

ORIGINAL ARTICLE

Socio-economic status influences the likelihood of undergoing surgical treatment for pancreatic cancer in the Netherlands

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Abstract

Surgical resection offers the only prospect of cure in pancreatic cancer patients. The probability of undergoing surgery is determined by several factors. The influence of socio-economic status (SES) on surgical treatment and survival was investigated in the Netherlands, a country with a widely accessible healthcare system.

Methods: Data on all patients with non-metastasised pancreatic cancer between 2005–2013 were analysed in the Eindhoven Cancer Registry (ECR). SES was categorized as low, intermediate or high. The influence of SES on the likelihood for surgery was assessed by multivariable logistic regression analyses. The influence on overall survival was analysed by multivariable Cox regression analyses.

Results: 698 M₀-patients were included, of whom 276 underwent surgery. Patients with low and intermediate SES were less likely to undergo surgery (32% vs 37%) than high-SES patients (48%) ($p = 0.002$; low SES: OR0.63, 95%CI [0.40–0.98]; intermediate SES: OR0.62, 95%CI [0.42–0.92]). Survival did not differ between SES groups (low SES: HR1.05 95%CI [0.85–1.30]; intermediate SES: HR1.11, 95%CI [0.91–1.35]), $p = 0.181$.

SES in pancreatic cancer patients determined the likelihood for surgery. However, SES had no influence on survival. It is important to provide more insights in the causes of these inequalities to minimize the effects of SES in pancreatic cancer care.

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Introduction

Pancreatic cancer is currently the fourth leading cause of cancer related death in Europe and the USA.¹ The only option to improve long-term survival is surgical treatment with or without neo-adjuvant chemotherapy, ideally followed by adjuvant chemotherapy.^{1,2} Nevertheless, up to 80% of pancreatic cancer patients are not treated with surgery.³ The most important reasons in refraining from surgical treatment are vascular

involvement of the primary tumour and the presence of metastatic disease at the time of diagnosis. However, the choice of treatment is not solely based on tumour characteristics. Patient characteristics such as age and general condition are usually taken into account given the complexity and impact of the surgical procedure. We recently described that presence of surgical experience in the hospital in which the patient is initially diagnosed with pancreatic cancer plays an important role in whether or not to proceed with surgery.⁴

Another factor that may also influence the choice of treatment in complex oncological procedures is the socio-economic status (SES) of the patient.⁵ In previous studies, the effect of SES was mostly attributed to the nature of the health care system such as

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in the USA, where care may not be equally accessible to all patients.^{6,7} The health care system in the Netherlands differs from that in the USA in that all Dutch residents regardless of income or social status are covered by equitable health care insurance. The current study was undertaken to investigate whether SES also plays a role in the treatment of pancreatic cancer.

Methods

Patient selection

Patients with a clinical or histological diagnosis of pancreatic cancer (C25) diagnosed between 1st January 2005 and 31st December 2013 in the southern region of the Netherlands were selected.⁸ This part of the Netherlands consists of approximately 15% of the Dutch population (16.7 million inhabitants in 2012). TNM classification or Clinical Extent of Disease (CEoD) was used in staging the pancreatic tumours. Only non-metastasised (M_0) pancreatic-cancer patients were included in the present study. Patients with missing tumour stage or diagnosed with tumour in situ (TNM 0) and patients with missing data on SES or categorised as institutionalised were excluded.

Data collection

Data on patient and tumour characteristics was collected from the Eindhoven Cancer Registry maintained by the Netherlands Comprehensive Cancer organization (IKNL). Specially trained registers routinely register all patients with a newly diagnosed malignancy in the southern part of the Netherlands. Comorbidities were scored according to a slightly modified Charlson comorbidity index.⁹

Socio-economic status (SES)

SES was determined at neighbourhood level using postal codes combined with mean value of housing and mean household income. These data were provided by the Netherlands Statistics Agency (CBS, Rijswijk, the Netherlands) and were derived from individual fiscal data available on an aggregated level.

