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Annual hospital volume and colorectal cancer survival in a population-based nationwide cohort study in Finland

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ABSTRACT

Purpose: To examine the annual hospital volume of surgery in relation to survival in colorectal cancer. Previous studies on hospital volume and survival following colorectal cancer surgery are conflicting.
Methods: All 49 032 patients who underwent resection for colorectal cancer in 1987–2016 in Finland were included, with complete follow-up until December 31, 2019. Primary outcome was 5-year mortality. Cox regression provided hazard ratios (HR) with 95% confidence intervals (CI) for quartiles of annual hospital volume for colorectal surgery, adjusted for calendar period, age, sex, comorbidity, stage, tumor location and oncological therapy. Additionally, colon and rectal cancer surgery were assessed separately. Sensitivity analysis of patients with confirmed curative intent was conducted.
Results: Compared to highest quartile (≥108 resections annually), lowest hospital volume (≤37 resections annually) was associated with slightly increased 5-year all-cause mortality (adjusted HR 1.07, 95% CI 1.02–1.12). A pre-planned subgroup-analysis suggested a slightly improved 5-year survival in high-volume institutions for rectal cancer, but not colon cancer surgery. Sensitivity analysis including only those operated with confirmed curative intent suggested no differences between hospital volume groups in colorectal, colon or rectal cancer for 5-year all-cause mortality.
Conclusion: Higher hospital volume is associated with slightly improved all-cause 5-year mortality in colorectal cancer surgery, but this effect may be limited to rectal cancer surgery only. Volume-outcome relationship in rectal cancer surgery should be investigated further using large datasets. These results do not support centralization of colon cancer surgery based on hospital volume only.

1. Introduction

Colorectal cancer is the fourth most common cancer in the world [1]. Colorectal cancer survival is highly dependent on stage, and typically ranges from a 90% 5-year survival rate for localized stage cancers to as low as 10% for those with distant metastasis [2]. Several studies have suggested that higher hospital volume might improve short-term prognosis of colorectal cancer patients [3–5]. However, the hospital volume in relation to long-term mortality in colorectal cancer is less well studied. An American study suggested better five year survival (48%) in a high volume hospital with over 93 annual colon resections yearly compared to in a low volume hospital (45%) with less than 43 operations yearly [6]. Furthermore, a Californian registry study from 1996 to 1999 suggested that both greater hospital and surgeon volumes improved outcomes for patients operated for colorectal cancer [7]. A Taiwanese population-based study suggested that higher hospital volume is associated with better 5-year survival in colorectal cancer, but no adjustment for cancer stage, location, or neoadjuvant treatment was done in that study, and further colon cancer and rectal cancer were not separately studied [8]. A meta-analysis suggested better long-term survival after colon and rectal cancer surgery in higher-volume hospitals, but this effect was attenuated after case-mix adjustment in colon cancer [9]. A Swedish nationwide cohort study showed that high hospital volume is associated to slightly better 5-year mortality in colon cancer and better 5-year all-cause mortality for some subgroups of rectal cancer patients [10]. Taken together, it is not completely clear whether hospital volume of colorectal

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cancer surgery is associated with long-term mortality.

We hypothesized that colorectal surgery carried out in higher-volume centers have a slightly better long-term prognosis compared to lower-volume hospitals, while short term prognosis is similar between volume groups. The aim of this study was to compare long- and short term mortality after colorectal surgery for cancer in an unselected, nationwide population-based cohort based on complete Finnish registries.

2. Methods

2.1. Study design

This was a Finnish population-based, nationwide retrospective cohort study. All patients with incident colorectal cancer undergoing resectional surgery in Finland from January 1, 1987 to December 31, 2016 within a year of cancer diagnosis were included. Follow-up for survival was 100% complete until December 31, 2019. The patients were identified from the Finnish Cancer Registry and Finnish Health Care Register HILMO using the relevant ICD-9, ICD-10 and operations codes. One-year limit between cancer diagnosis and surgery was chosen to take diagnostic lag and other delays, such as complications during neoadjuvant therapy into account.

