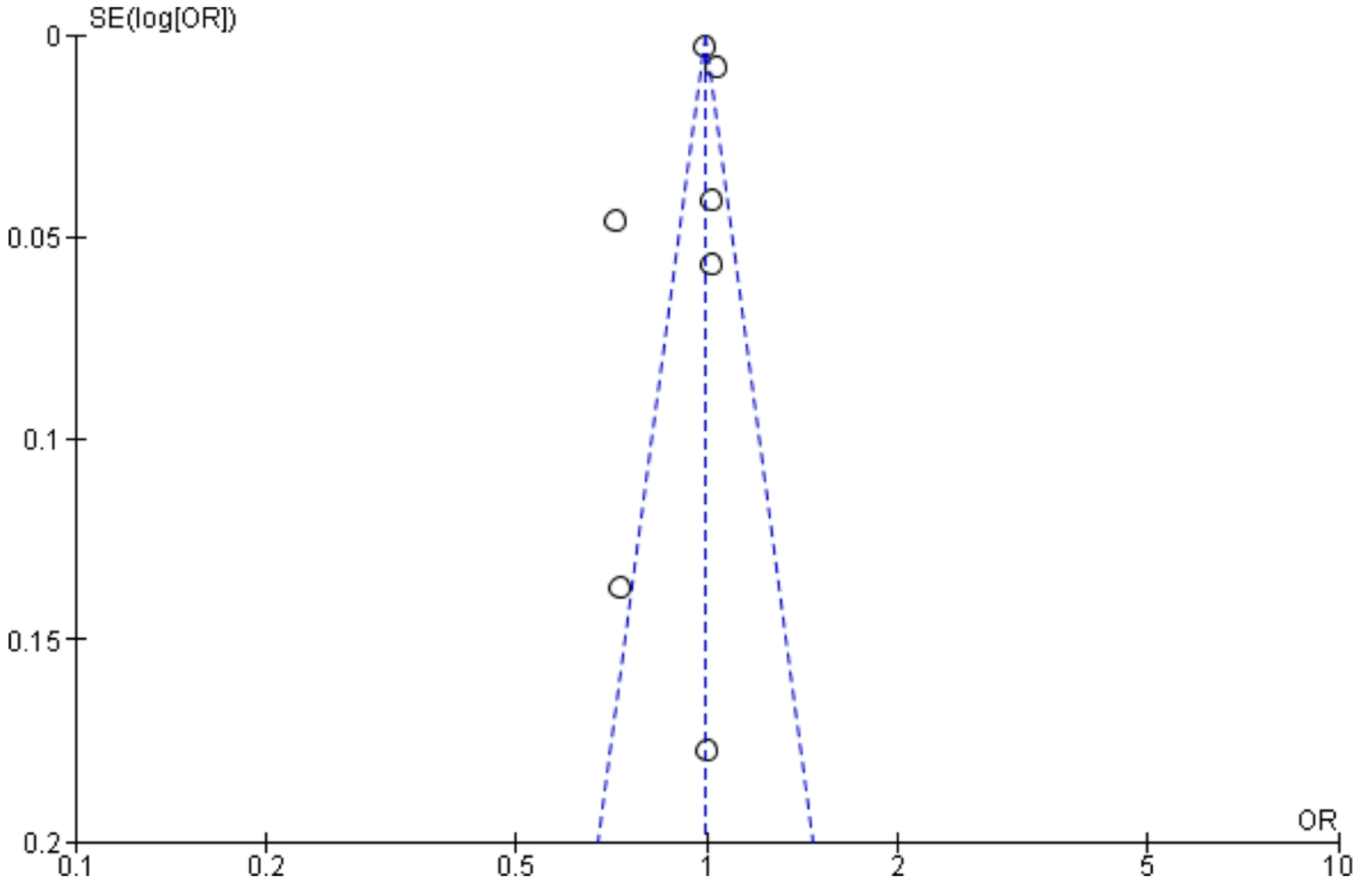

Figure A3:
Funnel plot of association between hospital volume and overall survival

