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Research Article

Do Multiple Deprivation Index Scores Correlate with the Prevalence and Outcome of Pancreatic and Periampullary Cancer in West Yorkshire?

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Abstract

Background: Pancreatic cancer is associated with both smoking and heavy alcohol consumption both of which are linked with social deprivation.

Objectives: The aim of this study was to assess whether the prevalence of pancreatic/periampullary carcinomas was related to multiple deprivation index (MDI) scores.

Methods: Patients discussed at pancreatic multidisciplinary team (MDT) meeting during the period 2006 - 2010 were identified from a departmental database and postcode data extracted for MDI score calculation.

Results: 782 patients were identified with MDI scores calculable for 766 (97.9%). MDI scores were grouped into quintiles [1 most and 5 least affluent]: 1 (n = 164); 2 (n = 175); 3 (n = 137); 4 (n = 135) and 5 (n = 155) with no variation in prevalence across MDI groups. Significant differences existed in gender distribution: a male predominance in 1 and 2 (186M/153F; $p < 0.05$), and a female predominance in 4 and 5 (157F/123M; $p < 0.05$). 122 (15.7%) patients subsequently underwent resection. The number of patients in 1 and 2 quintiles underwent surgery was significantly higher compared to those in the 4 and 5 quintiles (19.2% versus 11.7%; $p < 0.05$). Median age at presentation was higher in 1 and 2 quintiles at 69.4 versus 67.8 years in 4 and 5; $p < 0.05$. The overall median survival of the 1 and 2 quintiles was significantly better at 6.4 months [IQR: 2.4 - 12.7] versus 4.6 months [IQR: 1.9 - 11.3] in 4 and 5; $p < 0.05$. However, there was no significant difference following resection at 14.8 months [IQR: 7.4 - 24.5] for quintiles 1 and 2 versus 14.3 [IQR: 7.9 - 24.8] for quintiles 4 and 5.

Conclusions: Although the prevalence of periampullary carcinomas was comparable across MDIs, significant differences existed in relation to operability and overall survival in favour of MDI 1 and 2 quintiles although this disappears for patients undergoing resection suggesting that efforts should be made to identify reasons for delays/inoperability for those in the 4 and 5 quintiles.

Keywords: *Multiple Deprivation Index; Periampullary Carcinoma; Prevalence and Outcome*

Introduction

Periampullary cancers are defined as cancers originating 2 cm around the ampulla of Vater. They comprise of four heterogeneous types arising from; the head of the pancreas, distal common bile duct, ampulla of Vater and peri-ampullary duodenum [1].

Between 1998 and 2007, approximately 10 per 100,000 in males and 8 per 100,000 in females were diagnosed with pancreatic cancer. Biliary cancer incidence was reported at 2 per 100,000 for both males and females. Ampulla of Vater and duodenal cancers were much less common, with incidence found to be 0.6 per 100,000 for males and 0.4 per 100,000 for females for ampulla of Vater cancer and for duodenal cancer incidence was 0.4 - 0.6 per 100,000 for males and 0.3 - 0.5 per 100,000 for females respectively. The largest numbers of all periampullary cancer types were diagnosed between the ages of 75 and 79; with the more deprived areas having a higher proportion of cases [2].

Pancreatic cancer has notoriously poor outcomes, particularly when compared to other GI cancers. And survival rates are lower than for any other major cancer type [3,4]. A population-based study in the Lancet, looking at survival trends over the last 40 years (from 1971 - 2011), found one-year survival, five year and ten-year survival from pancreatic cancer to be 19.1%, 3.3% and 1.2% respectively [5]. This is in part related to the advanced stage of disease at diagnosis, contributed to by poor diagnostic markers and challenges obtaining a tissue diagnosis; as a result there are limited effective treatment options available at this time [6,7].

Management of these cancers is dependent on multiple factors including stage at diagnosis, as well as anatomical location, vascular involvement and patient co-morbidities. Chemotherapy and radiotherapy are rarely effective and so surgical resection is the only curative option for these tumours [8]. However, only 10 - 15% are amenable, due both to proximity to major vessels and the presence of metastases at diagnosis [1].

