Original article

Hospital of diagnosis and probability of having surgical treatment for resectable gastric cancer

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Background: **Gastric cancer surgery is increasingly being centralized in the Netherlands, whereas the diagnosis is often made in hospitals where gastric cancer surgery is not performed. The aim of this study was to assess whether hospital of diagnosis affects the probability of undergoing surgery and its impact on overall survival.**

Methods: **All patients with potentially curable gastric cancer according to stage (cT1/1b–4a, cN0–2, cM0) diagnosed between 2005 and 2013 were selected from the Netherlands Cancer Registry. Multilevel logistic regression was used to examine the probability of undergoing surgery according to hospital of diagnosis. The effect of variation in probability of undergoing surgery among hospitals of diagnosis on overall survival during the intervals 2005–2009 and 2010–2013 was examined by using Cox regression analysis.**

Results: **A total of 5620 patients with potentially curable gastric cancer, diagnosed in 91 hospitals, were included. The proportion of patients who underwent surgery ranged from 53·1 to 83·9 per cent according to hospital of diagnosis ($P < 0{\cdot}001$); after multivariable adjustment for patient and tumour characteristics it ranged from 57·0 to 78·2 per cent ($P < 0{\cdot}001$). Multivariable Cox regression showed that patients diagnosed between 2010 and 2013 in hospitals with a low probability of patients undergoing curative treatment had worse overall survival (hazard ratio 1·21; $P < 0{\cdot}001$).**

Conclusion: **The large variation in probability of receiving surgery for gastric cancer between hospitals of diagnosis and its impact on overall survival indicates that gastric cancer decision-making is suboptimal.**

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Introduction

Gastric cancer is the fifth most common cancer and the third leading cause of cancer death worldwide[1]. Although the incidence has decreased in recent decades in the Netherlands, prognosis is still poor. The 5-year overall survival rate for patients with stage I–III disease is 31 per cent and the median survival time for stage IV is only 6 months[2,3].

Surgery is the only potential curative treatment for gastric cancer[4]. Gastric surgery is associated with high morbidity and mortality rates, and performed mainly in low-volume hospitals[5,6]. Therefore, centralization by defining minimum volumes per centre has been initiated in the Netherlands. From 2012 onwards, hospitals should have performed a minimum of ten resections per year, increasing to a minimum of 20 resections annually from 2013. The probability of undergoing surgical treatment is influenced by several factors. Surgery with curative intent is generally not of benefit in patients with distant metastasis[2]. Patients can otherwise be regarded as less suitable for gastric cancer surgery because of advanced age, severe co-morbidity or decreased performance status.

Previous studies[7,8] have shown that the probability of receiving curative treatment for oesophageal and pancreatic cancer is associated with the hospital of diagnosis. Referring physicians may consider the patient too frail and unsuitable for surgery, and withhold possible curative options. In the study of patients with potentially curable oesophageal cancer[8], the proportion who underwent