2.2. Data collection

The Finnish Cancer Registry (FCR) was used to identify all cases of colon and rectum cancer, based on ICD-9 (1530-34, 1536-41, 1548) and ICD-10 diagnoses (C18.0, C18.2-9, C19 and C20). FCR has collected population-based data on cancer incidence since 1953 and after year 1961 reporting of all cancer cases has been compulsory by law. FCR is >95% complete regarding solid tumors [11]. Cancer registry provided information for tumor stage (classified as local, locally advanced, or advanced), tumor location (divided to right colon including cecum, ascending colon, hepatic flexure and transverse colon, and excluding appendix; left colon including splenic flexure, descending colon and sigmoid colon; and rectum including rectosigmoid junction and rectum), oncological treatment, and curative intent of surgery. Tumor stage has been validated as reasonably accurate, and location as very accurate, but some misclassification is known to exist.[12] Oncological treatment was defined as categorized by the FCR; i.e. oncological treatment (chemo- and/or radiotherapy) administered during the first 4 months after the first colorectal cancer diagnosis. The positive predictive value of oncological treatment for colorectal cancer patients in FCR is 94%, but a considerable number of oncological treatments are misclassified by FCR as no oncological treatment [12]. For curative intent of surgery, the number of missing values is known to be relatively high [12].

THL Care Register for Health Care (HILMO) (previously Hospital Discharge Register), was used to identify patients potentially missed by FCR using relevant ICD-9 and ICD-10 codes, and to identify all operations for incidental colorectal cancer. THL Care Register for Health Care HILMO (until 1993 Hospital Discharge Register) collects data for all hospital outpatient visits and ended inpatient admissions, and it has high positive predictive value for common diagnoses [13]. The operation type was collected from registers by using the classification for Finnish Hospital League 1983 (Sairaalaliiton Toimenpidenimikkeistö 1983) in years 1987–1996 and from year 1997 NOMESCO Classification for Surgical Procedures. In addition to the exposure variable annual procedural volume, patient registries provided information on year of surgery, patient sex, age at diagnosis, and comorbidity. Comorbidity was defined using the well-validated Charlson comorbidity index (CCI, Supplementary Table 1). All diagnoses prior to surgery were considered for comorbidity without weighting for different diagnosis groups, and excluding any colorectal cancer diagnoses [14].

The follow-up was based on Death Registry, which provided the dates of death and causes of death. The registry is 100% complete for vital status, and >99% accurate for cause of death due to manual checking of all death certificates by a forensic physician [15].

2.3. Identification of cases

All records representing colorectal cancer in 1997–2016 were identified using ICD-10 codes (C18.0, C18.2-9, C19 and C20) in databases. In years 1987–1996 all colorectal cancers were identified by using ICD-9 codes (1530-34, 1536-41, 1548). The operations in years 1987–1996 were identified using Sairaalaliiton Toimenpidenimikkeistö 1983 codes (6403-08, 6410, 6419, 6434-36, 6449), and the operations after year 1996 were identified using NOMESCO Classification for Surgical Procedures codes (JFB20-97, JFH00-96, JGA70-98, JGB00-36), and further divided to colon cancer surgery (for example right, left, or sigmoid colectomy) and rectal cancer surgery (for example anterior resection and abdominoperineal resection).

2.4. Exposures and outcomes

The main exposure, annual hospital volume of colorectal surgery was calculated as a number of colon and rectal cancer surgeries performed in each hospital and year in 1987–2016. Hospital volume was then divided into quartiles, i.e four equally sized groups. Secondary exposures were annual volume of colon cancer surgery and annual volume of rectal cancer surgery, which included only surgeries for that specific tumor type performed in each hospital and year.

The primary outcome was 5-year all-cause mortality, defined as mortality for any cause during 5 years from surgery. Secondary outcomes were 30-day and 90-day all-cause mortality, 5-year cancer-specific mortality, defined as mortality due to colon- or rectal cancer, and 5-year all-cause mortality excluding mortality during the first 90 days during follow up to exclude mortality due to postoperative complications.