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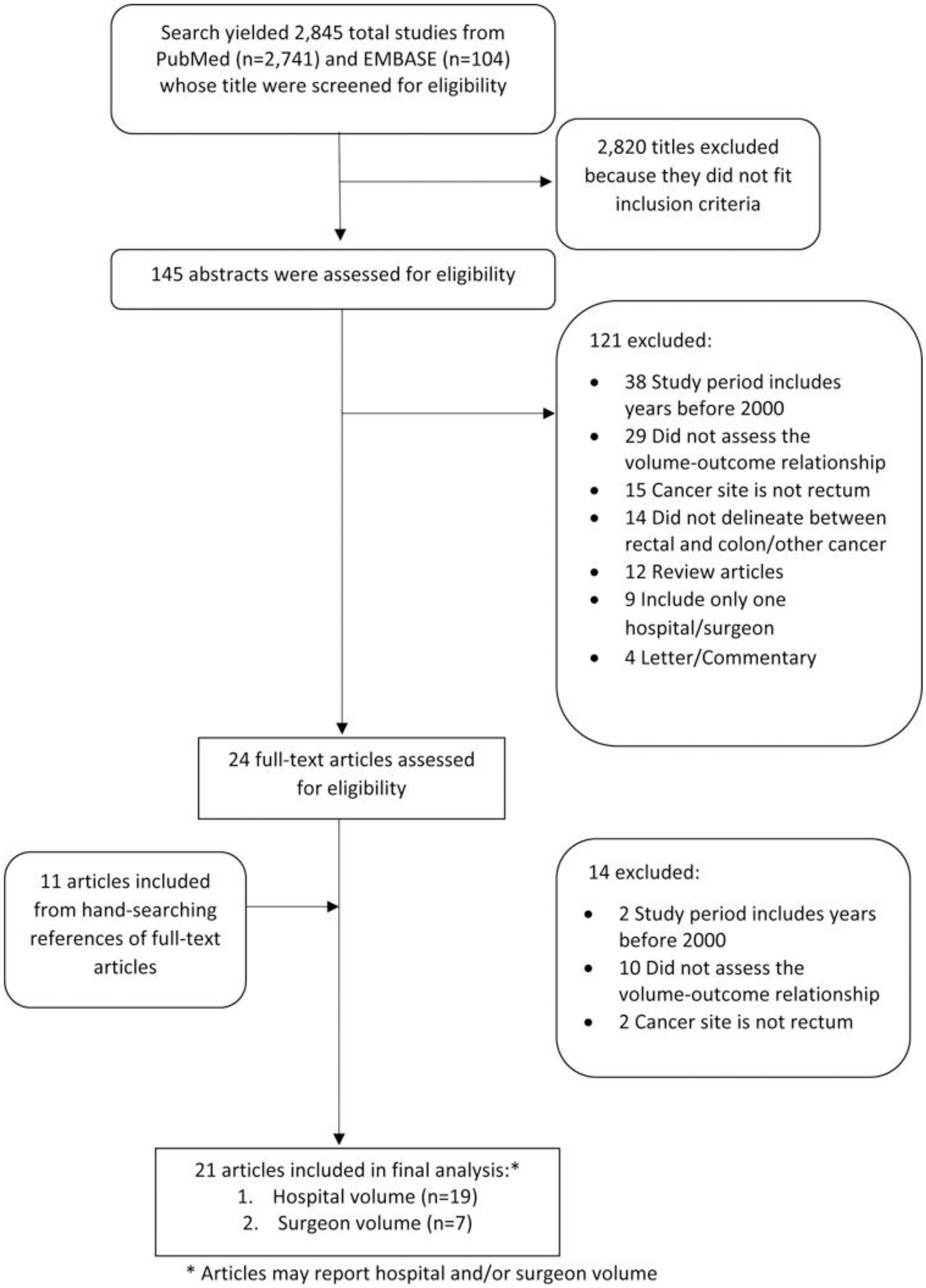


Figure 1.
Flow diagram of search strategy.