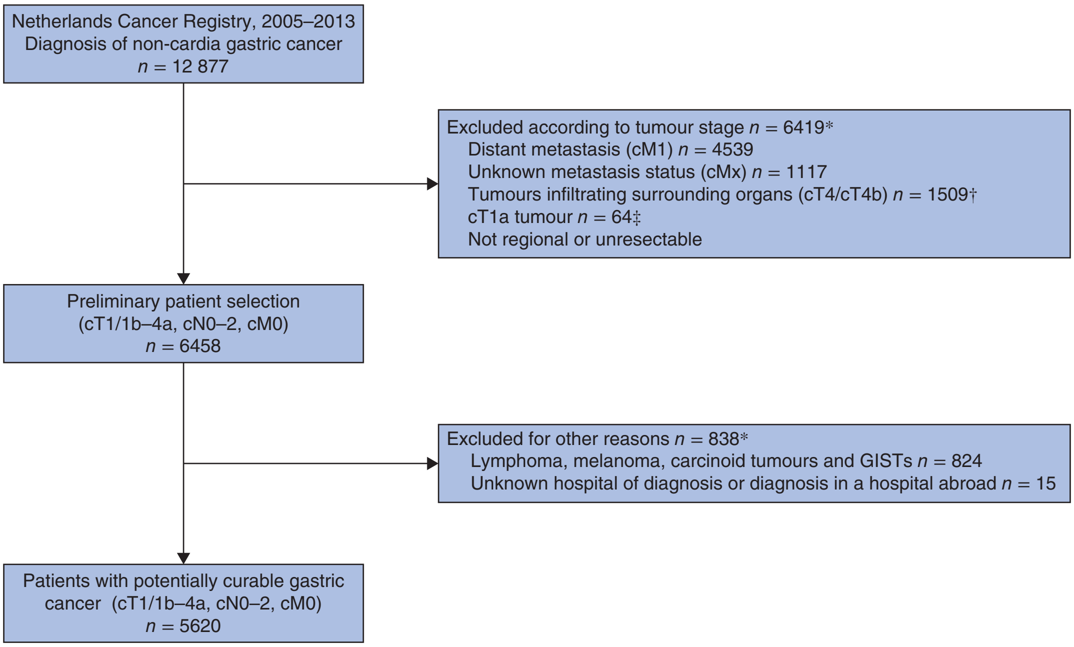

Fig. 1 Study flow chart. *Some patients met two exclusion criteria. †cT4 according to sixth edition of TNM classification and cT4b according to seventh edition. ‡Eligible for endoscopic mucosal resection instead of an operation. GIST, gastrointestinal stromal tumour

oesophagectomy varied between 33 and 67 per cent according to hospital of diagnosis.

It is of importance to evaluate the influence of hospital of diagnosis on referral for surgical treatment and, ultimately, survival, especially when surgical treatment for gastric cancer is being centralized within specialized centres. The aim of this study was, therefore, to examine the influence of hospital of diagnosis on the probability of undergoing surgery for gastric cancer in the Netherlands. The association between the variation in surgical treatment probability among hospitals of diagnosis and overall survival was also assessed.

Methods

Data were obtained from the Netherlands Cancer Registry (NCR). This registry serves the total Dutch population of 16·6 million inhabitants. The NCR is based on notification of all newly diagnosed malignancies in the Netherlands by the national automated pathological archive (PALGA). Additional sources are the national registry of hospital discharge, haematology departments and radiotherapy institutions. Information on diagnosis, staging and treatment is extracted routinely from the medical records by specially trained registration clerks of the cancer registry.

Patients with a potentially curable non-cardia gastric cancer were eligible for this study. The gastro-oesophageal junction could be involved, but the bulk of the tumour had to be in the stomach. Patients were considered potentially curable if they had no clinical distant metastasis, no tumour infiltrating surrounding organs, and no non-regional or unresectable conglomeration of suspicious nodes.

Topography and morphology were coded according to the International Classification of Diseases for Oncology (ICD-O-3)[9]. Distribution of the location in the stomach is divided as follows: proximal/middle (fundus, corpus, and lesser and greater curvature (C16.1, C16.2, C16.5, C16.6), pyloric and antrum (C16.3, C16.4), and overlapping or not otherwise specified (C16.8, C16.9).

Tumours were staged according to the International Union Against Cancer (UICC) TNM classification that was valid at the time of diagnosis. Patients diagnosed between 2005 and 2009 were staged using the sixth edition[10], and those diagnosed between 2010 and 2013 according to the seventh edition[11]. For this, the pathological stage of the resection specimen was used, or, if not available, clinical tumour stage was noted. Information on vital status was obtained from hospital records and by annual linkage with the Municipal Administrative Databases, which register all deceased and emigrated persons in the Netherlands.