SES was divided into 3 predefined SES categories, low (first to third decile), intermediate (fourth to seventh decile) and high (eight to tenth decile). Postal codes were assigned to one of these categories.

Hospital of diagnosis

Hospital of initial diagnosis was defined as the first hospital in which the clinical diagnosis of pancreatic cancer was made. Hospitals were classified as 'pancreatic centre' or 'non-pancreatic centre'. This classification was based on the annual volume of pancreatoduodenectomies (PD) performed in 2013 for a suspected malignancy in the pancreatic head. Centres performing 20 or more PDs annually were classified as 'pancreatic centre'. In the south region of the Netherlands 3 out of 10 hospitals fulfilled this criterion.

Study outcomes

Surgery

Surgical treatment was defined as any laparotomy with curative intent. Tumour resection included pancreatoduodenectomy, pancreatic body resection or distal pancreatectomy.

Survival

Overall survival was calculated making use of data retrieved from the Municipal Personal Records Database. This database contains all deaths or emigrations in the Netherlands. Overall survival was calculated from time of diagnosis to either death or end of follow-up (January 2014).

Statistical analysis

Differences in categorical variables between patients in the different SES and treatment groups were tested using Chi-square tests. A *p*-value under 0.05 was defined as statistically significant. The relationship between SES and likelihood of surgical treatment was tested by multivariable logistic regression analysis. Results were reported as Odds Ratios (OR) and 95% confidence intervals (95%CI). Survival analysis was performed by Kaplan–Meier method and differences were assessed by the log-rank test. Differences in median survival were tested for significance by Mann Whitney U test. Cox proportional hazards regression analysis was performed to assess the effect of treatment and SES on overall survival. Analyses were performed using Statistical Analysis Software (SAS) version 9.4.

Results

Population

Of the M_0 pancreatic cancer patients, 131 patients were excluded in this study.

There were 66 patients with missing tumour stage or diagnosed with tumour in situ (TNM 0) data were missing on SES or categorised as institutionalised ($n = 65$). In total, 698 patients diagnosed with M_0 -pancreatic cancer were included in the current study. Of these patients, 276 (40%) underwent a laparotomy and in 232 patients (33%) a resection of the tumour could be performed.

Baseline characteristics are provided in Table 1. Patients categorised as low SES were more often diagnosed in a non-pancreatic centre compared to high SES patients and patients with a high SES were more often diagnosed with a higher tumour stage. Surgical treatment was performed more often in patients categorized as high SES.

Logistic regression analysis

The likelihood for surgical treatment was higher in patients with high SES as compared to low and intermediate SES (Table 2) but decreased with age and diagnosis in a pancreatic centre. The likelihood for surgical treatment increased over time.

Table 1 Baseline characteristics of pancreatic cancer patients diagnosed between 2005 and 2013 in the Eindhoven Cancer Registry in the Netherlands, categorized by socio-economic status (SES)

Characteristics	Low SES (n = 184) (%)	Intermediate SES (n = 275) (%)	High SES (n = 239) (%)	p
Sex				
Male	83 (45)	136 (49)	117 (49)	0.628
Female	101 (55)	139 (51)	122 (51)	
Age (years)				
<60	51 (28)	77 (28)	77 (32)	0.074
60–69	23 (13)	61 (22)	51 (21)	
70–79	72 (39)	92 (33)	78 (33)	
≥ 80	38 (21)	45 (16)	33 (14)	
Diagnosis in pancreatic centre				
Yes	71 (39)	135 (49)	122 (51)	0.026
No	113 (61)	140 (51)	117 (49)	
Period of diagnosis				
2005–2007	64 (35)	83 (30)	74 (31)	0.205
2008–2010	76 (41)	104 (38)	83 (35)	
2011–2013	44 (24)	88 (32)	82 (34)	
Comorbidities				
0	36 (20)	57 (21)	58 (24)	0.453
1	48 (26)	92 (33)	65 (27)	
≥2	92 (50)	116 (42)	105 (44)	
Missing	8 (4)	10 (4)	11 (5)	
Tumour Stage				
I	65 (35)	81 (29)	48 (20)	0.002
II/III	119 (65)	194 (71)	191 (80)	
Laparotomy				
Yes	59 (32)	102 (37)	115 (48)	0.002
No	125 (68)	173 (63)	124 (52)	
Tumour resection				
Yes	48 (26)	84 (31)	100 (42)	0.001
No	136 (74)	191 (69)	139 (58)	

Survival

Median survival after surgical resection was 18 months (Interquartile range (IQR): 23) and 6 months without surgery (IQR: 8), $p = 0.010$. In addition, 5-year survival rates were significantly different for resection compared to no resection (20.4% vs 2.1%).