2.5. Statistical analysis

Statistical analyses were conducted by an experienced biostatistician (P.O.) according to an *a priori* study protocol. Descriptive statistics of patient and tumor characteristics and outcome indicators were presented in the total group and separately for the exposure groups. Follow-up time was calculated from the date of surgery until the date of death, the end of the specified follow-up time, or December 31, 2019 for all-cause mortality (December 31, 2018 for cancer-specific mortality), whichever occurred first. After checking the proportionality assumption, Cox regression provided hazard ratios (HR) with 95% confidence intervals (CI). There were three statistical models: 1) the crude model included only the exposure and the outcome variable, 2) multivariable model adjusted for calendar periods (5-year intervals; 1987–1991, 1992–1996, and so on), age at diagnosis (<60 years, 60–69 years, 70–79, or ≥80 years), sex (male, or female), Charlson comorbidity index (0, 1, or ≥2), tumor stage (local, locally advanced, or advanced), tumor location (right colon, left colon, or rectum), and oncological treatment (no, or yes). A sensitivity analysis (model 3) was conducted as in model 2, but including only those patients that were operated with curative intent according to the FCR. A preplanned effect modification analysis for confounding variables using statistical model 2 was done to explore the potential reasons for the results regarding 5-year all-cause mortality and 5-year cancer-

specific mortality after colorectal cancer surgery. Due to a proportion of missing tumor stage, multiple imputation for tumor stage was conducted. However, as the results in the imputed and non-imputed analyses were similar, only analyses with multiple imputation are presented for models 2 and 3.

3. Results

3.1. Patient characteristics (Table 1)

All 49 032 patients with surgical resection for colorectal cancer during 1987–2016 were included in the study. The number of surgically treated patients during years 1987–1991 was 5 413 (11.0%) and increased to 10 945 (22.3%) in years 2012–2016.

The patients were most frequently 70–79 years old (33.3%) with even distribution between the sexes. Most frequently patients had no comorbidities (59.5%), local cancer (29.1%), left colon tumor (37.3%) and no oncological therapy (81.6%). In the hospitals with lowest colorectal cancer operation volume, the patients had slightly higher median age, were more likely female, had less comorbidities, less advanced cancers, less rectal cancers and less oncological treatments compared to the highest volume quartile hospitals.

3.2. Annual hospital volume for colorectal cancer surgery (Table 2 and Fig. 1)

The 5-year survival of patients operated in the lowest volume quartile hospitals was 51.7%, compared to 63.7% in the highest volume quartile hospitals. In crude model for colorectal cancer surgery, the lowest hospital volume was associated with a higher risk of 5-year all-cause mortality, compared with the highest volume quartile (HR 1.41, 95% CI 1.36–1.47, lowest versus highest quartile), the five year cumulative survival is visualized in Fig. 1. After adjustment for confounders, the risk difference was much lower, but significant (HR 1.07, 95% CI 1.02–1.12, lowest versus highest quartile). However, in the sensitivity analysis including only those with confirmed curative intent, there were no differences in 5-year all-cause mortality comparing the lowest to highest volume quartile (HR 1.02, 95% CI 0.95–1.10), or between the other quartiles.

3.3. Secondary outcomes

The 30- and 90-day survivals of patients operated in the lowest volume quartile hospitals were 96.6% and 93.4%, compared to 97.1%, and 94.6% in the highest volume quartile hospitals respectively. No differences were observed in the adjusted analyses of 30-day (HR 0.90, 95% CI 0.76–1.05) and 90-day mortality (HR 0.91, 95% CI 0.72–1.14) comparing the lowest to highest volume quartiles of hospital volume. Similarly to the main outcome, the 5-year cancer-specific mortality (HR 1.11, 95% CI 1.06–1.17), and 5-year all-cause mortality excluding first 90 postoperative days (HR 1.06, 95% CI (0.98–1.14)) were slightly higher in lowest volume quartile hospitals compared to the highest volume quartile hospitals in the adjusted analysis, but not in the sensitivity analysis including only patients operated with confirmed curative intent.

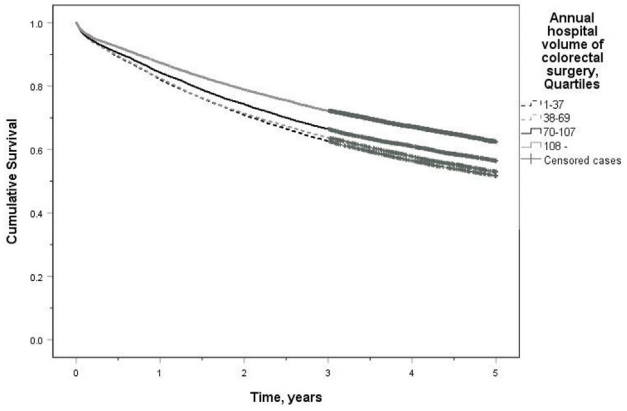

Fig. 1. The 5-year cumulative survival for patients with surgery of colorectal cancer.