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Table 1 Characteristics of patients with potentially curable gastric cancer (cT1/1b–4a, cN0–2, cM0), diagnosed between 2005 and 2013 in the Netherlands

	No. of patients (n = 5620)	Surgical treatment rate (%)	P†
Age (years)			< 0·001
< 60	883 (15·7)	86·6	
60–74	2119 (37·7)	81·2	
≥ 75	2618 (46·6)	53·3	
Sex			< 0·001
M	3345 (59·5)	71·0	
F	2275 (40·5)	66·2	
Interval of diagnosis			< 0·001
2005–2009	2853 (50·8)	73·4	
2010–2013	2767 (49·2)	64·6	
Morphology			< 0·001
Adenocarcinoma	5474 (97·4)	69·3	
Other	56 (1·0)	50	
No histological confirmation	90 (1·6)	0	
Clinical tumour category			< 0·001
cT1/1b*	248 (4·4)	68·2	
cT2	1038 (18·5)	74·0	
cT3	619 (11·0)	72·5	
cT4a	68 (1·2)	59	
cTx/missing	3647 (64·9)	67·3	
Clinical node category			< 0·001
cN0	2861 (50·9)	80·3	
cN1	1065 (19·0)	71·6	
cN2	258 (4·6)	61·6	
cNx/unknown	1436 (25·6)	46·2	
Type of hospital of diagnosis			0·694
Academic	370 (6·6)	68·1	
Teaching	3212 (57·2)	68·7	
Non-teaching	2038 (36·3)	69·7	
No. of gastric cancer resections in hospital of diagnosis			
≥ 10	1890 (33·6)	73·7	< 0·001
< 10	3730 (66·4)	68·0	

Values in parentheses are percentages. *cT1 according to sixth edition of TNM classification (2005–2009) and cT1b according to seventh edition (2010–2013). †χ^2 test.

Surgery

Surgery for gastric cancer was classified according to the NCR as subtotal gastrectomy, total gastrectomy and multiple organ resection, which was defined as a gastrectomy and surgical removal of other organs. Laparoscopy as a staging method was not regarded as surgery.

Hospital of diagnosis, hospital status, and volume

The hospital of diagnosis was defined as the hospital in which the histological diagnosis of gastric cancer was made. Patients were excluded from the study if the diagnosis was made in a hospital abroad. As the focus of this study was the decision-making process, the hospital of diagnosis was investigated rather than the hospital of resection.

In the Netherlands, patients can be diagnosed in any of the 91 hospitals, usually the one closest to their place of residence. If the hospital of diagnosis does not perform gastrectomies, patients are referred when gastrectomy is indicated. Type of hospital of diagnosis was classified as university (academic) hospital, teaching non-university hospital or non-teaching hospital.

Hospital of diagnosis was divided into two categories according to the number of gastric cancer resections: those that performed at least ten resections per year and those with a lower annual volume, according to the year of diagnosis. For example, if a patient was diagnosed in 2008 in a hospital that carried out ten or more resections in that year, the patient was included in the group of hospitals with an annual resection volume of at least ten.

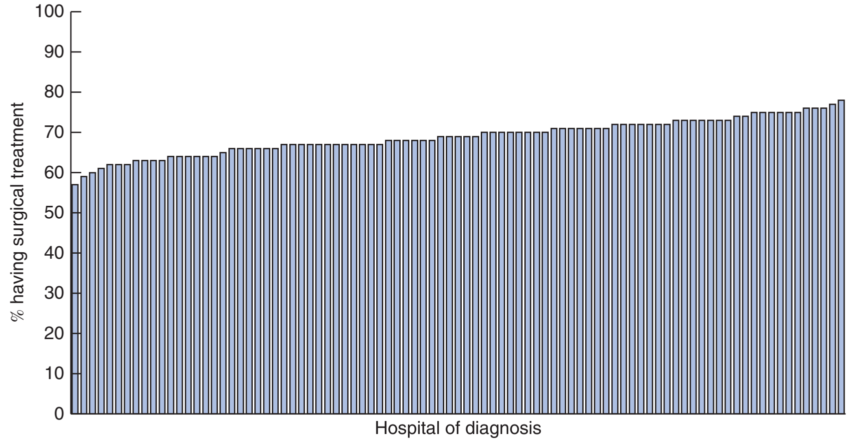
Outcome measures

Surgical treatment probability and survival were the outcomes investigated in this study. The surgical treatment probability of a hospital of diagnosis was defined as the proportion of patients diagnosed in a certain hospital who eventually underwent surgery, regardless of the hospital in which the surgery was performed. Survival time was defined as time from diagnosis to death, or until 1 January 2015 for patients who were still alive.