There is insurmountable evidence that modifiable risk factors including smoking and alcohol intake adversely affect health, with these behaviors being closely linked to social deprivation [9-11]. More specifically cigarette smoking has been found to increase the risk of developing pancreatic cancer by 66% when compared to non-smokers, making it arguably the most important modifiable risk factor for this disease [12]. Although smoking cessation reduces the risk of developing pancreatic cancer, the risk does not diminish to the level of a never smoker until over ten years after quitting [13]. It is thought that carcinogens in tobacco smoke and nicotine metabolites cause inflammation and fibrosis, which can result in chronic pancreatitis; and these ongoing inflammatory processes within pancreatic tissue can lead to dysplasia and ultimately malignant transformation. Smoking also directly affects cancer cells, leading to tumour progression through uncontrolled proliferation and inhibition of apoptosis [13,14].

The relationship between alcohol consumption and pancreatic cancer is less clear, with many of the current studies yielding inconsistent results [12]. However, this could be a result of the studies' limitations e.g. failing to control for confounding factors such as smoking [15] and limited sample size [13]. One meta-analysis exploring the relationship between alcohol intake and pancreatic cancer, suggested that high alcohol intake may play an important part in developing pancreatic cancer but these effects were not significant for low-moderate intake [13].

The pancreas has a role in metabolising alcohol through oxidative and non-oxidative pathways. It has been proposed that toxic metabolites, including reactive oxygen species, produced from these reactions could alter inflammatory response leading to chronic pancreatitis and fibrosis [15,16]. Approximately 2 - 4% of pancreatitis cases will develop pancreatic cancer in the future [13]. In this disease process alcohol sensitises the pancreas to immune mediated responses to inflammation. Carcinogenesis is thought to result from an interaction of immune, genetic and environmental pre-disposing factors [15,16]. Malnutrition, caused by alcohol excess, may indirectly promote pancreatic cancer development by promoting abnormal gene transcription, through depletion of important methylation cofactors required for this process. These genetic errors may cause activation of oncogenes, and switch off tumour-suppressor genes [13].

In order to guide service provision and funding for both cancer prevention and treatment programmes and to target future research; previous studies have explored the effect of socioeconomic deprivation on cancer incidence, distribution and survival [17]. This previous research includes a report carried out by National Cancer Intelligence Network (NCIN) in conjunction with the Upper Gastrointestinal

Cancer Site Specific Clinical Reference Group (UGI SSCRG) investigating the difference in survival between socioeconomic deprivation groups in upper GI cancers in England. This report looked specifically at survival for range of upper GI cancers, including pancreatic cancer at one month, one month to one year, and one year or more after diagnosis. They found that in the more deprived socioeconomic groups, there were a lower proportion of males diagnosed with pancreatic and ampulla of Vater cancer, in comparison to females.

Other research looking into the correlation between incidence, survival and socioeconomic deprivation includes a study by Downing., *et al.* from 2008 [17]. They mapped the incidence and survival rates for six different cancer types, including pancreatic across Yorkshire, investigating the impact of socioeconomic background on each. They found that pancreatic cancer was fairly evenly distributed across the region, and that living in a more deprived area was associated with increased risk of pancreatic cancer although this was not statistically significant [17].

The multiple deprivation index (MDI) is an overall relative measure of social deprivation for small areas across England. The MDI is calculated by combining seven key domains of deprivation, including income, employment, education, health deprivation and disability, crime, barriers to housing and services and living environment. Each domain has been given a different weighting. Every small area in England is ranked according their MDI, from most to least deprived.

Aim of the Study

The aim of this study was to assess whether the prevalence and outcome of periampullary carcinomas was related to MDI.

Methods

Patients discussed at multidisciplinary team (MDT) meeting at the Pancreatic Unit, St. James's University Hospital, Leeds, United Kingdom, during the period from January 2006 through December 2010 were identified from a prospectively maintained departmental database. Postcode data extracted for MDI score calculation, these MDI scores were obtained from the Office of National Statistics (ONS). West Yorkshire, including Bradford, Leeds and Hull is one of the most deprived areas in England according to calculated MDI scores. For the interests of this study, MDI scores have been divided into quintiles, quintile one being most affluent and quintile five being the most deprived. For analysis purposes, these quintiles have been further grouped, into quintiles 1 and 2, and quintiles 4 and 5.

