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Low Socioeconomic Status is not a Predictor of Worse Colorectal Cancer Survival

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Abstract

Purpose: Colorectal Cancer (CRC) is the third most common cancer in the UK. Factors with well-established relation to CRC survival include age, tumor site and stage. Socioeconomic Status (SES) is a factor that may play a role in survival but current evidence on this is conflicted. We aim to investigate the effect of SES on CRC survival.

Methods: This is a retrospective cohort analysis of all patients diagnosed with CRC in South Tees NHS Trust between January 2006-January 2019. Demographics were collected from a trust database. SES was defined using the Index of Multiple Deprivation (IMD). Cox- regression was used to investigate the effect of different factors on overall survival and Kaplan-Meier analysis to estimate survival.

Results: A total of 5,060 patients diagnosed with CRC, with a median follow-up of 60 months, were included. Overall survival was 77.2%, 59.6% and 50.3% at 1-year, 3-years and 5-years, respectively. Colon cancer was associated with worse survival than rectal cancer (p=0.003, hazard ratio=1.163). On multivariate analysis, socioeconomic deprivation was not associated with poorer CRC outcomes (hazard ratio=1.022, p=0.523).

Conclusion: There is a lack of uniformity in the reported effect of SES on CRC survival across different studies. This could be due to the heterogeneity of healthcare systems globally or a lack of uniform parameters used to assess SES. In this study, SES did not impact CRC survival. We therefore suggest that effective diagnosis and treatment, made available to all at the point of delivery, might mitigate any differences in survival across socioeconomic groups.

Keywords: Colon cancer; Rectal cancer; Survival; Socioeconomic class; Colorectal cancer.

Statements and Declarations

Funding: Not applicable. No funding was required for this project.

Conflicts of interest/Competing interests: I declare that the authors have no conflict of interest in regard to this study.

Availability of data and material: This data was extracted from an in-house trust database which belongs to the National Health Service.

Code availability: Not applicable

Ethics approval: The patients included in the study were treated as per the national and local guidelines. No additional ethical approval was required.

Consent to participate: No patient identifiable information was used in this study hence patient consent was not needed.

Consent for publication: All the authors involved in this study have read the paper and consented to its publication.

Introduction

Colorectal Cancer (CRC) is one of the most commonly diagnosed malignancies worldwide [1]. Around 42,300 new cases are diagnosed in the UK every year [2–5]. The overall survival for CRC has improved in recent years, with current five-year survival rates of almost 60% in England. Factors influencing survival include age, sex, tumour site and the American Joint

Committee on Cancer (AJCC) stage at the time of diagnosis. Other demographic factors such as race, marital status and Socioeconomic Status (SES) can similarly be implicated but the literature is conflicted on what impact these factors have on overall survival [6].

The association between SES and CRC survival in particular has been inconsistent across the literature. Globally, the incidence of CRC appears to be higher in more affluent socioeconomic groups, but the outcome of treatment remains less favourable in those with a lower SES [1,7,8]. This picture however varies between countries and even within different studies of the same populations. Although overall survival from CRC is improving, studies in Europe and the US suggest that a socioeconomic gradient does exist and is not reducing [9-13]. A post-hoc analysis of data from a Randomised Control Trial (RCT) in the United Kingdom (UK) however demonstrated no difference in the survival of CRC patients with resectable primary tumours across socioeconomic groups [14].

This study was designed to see whether the results of the UK-based RCT would reflect the outcomes seen within the North-East of England, where a notable proportion of the population live in some of the most deprived areas in the UK. As such, this study aims to investigate the impact of SES on the overall survival of patients diagnosed with CRC over a thirteen-year period in a large NHS trust within the North East of England.

Methods

Study population

This is a retrospective cohort study which used a prospectively maintained trust database to identify all patients diagnosed with CRC, in South Tees NHS trust between January 2006 to January 2019. This included patients across two hospital sites who all received treatment by the same team, using the same protocols as per the national guidelines [15].

Socioeconomic classification

Measure of relative deprivation was assigned to each patient using their postcode at the time of diagnosis to determine their Index of Multiple Deprivation (IMD) decile [16]. IMD is the official measure of relative deprivation for areas in England. These are divided into over 32,000 neighborhoods known as Lower-layer Super Output Areas (LSOA). The average population in each LSOA is 1,500 and all LSOAs are grouped into 10 equally sized IMD deciles. The IMD is calculated using 7 metrics: Income, employment, health deprivation and disability, education skills and training, barriers to housing and services, crime and living environment. After determining the LSOA and therefore the IMD decile of each patient, patients were then grouped into 3 categories: A (most deprived, IMD deciles 1-3), B (moderately deprived, IMD deciles 4-6) and C (least deprived, IMD deciles 7-10). These groupings were chosen to ensure a similar number of patients were included in each group.