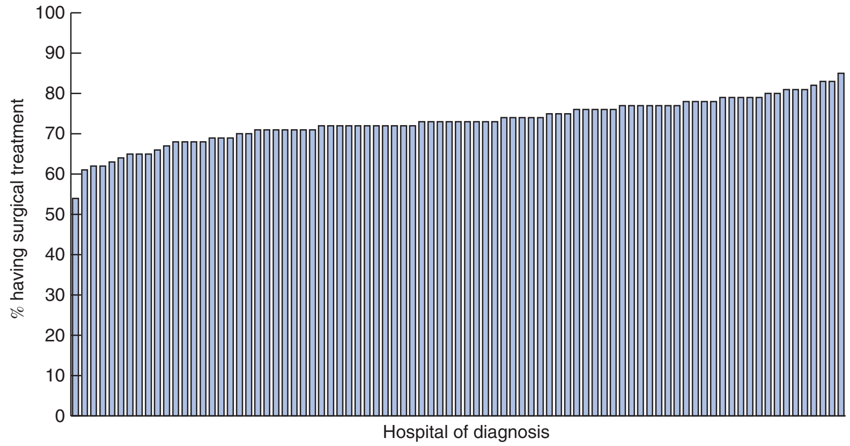
Statistical analysis

All analyses were conducted using SAS® version 9.4 (SAS Institute, Cary, North Carolina, USA). A multilevel logistic regression analysis was used to analyse the hierarchically structured data as patients were nested within hospitals. Multilevel regression analyses provide more accurate estimates when dealing with hierarchically structured data than traditional regression analyses as they account for dependency of patients within hospitals[12,13]. The outcome variable was surgery (0, no; 1, yes). A multivariable multilevel logistic regression model was generated, and patient- and tumour-related variables and type of hospital were added. The effect of a variable on the likelihood of surgical treatment was expressed as an odds ratio (OR) with 95 per cent c.i.

Each patient's adjusted chance of undergoing surgery was given by the following formula: $P = e^{L}/(1 + e^{L})$, where L is the calculated value from the logistic regression for that particular patient. The mean adjusted surgical probability for each hospital of diagnosis was defined as the mean adjusted surgical probability of the patients



a 2005–2013



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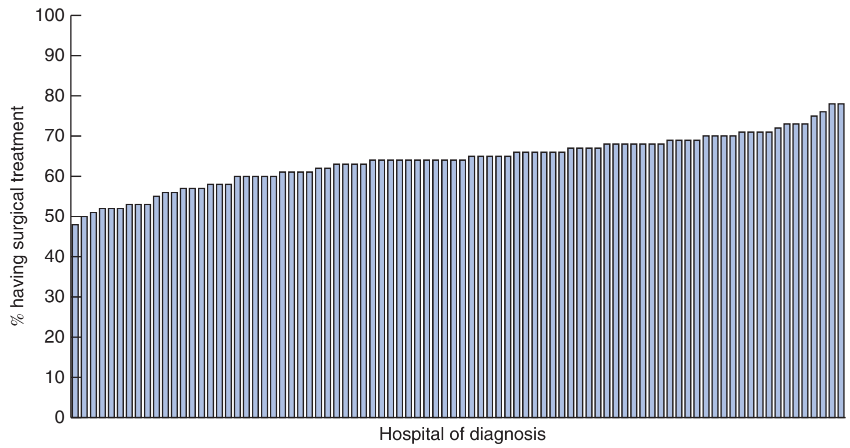

c 2010–2013

Fig. 2 Multilevel adjusted variation in the proportion of patients with potentially curable gastric carcinoma who received a gastrectomy in the interval **a** 2005–2013 (5620 patients), **b** 2005–2009 (2821 patients) and **c** 2010–2013 (2739 patients). Adjustment was made for age, sex, cT category, cN category, tumour location, morphology, interval of diagnosis, type of hospital of diagnosis, and annual number of resections in hospital of diagnosis. Each bar represents one hospital. Three hospitals were excluded from **b** and **c** because each had ten or fewer diagnoses in that interval

