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ORIGINAL ARTICLE

Impact of socioeconomic deprivation on short-term outcomes and long-term overall survival after colorectal resection for cancer

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Abstract

Purpose The aim of this study was to assess the effects of socioeconomic deprivation on short-term outcomes and long-term overall survival following major resection of colorectal cancer (CRC) at a tertiary hospital in England.

Method This was an observational cohort study of patients undergoing resection for colorectal cancer from January 2010 to December 2017. Deprivation was classified into quintiles using the English Indices of Multiple Deprivation 2010. Primary outcome was overall complications (Clavien-Dindo grades 1 to 5). Secondary outcomes were the major complications (Clavien-Dindo 3 to 5), length of hospital stay and overall survival. Outcomes were compared between most affluent group and most deprived group. Multivariate regression models were used to establish the relationship taking into account confounding variables.

Results One thousand eight hundred thirty-five patients were included. Overall and major complication rates were 44.9% and 11.5% respectively in the most affluent, and 54.6% and 15.6% in the most deprived group. Most deprived group was associated with higher overall complications (odds ratio 1.48, 95% CI 1.13–1.95, $p = 0.005$), higher major complications (odds ratio 1.49, 1.01–2.23, $p = 0.048$) and longer hospital stay (adjusted ratio 1.15, 1.06–1.25, $p < 0.001$) when compared with most affluent group. Median follow period was 41 months (interquartile range 20–64.5). Most deprived group had poor overall survival compared with most affluent, but it was not significant at the 5% level (hazard ratio 1.27, 0.99–1.62, $p = 0.055$).

Conclusion Deprivation was associated with higher postoperative complications and longer hospital stay following major resection for CRC. Its relationship with survival was not statistically significant.

Keywords Colorectal cancer · Deprivation · Complications · Survival

Introduction

In 2019, the National Health Service (NHS) Long-term Plan reaffirmed the UK's health service's commitment to take a concerted and systematic approach to reducing health inequalities and addressing unwarranted variation in care [1]. Socioeconomic deprivation (SED) is central to health inequality and influences outcomes of many diseases, including cancers. Cancer Research UK reports 19,000 extra cancer-related deaths in England every year due to the effects of socioeconomic deprivation [2]. SED effects are multifactorial, ranging from poor general health with higher rates of smoking, obesity and malnutrition, plus poor awareness of the implication of symptoms, impaired access to primary care and lower uptake of screening programmes [3, 4]. SED has been shown to be associated with higher incidence of surgical site infections in a large multicentre international cohort study [5]. In the context of colorectal cancer (CRC), these socioeconomic factors translate into more advanced stage at presentation, higher emergency resection rates, lower rates of curative treatment and diminished overall survival for more deprived patients [6–14].

The association between SED and complications after surgery for CRC has received relatively little attention in the surgical literature. Complications after major bowel resection directly influence short-term mortality, access to adjuvant therapy, quality of life, survival and overall cost of treatment.

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This study aims to assess the impact of SED on surgical complications, length of hospital stay and overall survival for patients undergoing major resection for CRC.

Methods

Design and patients

This was a retrospective analysis of a prospectively maintained database from January 2010 to December 2017 at a single high-volume colorectal unit. The unit has two hospital sites; both contribute to the National Bowel Cancer Screening Programme, UK (BCSP). Patients were identified from the colorectal cancer multidisciplinary meeting database which includes all elective and emergency resections. Polyp cancers treated with polypectomy only and early rectal cancers treated by transanal endoscopic microsurgery (TEMS) were excluded. Patients undergoing multivisceral resection, cytoreductive surgery and resections for recurrent rectal cancer were also excluded.

Data

Variables included patient demographics, date of diagnosis and surgery. Physiological status was recorded in American College of Anaesthesiology (ASA) grades. Cancer stage was recorded using the American Joint Committee on Cancer (AJCC/TNM) staging system 7th edition from I to IV. Surgical details included site of the primary cancer, anatomical type of resection, approach details (laparoscopic or open) and stoma creation. Presentation of the patients was defined as screening detected (screening), symptomatic elective (symptomatic) and emergency.