Analysis

Survival was estimated using Kaplan–Meier analysis and log-rank tests were used to compare the survival curves between each group. A multivariate cox proportional hazards regression model was used to investigate the effect of different factors on the overall survival. These multivariate analysis models included sex, age and the IMD group. The effect of sex, diagnosis (colon *vs* rectal cancer), age and IMD group on mortality was studied by creating a separate regression model. Additionally, we used a two-way analysis of variance (ANOVA) test to analyse the effect of any time lag between the diagnosis and surgical resection.

Results

A total of 5,073 patients presented with CRC between January 2006-January 2019 and were subsequently included in the study of these 2,978 were diagnosed with colon cancer and 2,095 patients were diagnosed with cancer in the rectum or recto-sigmoid junction. Thirteen patients were excluded from the survival analysis due to a missing postal address preventing IMD classification. In the remaining sample, there were 2,968 colon cancers and 2,092 rectal cancers with a slight male predominance for both colon (56%) and rectal cancer (66%). The median age at diagnosis for colon cancer was 71.0 years and for rectal cancer was 68.6 years. The median follow-up time over the two groups was 60 months (57 months for colon cancer and 65 months for rectal cancer). Figures 1 and 2 show the demographic distribution of the patients included in this study.

	Colon cancer (n = 2,968)			Rectal cancer (n = 2,092)		
	Median age	Sex		Median age	Sex	
IMD		Female	Male		Female	Male
A (1 – 3)	70.40	446	560	68.09	282	555
B (4 – 7)	71.21	368	422	69.18	194	354
C (8 – 10)	71.39	507	665	68.82	234	473
Total		1317	1647		710	1382
Percent (%)		44	56		34	66

Figure 1: Patient demographics- age and sex by IMD group and cancer type (IMD: Index of Multiple Deprivation (where group A were the most deprived, group B were

moderately deprived and group C were the least deprived), Median age: Median age at

time of diagnosis).

	Colorectal cancer (n = 5,060)				
	Median age	Sex		Total	Percentage (%)
IMD		Female	Male		
A (1 – 3)	69.25	730	1115	1,845	36
B (4 – 7)	70.20	529	776	1,305	28
C (8 – 10)	70.12	742	1140	1,882	34
Total		2001	3031	5060	
Percentage (%)		40	60		

Figure 2: Patient demographics overall- age and sex by IMD group for colorectal cancers combined (IMD: Index of Multiple Deprivation (where group A were the most deprived, group B were moderately deprived and group C were the least deprived), Median age: Median age at time of diagnosis).

Survival analysis

Overall survival for the entire cohort was 77.2%, 59.6% and 50.3% at 1 year, 3 years and 5 years, respectively (figure 3). Rectal cancer was associated with slightly better survival than colon cancer (p=<0.0001, hazard ratio: 0.865 (0.78-0.95)), (figure 4).

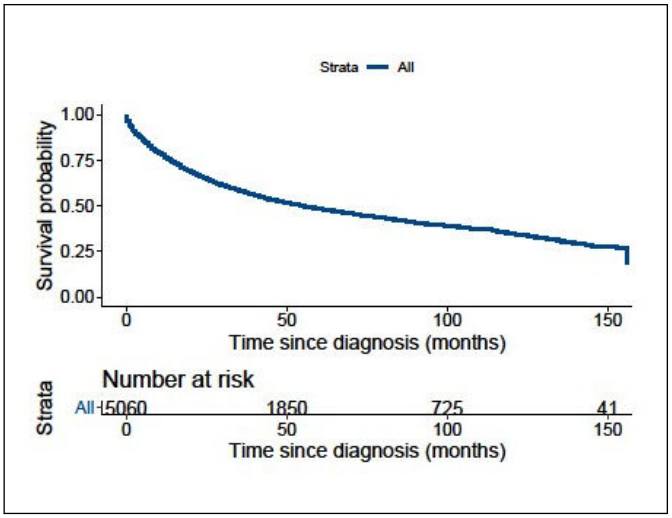

Figure 3: Overall survival for colorectal cancer. Overall survival for the entire cohort was

77.2%, 59.6% and 50.3% at 1 year, 3 years and 5 years respectively. Median follow up

time was 60 months. Kaplan-Meier analysis was used to estimate survival up to 150 months post-diagnosis.

