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Socioeconomic differences in selection for liver resection in metastatic colorectal cancer and the impact on survival☆

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ABSTRACT

Background: Socioeconomic inequalities in colorectal cancer (CRC) survival are well recognised. The aim of this study was to describe the impact of socioeconomic deprivation on survival in patients with synchronous CRC liver-limited metastases, and to investigate if any survival inequalities are explained by differences in liver resection rates.

Methods: Patients in the National Bowel Cancer Audit diagnosed with CRC between 2010 and 2016 in the English National Health Service were included. Linked Hospital Episode Statistics data were used to identify the presence of liver metastases and whether a liver resection had been performed. Multivariable random-effects logistic regression was used to estimate the odds ratio (OR) of liver resection by Index of Multiple Deprivation (IMD) quintile. Cox-proportional hazards model was used to compare 3-year survival.

Results: 13,656 patients were included, of whom 2213 (16.2%) underwent liver resection. Patients in the least deprived IMD quintile were more likely to undergo liver resection than those in the most deprived quintile (adjusted OR 1.42, 95% confidence interval (CI) 1.18–1.70). Patients in the least deprived quintile had better 3-year survival (least deprived vs. most deprived quintile, 22.3% vs. 17.4%; adjusted hazard ratio (HR) 1.20, 1.11–1.30). Adjusting for liver resection attenuated, but did not remove, this effect. There was no difference in survival between IMD quintile when restricted to patients who underwent liver resection (adjusted HR 0.97, 0.76–1.23).

Conclusions: Deprived CRC patients with synchronous liver-limited metastases have worse survival than more affluent patients. Lower rates of liver resection in more deprived patients is a contributory factor.

Introduction

Socioeconomic inequalities in survival have been reported for most adult cancers worldwide [1–3]. Even in the United Kingdom (UK) where there is a universal entitlement to healthcare within the National Health Service (NHS), the health inequalities between the most deprived and least deprived areas of the country are showing little sign of reducing [4]. The improved cancer survival that has occurred over the last two decades in the United Kingdom has been reflected more in patients living in affluent areas than for those living in deprived areas [5]. It is estimated that 11% of deaths from common cancers would be avoided if survival for all patients was as high as in the most affluent group [5].

Colorectal cancer (CRC) is one of the most common malignancies in the Western world and the fourth most common cancer in the United Kingdom (UK) [6]. There are over 40,000 new cases of CRC diagnosed per annum and CRC is the second most common cause of cancer-related deaths in the UK. Poorer cancer-specific and

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overall survival in CRC patients in lower socioeconomic groups has been reported in United States [7], European [8,9] and UK [9–11] populations. The origins of these disparities in survival are not fully understood. Although late stage at presentation is a commonly cited cause of the lower survival amongst more deprived patients [12], studies which correct for stage have reported that this difference remains [13]. Evidence now also points to both differential access to treatment and differential disease management within the healthcare system [14]. Access to specialist care is known to favour the affluent [15] and differences in rates of primary CRC resection [16–18] and receipt of chemotherapy [7,19–21] according to socioeconomic status have been demonstrated.

Synchronous liver metastases are present in around 20% of patients diagnosed with CRC [22]. Liver resection in suitable patients is the only curative treatment modality with 5-year survival rates from 44 to 74% reported following resection [23–25]. Relatively little is known about the impact of socioeconomic status on liver resection rates, with studies reporting conflicting findings. A study of selection for liver resection in an English CRC population diagnosed from 1998 to 2004 demonstrated higher socioeconomic status to independently predict liver resection [24]. Similarly, Wiggans and co-authors. (2015), reported that affluent patients were over-represented amongst a regional English cohort of patients undergoing liver resection when compared to the demographics of the local population [26]. In contrast, a population-based study of patients with synchronous liver-limited metastases in Sweden did not find either income or education to be independently associated with liver resection [27]. No previous study has examined socioeconomic status as an independent predictor of mortality in this cohort. In this paper we describe the association between socioeconomic deprivation and the rate of liver resection and survival in patients with synchronous CRC liver metastases. We also investigate if any survival inequalities related to deprivation within this cohort are explained by differences in rates of liver resection.