Median survival for low SES patients was 13 months (IQR: 13), for intermediate SES 13 months (IQR: 11) and for high SES 16 months (IQR: 16) ($p = 0.18$). Survival differences between SES groups were not different (Fig. 1A and B). When tested in a multivariable cox regression analysis, the influence of SES on

Table 2 Multivariable logistic regression analyses of likelihood for surgical treatment in pancreatic cancer patients diagnosed between 2005 and 2013 in the Eindhoven Cancer Registry, the Netherlands

Variable	Laparotomy n = 276	Odds Ratio [95%CI]
Sex		
Male	139 (41%)	1
Female	137 (38%)	1.05 [0.74–1.48]
Age (years)		
< 60	71 (53%)	1
60–69	105 (51%)	0.99 [0.62–1.58]
70–79	96 (40%)	0.62 [0.39–1.00]
≥80	4 (3%)	0.03 ^a [0.01–0.09]
Diagnosis in pancreatic centre		
Yes	155 (47%)	1.89 ^a [1.34–2.67]
No	121 (33%)	1
Period of diagnosis		
2005–2007	68 (31%)	0.32 ^a [0.21–0.50]
2008–2010	89 (34%)	0.50 ^a [0.33–0.76]
2011–2013	119 (56%)	1
Socio-economic Status		
Low	59 (32%)	0.63 ^a [0.40–0.98]
Intermediate	102 (37%)	0.62 ^a [0.42–0.92]
High	115 (48%)	1
Comorbidities		
0	65 (43%)	1
1	86 (42%)	1.40 [0.87–2.26]
≥ 2	115 (37%)	1.20 [0.76–1.91]
Missing	10 (35%)	1.05 [0.43–2.56]
Tumour Stage		
I	53 (27%)	1
II/III	223 (44%)	1.08 [0.71–1.65]

^a Significantly different.

survival showed no significant correlation (Table 3). In this regression analysis, surgical resection correlated with improved survival, whereas higher age and advanced tumour stage correlated with decreased survival (Table 3).

Discussion

This population-based study analysed the influence of SES on the likelihood for pancreatic cancer patients of receiving surgical treatment. This confirmed findings from previous studies that the hospital of initial diagnosis and age are important factors determining the prospect for surgical treatment.⁴ Besides previously known factors such as age and hospital of diagnosis, patients with a lower SES were identified to have a lower likelihood of receiving surgical treatment.⁴ In the present study, there