The English Indices of Deprivation 2010 were used to classify patients by socioeconomic status [15]. These indices use UK postcodes in England to define distinct geographical areas called 'lower layer super output areas' (LLSOA). Each LLSOA is given an Index of Multiple Deprivation (IMD) score based on per capita income, education and employment status, health, housing, crime and living environment. Based on IMD scores, areas are classified into IMD quintiles from 1 to 5: most affluent, affluent, middle, deprived and most deprived [12]. The IMD scores and quintiles were calculated for all the patients in the study from their respective postcodes [16].

Outcome measures

Surgical complication was defined as any adverse postoperative event until 30 days from the date of surgery according to the Clavien-Dindo classification (Table 1) [17]. Primary outcome was the overall complication rate; further outcomes were the recorded rates of major complications, length of hospital stay and overall survival. Major complications were defined as Clavien-Dindo (CD) grades 3 to 5. Length of hospital stay was calculated in days from date of admission to date of discharge or death. Overall survival time was calculated from date of diagnosis to date of death from any cause or censored on April 10, 2018. The dead/alive status of patients was ascertained from electronic hospital records.

Statistical analysis

Continuous variables were expressed as median and interquartile ranges and analysed using the Mann-Whitney *U* test or Kruskal-Wallis test where appropriate. Categorical variables were expressed as values and percentages and analysed using chi-square test. Multivariate logistic regression models were constructed for overall and major complication as dependent variables. Variables which were clinically important or with p value < 0.25 on univariate analysis were included in the logistic regression model. Hosmer-Lemeshow's test was used to confirm the 'good fit' of the model. Multiple linear regression was used to assess effects of variables on length of hospital stay. Log transformation of length of stay was used as the dependent variable in order to normalize skewed distribution. Variables which were clinically important and significant on univariate analysis were included in the model. Kaplan-Meier curves were used to illustrate the survival analysis. Log rank test was used to compare overall survival between groups. Cox proportional hazards model was constructed to identify factors related to overall survival. For all analyses, a p value of < 0.05 was considered as statistically significant. To evaluate the effect of SED on outcomes, the most deprived group (quintile 5) was compared with most affluent (quintile 1). This methodology is similar to previously reported studies [6, 8, 12]. We also calculated the global p values for SED and other variables with more than 2 subgroups to assess their overall impact on complications and length of hospital stay. Data analysis was undertaken using R Foundation Statistical Software (R 3.5.1, R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Results

Patients

The study cohort was identified from the total number of diagnosed CRC in the unit during the study period January 2010 to December 2017 (Fig. 1). A total of 1835 patients underwent major resection and were included for analysis. Three hundred twenty-three were emergency presentations, 202 patients were

Table 1 Clavien-Dindo classification of surgical complications [17]

Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are drugs as anti-emetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications.Blood transfusion and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention
- IIIa	- Intervention not under general anaesthesia
- IIIb	- Intervention under general anaesthesia
Grade IV	Life-threatening complication requiring ICU management
- IVa	- Single organ dysfunction (including dialysis)
- IVb	- Multi-organ dysfunction
Grade V	Death of a patient

diagnosed by the BCSP and 1310 patients had elective resections for symptomatic cancers.

Patients were grouped into the IMD quintiles from most affluent to most deprived (Table 2). The distributions of gender, ASA grades, TNM stage, primary site and stoma rate were similar across the five groups. The median age in years at diagnosis appeared to decrease with increasing levels of deprivation (most affluent group, 72.5 years; most deprived group, 69 years, $p < 0.001$). Mode of presentation was differentially distributed across the 5 groups ($p = 0.004$), with presentation by 'screening' being highest in the most affluent (66/418, 15.8%) and lowest in the most deprived group (33/513, 6.4%). Conversely, 'emergency' presentation was highest in the most deprived (98/513, 19.1%) and lowest in the most affluent group (63/418, 15.1%).