Statistical analysis

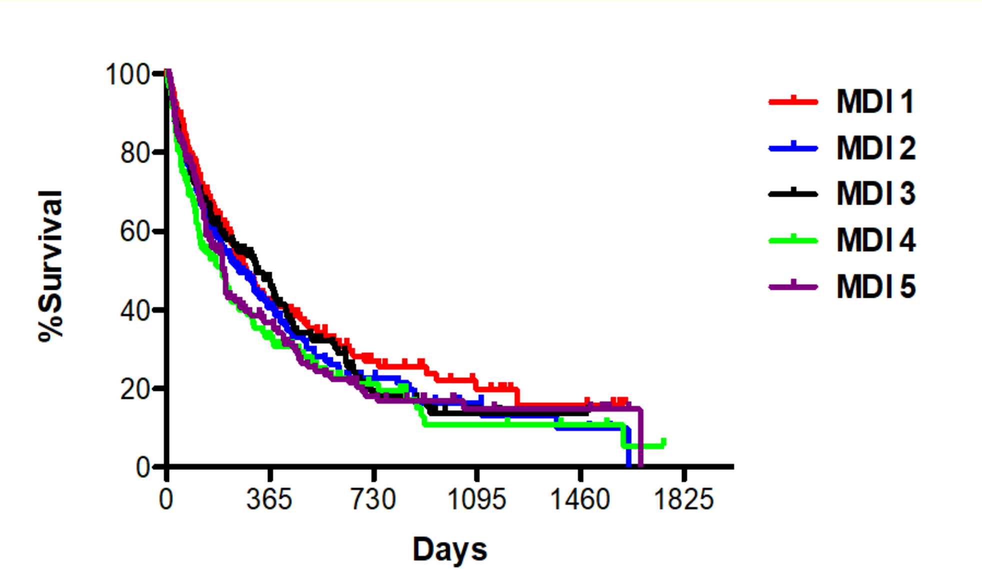
Continuous data was expressed as the median and interquartile range (IQR), and was assessed using the Mann Whitney test. Categorical data was expressed as frequency and proportions (%), and was assessed with the Pearson's chi-squared test. SPSS for Windows™ v18.0 (SPSS Inc, Chicago, Illinois, USA) was used for all analyses. Analyses were two sided and a *p*-value of < 0.05 was considered significant. The Kaplan-Meier method was used to assess survival outcomes.

Results

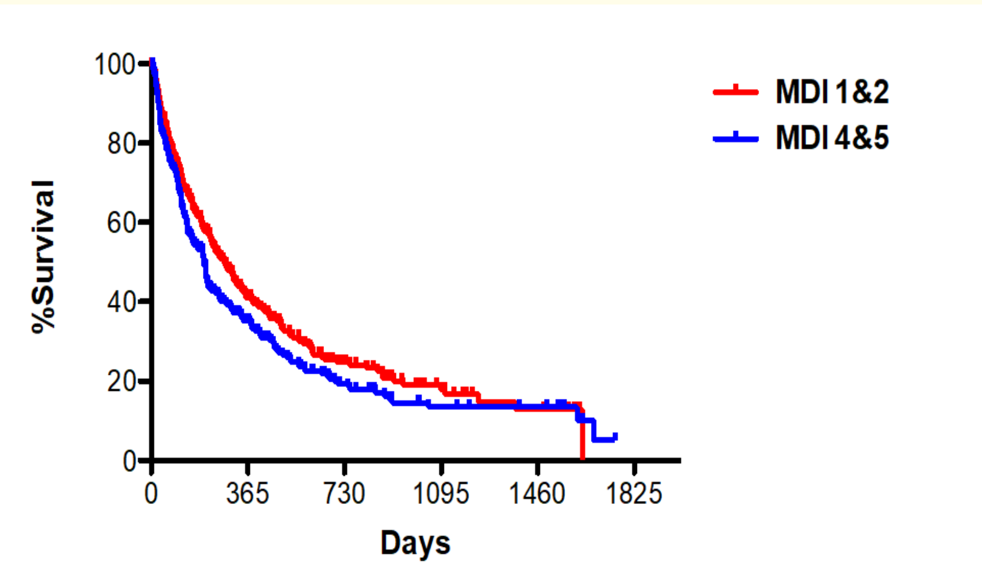
782 patients were identified with MDI scores calculable for 766 (97.9%). MDI scores were grouped into quintiles [1 most and 5 least affluent]: 1 (n = 164); 2 (n = 175); 3 (n = 137); 4 (n = 135) and 5 (n = 155) with no variation in prevalence across MDI groups (Table 1). Significant differences existed in gender distribution: a male predominance in 1 and 2 (186M/153F; $p < 0.05$), and a female predominance in 4 and 5 (157F/123M; $p < 0.05$). 122 (15.7%) patients subsequently underwent resection (Table 1). The number of patients in 1 and 2 quintiles underwent surgery was significantly higher compared to those in the 4 and 5 quintiles (19.2% *versus* 11.7%; $p < 0.05$; Table 1). Median age at presentation was higher in 1 and 2 quintiles at 69.4 *versus* 67.8 years in 4 and 5; $p < 0.05$ (Table 1). The overall median survival of the 1 and 2 quintiles was significantly better at 6.4 months [IQR: 2.4 - 12.7] *versus* 4.6 months [IQR: 1.9 - 11.3] in 4 and 5; $p < 0.05$ (Table 1 and Figure 1). However, there was no significant difference following resection at 14.8 months [IQR: 7.4 - 24.5] for quintiles 1 and 2 *versus* 14.3 [IQR: 7.9 - 24.8] for quintiles 4 and 5 (Table 1 and Figure 2).