Methods

Study population

Data from patients included in the National Bowel Cancer Audit (NBOCA) [28] were linked to Hospital Episode Statistics (HES) data. NBOCA data is prospectively collected and submission of patient data for those with a new diagnosis of CRC is mandatory for NHS trusts in England. In this study we included all patients recorded in the NBOCA dataset with a diagnosis of primary CRC from 1st January 2011 to 31st December 2015 with synchronous liver-limited metastases.

Study variables

Diagnostic information is captured in HES according to ICD-10 [29]. Synchronous liver metastases and extra-hepatic metastases were defined as an ICD-10 code for secondary cancer within the liver (C787) or secondary cancer elsewhere (C780-784, C786, C790-96) recorded up to one year before and 30-days after diagnosis of CRC. A year before CRC diagnosis was chosen to include patients who are found to have metastases before determining the site of the primary CRC.

Admission type (elective or emergency) was obtained from the linked HES records. The Royal College of Surgeons Charlson co-morbidity score [30] was used to identify co-morbid conditions in the HES records in the preceding year.

Socioeconomic status was calculated by the English Indices of Deprivation according to the patient's postcode [31]. This is the official measure of relative deprivation for neighbourhoods in England. The Index of Multiple Deprivation (IMD) ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area). Every such neighbourhood covers an average population of around 1500 people or 400 households. This measure is based on 37 indicators organised across 7 distinct domains of deprivation. These are combined to calculate the Index of Multiple Deprivation (IMD). The 7 domains of deprivation relate to 1) income, 2) employment, 3) education, 4) health and disability, 5) crime, 6) barriers to housing and services and 7) living environment. Quintiles are calculated by ranking the 32,844 small areas in England from most deprived to least deprived and dividing them into five equal groups.

Liver metastases were identified in HES data because the NBOCA records only the presence, but not the site, of metastatic disease. Of all patients with CRC identified in the NBOCA database as having metastatic disease at diagnosis, 60% had a metastases code recorded in HES data. Despite the potential under-reporting of liver metastases in HES, odds ratios still represent a valid measure of the relationship between patient characteristics and the liver resection rate, in the same way that an odds ratio provides a valid measure of relative risk in case–control studies. This is valid as long as under-recording is not dependent on the risk factor under investigation (socioeconomic status). The use of patients with recorded liver metastases in HES as a representative sample of all patients with liver metastases has been previously validated by comparing the characteristics of patients with metastases, irrespective of their site, identified in the NBOCA database and corresponding patients in the HES database [32].

Procedure information is captured in HES according to OPCS-4 [33]. All HES records in the year following the date of CRC diagnosis were searched for codes indicating a liver resection: right hemihepatectomy (J021), left hemihepatectomy (J022), resection of segment of liver (J023), wedge excision of liver (J024), extended right hemihepatectomy (J026), extended left hemihepatectomy (J027), partial excision of liver (J028/9), excision of lesion of liver (J031) and extirpation of lesion of liver (J038/9).

Study endpoints

The primary endpoints were receipt of liver resection within one year of date of CRC diagnosis and three-year all cause survival from date of CRC diagnosis. These two outcomes as well as demographic and tumour characteristics were compared between IMD quintiles to highlight any differences between groups of decreasing deprivation.

Statistical analysis

The statistical significance of differences in patient characteristics according to IMD quintile were assessed using the χ^2 test. Multivariable random-effects logistic regression was used to estimate the odds ratio of liver resection by IMD quintile, firstly adjusted for the following risk factors: gender, age, Charlson co-morbidity score, primary cancer site within the colon and rectum, admission type, T-stage and N-stage. A further model was fitted additionally adjusting for the presence of hepatobiliary surgical services on-site. A random intercept was modelled for each hospital trust to reflect the possible clustering of results within trusts. Missing values for the risk factors were imputed with multiple imputation using chained equations, creating ten data sets and using Rubin's rules to combine the estimated odd ratios across the data sets. Survival curves were estimated using the Kaplan–Meier method. Difference in 3-year survival in the first three years after diagnosis between IMD quintiles was tested with the log rank test.

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