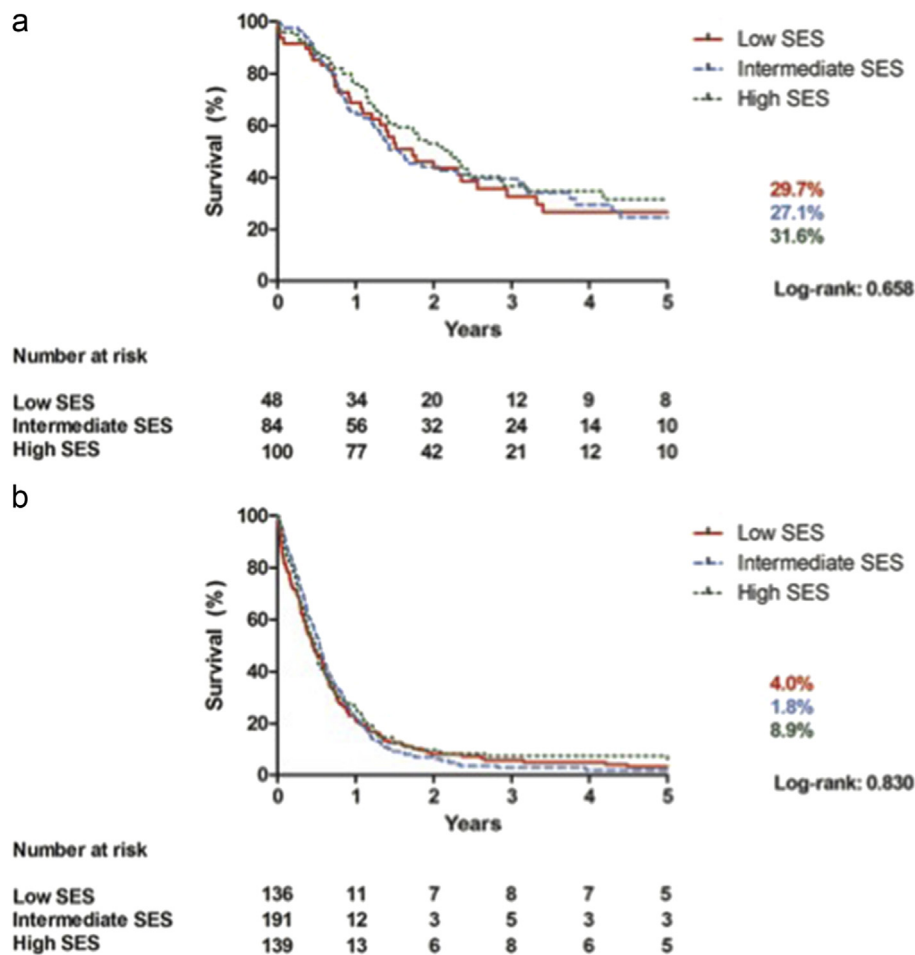


Figure 1 a) Kaplan-Meier of M₀-pancreatic cancer patients diagnosed between 2005-2013 in het ECR in the Netherlands and treated by surgical resection, divided in SES groups. b) Kaplan-Meier of M₀-pancreatic cancer patients diagnosed between 2005-2013 in het ECR in the Netherlands and not surgically treated, divided in SES groups

was a non-significant trend that patients with fewer comorbidities or a lower tumour stage were more likely to undergo surgical treatment.

The effect of SES on choice of treatment in pancreatic cancer has been previously reported in two studies from the USA. Our own findings concur with those of Seyedin *et al.* who reported that tumours of patients categorised to a low-income group were resected less often (33%) compared to patients in the high-income group (46%).⁷

Sun *et al.* showed that SES was a predictor for survival, with a mean overall survival in the low-SES group of 40 months compared to 50 months in the high SES group.⁶ The authors explained that these survival differences were a possible result of less medical consultation and less treatment in the low SES group. A correlation between SES and survival was not observed in the current study, potentially because it was underpowered or possibly as a result of the poor survival in pancreatic cancer in general even after surgical treatment. However, age, tumour stage

and surgical resection did show a significant correlation with survival.

In a recent German study, self reported SES-surrogates in pancreatic cancer patients were analysed. In contrast to the current study, this did not reveal an influence of any of the surrogate parameters of SES on the likelihood for a curative resection.¹⁰ These results were in line with the authors' expectations as in the German multi-payer health care system, all patients have equal access to health care. This is however similar to the situation in the Netherlands, although our study and the previously mentioned US study did reveal differences in the chance to receive surgery. An explanation may be that the method to determine the SES varied between these studies. SES was determined by median family income in the USA studies and in the German study only self-reported SES surrogates such as education level were used. The current study determined SES by using data on mean value of housing and mean household income at a neighbourhood level and may therefore be a more

Table 3 Cox regression analyses in pancreatic cancer patients diagnosed between 2005 and 2013 in the Eindhoven Cancer Registry, the Netherlands