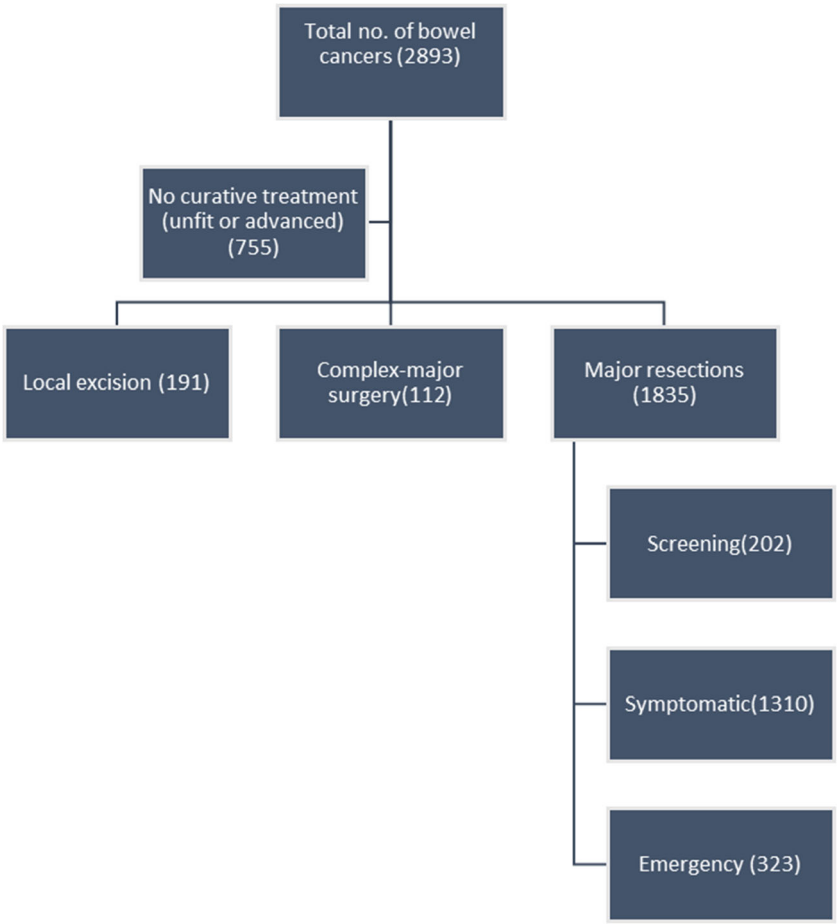

Fig. 1 Case mix of colorectal cancers diagnosed from January 2010 to December 2017 in the unit

Table 2 Distribution of population split by Index of Multiple Deprivation (IMD) quintiles

Variables		IMD Quintiles					*p* value
		1 Most affluent	2 Affluent	3 Middle	4 Deprived	5 Most deprived	
Number of patients		418	320	327	257	513	
Age (years) Median (IQR)		72.5 (65–80)	72 (65–78)	71 (63–78)	71 (62–77)	69 (60–77)	< 0.001
Gender Value (percentage)	Female	171 (40.9)	140 (43.7)	145 (44.3)	124 (48.2)	196 (38.2)	0.077
ASA	3, 4	105 (25.1)	69 (21.6)	79 (24.1)	63 (24.5)	131 (25.5)	0.75
Approach	Laparoscopic	214 (51.1)	144 (45)	143 (43.7)	109 (42.4)	229 (44.6)	
	Open	204 (48.9)	176 (55)	184 (56.3)	148 (57.6)	284 (55.4)	0.135
TNM stage	1	107 (25.6)	65 (20.3)	60 (18.3)	51 (19.8)	91 (17.7)	
	2	108 (25.8)	93 (29.1)	103 (31.4)	85 (33.0)	146 (28.4)	
	3	160 (38.2)	124 (38.7)	130 (39.7)	95 (36.9)	213 (41.5)	
	4	43 (10.2)	38 (11.9)	34 (10.4)	26 (10.1)	63 (12.3)	0.284
Presentation	Screening	66 (15.8)	38 (11.9)	37 (11.3)	28 (10.9)	33 (6.4)	
	Symptomatic	289 (69.1)	229 (71.5)	228 (69.8)	182 (70.8)	382 (74.5)	
	Emergency	63 (15.1)	53 (16.6)	62 (18.9)	47 (18.3)	98 (19.1)	0.004
Primary site	Rt and transverse	161 (38.5)	125 (39.1)	126 (38.5)	109 (42.4)	183 (35.6)	
	Left and sigmoid	129 (30.8)	76 (23.7)	104 (31.8)	72 (28.0)	172 (33.5)	
	Rectum	128 (30.6)	119 (37.2)	97 (29.6)	76 (29.6)	158 (30.8)	0.102
Stoma		139 (33.2)	114 (35.6)	101 (30.8)	77 (29.9)	190 (37.0)	0.21
Overall complication		188 (44.9)	158 (49.3)	165 (50.4)	133 (51.7)	280 (54.6)	0.065
Major complication		48 (11.5)	48 (15)	39 (11.9)	34 (13.2)	80 (15.6)	0.312
Length of hospital stay (days)		6.5 (5–10)	7 (5–11)	7 (5–12)	7 (5–12)	8 (5–12)	0.003

