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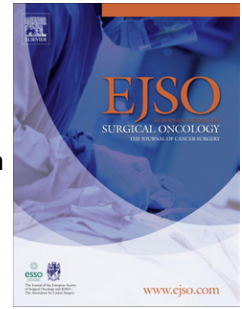
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Lymph node examination among patients with gastric cancer: variation between departments of pathology and prognostic impact of lymph node ratio

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Abstract**Introduction**

At least 15 lymph nodes should be retrieved for proper TNM-staging in gastric cancer. We evaluated nodal harvest and examined its relation to stage distribution and survival at a population-based level, including the value of N-ratio (metastatic/evaluated) as a staging modality.

Methods

All patients resected for primary M0 gastric cancer diagnosed in 1999-2007 in the Dutch Eindhoven Cancer Registry area were included (N=880). Determinants of lymph node evaluation and their relationship with stage and survival were assessed in multivariable regression analyses. N-ratio categories were determined (N ratio 0, 0%; N ratio 1, 0.1%–19%; N ratio 2, 20%–29%; N ratio 3, ≥ 30%)

Results

The median number of lymph nodes examined was 7, dependent on N-category (N0: 7; N+: 8). It varied between departments of pathology from 5 to 9. This variation remained after adjustment for relevant patient- and tumour factors. Stage distribution differed between pathology departments (proportion N0 ranging from 14% to 21%, $p=0.003$). Among resected patients with N0M0 disease and <7 nodes examined, 5-year survival was 56%, compared to 69% among patients with ≥7 nodes examined ($p=0.012$). Five-year survival for N-ratio 0 was 58%, N-ratio 1 50%, N-ratio 2 18% and N-ratio 3 11% ($p<0.0001$), while 5-year survival ranged from 58% for N0, 17% for N1, and 11% for N2/3 ($p<0.0001$).

Conclusion

In this series of patients with a relatively low number of evaluated lymph nodes, a high prognostic accuracy of N-ratio was found. However, improvement in nodal assessment is mandatory.

Introduction

Gastric cancer is still one of the leading cancers in incidence and mortality throughout the world. Mortality of gastric cancer ranks fourth in Europe for males and fifth in females[1]. Although mortality and incidence declined since the second half of the previous century, survival rates remained dismal in Europe with a relative 5-year survival of 14-32%[2]. In the southern Netherlands, overall 5-year survival is 18%[3]. The only curative treatment is surgery with (partial) gastric resection and lymph node dissection. The type of lymph node dissection is still under discussion. Japan and some other countries perform an extended lymphadenectomy, the so-called D2- or D3-dissection. Several large studies have been conducted to evaluate the outcome of patients after a D2-dissection in the West[4, 5]. As they found no survival benefit for this type of dissection, with higher post-operative morbidity a D2-dissection is therefore no general practice in our country. The long-term results after a median survival of 15 years did find lower regional recurrence and gastric cancer related deaths after a D2 dissection. It was suggested that a D2 dissection should be recommended, especially in view of the availability of a spleen-saving (and therefore safer) D2-dissection[6].

It is widely accepted that lymph node status and lymph node ratio, together with T and M category, are the most important prognostic factors[7, 8]. According to several studies and guidelines (UICC) a resection with at least 15 lymph nodes should be performed for proper staging and disease control. As in most countries where a D1-dissection is performed these numbers cannot be met, N-ratio (metastatic/evaluated) is proposed as a new N-staging modality.

In this perspective, we conducted a retrospective study in the southern part of the Netherlands to evaluate the amount of lymph nodes dissected and examined its relation to stage distribution and survival.

Patients and methods

Data collection

The Eindhoven Cancer Registry collects data on all patients with newly diagnosed cancer in a large part of the southern Netherlands. The registry area grew from an area covering 850,000 to about 2.3 million inhabitants. This population-based registry was notified by 6 pathology departments, 10 community hospitals (20 at the beginning of the 1970's but many of them have merged) at 15 locations, and 2 radiotherapy institutions.

All patients resected for primary gastric cancer (ICD-O (International Classification of Diseases for Oncology) code C16) without evidence for distant metastasis, diagnosed between 1999 and 2007 in the Dutch Eindhoven Cancer Registry area were included (N=880). Information on diagnosis, staging, and treatment is routinely extracted from the medical records by specially trained administrators of the cancer registry. Registration takes place 6 to 18 months after diagnosis. By means of an independent case ascertainment method, the completeness of the registration is estimated to exceed 95%.

Stage distribution is based on the Tumour Node Metastasis (TNM) system (International Union Against Cancer (UICC) classification 6th edition). Subsite distribution is divided as follows: cardia (comprising gastro-esophageal junction, C16.0), middle part (fundus, corpus, lesser curvature, and greater curvature (the two latter not classifiable to C16.0 - C16.4], C16.1, C16.2, C16.5, and C16.6), pyloric part (antrum and pylorus, C16.3 and C16.4), overlapping lesions (C16.8), and not otherwise specified (C16.9). Tumour characteristics registered furthermore include number of lymph nodes examined, number of positive lymph nodes, and grade of tumour differentiation. Prognostically relevant concomitant conditions are recorded from the medical records according to a slightly adapted version of the Charlson Index. This item was not registered before 1993; since 1995 these data are reliable and validated[8,9]. Socio-economic status (SES) of the patient was defined at neighborhood level (based on postal code of residence area, 17 households on average) combining mean household income and mean value of the house/apartment. The latter was derived from individual fiscal data made available at an aggregated level. Postal codes were assigned to one of 3 SES categories: low (1st-3rd decile), intermediate (4th-7th decile), and high (8th-10th decile)[9]. For patients residing in nursing homes, a special SES category was assigned. Vital status of all patients diagnosed until 1st of January 2007 was assessed on 1st of January 2008 through merging with the Municipal Administrative Databases, where all deceased and emigrated persons in the Netherlands are

registered. Population and mortality data were obtained from Statistics Netherlands (CBS) (CBS, 2007. Voorburg/Heerlen).