Table 2 Multivariable multilevel logistic regression analysis to examine predictors of surgery in patients diagnosed with potentially curable gastric cancer.

	Odds ratio
Age (years)	
< 60	1·00 (reference)
60–74	0·61 (0·48, 0·78)
≥ 75	0·16 (0·13, 0·21)
Sex	
M	1·00 (reference)
F	0·83 (0·73, 0·95)
Interval of diagnosis	
2005–2009	1·00 (reference)
2010–2013	0·47 (0·41, 0·55)
Clinical tumour category	
cT1/1b	0·60 (0·41, 0·88)
cT2	0·92 (0·71, 1·19)
cT3	1·00 (reference)
cT4a	0·59 (0·33, 1·05)
cTx/missing	0·86 (0·68, 1·07)
Clinical node category	
cN0	2·50 (1·85, 3·38)
cN1	1·16 (0·85, 1·60)
cN2	1·00 (reference)
cNx/unknown	0·45 (0·32, 0·61)
Type of hospital of diagnosis	
Academic	1·00 (reference)
Teaching	1·19 (0·85, 1·67)
Non-teaching	1·34 (0·95, 1·90)
No. of gastric cancer resections in hospital of diagnosis	
≥ 10	1·55 (1·27, 1·89)
< 10	1·00 (reference)

Values in parentheses are 95 per cent c.i. Analyses adjusted for morphology, tumour location and all variables listed in this table.

diagnosed within that hospital. This resulted in a range of surgical probabilities adjusted for differences in patient characteristics between hospitals. The variation in surgical probabilities between hospitals of diagnosis was tested for statistical significance by means of ANOVA with Bonferroni correction. Information on co-morbidity and socio-economic status was not collected routinely by the NCR but solely by the Eindhoven Cancer Registry (ECR), which is representative of the NCR. Therefore, a similar analysis was performed in the subgroup of patients within the ECR to examine the influence of co-morbidity and socio-economic status on changes in surgical probabilities among hospitals of diagnosis.

Multivariable Cox regression analyses were undertaken to investigate the prognostic impact of the variation in surgical treatment probability among hospitals of diagnosis on overall survival, after adjustment for patient characteristics. The hospitals of diagnosis, and thereby the patients, were clustered within four groups with a comparable number of patients according to the adjusted surgical probabilities of the hospitals. Two multivariable Cox regression analyses were performed to investigate the prognostic impact of the variation separately in the intervals 2005–2009 and 2010–2013. These two intervals were defined because from 2010 an increasing effect of centralization of gastric cancer surgery in the data set might influence the surgical probabilities of hospitals of diagnosis. Furthermore, the interval 2005–2013 included a new treatment paradigm: the introduction of perioperative chemotherapy in the earlier time period. Therefore, calculation of the surgical probabilities of hospitals in the entire study interval (2005–2013) would not provide an accurate estimate. Patients without histological confirmation were classified as having an adenocarcinoma in multivariable analyses, as approximately 99 per cent of the patients with histological confirmation of gastric cancer had an adenocarcinoma. Results from survival analyses using Cox regression analyses were reported as hazard ratios (HRs) with 95 per cent c.i. $P < 0{\cdot}050$ was considered statistically significant.

Results

Between January 2005 and December 2013, 12 877 patients were diagnosed with non-cardia gastric cancer. Exclusion of patients for several reasons (*Fig. 1*) resulted in a study population of 5620 patients with potentially curable gastric cancer (cT1/1b–4a, cN0–2, cM0).