Postoperative complications

The overall complication rate was 54.6% in the most deprived and 44.9% in the most affluent group. Multivariate logistic regression demonstrated the effects of the variables on overall complication rate (Table 3). The most deprived group had significantly higher overall complication rate (odds ratio (OR) 1.48, 1.13–1.95, $p = 0.005$) compared with the most affluent group. A rising trend in the OR for overall complications from IMD quintile 2 to 5 was evident. On analysing SED as a 5 level variable, its global p value was 0.077. Female gender was associated with lower overall complication rate (OR 0.74, 0.61–0.91, $p = 0.002$). ASA grades 3 or 4 (OR 1.76, 1.39–2.24, $p < 0.001$), emergency presentation (OR 1.68, 1.12–2.53, $p = 0.012$), open approach (OR 2.00, 1.63–2.45, $p < 0.001$) and rectal primary (OR 1.54, 1.21–1.96, $p < 0.001$) were independent predictors of higher overall complication.

The major complication rate was 15.6% in the most deprived and 11.5% in the most affluent group. Most deprived group was an independent risk factor for major complications compared with the most affluent group (OR 1.49, 1.01–2.23, $p = 0.048$) (Table 4). The global p value for impact of SED on major complications was 0.24. Other variables with significant impact on major complication were age (OR 1.02, 1.01–1.04, $p < 0.001$), female gender (OR 0.73, 0.55–0.97, $p = 0.033$), ASA grades 3 or 4 (OR 2.19, 1.62–2.95, $p < 0.001$) and open approach (OR 2.00, 1.45–2.76, $p < 0.001$).

Length of hospital stay

The median length of hospital stay was 6.5 days in the most affluent and 8 days in the most deprived group ($p = 0.003$). The linear regression model used log transformation of length of hospital stay as an outcome variable. There were no zero values in the length of hospital stay, with the minimum value being 1 day. The exponentiated coefficients generated from the model can be seen in Table 4. These represent fold increase or decrease in the length of hospital stay of a group to its reference. Based on this model, the estimated of length of hospital stay of the most deprived group was 15% higher or 1.15 times that of the most affluent group (coefficient 1.15, 1.06–1.25, $p < 0.001$). The overall effect of SED on length of hospital stay was significant (global $p < 0.001$). Other variables associated

Table 3 Multivariate regression model for primary outcome

		Overall complication			
Variable	Subgroups	Odds ratio	95% confidence intervals	*p* value	*p* value (global)
Age		1.01	1.00–1.02	0.001	-
Gender	Male	REF			
	Female	0.74	0.61–0.91	0.002	-
ASA	1–2	REF			
	3–4	1.76	1.39–2.24	< 0.001	-
Presentation	Screening	REF			0.005
	Symptomatic	1.07	0.77–1.47	0.692	
	Emergency	1.68	1.12–2.53	0.012	
Primary site	Right and transverse colon	REF			< 0.001
	Left and sigmoid colon	0.86	0.77–1.47	0.218	
	Rectum	1.54	1.21–1.96	< 0.001	
Surgical approach	Laparoscopic	REF			-
	Open	2.00	1.63–2.45	< 0.001	
IMD quintiles	1 (most affluent)	REF			
	2	1.15	0.85–1.56	0.362	0.077
	3	1.23	0.91–1.67	0.174	
	4	1.32	0.95–1.83	0.098	
	5 (most deprived)	1.48	1.13–1.95	0.005	

with longer length of stay were age, ASA grades 3 or 4, rectal primary and open approach. Both symptomatic and emergency presentations had longer hospital stay compared with screening patients.