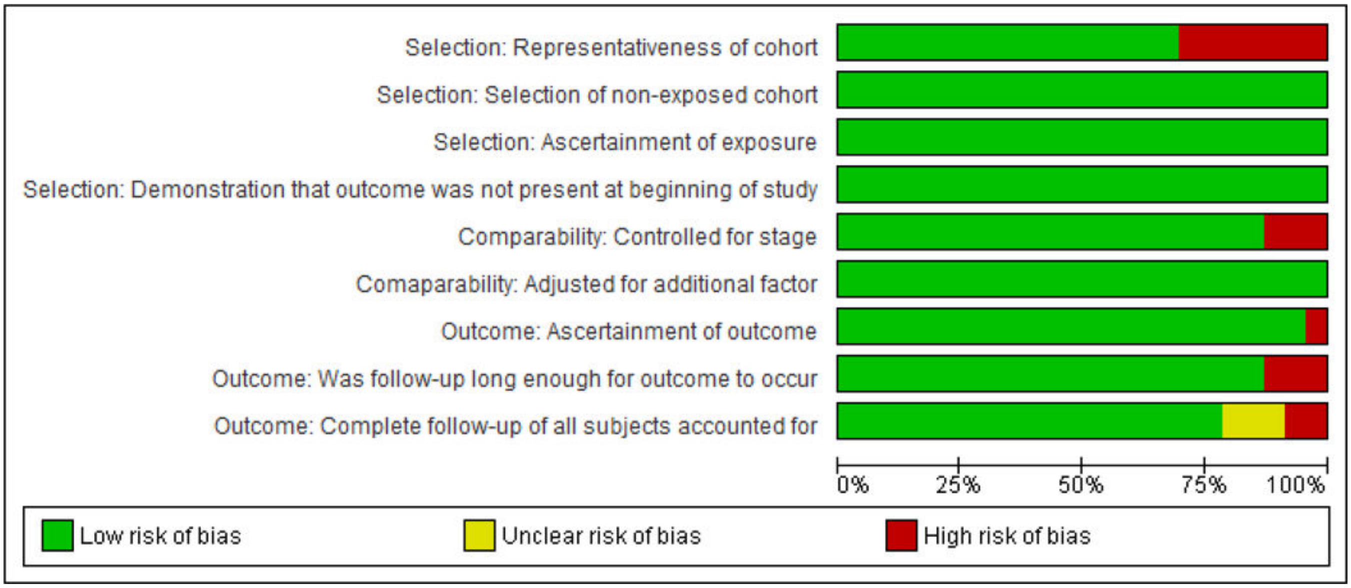


Figure 2.
Newcastle Ottawa Risk of Bias Assessment Summary

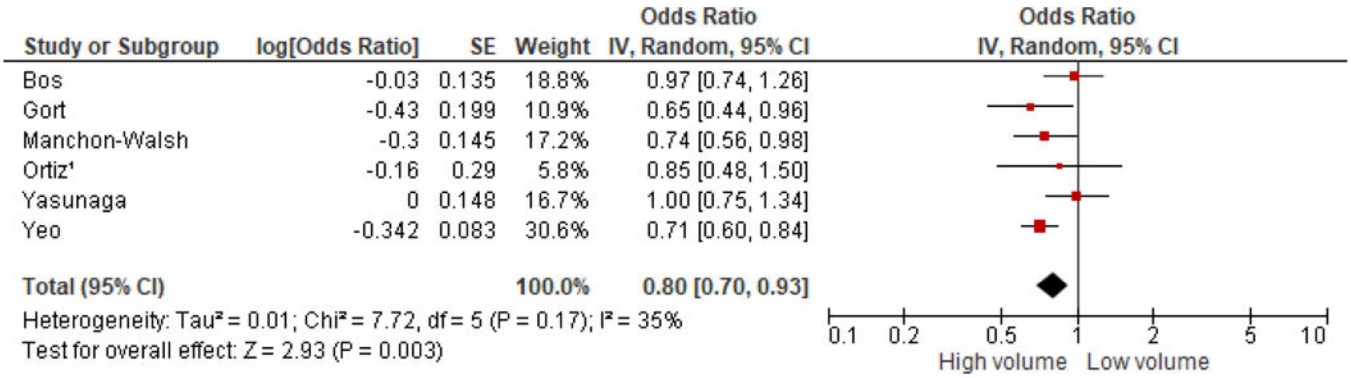
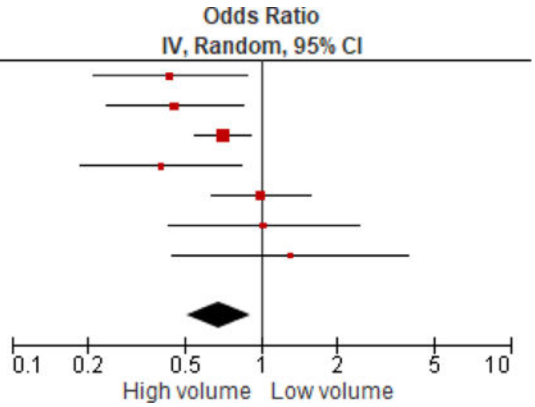