Variable	Hazard Ratio [95%CI]
Sex	
Male	1
Female	1.01 [0.85–1.19]
Age (years)	
< 60	1
60–69	1.21 [0.94–1.56]
70–79	1.62 ^a [1.26–2.08]
≥ 80	2.53 ^a [1.87–3.44]
Diagnosis in pancreatic centre	
Yes	0.99 [0.84–1.17]
No	1
Period of diagnosis	
2005–2007	1.24 [0.99–1.55]
2008–2010	1.24 [1.00–1.53]
2011–2013	1
Surgical tumour resection	
Yes	0.37 ^a [0.30–0.47]
No	1
Adjuvant chemotherapy	
Yes	0.79 [0.57–1.11]
No	1
Socio-economic Status	
Low	1.05 [0.85–1.30]
Intermediate	1.11 [0.91–1.35]
High	1
Comorbidities	
0	1
1	1.00 [0.79–1.26]
≥ 2	1.03 [0.82–1.30]
Missing	0.74 [0.48–1.15]
Tumour Stage	
I	1
II/III	1.33 ^a [1.09–1.63]

^a Significantly different.

accurate measure to assess SES. However, using zip-code equivalents to determine SES might still confound results.

Several mechanisms may be responsible for the difference in the chance for surgical treatment regarding SES. Some studies have argued that patients with a low SES present at a later stage of their disease, possibly caused by a delay in symptom awareness.^{5–7,11,12} This was for instance observed in a study on oesophageal cancer patients investigating the effect of SES on treatment.⁵ Patients in the low-SES group were diagnosed at a

later stage compared to high SES patients but this was not the case in the current study.

The level of education might be another mechanism responsible for the differences between SES groups. Patients categorised as low SES more often have a lower educational level compared to patients categorised as high SES. A higher educational level might result in better-informed patients seeking for the best treatment options. This might explain a contribution of educational level to socioeconomic inequalities.¹³ Another factor may be life-style related factors associated with low SES such as smoking, alcohol consumption and obesity, making patients less suitable for undergoing major surgery.¹¹ Unfortunately these factors are not registered in the cancer registry (NCR) but smoking, alcohol consumption and obesity are known to be more prevalent in patients with low SES. Social support may also play a role. Given the impact of pancreatic surgery on quality of life, elderly patients, in particular, may require long-lasting support after surgery.^{14,15} The possibility of securing such support may depend on SES and affect the choice of treatment.

The effect of SES in the USA was mostly attributed to their health care system which is not equally accessible to all patients.^{6,7,16} Abraham *et al.* showed that patients' insurance status was of great importance in terms of likelihood for surgical treatment. The health care system in the Netherlands differs from that in the USA with all Dutch inhabitants being insured and having equal access to health care facilities regardless of the SES. Nevertheless, in the current study, patients with a high SES were more likely to be referred to a centre with surgical expertise. The insurance status is not a likely explanation for this practice in the Dutch situation. It may be that patients or their relatives are responsible for this phenomenon with high SES patients, being more well-informed and demanding about their treatment possibilities, requesting referral to a pancreatic centre. Additionally, low SES patients might more often refuse treatment, as suggested by Zell *et al.* in a California population.¹⁶

The differences in treatment between SES groups might also be influenced by decision making of physicians. Bernheim *et al.* showed that patients' SES affected physician clinical management decisions.¹⁷ Furthermore, Williams *et al.* showed that in medical decision-making high SES patients were more likely to receive treatment according to recommendations.¹⁸

The strength of this study is the complete database including all consecutive patients with a clinically or pathologically proven malignancy in the South of the Netherlands. Only pancreatoduodenectomies for pancreatic cancer were included in the current study as these procedures are now centralised in the Netherlands as opposed to distal pancreatectomies. Unfortunately no information on patients' lifestyle such as BMI, smoking, education or race are registered which may have played a role in decision making. Overall, the inequalities probably have multifactorial causes and can be both patient-related as well as physician-related.¹⁹ Information on the influence of patient's SES on physician decision-making has not been studied before and

might be an interesting topic for future research. By addressing this issue and making physicians aware of this phenomenon differences in health care within the population may be reduced which is one of the targets of the WHO.²⁰

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Conflicts of interest

None to declare.

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