Table 4 Multiple regression for secondary outcomes

		Major complication (CD 3–5)				Length of hospital stay (LOS)			
Variable	Subgroups	Odds ratio	95% confidence intervals	*p* value	*p* value (global)	Coefficients* (exponentiated)	95% confidence intervals	*p* value	*p* value (global)
Age		1.02	1.01–1.04	< 0.001	-	1.01	1.00 to 1.01	< 0.001	-
Gender	Male	REF				REF			
	Female	0.73	0.55–0.97	0.033	-	0.97	0.92 to 1.03	0.295	-
ASA	1–2	REF				REF			
	3–4	2.19	1.62–2.95	< 0.001	-	1.17	1.09 to 1.25	< 0.001	-
Presentation	Screening	REF			0.18	REF			< 0.001
	Symptomatic	0.85	0.51–1.45	0.532		1.11	1.01 to 1.22	0.023	
	Emergency	1.17	0.65–2.18	0.600		1.52	1.35 to 1.70	< 0.001	
Surgical approach	Laparoscopic	REF				REF			
	Open	2.00	1.45–2.76	< 0.001	-	1.43	1.34 to 1.52	< 0.001	-
Primary site	Right and transverse colon	REF			0.16	REF			< 0.001
	Left and sigmoid colon	1.05	0.74–1.48	0.778		1.03	0.96 to 1.10	0.368	
	Rectum	1.38	0.97–1.96	0.070		1.22	1.14 to 1.31	< 0.001	
IMD quintiles	1 (most affluent)	REF			0.24	REF			< 0.001
	2	1.40	0.90–2.18	0.134		0.99	0.91 to 1.08	0.896	
	3	1.04	0.65–1.65	0.874		1.02	0.93 to 1.11	0.708	
	4	1.23	0.75–1.99	0.386		1.05	0.95 to 1.15	0.315	
	5 (most deprived)	1.49	1.01–2.23	0.048		1.15	1.06 to 1.25	< 0.001	

*The coefficients (exponentiated) represent fold increase or decrease of estimated LOS of a group to that of its reference group; e.g. the LOS in ASA 3 or 4 is 1.17 times or 17% more than that of its reference group ASA 1 or 2

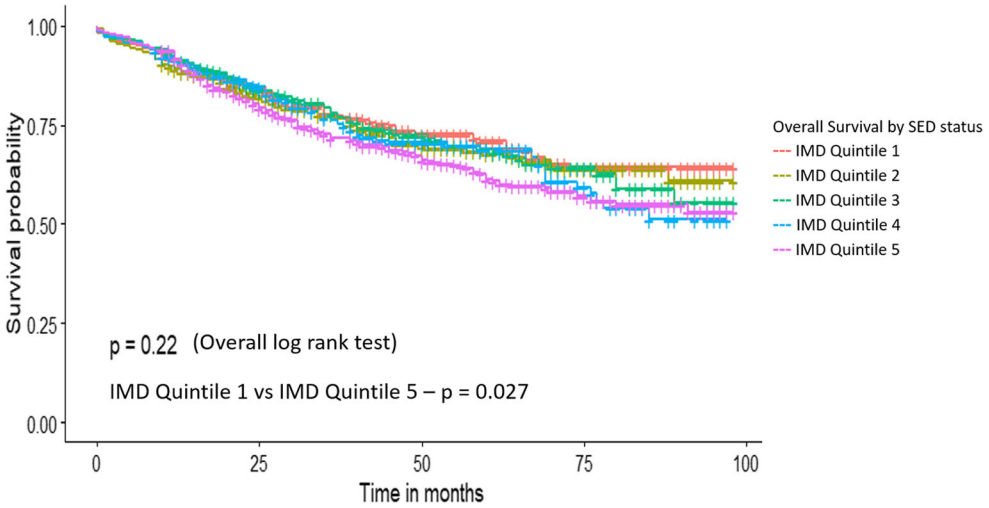

Fig. 2 Overall survival by SED status

Overall survival

The median follow period in the study was 41 months with an interquartile range of 20 to 64.5 months. Figure 2 shows the Kaplan-Meier survival curves for all the five deprivation groups. Log rank test could not show a significant trend of difference in the overall survival of the five quintiles (p = 0.22). However, there was a significant difference between the overall survival of the most deprived and the most affluent groups (Log rank test, p = 0.027).