3.4. Annual hospital volume of colon, or rectal cancer surgery (Table 3)

For the pre-specified subgroup analysis of colon cancer surgery, i.e. those undergoing e.g. segmental, right, left or sigmoid colectomies, the 5-year survival of patients operated in the lowest volume quartile hospitals was 51.6%, compared to 61.0% in the highest volume quartile hospitals. The lowest hospital volume quartile was associated with a higher risk of 5-year all-cause mortality in colon cancer in the crude model (HR 1.30, 95% CI 1.24–1.37) but not in the adjusted model (HR 1.02, 95% CI 0.96–1.08), compared to the highest hospital volume quartile. In the sensitivity analysis including only those with confirmed curative intent, no difference was found between the lowest volume quartile (HR 1.01, 95% CI 0.92–1.12) compared to the highest.

In the subgroup analysis of rectal cancer surgery, i.e. those undergoing anterior-, abdominoperineal- or transrectal resections for cancer, the 5-year survival of patients operated in the lowest volume quartile hospitals was 51.4%, compared to 67.4% in the highest volume quartile hospitals. The lowest hospital volume quartile was associated with a higher risk of 5-year all-cause mortality (HR 1.65, 95% CI 1.54–1.76). In the adjusted model this risk difference was lower but still significantly higher comparing lowest to highest volume quartiles (HR 1.17, 95% CI 1.09–1.26). When only patients with curative intent were included, no statistically significant difference was observed between the lowest and highest volume quartiles (HR 1.05, 95% CI 0.94–1.17).

3.5. Annual volume of colorectal surgery and 5-year mortality, stratified by age, sex, tumor stage, tumor location and oncological treatment (Table 4)

The risk of all-cause mortality was slightly elevated in lowest volume hospitals compared to highest volume hospitals among patients under 72 years (median), (HR 1.12, 95% CI 1.05–1.20), but not for older patients. Similar point estimates were observed between the sexes, tumor stage groups and oncological treatment groups. Tumors located in the rectum had higher mortality in lowest volume hospitals compared to the highest volume (HR 1.33, 95% CI 1.20–1.48), with a dose-response relationship in the point estimates, while no differences between volume groups were present for right- or left colon tumors.

4. Discussion

The results of this population-based, nationwide cohort study suggest that increasing annual hospital volume of colorectal cancer surgery might be associated with a lower 5-year all-cause mortality. Subgroup analysis suggested survival differences between hospital volume groups for rectal, but not colon cancer. However, in sensitivity analyses including only patients operated with confirmed curative intent, no difference was observed in any of the groups.

The main strengths of this study are the population-based design and virtually complete inclusion of all patients undergoing

Table 1
Clinical characteristics of the patients.

Variable	N (%)
Calendar period	
1987–1991	5 413 (11.0)
1992–1996	6 504 (13.3)
1997–2001	7 872 (16.1)
2002–2006	8 698 (17.7)
2007–2011	9 600 (19.6)
2012–2016	10 945 (22.3)
Age at diagnosis	
<60 years	9 510 (19.4)
60–69 years	13 426 (27.4)
70–79 years	16 306 (33.3)
≥80 years	9 790 (20.0)
Sex	
Male	24 521 (50.0)
Female	24 511 (50.0)
Charlson comorbidity index	
0	29 172 (59.5)
1	12 287 (25.1)
>1	7 573 (15.4)
Tumor stage	
Local	14 247 (29.1)
Locally advanced	11 386 (23.2)
Advanced	13 106 (26.7)
Missing	10 293 (21.0)
Tumor Location	
Left colon	18 265 (37.3)
Right colon	16 208 (33.1)
Rectum	14 388 (29.3)
Oncological treatment	
No	40 030 (81.6)
Yes	9 002 (18.4)
Hospital volume of colorectal surgery	
Q1 (1–37)	12 530 (25.6)
Q2 (38–69)	12 547 (25.6)
Q3 (70–107)	12 106 (24.7)
Q4 (108-)	11 849 (24.2)