General characteristics of the patients are shown in *Table 1*. The median age was 73 (i.q.r. 64–73) years. The overall surgical resection rate was 69·1 per cent (3881 patients); 59·5 per cent of these patients underwent resection without neoadjuvant or adjuvant treatment, 16·3 per cent received only neoadjuvant chemotherapy, 20·9 per cent received neoadjuvant chemotherapy as well as adjuvant chemotherapy or chemoradiotherapy, and 3·3 per cent received adjuvant treatment alone. The most commonly performed operation was subtotal gastrectomy (64·3 per cent). Some 36·3 per cent of the patients were diagnosed in a non-teaching hospital and 69·7 per cent of these underwent surgery, either in the hospital of diagnosis or in a referral hospital (*Table 1*).

Surgical treatment

Surgical treatment rates were 74·0, 72·5 and 59 per cent for cT2, cT3 and cT4a tumours respectively ($P < 0{\cdot}001$) (*Table 1*). Surgical treatment decreased with age. In addition, a small decline was noted in the use of surgery during the study; 73·4 per cent of the patients underwent surgical treatment in 2005–2009 compared with 64·6 per cent in 2010–2013 ($P < 0{\cdot}001$).

Table 3 Univariable and multivariable Cox proportional hazards analyses of overall survival for patients with potentially curable gastric cancer in the Netherlands, 2010–2013

Surgical treatment probability (%)*	No. of patients ($n = 2739$)	Crude 2-year overall survival (%)	Hazard ratio: Univariable analysis	Hazard ratio: Multivariable analysis†
48–59	473	37·5	1·45 (1·25, 1·68)	1·21 (1·04, 1·41)
60–64	841	45·1	1·17 (1·03, 1·34)	1·04 (0·91, 1·19)
65–68	722	44·6	1·20 (1·04, 1·37)	1·10 (0·95, 1·26)
69–78	703	50·3	1·00 (reference)	1·00 (reference)

Values in parentheses are 95 per cent c.i. *Patients are included in one of the four groups according to the adjusted mean surgical treatment probability of the hospital where they were diagnosed in the interval 2010–2013. Twenty-eight patients were excluded from the analysis because they were diagnosed in a hospital that diagnosed ten or fewer patients in this interval. †Adjusted for age, sex, tumour stage, tumour location, morphology, tumour differentiation, type of hospital of diagnosis, and annual number of resections in hospital of diagnosis.

Table 4 Univariable and multivariable Cox proportional hazards analyses of overall survival for patients with potentially curable gastric cancer in the Netherlands, 2005–2009

Surgical treatment probability (%)*	No. of patients ($n = 2821$)	Crude 2-year overall survival (%)	Hazard ratio: Univariable analysis	Hazard ratio: Multivariable analysis†
54–69	594	50·0	1·11 (0·98, 1·25)	1·00 (0·88, 1·13)
70–72	604	48·2	1·15 (1·02, 1·30)	1·04 (0·91, 1·18)
73–75	766	48·8	1·13 (1·01, 1·27)	1·03 (0·91, 1·16)
76–85	857	52·0	1·00 (reference)	1·00 (reference)

Values in parentheses are 95 per cent c.i. *Patients are included in one of the four groups according to the adjusted mean surgical treatment probability of the hospital where they were diagnosed in the interval 2005–2009. Thirty-two patients were excluded from the analysis because they were diagnosed in a hospital that diagnosed ten or fewer patients in this interval. †Adjusted for age, sex, tumour stage, tumour location, morphology, tumour differentiation, type of hospital of diagnosis, and annual number of resections in hospital of diagnosis.

Patients were diagnosed with gastric cancer in 91 hospitals. Seven hospitals performed at least 20 gastric cancer resections in 2013, whereas no hospital reached a volume of 20 resections in 2005. Surgery was not performed in six hospitals in which the diagnosis of gastric cancer was made in 2005; this increased to 47 hospitals in 2013. Furthermore, 6·0 per cent of the patients were referred to another hospital for surgery in 2005, whereas 57·6 per cent of the patients were referred from a hospital that did not perform gastrectomies in 2013.

