Resection rate, hospital procedure volume and survival in pancreatic cancer patients in England: Population-based study, 2005-2009

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ABSTRACT

Objective

We assessed the association between population resection rates, hospital procedure volume and death rates in pancreatic cancer patients in England.

Design

Patients diagnosed with pancreatic cancer were identified from a linked cancer registration and Hospital Episode Statistics dataset. Cox regression analyses were used to assess all-cause mortality according to resection quintile and hospital volume, adjusting for sex, age, deprivation and comorbidity.

Results

There were 31,973 pancreatic cancer patients studied, 2,580 had surgery. Increasing resection rates were associated with lower mortality among all patients (χ^2(1df)=176.18, p_{trend}<0.001), with an unadjusted hazard ratio (HR) of 0.78 95%CI[0.75 to 0.81] in the highest versus the lowest resection quintile. Adjustment changed the estimate slightly (HR 0.82, 95%CI[0.79 to 0.85], (χ^2(1df)=99.44, p_{trend}<0.001)). Among patients that underwent surgery, higher procedure volume was associated with lower mortality (HR=0.88 95%CI[0.75-1.03] in hospitals carrying out 30+ versus <15 operations a year, shared frailty model, χ^2(1df)=1.82, p_{trend}=0.177).

Conclusion

Higher population resection rates were associated with lower mortality. The association with hospital procedure volume was less clear possibly due to small number of patients who underwent surgery. Nevertheless these results suggest survival is higher in hospitals that carry out a greater number of operations a year, particularly those doing 30+ operations, supporting the benefit of centralising perioperative expertise in specialist centres. Ensuring people are increasingly diagnosed when they are suitable candidates for surgery, and have access to these specialist centres may lead to an increase in the proportion of patients that undergo surgical resection which could plausibly increase survival of pancreatic cancer patients.

Key words: Population resection rate, hospital procedure volume, survival, pancreatic cancer, England

INTRODUCTION

In 2010, around 7,000 persons were diagnosed with pancreatic cancer in England.[1] Pancreatic cancer survival is poor with 3.7% of patients surviving five or more years after diagnosis.[2] Surgical resection offers the chance of a cure for patients with early stage tumours, but pancreatic cancer is often diagnosed at an advanced stage of disease and curative surgery is only possible for a minority of patients.[3, 4]

Pancreatic resection is a complex surgical procedure with a high risk of postoperative mortality and morbidity. A study in the US by Birkmeyer *et al* of Medicare patients treated between 1994 and 1999 found that across all 14 procedures studied (8 of which were for cancer) mortality was lower in higher volume hospitals, with absolute differences in mortality between very-low and very-high volume groups most pronounced for pancreatic resections.[5] In general, studies have found an association between higher hospital procedure volume, lower post-operative mortality and long-term survival following surgery for pancreatic cancer, although not all these studies reported a statistically significant association.[5-10] In 2001, the Upper Gastrointestinal Cancer Improving Outcomes Guidance proposed that surgical referrals for pancreatic cancer should be centralised to specialist centres.[11] Within this framework, the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS) recommend that hospitals should draw from a population of 2-4 million which should result in at least 80-100 pancreatic resections being carried out per year, of which some would be carried out for related peri-ampullary tumours and other conditions such as chronic pancreatitis.[12] In most centres, pancreatic cancer accounts for less than half of all pancreatic resections.[13]

Previous studies from our group that focused on oesophageal and gastric cancer [14] and on lung cancer [15] found lower death rates in areas where a higher proportion of patients underwent surgical resection. We also found lower death rates in patients operated in hospitals that carry out a greater number of operations a year despite an adverse case-mix in the higher procedure volume hospitals.[14, 16] No study has investigated the association between population-based resection rates and mortality or the impact of hospital procedure volume on survival in pancreatic cancer patients in England following the 2001 Improving Outcomes Guidance. The present study aimed to assess the associations between population resection rate, hospital procedure volume and survival for patients with pancreatic cancer in England, taking into account differences in case-mix including age, sex, socioeconomic deprivation and comorbidity.