surgery for colorectal cancer in the entire Finland. Accurate information about the exposures, outcomes and relevant covariates was made possible by data retrieval from validated nationwide registers. The use of a predefined data retrieval and specific study protocol reduced the risk of chance findings and systematic errors. The reliable identification of all eligible patients and the complete follow-up was made possible by the uniquely assigned personal identity numbers and high-quality cancer and patient registries. The use of quartiles reduced bias compared to arbitrary or "optimal" cut-offs for hospital volume. A limitation of observational studies is confounding. However, this was mitigated by adjusting for several potential confounders, though residual confounding cannot be ruled out. The long inclusion period might be considered a weakness.The patients operated during the latest study period had a minimum of 2 years of follow up for disease-specific mortality and 3 years for all-cause mortality. However, they were only a minor part of the whole cohort, so this limitation only reduces the statistical power, and does not impact the risk estimates. The care for colorectal cancer patients has much improved in the last three decades. Long term survival has been much impacted by better perioperative care and introduction of neoadjuvant and adjuvant treatment strategies. Furthermore, minimally invasive surgery has become an integral part of CRC management. However, the 5-year calendar periods were adjusted for in the analyses, which mitigates this confounding to some extent. Registration of stage and oncological treatments are not 100% complete in the FCR and suffer of some non-differential misclassification due to underestimating the proportion of advanced cancers and patients receiving oncological treatments. This may cause some under-adjustment in statistical models, but should not change the overall result of the study. Furthermore, defining curative therapy is based on FCR records and some patients undergoing curative therapy might have been left out from the sub-analyses (Model 3), leading to lower power in the respective analyses but should not cause major changes in the point estimates. There were some missing data on tumor stage, which was handled using multiple imputation. Lack of complication data can be considered as a weakness in this study. Lastly, all abdominal surgeons in Finland, which is a relatively small country, practicing during the study period have been required to train at least half of their residency in the highest volume university hospitals. This training might mitigate some of the differences in surgical techniques between surgeons working in lower hospital volume compared to higher volume hospitals. However, only hospital volume but not the surgeon volume could be assessed as no data on individual surgeons were available.

Some previous research on hospital volume of colorectal cancer surgery in relation to long-term mortality has been conducted. The American landmark studies in 1992–2002 have demonstrated slightly better short and long-term survival in hospitals with higher volume of colorectal cancer surgery, compared to lower volume centers [3,6]. A Californian study in 1996–1999 suggested better survival for colorectal cancer patients operated in higher volume centers and higher volume surgeons, compared to lower volume [7]. A Taiwanese population-based study suggested that surgeon volume has more impact on colorectal cancer than hospital volume [11]. However, the Taiwanese study did not assess colon and rectal cancer separately, nor adjust for important confounding factors such as stage or oncological treatment. Another study from the US in 1991–1994 (N = 3200) suggested that differences in survival after curative resection for colorectal cancer among surgeons appear to reflect the degree of specialization rather than case volume [16]. For colon cancer, a Medicare linked database study suggest that higher hospital volume is associated with lower mortality, although the differences are modest in comparison with the variation observed for higher-risk cancer surgeries [17]. For rectal cancer surgery, a SEER -database based study (N = 6432) treatment at higher-volume hospitals with specialized surgeons was associated with improved longterm survival compared to lower volume [18]. Furthermore, one meta-analysis suggested no relationship between center volume and colon and rectal cancer surgery outcomes [19], while another meta-analysis suggested better long-term survival in high-volume institutions but not in colon cancer after case-mix adjustment [9]. A more recent nationwide study from Sweden suggested that colon cancer surgery, but not rectal cancer surgery, in higher volume hospitals was associated with survival benefit [10]. However, the differences between the groups were rather modest, and colon cancer surgery is also often conducted for palliation, which was not taken into account in the Swedish study.

In the present study, a weak association between increased 5-year all-cause mortality was observed in the three lower-volume quartiles compared to the highest. Similarly, 5-year cancer-specific mortality was increased in the three lower-volume quartiles compared to the highest. However, no dose-response relationship was observed, suggesting that the finding might have also occurred by chance. In analyses limited to those operated with confirmed curative intent, and those undergoing colon cancer surgery only, no volume-outcome relationship was present. For

Table 2
Annual hospital volume in relation to mortality in colorectal cancer patients.