Hospital of diagnosis and probability of surgical treatment

The proportion of patients who underwent surgical treatment differed significantly between hospitals of diagnosis, varying from 53·1 to 83·9 per cent ($P < 0·001$). Multivariable multilevel analysis confirmed the effect of hospital of diagnosis on the probability of undergoing surgery. After adjustment for patient-related factors and type of hospital, surgical treatment rates ranged from 57·0 to 78·2 per cent according to hospital of diagnosis ($P < 0·001$) (*Fig. 2a*). Comparing 2005–2009 with 2010–2013, the adjusted variation in surgical treatment probability between hospitals of diagnosis was comparable (56·9–84·8 per cent in 2005–2008 *versus* 46·8–78·6 per cent in 2010–2013) (*Fig. 2b,c*). Subgroup analysis of patients within the ECR showed that, after adjustment for co-morbidity and socioeconomic status, the mean probability of surgical treatment changed by 0·2–2·3 per cent in the hospitals of diagnosis.

Results of the multivariable multilevel analysis showed that, in addition to hospital of diagnosis, the following factors were associated with a lower probability of undergoing surgical treatment: older age, female sex, a cT1 tumour and clinically lymph node-positive disease. Being diagnosed in a hospital that performed ten or more resections per year was associated with a higher probability of having surgery (OR 1·55; $P < 0·001$) (*Table 2*). However, there was no association with type of hospital of diagnosis in either 2005–2009 or 2010–2013.

Hospital of diagnosis and overall survival

Multivariable Cox regression analysis showed that patients diagnosed between 2010 and 2013 in hospitals with a lower probability of undergoing surgical treatment (48–59 per cent) had worse overall survival than those diagnosed in hospitals with a higher probability (69–78 per cent) (adjusted HR 1·21; $P < 0·001$ (*Table 3*). However, in 2005–2009 no such association was found (*Table 4*).

Discussion

In this population-based nationwide study the proportion of patients who underwent surgery varied between 53·1 and 83·9 per cent according to hospital of diagnosis. Multivariable multilevel logistic regression analysis confirmed the effect of hospital of diagnosis on the probability of undergoing surgical treatment. Patients with gastric cancer who had been diagnosed more recently in hospitals with a low probability of surgical treatment had worse overall survival than those diagnosed in hospitals with a high probability.

Variation in the probability of surgical treatment between hospitals of diagnosis remained after adjustment for differences in patient characteristics and type of hospital of diagnosis. In a previous study[14], it was suggested that co-morbidity and socioeconomic status could also have influenced the probability of undergoing surgery[14]. Subgroup analysis of data from the ECR in the present study revealed only slight changes in probability of surgery after adjustment for co-morbidity and socioeconomic status, indicating a minimal contribution of these factors to the variation in probabilities between hospitals of diagnosis. The present study has confirmed the variation in treatment probability among patients with gastric cancer, as shown previously for numerous other types of cancer, including bladder, breast and colonic cancer[15–17].

Factors associated with a lower probability of surgery were older age and female sex. In concordance with this, previous Dutch studies[18,19] found that older age was associated with a lower probability of having surgery. There are no published reports on the relationship between sex and likelihood of gastric cancer surgery. However, four Dutch studies[8,18–20] noted that sex did not affect the probability of surgery for oesophageal cancer, whereas a North American study[21] found a significantly lower probability of oesophagectomy among women. Furthermore, patients with cT1 tumour were less likely to undergo surgical treatment. This was probably a result of the introduction of endoscopic mucosal resection in recent years.

In the present study, patients diagnosed between 2005 and 2009 had a higher probability of having surgery than those diagnosed between 2010 and 2013. These findings may be explained by developments in more sensitive diagnostic modalities that have led to more accurate tumour staging[22]. The decrease in resection rates could also be related to the introduction and extensive use of perioperative chemotherapy more recently, with some patients progressing to incurable disease during preoperative chemotherapy.