Figure 3 shows effect of major complications on overall survival (after excluding postoperative deaths—CD grade 5). Presence of CD grades 3 or 4 led to poor overall survival compared with patients with no major complication—CD 0, 1 and 2 (p = 0.004).

Table 5 shows the Cox proportional hazards model constructed for overall survival. In this model, we first analysed SED as an individual variable; secondly, with TNM stage and presentation and lastly, along with all the variables. When SED was considered as the only independent variable, a significant difference was seen in overall survival of most deprived versus the most affluent group (unadjusted hazard ratio (HR) 1.30, 1.01–1.63, p = 0.029). However when TNM stage and mode of presentation were added to the model, the adjusted hazard ratio for SED did not reach statistical significance (most deprived vs. most affluent, HR 1.15, 0.90–1.47, p = 0.235). On inclusion of other variables in the model, the adjusted hazard ratio for SED was 1.27, 0.99–1.62, p = 0.055. TNM stage 3 or 4, age, ASA status 3 or 4, open approach,

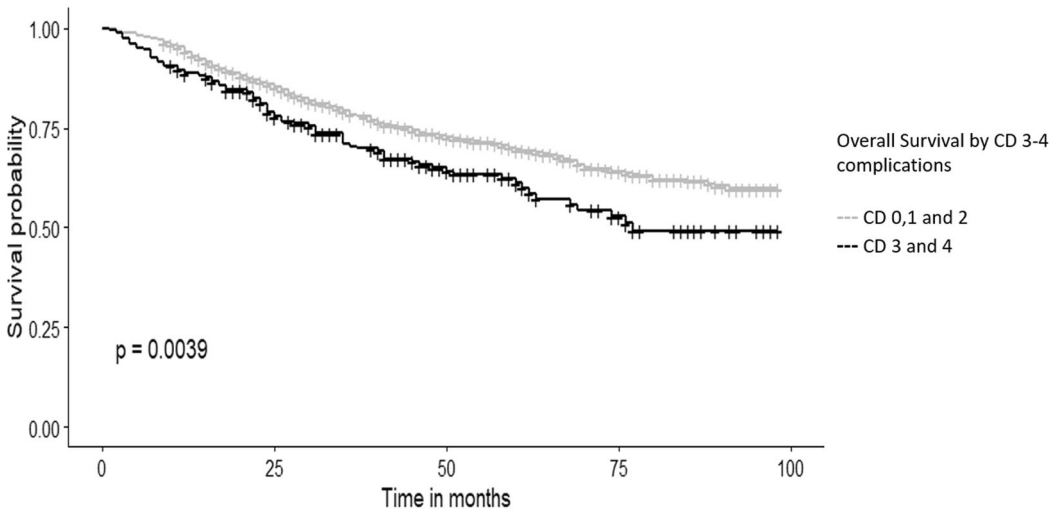

Fig. 3 Overall survival by CD 3–4 complication

Table 5 Cox proportional hazard models for overall survival

Variables included	Overall survival								
	IMD quintile only			IMD quintile + TNM stage + presentation			IMD quintile + TNM stage + presentation +all variables as below		
	Hazard ratio	95% confidence intervals	*p* value	Hazard ratio	95% confidence intervals	*p* value	Hazard ratio	95% confidence intervals	*p* value
IMD quintiles									
1 (most affluent)	REF			REF			REF		
2	1.09	0.81–1.42	0.535	0.99	0.75–1.31	0.962	1.08	0.81–1.43	0.566
3	1.07	0.79–1.39	0.638	0.97	0.73–1.29	0.859	1.00	0.76–1.33	0.953
4	1.17	0.87–1.55	0.273	1.12	0.84–1.50	0.424	1.20	0.89–1.61	0.215
5 (most deprived)	1.30	1.01–1.63	0.029	1.15	0.90–1.47	0.235	1.27	0.99–1.62	0.055
Presentation	NA								
Screening				REF			REF		
Symptomatic				2.19	1.45–3.30	< 0.001	1.58	1.04–2.40	0.031
Emergency				3.97	2.58–6.10	< 0.001	2.10	1.33–3.32	0.001
TNM Stage	NA								
1				REF			REF		
2				1.12	0.83–1.52	0.451	1.04	0.77–1.41	0.778
3				1.62	1.23–2.13	< 0.001	1.65	1.25–2.17	< 0.001
4				5.65	4.19–7.62	< 0.001	5.47	4.03–7.44	< 0.001
Age	NA			NA			1.02	1.01–1.03	< 0.001
Gender—male	NA			NA			REF		
Gender—Female							0.89	0.75–1.06	0.20
ASA status 1–2	NA			NA			REF		
ASA status 3–4							1.92	1.59–2.31	< 0.001
Surgical approach	NA			NA					
Laparoscopic							REF		
Open							1.57	1.28-1.91	< 0.001
Primary site	NA			NA					
Right and transverse colon							REF		
Left and sigmoid colon							0.85	0.69–1.04	0.108
Rectum							0.73	0.58–0.91	0.007