Model	Number	Hospital volume quartile of colorectal cancer surgery			
		Q1 (1–37) HR (95% CI)	Q2 (38–69) HR (95% CI)	Q3 (70–107) HR (95% CI)	Q4 (≥108) HR (95% CI)
Primary outcome: 5-year all-cause mortality					
Crude	49 032	1.41 (1.36–1.47)	1.37 (1.31–1.42)	1.23 (1.18–1.28)	1 (reference)
Model 2	49 032	1.07 (1.02–1.12)	1.05 (1.01–1.10)	1.07 (1.02–1.12)	1 (reference)
Model 3	24 457	1.02 (0.95–1.10)	1.04 (0.96–1.11)	0.98 (0.91–1.05)	1 (reference)
Secondary outcome: 30-day all-cause mortality					
Crude	49 032	1.19 (1.03–1.37)	1.23 (1.07–1.42)	1.23 (1.06–1.42)	1 (reference)
Model 2	49 032	0.90 (0.77–1.06)	1.01 (0.86–1.19)	1.09 (0.94–1.27)	1 (reference)
Model 3	24 457	0.90 (0.76–1.05)	1.00 (0.86–1.18)	1.09 (0.94–1.27)	1 (reference)
Secondary outcome: 90-day all-cause mortality					
Crude	49 032	1.24 (1.12–1.38)	1.28 (1.16–1.43)	1.23 (1.10–1.35)	1 (reference)
Model 2	49 032	0.93 (0.83–1.05)	1.01 (0.90–1.14)	1.06 (0.95–1.18)	1 (reference)
Model 3	24 457	0.91 (0.72–1.14)	1.08 (0.87–1.35)	1.08 (0.88–1.33)	1 (reference)
Secondary outcome: 5-year cancer-specific mortality					
Crude	49 032	1.56 (1.49–1.63)	1.50 (1.44–1.57)	1.32 (1.26–1.38)	1 (reference)
Model 2	49 032	1.14 (1.08–1.20)	1.11 (1.05–1.16)	1.11 (1.06–1.17)	1 (reference)
Model 3	24 457	1.11 (1.06–1.17)	1.09 (1.04–1.15)	1.11 (1.06–1.17)	1 (reference)
Secondary outcome: 5-year overall mortality excluding first 90 postoperative days					
Crude	45 933	1.44 (1.38–1.50)	1.38 (1.32–1.44)	1.23 (1.18–1.28)	1 (reference)
Model 2	45 933	1.12 (1.06–1.17)	1.08 (1.02–1.13)	1.07 (1.02–1.12)	1 (reference)
Model 3	24 457	1.06 (0.98–1.14)	1.04 (0.97–1.13)	0.98 (0.91–1.05)	1 (reference)

Table 3
Annual hospital volume of colorectal cancer surgery in relation to mortality, stratified by surgery type (colon cancer surgery, or rectum cancer surgery).

Annual hospital volume of colon cancer surgery					
Model	Number	Q1 (1–23) HR (95% CI)	Q2 (24–42) HR (95% CI)	Q3 (43–68) HR (95% CI	Q4 (≥69) HR (95% CI)
Crude	29 668	1.30 (1.24–1.37)	1.21 (1.15–1.27)	1.16 (1.10–1.22)	1 (reference)
Model 2	29 668	1.02 (0.96–1.08)	1.03 (0.97–1.09)	1.04 (0.99–1.10)	1 (reference)
Model 3	14 169	1.01 (0.92–1.12)	1.05 (0.95–1.16)	0.95 (0.87–1.04)	1 (reference)
Annual hospital volume of rectal cancer surgery					
Model	**Number**	**Q1 (1–17) HR (95% CI)**	**Q2 (18–28) HR (95% CI)**	**Q3 (29–43) HR (95% CI)**	**Q4 (≥44) HR (95% CI)**
Crude	19 364	1.65 (1.54–1.76)	1.54 (1.45–1.65)	1.31 (1.22–1.40)	1 (reference)
Model 2	19 364	1.17 (1.09–1.26)	1.14 (1.06–1.22)	1.11 (1.03–1.19)	1 (reference)
Model 3	10 288	1.05 (0.94–1.17)	1.01 (0.90–1.12)	0.98 (0.88–1.09)	1 (reference)

short-term outcomes no differences were observed after case-mix adjustment, but the power in these analyses were limited due to low number of events. Patient factors or time trends could explain some of the mortality differences, for example lower-volume hospitals operating on more palliative patients, or that outcomes improved over time irrespective of hospital volume.