METHODS

Data on 34,135 pancreatic (ICD10 C25) cancers diagnosed in England between 2005 and 2009 were extracted from the National Cancer Data Repository, which contains information collected by the former regional cancer registries in England. Death information was obtained from the National Health Service central register via the Office for National Statistics. Registrations which only had information from a death certificate (n=2,099) and had no NHS number (n=61) were excluded. For patients registered with more than one primary pancreatic cancer tumour the earlier tumour was selected which excluded a further two records, leaving 31,973 patients in the final dataset.

Patient characteristics

Age at diagnosis was aggregated into five-year groups. Patients were grouped into quintiles of socioeconomic deprivation based on their postcode and lower super output area (each comprising a population of around 1,500 people) of residence. The income domain of the 2007 Indices of Deprivation [17] was used for patients diagnosed between 2005 and 2006, and the income domain of the 2010 Indices of Deprivation [18] was used for patients diagnosed between 2007 and 2009. Comorbidity information was obtained from a linked Hospital Episode Statistics (HES) admitted patient dataset supplied by the Health and Social Care Information Centre. For each patient, a comorbidity score was derived using non-cancer diagnosis codes recorded within inpatient and day case episodes between two years prior to and three months after the patient's date of cancer diagnosis.[19] Standard weights were assigned according to the severity of the condition,[20] and the resulting scores were aggregated into four categories of increasing severity of comorbidity: 0 (no comorbidity) through to 3+ (score of 3 or higher).

Pancreas surgery information, defined as pancreatectomy, pancreaticoduodenectomy and other total or subtotal excisions of the pancreas (OPCS4 J55.1-J55.2, J55.8-J55.9, J56.1-J56.9, J57.1-J57.5, J57.8-J57.9), was obtained from the HES dataset. The first surgical procedure for each patient from one month before to six months after the diagnosis date was extracted.

Population resection quintile and hospital procedure volume

The resection rate was defined as the proportion of pancreatic cancer patients in each primary care trust geographical area that underwent surgical resection in each year of diagnosis. These proportions were then grouped into population resection quintiles representing areas with increasing proportions of resected patients.

The number of operations was available at the organisation level of NHS hospital trust. In England, an NHS hospital trust manages one or more local hospitals. In this paper, we refer to NHS hospital trusts simply as "hospitals", and the annual number of operations in a trust is referred to as the "hospital procedure volume". For each pancreatic cancer patient that underwent surgical resection, hospital procedure volume was computed as the number of pancreatic cancer operations carried out in the hospital in which they were

treated and in the same year as their diagnosis. Three groups were defined based on quantiled distributions with the boundaries readjusted slightly to form sensible groupings: <15 operations per year, 15-29, and 30+ operations per year. There were 91 individual hospitals included in the analysis, of which 62 individual hospitals contributed to the <15 volume group and nine individual hospitals to the 30+ group in at least one diagnosis year.

Data analysis

The numbers and proportions of patients who underwent surgical resection by population resection quintile, hospital procedure volume and case-mix variables, i.e. sex, age, socioeconomic deprivation and comorbidity, were tabulated. P-values for trend or heterogeneity were calculated, as appropriate. Univariate and multivariate Cox proportional hazards regression analyses were used to estimate the all-cause mortality hazard ratios (HRs) and 95% confidence intervals (CIs) according to population resection quintile, hospital procedure volume and the case-mix variables. Analyses of hospital procedure volume were performed on the subset of patients who underwent surgical resection (n=2,580).

For all patients, survival time was calculated from the diagnosis date until death from any cause or censored at end of study on 31st December 2010. In the analysis restricted to patients who underwent surgical resection, survival time was calculated from the operation date. Adjustment was made for identified potential confounders including sex, age, socioeconomic deprivation, comorbidity and population resection quintile. To account for any potential variation in the risk of death between groups of patients treated in particular hospitals, a shared frailty Cox model was used, with hospital as a random effect.