Figure 3.
Association between hospital volume and surgical morbidity



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aquina	-0.84	0.363	11.7%	0.43 [0.21, 0.88]
Baek	-0.8	0.32	13.9%	0.45 [0.24, 0.84]
Bos	-0.35	0.134	29.3%	0.70 [0.54, 0.92]
Elferink	-0.92	0.379	11.0%	0.40 [0.19, 0.84]
Kolfschoten	0	0.236	19.6%	1.00 [0.63, 1.59]
Manchon-Walsh	0.02	0.451	8.5%	1.02 [0.42, 2.47]
Ortiz²	0.269	0.554	6.1%	1.31 [0.44, 3.88]
Total (95% CI)			**100.0%**	**0.67 [0.50, 0.90]**

Heterogeneity: Tau² = 0.06; Chi² = 10.15, df = 6 (P = 0.12); I² = 41%
Test for overall effect: Z = 2.65 (P = 0.008)

Figure 4.

Association between hospital volume and post-operative mortality

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bos	0.02	0.041	15.9%	1.02 [0.94, 1.11]
Comber	0.03	0.008	26.4%	1.03 [1.01, 1.05]
Elferink	0.02	0.057	11.5%	1.02 [0.91, 1.14]
Leonard	-0.01	0.003	27.0%	0.99 [0.98, 1.00]
Ortiz[a]	-0.32	0.137	3.1%	0.73 [0.56, 0.95]
van Erning	0	0.177	1.9%	1.00 [0.71, 1.41]
Yun	-0.33	0.046	14.3%	0.72 [0.66, 0.79]
Total (95% CI)			**100.0%**	**0.95 [0.91, 1.00]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 77.50$, df = 6 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: $Z = 1.83$ ($P = 0.07$)

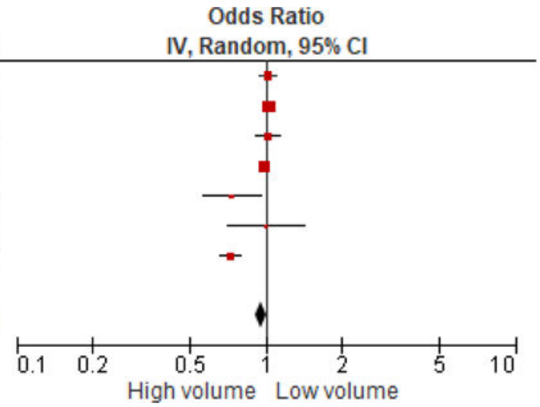


Figure 5.
Association between hospital volume and overall survival

Table 1.

Description of included studies

Study (Dates)	Study Type, Data source	Hospital, n Surgeon, n Patient, n	Patient characteristics: Location (Country/ State)	Patient characteristics: Age (years)[a] /M:F	Patient characteristics: Stage	Surgery type	Volume definition	Adjusted Results
Ptok 2007 [39]; (2000–2001)	Prospective cohort, study data (voluntary)	Patients: 1557	Germany	Median 66 26–92) / 1.6:1	UICC stage I = 16% II= 35% III =48%	LAR = 39% APR = 61%	Hospital volume *Number of annual surgeries* Low <10, Medium 10–19, High ≥20	Hospital HR (95%CI) [ref = High] ***Local recurrence rate***: Low 1.01 (0.83–1.52) Medium 1.39 (1.06–1.81) *
Yasunaga 2009 [33]; (2006–2007)	Retrospective cohort; Web based registration system (voluntary)	Hospital: 371 Patients: 2285	Japan	Mean = 67 (SD=11) / 1.8:1	*Stage* 0 = 2% I = 21% II = 28% III = 37% IV = 12%	HAR = 20% LAR = 55% APR = 19% Hartman = 6%	Hospital volume *Number of 2005 surgeries* Low ≤ 9 High ≥10 Surgeon volume *Number of cumulative surgeries* Very low ≤49 Low 50–99 High 100–499 Very High ≥500	OR (95%CI) [ref =Low] ***Intraoperative blood loss***: *Hospital*: High 1.09 (0.81–1.48) *Surgeon*: Low: 1.02 (0.73–1.42) *Surgeon*: High: 0.93 (0.67–1.28) *Surgeon*: Very High: 0.67 (0.46–0.99) * RR ratio (95%CI)(ref =Very low) ***Postoperative complications***: *Hospital*: High: 1.00 (0.75–1.34) *Surgeon*: Low: 0.92 (0.64–1.33) *Surgeon*: High: 0.94 (0.69–1.28) *Surgeon*: Very High: 0.93 (0.65–1.36) ***Length of stay***: *Hospital*: High 1.41 (1.23–1.62) * *Surgeon*: Low 0.99 (0.83–1.17) *Surgeon*: High 0.99 (0.85–1.16) *Surgeon*: Very High 1.09 (0.87–1.36)
Gort 2010 [28]; (2001–2005)	Retrospective cohort; North East cancer registry	Hospital: 16 Patients: 819	North East Netherlands	<70 = 58% ≥70 = 42% / 1.6:1	*TNM Stage* I = 32% II = 30% III = 38%	LAR = 40% APR = 42% Hartmann = 18%	Hospital volume *Mean annual surgeries* Low <20, Medium 20–40 High ≥40 Surgeon volume *Mean annual surgeries* Low <5, Medium 5–10, High ≥10	Hospital OR (95%CI) [ref = Low] ***Complications:*** Medium: 0.79 (0.52–1.20); High: 0.65 (0.44–0.96) * Surgeon HR (95%CI) [ref = Low] ***Overall Survival (3 years)***: Medium: 1.02 (0.73–1.42); High: 0.70 (0.47–1.03)