Deprivation Quintile	Total Cases		Gender		Age at Presentations Median (IQR)	Underwent Surgery		Overall Survival Months Median (IQR)	Survival Following Resection Median (IQR)
	No	%	M	F		No	%		
Quintile 1 (Most Affluent)	164	21	89	75	69.7 (61.5 - 77)	32	20	6.4 (2.4 - 12.7)	16.6 (7.4 - 24.5)
Quintile 2	175	23	97	78	70.6 (62.8 - 78.4)	33	19	6.2 (1.94 - 12.6)	13.3 (8.2 - 22.6)
Quintile 3	137	18	76	61	67.5 (61 - 76.3)	23	17	6.8 (2.5 - 14.8)	14.9 (12.7 - 28.1)
Quintile 4	135	18	52	83	68.8 (61.9 - 78.5)	12	8	3.8 (1.7 - 10.1)	14.9 (9.6 - 22.3)
Quintile 5 (Most Deprived)	155	20	71	84	68.1 (59.2 - 76.9)	22	14	4.6 (1.9 - 11.3)	14.73 (7.2 - 31.0)
Total	766	100	385	381	67.2 (60.6 - 76.4)	122	15.7	5.4 (1.9 - 12.7)	14.9 (8.5 - 25.5)
Quintiles 1 and 2	339	44	186*	153	70.0 (62.3 - 78.5)*	65	19*	6.4 (2.4 - 12.7)*	14.8 (7.4 - 24.5)
Quintiles 4 and 5	290	38	123	157*	68.2 (60.4 - 77.4)	38	12	4.6 (1.9 - 11.3)	14.3 (7.9 - 24.8)

Table 1: *Prevalence, demographics and survival of periampullary cancer patients across MDI groups.*
p - value < 0.05.