RESULTS

Of 31,973 patients diagnosed with pancreatic cancer in England between 2005 and 2009 included in this study, 2,580 (8.1%) underwent surgical resection (Table 1). The annual proportion of patients that had surgery in each of the 151 primary care trusts of residence ranged from 0% to 29% and the annual number of patients undergoing surgery in each hospital ranged from 1 to 55.

The proportion of patients that had surgery decreased with age (from 17.9% in patients aged 55 or less to 0.2% for patients aged 85+), socioeconomic deprivation (from 9.1% to 7.2% in the least to most deprived quintile), and severity of comorbidity (from 10.1% for patients with no recorded comorbidity to 5.2% for patients with a comorbidity score of 3 or more), (all with $p_{trend}<0.001$). Women were less likely to undergo surgery than men (7.6% vs. 8.6%, p=0.002). Patients that underwent surgery in high volume hospitals were more likely to live in areas where a higher proportion of patients underwent surgical resection ($\chi^2(1df)=132.65$, $p<0.001$) and were more likely to have more severe comorbidity ($\chi^2(1df)=4.58$, p=0. 032).

Among all patients, increasing resection rates were associated with lower death rates ($\chi^2(1df)=176.18$, $p_{trend}=<0.001$), with a HR of 0.78 (95%CI 0.75 to 0.81) in the highest compared with the lowest population resection quintile (Table 2). Adjustment for age and sex (HR=0.82, 95%CI 0.79 to 0.85, $\chi^2(1df)=105.03$, $p_{trend}<0.001$), and further adjustment for socioeconomic deprivation and comorbidity attenuated the association a little (HR=0.82, 95%CI 0.79 to 0.85, $\chi^2(1df)=99.44$, $p_{trend}<0.001$). Without any adjustment, one-year survival ranged from 12.8% to 21.4% in the lowest to the highest resection quintile. Five-year survival ranged from 2.0% to 4.4% respectively.

Over the five-year period studied, there was an increase in the proportion of patients who underwent surgical resection in hospitals carrying out 30+ operations a year (20% in 2005 to 57% in 2009), and a corresponding decrease from 50% to 15% in hospitals carrying out <15 operations a year (Figure 1).

Regarding hospital procedure volume, the unadjusted HR for the highest (30+ operations per year) compared with the lowest volume group (<15 operations a year) was 0.96, 95%CI 0.85 to 1.08, $\chi^2(1df)=0.52$, $p_{trend}=0.472$ (Table 3). Adjustment for age and sex made little material difference (0.94 (95%CI 0.84 to 1.06, $\chi^2(1df)=0.92$, $p_{trend}=0.338$). The shared frailty model strengthened the HR to 0.88 (95%CI 0.75 to 1.03, $\chi^2(1df)=1.82$, $p_{trend}=0.177$) suggesting a marginal survival benefit in the largest procedure volume group but not reaching statistical significance. The hazard ratios in the short term (<30 days after surgery) were lower (HR 0.69 [0.37 to 1.32]) than those in the longer term; 31-365 days (HR 0.93 [0.74 to 1.17]) and >365 days (HR 0.91 [0.75 to 1.11]), after adjusting for case mix and resection quintile.

DISCUSSION

This study found variation in the proportion of pancreatic cancer patients that underwent surgical resection in England in the five-year period between 2005 and 2009. In absolute terms, the difference in the unadjusted survival between the lowest and the highest resection quintile was greater at one-year compared with five-years after diagnosis. After adjustment for age, sex, socioeconomic deprivation and comorbidity, areas with higher resection rates had higher survival. This is consistent with our previous studies for oesophageal and gastric cancer [14] and for lung cancer.[15] The association between hospital procedure volume and survival was in the direction of higher survival in larger volume hospitals, but the association was not statistically significant.