symptomatic and emergency presentations were found to be associated with diminished overall survival. Screening presentation and rectal primary were markers of better overall survival.

Discussion

Socioeconomic deprivation is known to be associated with poor cancer outcomes but its impact on surgical complications following CRC resection has received rather less attention. In this study, we have shown that the most deprived socioeconomic status is an independent risk factor for higher overall and major complications following major resection of colorectal cancer compared with the most affluent status. Although we could not establish the effects of SED on complications across 5 quintiles of deprivation, significant differences were demonstrated between most deprived and most affluent groups. SED was also an independent predictor of longer length of hospital stay and this was seen across all the deprivation quintiles. These associations between SED and the outcomes persisted despite adjusting for other prognostic variables.

Data on surgical complications is not currently included in regional or national databases such as the National Bowel Cancer Audit, UK [18]. Surgical complications have direct impact on length of stay, cost of treatment and quality of life [19]. Occurrence of complications such as anastomotic leak may result in delays in starting adjuvant chemotherapy and can impact on

long-term oncolo
gical outcomes [20, 21].

As other studies, we found that increasing age, male gender and ASA grade 3 or 4 were associated with higher overall and major complications [22]. Adverse risk factors for survival were age, ASA grade 3 or 4, TNM stage 3 or 4, open approach and emergency presentation. Rectal cancers had higher overall complications and better survival compared with right colon cancers [23, 24]. Age, ASA grade 3 or 4, open surgery and rectal primary were associated with longer hospital stay [25]. Emergency presentation was associated with extended hospital stay, higher overall complication but not major complications. Laparoscopic surgery was associated with fewer complications, shorter length of stay and better overall survival compared with open surgery. This may reflect the inherent advantages of laparoscopy, but it also may be related to selection bias, with generally fitter patients being selected for laparoscopy rather than open surgery [26].

A recent study from the Netherlands has reported better postoperative outcomes for patients with colon cancer referred through the faecal immunochemical test-based screening program compared with non-screen-detected patients. However, in this study, there were no differences in rate of postoperative complications between screening and symptomatic patients [27]. Screening status was associated with better overall survival compared with symptomatic and emergency presentations even after adjustment for TNM stage. This is consistent with reported literature, which may be due to better tumour pathology or because of lead time bias that is seen with screening [28, 29].

We demonstrated a significant difference in overall survival between most affluent and most deprived groups on univariate analysis. On multivariate analysis, the difference was not statistically significant ($p = 0.055$). This could be a result of relatively lower numbers of events (deaths) in each of the 5 subgroups (quintiles 1–5), which in turn could be an effect of a relatively lower sample size.

Limitations of the study include the recognized shortcomings of retrospective analysis, as data were collated from discharge summaries and clinic follow-up letters. Major complication (CD 3, 4, 5) data were accurate because of its consistent inclusion in the electronic records, but CD 1, 2 data could have been recorded with less fidelity. SED is finally a surrogate marker of various unstudied variables like nutritional status, smoking, alcohol and lifestyle. We have not analysed any of these variables individually due to unavailability of such details in electronic patient records. Future studies looking at these specific variables may be able to explain the reason why SED affects disease outcomes.

Current risk stratification tools do not consider SED as a variable and this study emphasizes the importance of SED in risk stratification for patients undergoing CRC resection [30]. The importance of SED could be further emphasized by its inclusion in regional or national level audits which report and compare CRC outcomes.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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