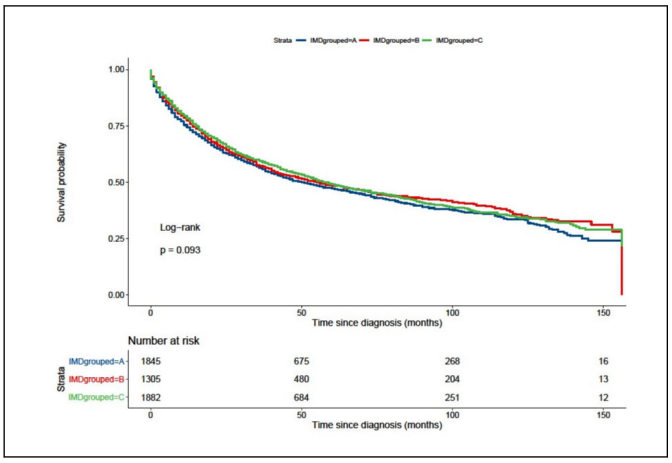

Figure 4: Overall survival for colon and rectal cancer. Kaplan-Meier analysis was used to estimate survival up to 150 months post-diagnosis and log-rank tests were used to compare survival curves between colon and rectal cancer. Rectal cancer was associated with slightly better survival than colon cancer (p=<0.0001, hazard ratio=0.86).

To analyses the impact of SES on overall survival, a multivariate analysis model was created. In this cohort, socioeconomic deprivation was not associated with poorer CRC survival outcome (hazard ratio: 1.022, p=0.523). Both male and female patients showed similar survival (hazard ratio: 0.983 and 0.934, respectively; p=0.986 and 0.946 respectively). Age however was found to be a significant factor with relatively poorer outcomes being associated with increasing age (p=<0.001, hazard ratio: 1.035 (1.03–1.04)).

The effect of sex, diagnosis, and age and IMD group on mortality was studied by creating a separate regression model. The analysis found that IMD group did not have a significant impact on mortality (figure 5). Group A (most deprived), hazard ratio: 0.995 (0.90–1.09; p=0.801); Group C (least deprived), hazard ratio: 0.970 (0.88–1.06; p=0.422).

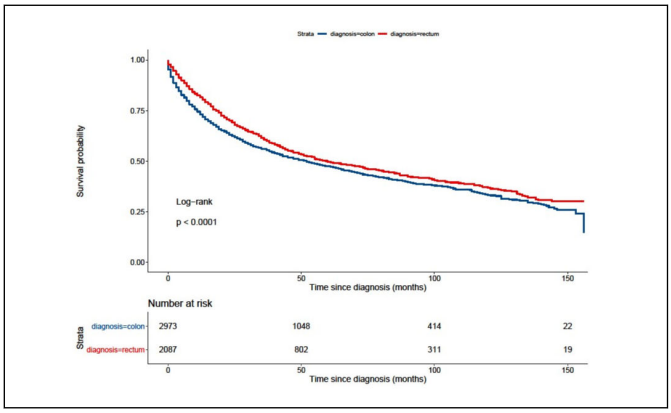

Figure 5: Overall survival for colorectal cancer by IMD. Multivariate Cox proportional hazards regression models were used to investigate the effect of socioeconomic status on overall survival. Survival was estimated using Kaplan-Meier analysis and log-rank tests were used to compare survival curves between the three socioeconomic groups. This showed that a patient's IMD group had no significant impact on survival.

The time lag between the diagnosis and surgical resection was then analyzed using a two-way ANOVA test. This showed no significant difference across the socioeconomic groups (A and B, p=0.733, A and C, p=0.921, B and C, p=0.909).

Discussion

The impact of socioeconomic deprivation on survival has been previously investigated for a variety of adult malignancies but the roots of disparity in survival remain largely controversial. The disease stage at the time of presentation, access to treatment, likelihood to participate in screening, and the different indices used to assess deprivation could in part, explain some of these differences.

Our regression analysis investigated the effect of sex, diagnosis, age and IMD group on mortality. The results demonstrated that being in a more affluent IMD group was not associated with a reduced risk of death which supports the findings of the previous UK- based study suggesting that a deprivation gradient does not exist across socioeconomic groups

for CRC in the UK [14]. There was also no significant difference in survival seen between males and females.