Whether or not a patient undergoes surgical resection depends on several factors. Adjustment for case-mix variables, which frequently affect long-term survival such as age, sex, socioeconomic deprivation and comorbidity made little material difference to the findings which could suggest, at the very least these, patient-level factors were not the main reason for the lower death rates in the higher resection rate areas. Therefore, we propose that factors related to service provision, such as the availability of specialist surgical teams and appropriate supportive care, the presence of effective multidisciplinary team decision making and the tendency and/or ability to operate on higher-risk patients in some areas, may be relatively more important. If these findings are the result of non-patient related factors, increasing the proportion of patients who undergo surgical resection could plausibly lead to an increase in survival for patients with pancreatic cancer. Quality of life will also be an important consideration when deciding whether it is appropriate to offer surgery to a greater number of patients. Therefore, it is important to ensure all pancreatic cancer patients who could potentially benefit from specialist expertise are referred to dedicated multidisciplinary teams.

Our previous studies on the association between hospital procedure volume and death rates in England for oesophageal and gastric cancer [14] and for lung cancer [16] found there was lower mortality in hospitals that carried out a greater number of operations per year. Other studies have found an association between higher hospital volume and lower post-operative mortality following surgery for pancreatic cancer.[5-9, 21] In the present study the association between hospital procedure volume and survival was strengthened by adjustment for case-mix and resection quintile but it did not reach statistical significance. It is feasible that this study was underpowered since only nine hospitals carried out 30 or more procedures per year in at least one year during the period. It is recognised that this study does not completely reflect the volume of pancreatic resections carried out in these hospitals as the volume measure was only based on pancreatic cancer patients, however, it suggests a survival benefit for patients operated on in hospitals undertaking 30 or more pancreatic cancer operations a year.

The principal strength of this study was that it used a population-based cancer registration and Hospital Episode Statistics linked dataset which included all patients diagnosed with pancreatic cancer in a five-year period in the whole of England. It also covered a period when centralisation of surgical services in England was on-going with a clear increase in the proportion of pancreatic cancer patients who underwent surgical

resection in hospitals carrying out 30+ operations a year. Surgical information was obtained from the HES admitted patient dataset and was more complete than surgery information recorded in the cancer registration process. A systematic review found acceptable accuracy for procedure codes from NHS administrative data.[22]

Information on tumour stage, performance status and location of the tumour was not available in our dataset. These factors are associated with survival and define a patient's suitability to undergo surgery. It could be argued that the lower mortality in higher volume hospitals is associated with the selective referral of patients who have less advanced stage and have better fitness for surgery. However, it is evident that patients undergoing surgery in higher volume hospitals included a greater proportion of patients with comorbidity and adverse case-mix. Adjustment for the available case-mix factors strengthened the association between volume and mortality. Therefore, the absence of adjustment for other factors like stage may imply that the analysis actually underestimates the true difference between hospital volume groups. It was also not possible to take into account other non-surgical treatments such as chemotherapy and radiotherapy. Patients in the higher volume groups may be more likely to get other non-surgical treatments in combination with their surgery which could lead to better outcomes. Therefore, taking these other treatments into account could explain part of this association between hospital volume and survival. As the association between population resection quintiles and death rates was not affected by adjustment for other case-mix factors including comorbidity it suggests, as discussed earlier, that non-patient factors are more likely to explain the variation in resection rates. Therefore it is considered unlikely that the inclusion of stage information would materially change the resection rate findings.

Higher population resection rates were associated with lower mortality in pancreatic cancer patients. Due to the absence of information on stage and non-surgical treatment, future studies to assess the relationship between resection rate, stage, survival and quality of life in more detail should be carried out in order to ascertain whether there is genuine scope to offer surgical resection to a greater number of patients. The association between hospital procedure volume and survival was in the direction of higher survival in larger volume hospitals particularly those doing 30 or more operations a year, but it did not reach statistical significance. This study supports the benefit of centralising expertise including surgery and perioperative care in specialist centres.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no conflicts of interest.