Study (Dates)	Study Type, Data source	Hospital, n Surgeon, n Patient, n	Patient characteristics: Location (Country/ State)	Patient characteristics: Age (years)[a] /M:F	Patient characteristics: Stage	Surgery type	Volume definition	Adjusted Results
Elferink 2010 [26]; (2001–2006)	Retrospective cohort; Netherlands cancer registry	Hospital: 97 Patients: 16039	Netherlands	<60 = 26% 60–74 = 43% 75+= 30% / 1.4:1	*Clinical Stage* T0/IS-M0 = <1% T1-M0 = 9% T2/T3-M0 = 59% T4-M0 = 10% T/Nany-M1 = 17% Missing = 5%	LAR = Included APR = Included Other = Included	*Hospital volume* *Number of annual surgeries* Low <25 Medium 25–50 High >50	Hospital OR (95%CI) [ref = Low] ***Postoperative Mortality***: Medium: 0.70 (0.44–1.14) High: 0.40 (0.19–0.84) * RER (95%CI) [ref = Low] ***Overall survival (2 years)***: Medium: 0.95 (0.88–1.04) High: 1.02 (0.91–1.14)
Manchon-Walsh 2011 [24]; (2005 & 2007)	Retrospective cohort; Hospital data (Catalonian Hospital Discharge Minimum Basic Data Set)	Hospital: 51 Patients: 1831	Spain/ Catalonia	Median =70 (29–92) / 1.9:1	*TNM Stage* 0 = <1%; I = 12%; II = 28%; III = 43%; IV = 7%; Missing = 8%	LAR = 73% APR = 21% Hartmann = 5% Missing = 2%	*Hospital volume* *Number of annual surgeries* Low ≤ 11 Medium 12–30 High ≥30	OR (95%CI) [ref=Low] ***Postoperative complications***: Medium: 0.65 (0.49–0.88) * High: 0.74 (0.56–0.99) * ***Postoperative Mortality***: Medium: 0.93 (0.38–2.31) High: 1.02 (0.42–2.46)
Kolfschoten 2011 [25]; (2010)	Retrospective cohort; Dutch Surgical Colorectal Audit	Hospital: 90 Patients: 2419	Netherlands	<70 = 59% 70–80 = 30% 80+ = 11% / 1.6:1	*TNM Stage* I = 30%; II = 27%; III = 32%; IV = 10%; X = 1%	LAR = 67% APR = 30% Other = 3%	*Hospital volume* *Number of annual surgeries* Low <50, High 50–100	Hospital SMR (95%CI) ***Postoperative Mortality***: Low: 1.00 (0.72–1.38) High: 1.0 (0.63–1.59)
Yun 2012[35]; (2001–2005)	Retrospective cohort; Korean cancer registry	Hospital:>180 Patients: 19028	South Korea	Composite[##]	Composite[##]	Composite[##]	Hospital volume *Mean 5 year surgeries* Low <23, High ≥23	Hospital HR (95%CI) [ref = High] ***Overall survival (5 years)***: Low: 1.39 (1.27–1.52) *
Comber 2012 [40]; (2007)	Retrospective cohort; National cancer registry	Hospital: 49 Surgeon: 86 Patients: 457	UK/ Ireland	30–49 = 11% 50–69 = 51% 70+ = 34% Missing=4%/NR‡	NR[‡]	NR[‡]	Hospital volume *Number of annual surgeries* Low <10, Medium 10–19, High ≥20 Surgeon volume Continuous	Hospital OR (95%CI) [ref = High] ***Overall survival (1 year)***: *Hospital*: 1.03 (1.00–1.06) * *Surgeon*: 0.97 (0.93–1.01)
Richardson 2013 [36]; (2002–2006)	Retrospective cohort; Nova Scotia Cancer Registry	Hospital: 10 Surgeon: 51 Patients: 466	Canada/ Nova Scotia	Mean=66 (27–94) / 1.9:1	AJCC stage I = 31% II= 27% III =35% IV = 7%	LAR = Included APR = Included Hartman= Included Other= Included	Hospital and surgeon volume *Mean annual surgeries* *Hospital and surgeon volume*: based on volume distribution	OR (95%CI)(ref = High) ***Permanent colostomy***: *Hospital:* Medium: 2.02 (0.90–4.57) *Hospital*: Low: 2.10 (0.85–5.20) *Surgeon*: Low: 1.23 (0.58–2.62) RR ratio (95%CI)(ref = High) ***Inappropriate colostomy***:

Study (Dates)	Study Type, Data source	Hospital, n Surgeon, n Patient, n	Patient characteristics: Location (Country/ State)	Patient characteristics: Age (years)[a] /M:F	Patient characteristics: Stage	Surgery type	Volume definition	Adjusted Results
							(actual definitions not reported)	Medium: 3.32 (1.08–10.27)[*]; *Hospital*: Low: 5.03 (1.44–17.54)[*] *Surgeon*: Low: 1.50 (0.54–4.16)
Richardson 2013[37]; (2002–2006)	Retrospective cohort; Nova Scotia Cancer Registry and surgeon survey (voluntary)	Surgeon: 25 Patients: 377	Canada/ Nova Scotia	Mean=67 (27–96) / 1.8:1	AJCC stage I = 31% II = 28% III =35% IV = 7%	NR[‡]	Surgeon volume *2002–2006 mean surgeries* based on volume distribution (actual definitions not reported)	Surgeon OR (95%CI) [ref = Low] ***Permanent colostomy***: High: 0.49 (0.25–0.97)[*] ***TME***: High: 3.59 (2.21–5.83)[*1] ***12 nodes examined:*** High: 0.95 (0.55–1.64)[*] HR (95%CI) [ref = Low] ***Local recurrence***: High: 0.54 (0.29–0.99)[* 1] ***Disease specific survival***: High: 0.71 (0.42–1.02) ***Overall survival***: High: 0.67 (0.43–1.02)
van Erning 2013[27]; (2008–2011)	Retrospective cohort; Eindhoven cancer registry	Hospital: 10 Patients: 1721	Southern Netherlands	<60 = 26% 60–69 = 31% 70–79 = 32% ≥80 = 8% / 1.7:1	AJCC T stage (%) T1 = 9%; T2 = 32%; T3 = 52% T4 = 7% AJCC N stage (%) N0= 65%; N1= 23%; N2= 12% AJCC M stage (%) M0 = 92%; M1 = 8%	LAR = Included APR = Included	Hospital volume *Number of annual surgeries* Low <130 High ≥130	Hospital OR (95%CI)[ref = <130] ***Overall survival (3 years):*** High: 1.0 (0.7–1.4)
Leonard 2014[38]; (2006–2010)	Retrospective cohort; Belgian cancer registry (BCR); (exclude PROCARE results)	Hospital: 108 Patient: 5869	Belgium	NR[‡]	NR[‡]	NR[‡]	Hospital volume Continuous	Hospital HR (95%CI) ***Postoperative mortality***: 0.99 (0.98–1.00)[*2] ***Overall survival (5-years):*** 0.99 (0.99–1.00)[*]
Ortiz 2015[22]; (2006–2013)	Prospective cohort; Rectal Cancer Project of the Spanish Society of Surgeons (voluntary)	Hospital: 84 Patients: 9809	Spain	<65 =39%, 65–80=48% >80=13% / 1.5:1	AJCC T stage (%) T0 = 11%; T1 = 7%; T2 = 26%; T3 = 49%; pT4 = 6% AJCC N stage (%) Nx-0= 67%; N1–2= 33% AJCC M stage (%) pM0 = 90%;	LAR = 74% APR = 26%	*Hospital volume* *Median annual surgeries* Very low 11 Low 12–23 Medium 24–35 Very high ≥36	Hospital OR (95%CI) [ref=Low] ***Postoperative mortality***: Low 1.852 (0.710, 5.881) High 1.700 (0.649, 5.248) Very high 1.309 (0.483, 4.238)