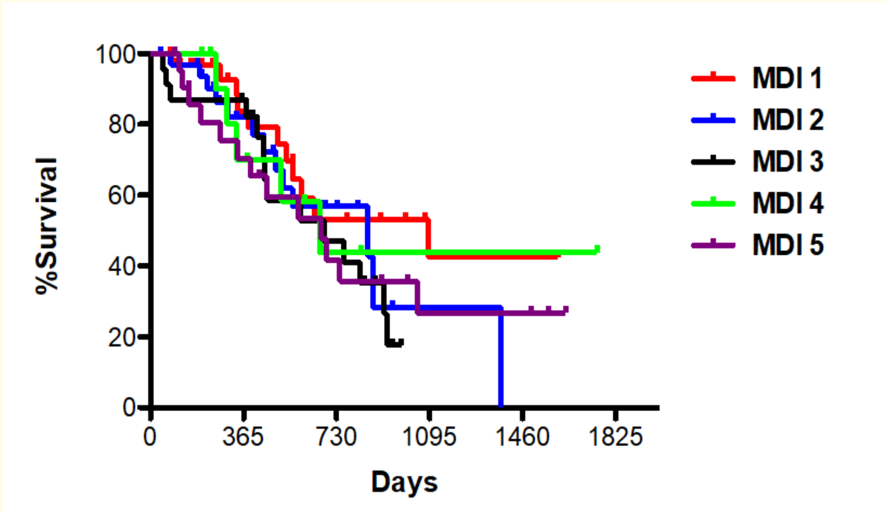


(a)

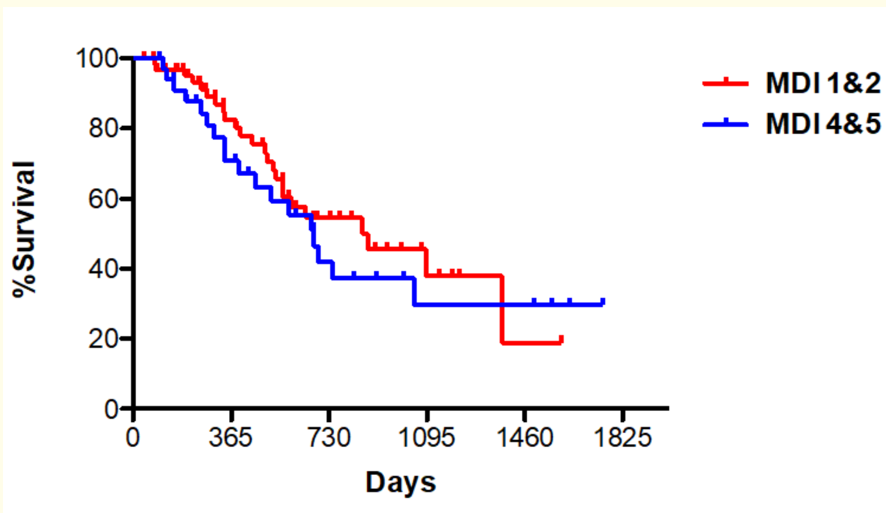


(b)

Figure 1: *Overall survival.*
(a) ***5 MDI groups****: There were no significant differences among the 5 MDI groups in term of overall survival (p = 0.23).*
(b) ***MD1 1 and 2 groups vs. MDI 4 and 5 groups:*** *The overall survival of the 1 and 2 quintiles was significantly higher compared to 4 and 5 quintiles (p = 0.03).*



(a)



(b)

Figure 2: *Survival following surgical resection of periampullary cancer.*

(a) ***5 MDI groups:*** *There were no significant differences among the 5 MDI groups in term of survival following surgical resection of periampullary cancer (p = 0.69).*

(b) ***MD1 1 and 2 groups vs. MDI 4 and 5 groups:*** *There was no significant difference between 1 and 2 quintiles compared to 4 and 5 quintiles in term of survival following surgical resection of periampullary cancer (p = 0.46).*

Discussion

Several previous studies have investigated the association of socioeconomic deprivation index and different types of the most common cancers (breast, lung and colon) as well upper GI cancers, which are less prevalent. These studies showed that the incidence and outcome of cancer were affected by MDI [2,18-20].

For lung cancer, incidence was found to be higher in more deprived areas than in affluent areas and it has been suggested that this difference, in part, can be linked with tobacco smoking [21,22]. And similarly, to other cancers, lung cancer survival was higher in affluent areas than in deprived areas [23,24].

In breast cancer, there is mounting evidence that women from deprived areas have a significantly poorer outcome and reasons for this are multi-factorial [25,26]. They often present with more advanced disease suggesting that there might be an element of delay in presentation, poorer general health and life style [27,28]. These factors may contribute to more co-morbidities, less resistance to malignancy, being unfit for surgery or having poor post-operative recovery.