However, for those with cancer located in the rectum, or for those undergoing rectal cancer surgery (i.e. anterior or abdominoperineal resections), surgery in lower volume centers was associated with a slightly, but significantly increased risk of 5-year all-cause, with clearly increasing point estimates with decreasing volume. Taken together, these findings suggest that annual hospital volume is not relevant for colon cancer surgery outcomes, but might be for rectal cancer surgery.

The present study has several research and clinical implications. Firstly, larger studies with adjustment for more granular clinical data could improve the knowledge on volume-outcome relationships in especially rectal cancer. Assessing whether the potential volume-outcome relationship is driven by surgeon volume only, or both surgeon and hospital volume is of particular importance as individual surgeons in smaller centers might still have considerably high individual annual volumes of colorectal cancer surgery. The relationship between surgeon and mortality appears stronger compared to hospital volume and mortality, especially for overall long-term survival and surgery-related mortality [8,9]. This might also be reflected in the results of the present study as lack of associations. It remains unknown whether the association exists for any rectal cancer surgery, or if it is limited to a certain procedure, e.g. abdominoperineal resection of low rectal cancer. Audits and other quality control measures, in addition to locally centralizing surgery to high-volume surgeons are accessible options to improve outcomes after colorectal cancer surgery. While centralization of rectal cancer surgery might be appropriate, the present study does not support centralization of colon cancer surgery based on volume requirements only. Furthermore, the accessibility of surgical care should be taken into consideration when centralizing surgical services.

In conclusion, in this nationwide, population-based cohort study higher hospital volume is associated with slightly improved all-cause 5-year mortality in colorectal cancer surgery, but not in patients undergoing surgery with confirmed curative intent. Volume-outcome relationship in rectal cancer surgery should be

Table 4
Annual volume of colorectal surgery and 5-year all cause mortality effect modification by age, sex, tumor stage, tumor location and oncological treatment.

Variable	N	Hospital volume quartile of colorectal cancer surgery			
		Q1 (1–37) HR (95% CI)	Q2 (38–69) HR (95% CI)	Q3(70–107) HR (95% CI)	Q4 (≥108) HR (95% CI)
5-year all cause mortality					
Age					
<72 years	26 109	1.12 (1.05–1.20)	1.11 (1.03–1.18)	1.10 (1.03–1.17)	1 (reference)
≥72 years	22 923	1.04 (0.98–1.11)	1.03 (0.97–1.09)	1.05 (1.00–1.11)	1 (reference)
Sex					
Male	24 521	1.05 (0.99–1.12)	1.05 (0.99–1.12)	1.05 (0.99–1.11)	1 (reference)
Female	24 511	1.09 (1.02–1.17)	1.06 (0.99–1.13)	1.10 (1.03–1.17)	1 (reference)
Tumor stage					
Local	14 247	1.06 (0.95–1.18)	1.06 (0.95–1.18)	1.07 (0.96–1.19)	1 (reference)
Locally advanced	11 386	1.07 (0.98–1.17)	1.05 (0.96–1.15)	1.04 (0.96–1.12)	1 (reference)
Advanced	13 106	1.07 (1.00–1.15)	1.05 (0.99–1.13)	1.08 (1.02–1.15)	1 (reference)
Tumor location					
Right colon	16 208	1.01 (0.93–1.09)	0.98 (0.91–1.06)	1.02 (0.95–1.10)	1 (reference)
Left colon	18 265	1.02 (0.95–1.10)	1.05 (0.98–1.13)	1.07 (1.00–1.15)	1 (reference)
Rectum	14 388	1.22 (1.11–1.33)	1.15 (1.06–1.26)	1.11 (1.03–1.21)	1 (reference)
Oncological treatment					
Yes	9 002	1.15 (1.03–1.27)	1.03 (0.94–1.13)	1.16 (1.06–1.27)	1 (reference)
No	40 030	1.06 (1.01–1.12)	1.07 (1.01–1.12)	1.06 (1.01–1.11)	1 (reference)

investigated further using large datasets. These results do not support centralization of colon cancer surgery based on hospital volume.

CRediT author statement

Elise Sarjanoja: conceptualization, methodology, writing original draft, visualization. Kai Klintrup: methodology, writing review and editing. Pasi Ohtonen: software, methodology. Joonas Kauppila: methodology, writing review and editing, supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2022.02.017.

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