Study (Dates)	Study Type, Data source	Hospital, n Surgeon, n Patient, n	Patient characteristics: Location (Country/ State)	Age (years)[a] /M:F	Stage	Surgery type	Volume definition	Adjusted Results
					pM02 = 10%			
Aquina 2016 [31]; (2000–2011)	Retrospective cohort; New York Statewide Planning and Research Cooperative System	Hospitals: 206 Surgeons: 849 Patients: 7798	US/ New York	18–65 = 50% 65–79 = 38% ≥80= 12% / 1.4:1	NR[ǂ]	LAR = 64% APR = 35%	Hospital and Surgeon volume *Mean surgeries/ period* *Hospital*: Low <25, High ≥25 *Surgeon*: Low <10, High ≥10 Categories[1] LVS/LVH, HVH only, HVS only, HVS/HVH	OR (95%CI) [ref = LVS/LVH] ***Non-restorative protectomy***: HVH only: 0.86 (0.70–1.05); HVS only: 0.84 (0.60–1.17); HVS/HVH: 0.65 (0.48–0.89)* ***Postoperative mortality***: HVH only: 1.06 (0.52–2.15); HVS only: 0.72 (0.32–1.62); HVS/HVH: 0.43 (0.21–0.87)*
Baek 2016 [32]; (2000–2011)	Retrospective cohort; California Office of Statewide Health Planning and Development	Hospital: 321 Patients: 7187	US/ California	<65 = 38% ≥65 = 49% Missing= 13% / 1.7:1	NR[ǂ]	LAR = Included APR = Included	Hospital volume *Number of 20006–2007 surgeries* Low 1–5, Medium 6–10, High 11–24	Hospital OR (95%CI) [Low] ***Sphincter preserving surgery***: Medium: 1.14 (0.99–1.29) High: 1.63 (1.40–1.89)* ***Postoperative mortality***: Medium: 0.46 (0.27–0.78)* High: 0.45 (0.24–0.84)*
Yeo 2016 [20]; (2000–2013)	Retrospective cohort; New York Statewide Planning and Research Cooperative System	Surgeons: 1860 Patients: 14833	US/New York	<65 = 48% 65–75 = 26% ≥75= 26% / 1.2:1	NR[ǂ]	LAR = 74% APR = 26%	*Surgeon volume* Low cumulative; 0–23 High cumulative; ≥24 Low annual; 0–4 High annual; ≥5 *Categories*[2] LC/LA, LC/HA, HC/LA and HC/HA	*Surgeon* HC/HA OR (95%CI) [ref=LC/LA] ***Major events***: 0.82 (0.67–0.99)* **Prolonged LOS**: 0.74 (0.65–0.85)* ***Surgical complications***: 0.71 (0.60–0.83)* ***Anastomic leak***: 1.04 (0.88–1.24) ***Nonroutine discharges***: 0.89 (0.79–1.00) ***High charges***: 0.73 (0.63–0.86)* ***30-day readmission***: 0.92 (0.80–1.05) ***Reoperation:*** 0.98 (0.82–1.17)
Bos 2016 [29]; (2005–2012)	Retrospective cohort; Netherlands cancer registry	Hospital: 95 Patients: 20481	Netherlands	<60 = 24% 60–69 = 32% 70–79= 31% ≥80 = 13% / 1.5:1	AJCC T stage (%) T1 = 11%; T2 = 33%; T3 = 25%; T4 = 28% AJCC N stage (%)	NR[ǂ]	Hospital volume *Number of annual surgeries* Low <20 Medium 20–39 High ≥40	Hospital OR (95%CI) [ref = High] ***Anastomic leakage***: Low: 1.03 (0.79–1.34) Medium: 0.97 (0.83–1.15) ***Postoperative Mortality***:

Study (Dates)	Study Type, Data source	Hospital, n Surgeon, n Patient, n	Patient characteristics: Location (Country/ State)	Patient characteristics: Age (years)[a] /M:F	Patient characteristics: Stage	Surgery type	Volume definition	Adjusted Results
					N0= 67%; N1= 22%; N2= 11%			Low: 1.42 (1.09–1.84)* Medium: 1.12 (0.92–1.36) Hospital HR (95%CI)(ref = High) ***Overall survival (5 years)***: Low: 0.98 (0.91–1.07) Medium: 1.00 (0.95–1.06)
Ortiz 2016 [23]; (2006–2010)	Prospective cohort; Rectal Cancer Project of the Spanish Society of Surgeons (voluntary)	Hospital: 36 Patients: 2910	Spain	<65 =37%, 65–80=49% >80=14% / 1.4:1	AJCC T stage (%) T0 = 8%; T1 = 10%; T2 = 28%; T3 = 49%; T4 = 5% AJCC N stage (%) pN0-ypN0= 68%; pN1-pN2= 32%	LAR = 69% APR = 23% Hartmann = 8%	*Hospital volume* *Number of annual surgeries* Low 12–23 Medium 24–35 High ≥36	Hospital OR (95%CI) [ref=Low] ***Overall survival (5 years)***: Medium: 0.858 (0.653, 1.126) High: 0.727 (0.556, 0.951)* ***Local recurrence***: Medium: 1.098 (0.630, 1.916) High:0.835 (0.480, 1.452) ***Metastasis***: Medium: 0.951 (0.683, 1.324) High: 0.727 (0.636, 1.217)
Ortiz 2016 [21]; (2006–2013)	Prospective cohort; Rectal Cancer Project of the Spanish Society of Surgeons (voluntary)	Hospital: 84 Patients: 7231	Spain	<65 =41%, 65–80=47% >80=12% / 1.9:1	AJCC T stage (%) T0 = 11%; T1 = 8%; T2 = 26%; T3 = 50%; T4 = 6% AJCC N stage (%) Nx-0= 67%; N1–2= 33% AJCC M stage (%) M0= 90%;M1= 10%	LAR = 100%	*Hospital volume* Median number of annual surgeries Very low 11 Low 12–23 High 24–35 Very high ≥36	Hospital OR (95%CI) [ref=Very low] ***Anastomic leakage***: Low: 0.836 (0.492, 1.449); High: 0.833 (0.485, 1.455); Very high: 0.852 (0.487, 1.518)
Gietelink 2016 [30]; (2011–2012)	Retrospective cohort; Dutch Surgical Colorectal Audit	Hospital: 91 Patients: 5161	Netherlands	<75= 72–74% >75= 26–28% / 1.7:1	AJCC T stage (%) T1-T2 = 32%; T3 = 54%; T4 = 9%	LAR = 67% APR = 30% Other = 12%	Hospital volume *Mean annual surgeries* Low <20 High ≥20	Hospital OR (95%CI) [ref = High] ***CRM involvement***: Low: 1.54 (1.12–2.11)*
Lorimer 2017 [34]; (2004–2014)	Retrospective cohort; National Cancer Database	Hospital: 1179 Patients: 27532	US	Mean = 59 (18–90) / 1.7:1	Stage II/III only AJCC T stage (%) T1 = <1%; T2 = 5%; T3 = 87%; T4 = 8% AJCC N stage (%) N0= 46%; N1= 46%; N2= 8%	NR[‡]	Hospital volume *Mean annual surgeries* Low <2.2 Very low 2.2–4.37 High 4.37–7.82 Very high >7.82	Hospital OR (95%CI) [ref =Very high] ***Pathological complete response***: Low: 0.66 (0.58–0.74)*; Very low: 0.96 (0.86–1.08); High: 0.93 (0.83–1.04) ***Positive surgical margins***: Low: 1.45 (1.25–1.70)*; Very low: 1.32 (1.13–1.54); High: 0.96 (0.82–1.13)

[*] **Key**: = Significant p-value<0.0005

[ǂ] NR =Not reported in the article

[ǂǂ] Composite = Cannot delineate between rectal and other cancer with regard to information for this variable

[1] High volume hospital (HVH), Low volume hospital (LVH), High volume surgeon (HVS), Low volume surgeon (HVS)

[2] High cumulative volume surgeon (HC), Low cumulative volume surgeon (LC), Low annual volume surgeon (HA), Low annual volume surgeon (LA); Odds ratio (OR); Hazard ratio (HR); Relative risk ratio (RR); Relative excess risks (RER); Standard mortality ratio (SMR); High anterior resection (HAR; Low anterior resection (LAR); Abdominoperineal resection (LAR); American Joint Committee on Cancer (AJCC); Union for International Cancer Control's (UICC), Complete resection margin (CRM)