The type of hospital of diagnosis was not associated with the probability of surgery for gastric cancer in either time interval. This means that patients diagnosed in non-teaching hospitals do not have a lower chance of having surgery than those diagnosed in a teaching or academic hospital. Referral of patients diagnosed in non-teaching hospitals results in their likelihood of undergoing surgery being comparable to that of patients diagnosed in teaching and academic hospitals. However, there is still a large variation in probability of resection across hospitals of diagnosis that could probably be explained by factors other than institution type, such as patient frailty, patient preference, specialization of the hospital and multidisciplinary team (MDT) meetings[23].

In the Netherlands, gastric cancer surgery is increasingly being performed in higher-volume hospitals[24], the minimum volume having been increased to 20 gastrectomies per year from 2013. In Denmark, centralization of gastric cancer has been associated with better surgical quality and a significant decline in mortality[25]. Similarly, centralization of surgical treatment for oesophageal and pancreatic cancer in the Netherlands has also been associated with improved outcomes[24,26,27]. Because centralization of gastric cancer surgery has been introduced in the Netherlands more recently, the effect on mortality and survival could not be examined here.

The probability of surgical treatment could be influenced by organizational structures within a hospital or department, radiotherapy and endoscopic facilities, established clinical pathways or regional agreements, and protocols between one or multiple hospitals. In general, all hospitals in the Netherlands have an endoscopy unit and CT available at least. The probability of having surgical treatment could also be affected by the grade of specialization of the hospital and medical specialists. The present study has shown that patients diagnosed in high-volume hospitals had a greater likelihood of receiving surgery than those diagnosed in low-volume hospitals. Two previous studies[22,28] reported that patients treated by medical specialists with higher caseloads were more likely to undergo surgery and other treatments than patients treated by lower-volume medical specialists. Higher-volume specialists used a wider range of investigations, which could not be explained by better access to these facilities[22].

In the Netherlands, all patients with gastric cancer should be discussed in a MDT meeting for proper treatment decisions to be made. A MDT meeting could improve the adequacy and uniformity of treatment decisions, which may increase the probability of curative surgical treatment. Regional expert MDT meetings have been shown to alter initial treatment plans frequently in patients with gastric, oesophageal, colorectal and breast cancer[29]. However, it is unknown whether a surgeon with experience in gastrectomies is always present. Implementation of regional expert MDT meetings with involvement of experienced surgeons may increase the overall survival of patients with gastric cancer through better selection for curative treatment or optimal palliative treatment.

Centralization could have led to a greater influence of hospitals of diagnosis in the recent time interval. Centralization would have led to an overall decrease in the number of gastric cancer specialists in the hospitals of diagnosis with sufficient experience in clinical decision-making, possibly resulting in fewer referrals to a specialized centre for curative treatment. However, in the earlier interval the introduction of perioperative chemotherapy, and thereby variation in quality of care, could have influenced survival more than hospital of diagnosis.

A limitation of the present study was that some factors influencing treatment decisions, such as frailty of the patient and performance status, were not registered adequately and could not therefore be included in the analyses. Furthermore, patients with distant metastasis (M1) and T4b tumours were excluded. However, the accuracy of the clinical staging and diagnostic methods used are unknown. Because endoscopic ultrasonography is not always performed in patients with gastric cancer, clinical stage was unknown in a relatively high proportion of patients. The variation in missing data on cT and cN status between hospitals was much smaller than the interhospital variation in resection probabilities, however, and is unlikely to have influenced the results substantially. In addition, clinical decision-making in gastric cancer is more often based on cN and cM than cT status; the exact cT category is often unknown because endoscopic ultrasonography is not performed and so the cT status is estimated by CT.

This study also has several strengths, such as its observational nature resulting in a representative population. This nationwide population-based study, including a large number of patients with potentially curable gastric cancer, has enabled evaluation of the probability of undergoing surgical treatment and its impact on survival.

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