More specifically, there were similar findings for upper GI cancers, including periampullary, to those of lung and breast cancers. For both pancreatic and biliary cancers one-year survival was lower in the more deprived than the least deprived areas, for both males and females. But interestingly this difference diminished over a longer time period, with five-year pancreatic cancer survival rates being comparable across all socioeconomic deprivation groups for both males and females. In contrast, for biliary cancer there were differences between males and females. For five-year survival, survival rates for males were higher in the least deprived versus most deprived areas, but this was not the case for females where there was no significant association between survival and socioeconomic deprivation [20].

In our study, the results indicate that the prevalence of periampullary carcinomas is not related to the degree of affluence/deprivation in the population of West Yorkshire. However, variation did exist in age and gender in relation to the MDI quintiles. Median age at diagnosis in the quintiles 1 and 2 was higher than in quintiles 4 and 5 (69.4 years versus 67.8 years respectively). And interestingly, there were a higher proportion of males diagnosed with periampullary cancer than females in quintiles 1 and 2; the converse being true for quintiles 4 and 5, where females made up the majority.

The outcome of periampullary cancer was found to be influenced by MDI, with patients from the most deprived regions (quintiles 4 and 5) less commonly undergoing surgery, and exhibiting a poorer overall median survival following diagnosis, 6.4 months for quintiles 1 and 2 was versus 4.6 months for quintiles 4 and 5. The data on survival post-resection would appear to suggest that outcomes in the upper and lower quintiles are comparable after surgery, with no significant difference demonstrated (14.8 months versus 14.3 months for quintiles 1 and 2 and quintiles 4 and 5 respectively).

There are a number of limitations with regards to our study. One of the main ones was the inability to determine reasons for poorer overall survival post diagnosis for patients living in more deprived areas; we were unable to ascertain whether the reduced rates of operability and overall survival were due to a delayed presentation and hence more advanced disease or due to co-morbidities preventing resection as both details of presentation (including cancer staging) and co-morbidities were not assessed.

Secondly, as smoking and high alcohol intake have been shown to be associated with periampullary cancers, it would have been informative to analyse smoking statuses and alcohol consumption for all the patients involved in this study. This would enable us to establish if there were any correlations between age at diagnosis, operability and overall survival with smoking history and alcohol intake. And, in addition, to determine whether there were higher rates of smoking and alcohol excess within the more deprived areas.

Finally, the data and findings from this study may not be comparable to other regions within the England/UK. West Yorkshire (including inner city areas of Leeds and Bradford) has particularly high concentrations of MDI 5 populations, and therefore other regions may not have such a large proportion of residents living in deprived areas. It may be that these overall survival figures are especially pessimistic due to the nature of the West Yorkshire's population demographics.

One of the strengths of this study is that we have looked at a specific intervention, i.e. surgery, which few other similar studies have. By analyzing the percentage of patients undergoing surgery in each quintile, we can explore reasons for these differences (65% of patients in quintiles 1 and 2 underwent surgery compared to just 38% in quintiles 4 and 5). We have also been able to compare overall median survival (in months) with median survival following surgical resection, which is particularly important as this only curative option for periampullary cancers. From analysis, we have found that the better outcomes for patients in least deprived areas, do not exist following surgical resection, in other words there is no significant difference in survival post-surgical resection for those in the least versus the most deprived areas.

Further research needs to focus on exploring reasons why those from more deprived areas have delays to diagnosis and particularly if these delays directly impact on the chances of operability and therefore curative management. One of the issues resulting in delayed presentation is a lack of awareness of the signs and symptoms of pancreatic cancer, crucially in the more deprived socioeconomic groups. In order to minimise this, we need to invest in public health campaigns promoting recognition of the common signs and symptoms of this malignancy. And additionally, by ascertaining other reasons for delayed presentation in lower socioeconomic deprivation groups (MDI quintiles 4 - 5), we can look to eliminate further barriers preventing individuals seeking medical attention at an earlier stage and thereby potentially improve overall survival.

Conclusions

Although the prevalence of periampullary carcinomas was comparable across MDIs, significant differences existed in relation to operability and overall survival in favour of MDI 1 and 2 quintiles although this disappears for patients undergoing resection suggesting that efforts should be made to identify reasons for delays/inoperability for those in the 4 and 5 quintiles.

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