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CONTRIBUTORS

This study was conceived and designed by VHC, ML and HM. VHC prepared and managed the dataset and VHC, SPR, JK, RHJ and ML carried out the statistical analysis. HMK and WA provided critical clinical insight into these data. VHC drafted the paper and all authors reviewed and revised the drafts and provided interpretation of results. All authors have approved the final version of the manuscript.

ETHICS COMMITTEE APPROVAL

This study was covered by section 251 of the Health and Social Care Act 2006 (and formally under Section 60 of the Health and Social Care Act 2001) which enables the collection and analysis of cancer registration data for the UK population. Therefore separate ethical approval was not required for this study.

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Table 1: Characteristics of patients diagnosed with pancreatic cancer (ICD10 C25) in England between 2005 and 2009

				Hospital procedure volume			
	Total number of patients	Total number resected	% resected χ^2 (1) df[3], p-value	<15 %	15-29 %	30+ %	Mantel-Haenszel χ^2 (1) df[c], p-value
	31,973	2,580	8.1	n = 802	n = 854	n = 924	
Hospital procedure volume[a]							
<15		802	31.1				
15-29		854	33.1				
30+		924	35.8				
No surgery	29,393						
Resection quintile[b]							
Quintile 1 (0.0-4.5)	6,411	145	2.3	8.4	4.7	4.1	
Quintile 2 (4.5-6.3)	6,549	356	5.4	20.8	13.2	8.2	
Quintile 3 (6.3-8.5)	6,276	468	7.5	23.6	15.8	15.6	
Quintile 4 (8.5-11.3)	6,360	621	9.8	19.6	32.1	20.6	
Quintile 5 (11.4-29.2)	6,377	990	15.5	27.7	34.2	51.5	
			763.02				**132.65**
			<0.001				**<0.001**
Sex							
Male	15,691	1,342	8.6	49.3	53.5	53.0	
Female	16,282	1,238	7.6	50.7	46.5	47.0	
			9.69				**2.32**
			0.002				**0.128**
Age group							
<55	2,547	457	17.9	17.2	19.2	16.8	
55-59	2,366	315	13.3	12.2	11.8	12.6	
60-64	3,429	434	12.7	16.6	18.1	15.8	
65-69	4,198	495	11.8	19.2	19.2	19.2	
70-74	4,915	439	8.9	18.5	14.6	18.0	
75-79	5,317	366	6.9	13.8	14.4	14.3	
80-84	4,654	66	1.4	2.2	2.3	3.0	
85+	4,547	8	0.2	0.2	0.2	0.4	
			1095.76				**0.43**
			<0.001				**0.510**
Socioeconomic deprivation							
1 = Most affluent	6,137	560	9.1	20.7	20.4	23.8	
2	6,978	600	8.6	26.9	21.3	21.9	
3	6,935	556	8.0	21.8	22.0	20.9	
4	6,430	466	7.2	18.3	17.9	18.0	
5 = Most deprived	5,493	398	7.2	12.2	18.4	15.5	
			21.60				**0.42**
			<0.001				**0.518**
Comorbidity score							
0	15,027	1,514	10.1	61.1	59.8	55.5	
1	8,302	737	8.9	26.7	27.9	30.8	
2	3,080	209	6.8	8.2	7.8	8.2	
3+	2,316	120	5.2	4.0	4.4	5.4	
Not known	3,248	-	-	-	-	-	
			78.99				**4.58**
			<0.001				**0.032**

[a] The proportion resected for hospital procedure volume is calculated out of those who underwent surgery

[b] Proportion of pancreatic cancer patients in each primary care trust area that underwent surgical resection

[c] For comorbidity, those with a not known comorbidity score were excluded

Table 2: Hazard ratios (HR) and 95% confidence intervals (95%CI) according to population resection quintile for all patients diagnosed with pancreatic cancer between 2005 and 2009