The slightly (though still statistically significant) improved survival seen in the rectal cancer group compared to the colonic cancer group may reflect adherence to a standardised protocol (i.e.TME) for rectal cancer treatment as opposed to the lack of any unified approach for colonic cancer. As expected, increasing age was a less favorable parameter in our study which we presume may have correlated with ASA grades however further analysis of this was beyond the scope of this study.

As previously discussed, this data demonstrates no difference in CRC outcomes between different socioeconomic groups. We hypothesis that this absence of variation in survival is related to the uniform accessibility of treatment within the NHS. Lower survival among socio-economically deprived populations in other countries might therefore be explained by the differences in healthcare provision, which are unfortunately seen across socioeconomic groups [17]. This may include disparities in insurance coverage as well as accessibility to early diagnosis and prompt treatment.

Pre-existing co-morbidities, such as smoking, sedentary lifestyle, adherence to treatment and obesity might also be related to worse outcomes in CRC specific survival [18]. Although we did not investigate these factors in our analysis, it is well established that they are more prevalent in the lower social classes and could therefore be viewed as surrogates of socioeconomic deprivation [19]. Yet despite this association between increasing comorbidity and lower SES, in the UK at least, this does not translate into worse CRC survival.

Another factor to consider is the uptake of bowel cancer screening. Endoscopic screening is known to be one of the most important factors in reducing the mortality of CRC [6,20,21]. Some studies suggest that inequality in access to screening might be associated with increased likelihood of late-stage diagnosis [22,23]. In the UK, the NHS-run bowel cancer screening programme is free and involves an at-home Faecal Immunochemical Test (FIT) done with the aid of a mailed test kit [24-26]. Since the introduction of the FIT programme, uptake of bowel cancer screening has increased from 56% to 66% but still varies dramatically with socioeconomic status with uptake in the lower social classes of only 35% [25-28]. Although a socioeconomic gradient is seen in many cancer screening programmes in the UK, the gradient seen in the uptake of bowel cancer screening is the widest. This difference in screening uptake however has not manifested as a measurable difference in CRC survival across different socioeconomic groups according to both the UK based study and our own data [14].

Strengths and weaknesses of the study

This is a relatively large study comprising over 5,000 CRC patients diagnosed in a single NHS trust. All patients with a diagnosis of CRC over a 13 year period were included with only a handful of exclusions due to missing patient postcodes. We believe this data adds to the results of the previous UK based study [14] which was smaller than our own (with 2,481 patients) and only included patients with resectable colorectal adenocarcinoma who were fit enough to receive adjuvant radiotherapy and/or chemotherapy. Our data set included all patients, regardless of their staging or treatment modality.

Furthermore, our procedures were all carried out in the same trust by a group of highly trained colorectal surgeons, using the same protocols.

At the time of comparison, we did not have staging data for all the patients due to a changeover of data-storing software during the study period which unfortunately resulted in a loss of some data. As such, staging information was omitted from the analysis as imputations to account for the missing data were not possible. Although being able to match for cancer stage would have strengthened our data set, we do believe that there were similarities in the staging across the groups as a similar proportion of patients went on to have curative surgery in all three groups.

A potential limitation of this study is the different parameters used by different studies to determine SES. As previously discussed, survival comparisons can be inconsistent between countries and even within the same population as different indices are used to assess SES. This unfortunately affects the comparability across studies investigating the impact of SES on CRC survival.

Furthermore, in England and therefore in this study, information on deprivation status (IMD) is not a household-specific measure and is based on a patient's residence and neighbourhood. By using geographical factors instead of individual measures, confounding influences on a patient's SES, such as external sources of income, or changing post-code during the study period may be overlooked. As such, the patient's assigned IMD group may not always be an accurate reflection of their SES. Nevertheless, it provides a uniform parameter and allows a fair comparison of studies within the UK.

Conclusion

There is a lack of uniformity in the reported effect of SES on CRC survival across different studies. This could in part be due to the heterogeneity of healthcare systems and non-uniform parameters used to assess SES in different parts of the world. The availability of screening, access to diagnosis, prompt treatment and provisions for regular follow-up can all have bearings on survival. Despite SES playing a well-defined role in a patient's likelihood to participate in screening and their risk of having additional co-morbidities, in the UK this does not translate to an increase in CRC deaths in socioeconomically deprived groups. We therefore conclude that a highly effective treatment, made available to all at the point of delivery, might mitigate any expected differences in survival across the socioeconomic groups.

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