Resection Quintile	Unadjusted		Adjusted for age and sex		Adjusted for age, sex, socioeconomic deprivation and comorbidity	
Quintile 1 (0.0-4.5)	1.00		1.00		1.00	
Quintile 2 (4.5-6.3)	0.90	(0.87-0.93)	0.90	(0.87-0.93)	0.91	(0.88-0.95)
Quintile 3 (6.3-8.5)	0.90	(0.87-0.94)	0.93	(0.89-0.96)	0.94	(0.91-0.97)
Quintile 4 (8.5-11.3)	0.86	(0.83-0.90)	0.89	(0.86-0.92)	0.90	(0.87-0.93)
Quintile 5 (11.4-29.2)	0.78	(0.75-0.81)	0.82	(0.79-0.85)	0.82	(0.79-0.85)
χ^2 (1)	**176.18**		**105.03**		**99.44**	
p for trend	**<0.001**		**<0.001**		**<0.001**	

Figure 1: Proportion of patients undergoing surgical resection in each hospital procedure volume group, <15 operations a year, 15-29 operations a year, and 30 or more operations a year.

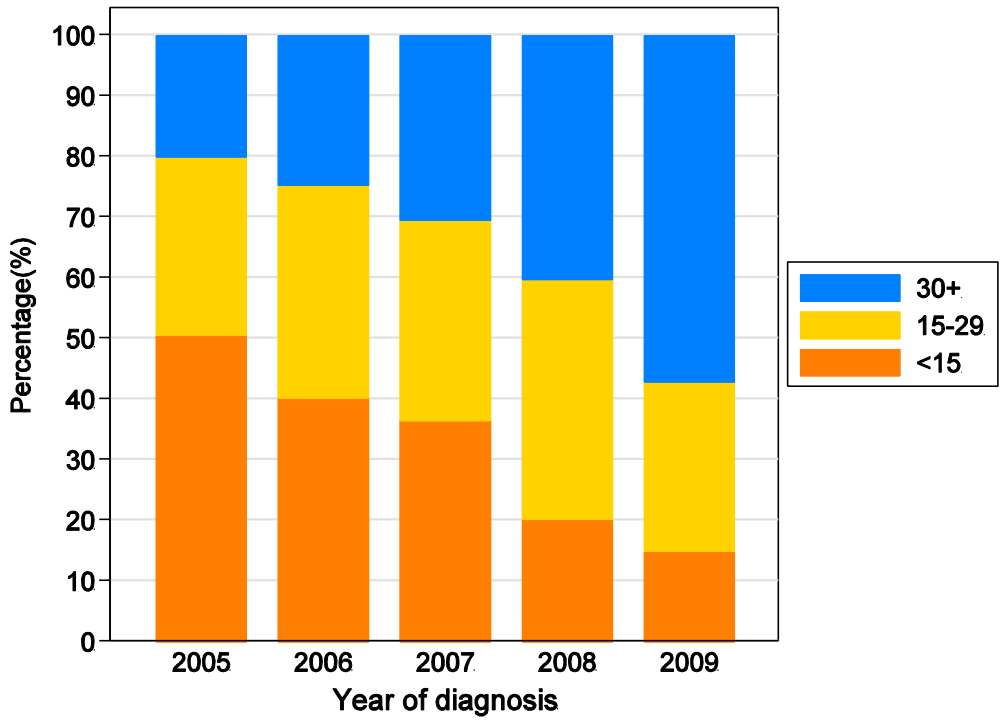

Table 3: Hazard ratios (HR) and 95% confidence intervals (95%CI) according to hospital procedure volume among resected patients diagnosed with pancreatic cancer

Hospital procedure volume	Unadjusted		Adjusted for age and sex		Shared frailty model adjusted for age, sex, socioeconomic deprivation, co-morbidity score, resection quintile and hospital (random effect)	
<15	1.00		1.00		1.00	
15-29	1.07	(0.96-1.21)	1.09	(0.97-1.23)	1.02	(0.89-1.16)
30+	0.96	(0.85-1.08)	0.94	(0.84-1.06)	0.88	(0.75-1.03)
χ2 (1)	**0.52**		**0.92**		**1.82**	
p for trend	**0.4722**		**0.3377**		**0.1774**	