Analyses

Differences between the departments of pathology according to the number of lymph nodes evaluated and the postoperative nodal status were tested by means of a Kruskal Wallis test. The independent influence of institution or patient and tumour characteristics on the number of lymph nodes evaluated was analyzed by means of a logistic regression analysis. To examine the hypothesis that the number of lymph nodes examined is related to survival, 5-year crude overall survival differences between patients with the median number or less versus more than the median number of nodes examined were tested using a log-rank test, stratified for N status. Furthermore, the ratio between the number of metastatic and evaluated lymph nodes was determined. Cutoff values for N-ratio intervals were determined based on the prognosis of patients and the number of patients included within each category. Patients were categorised into 4 groups: N-ratio 0 (number of metastatic nodes / number of evaluated nodes * 100%=0%), N-ratio 1 (0.1-19%), N-ratio 2 (20-29%), and N-ratio 3 ($\geq 30\%$). Five-year survival was compared between these groups using a log-rank test. A multivariable proportional hazards regression analysis was used to discriminate independent risk factors for death. To compare the prognostic value of nodal status and N-ratio, the model was first built with inclusion of nodal status and lymph node count, and then repeated with N-ratio instead of the aforementioned variables. All tests were two-sided. P-values < 0.05 were considered statistically significant. All analyses were performed using SAS/STAT[®] statistical software (SAS system 9.1.3, SAS Institute, Cary, NC).

Results

General characteristics and departments of pathology

Three out of the six departments of pathology served one hospital, while two departments covered 3 hospitals each. One hospital has been served by two departments of pathology during the study period for logistic reasons.

The general characteristics of all patients are shown in table 1. The median age was 69 years. The majority of patients was male, and presented with comorbidity. A large proportion of patients had poorly differentiated tumours. Few patients received neoadjuvant treatment; the most commonly performed resection was a subtotal gastrectomy. Twelve percent of patients had 15 or more lymph nodes examined.

Nodal evaluation

The median number of lymph nodes evaluated varied between 5 in department #6 to 9 in departments #1 and #4 ($p < 0.0001$) (table 2). In total, a median number of 7 nodes was evaluated between 1999 and 2007. There was also a large variation between the departments concerning the proportions of patients with no exact number of evaluated nodes stated in the pathology report. Often, terms were used such as 'a few' or 'a number of', indicating that lymph nodes were indeed evaluated.

Five out of six departments of pathology showed an increasing trend over time in the number of evaluated lymph nodes. In total, the median number of evaluated nodes increased from 6 in the period 1999-2001, to 8 in 2004-2007. Within the last period, the median number of nodes evaluated continued to rise to 13 in department #3 and to 14 in department #4 in 2007 (results not shown).

Among patients with N+ disease, there was a larger proportion of patients with an unknown exact number of nodes evaluated, but also a larger proportion of patients with 15 or more nodes evaluated (median 8 nodes compared to 7 among N0 patients). Postoperative N category differed between the departments of pathology ($p = 0.003$) (table 2). In the departments with a higher median number of lymph nodes evaluated, a smaller proportion of patients was diagnosed with N0 disease. Compared to the other departments, in department #1 a higher proportion of patients was diagnosed with N3 disease, and a smaller proportion with unknown N category.

In table 3, the results of a multivariable logistic regression analysis (adjusting for all variables listed) show that patients with two or more comorbid conditions, patients with a T1 or T4 tumour, and patients whose resection specimen was examined in department of pathology #2 had a significantly lower

chance of having 7 or more nodes evaluated compared to the respective reference groups. Patients with N+ disease and patients undergoing a total gastrectomy or a multi-organ resection had a higher chance of having 7 or more nodes examined. Patients being diagnosed more recently also had a higher odds of having more nodes evaluated, but this reached borderline significance only ($p=0.06$).

Survival

Five-year survival was significantly higher among patients with N0, M0 disease which had 7 or more nodes evaluated compared to patients with less than 7 nodes evaluated (figure 1a). Among patients with N+, M0 disease, no prognostic effect of lymph node count could be noted (figure 1b). Five-year survival clearly differed according to nodal status, ranging from 58% for patients with N0 disease, 17% for patients with N1 disease, and 11% for patients with N2/3 disease (figure 1c). Classifying patients according to lymph node ratio yielded a comparable survival gap between patients with N-ratio of 0 and patients with an N-ratio of 2 or 3 (figure 1d). Patients with an N-ratio of 1 however, only fared slightly less well than patients with an N-ratio of 0 (50% vs. 58%). After adjustment for relevant patient and tumour characteristics, the risk of death (hazard ratio (HR)) was strongly correlated with nodal category and with lymph node count (table 4). Exchanging these two variables for N-ratio yielded comparable effects, but note again the only borderline significant worse survival of patients with N-ratio 1 compared to N-ratio 0. To a lesser degree, T-category and having two or more comorbid conditions also were of prognostic importance.

Without inclusion of N-ratio or lymph node count and nodal status in the model, patients who had their resection specimen examined in department of pathology #2 exhibited a significant increased risk of death (HR 1.3, 95% confidence limits 1.01-1.7) (results not shown).

Discussion

Nodal category (N-category) is one of the most important prognostic factors in gastric cancer. Proper N-staging is therefore needed to predict outcome in patients. According to UICC guidelines in gastric cancer at least 15 lymph nodes should be investigated to correctly assess N-category (6th and 7th edition). Additionally, several studies have shown the importance of N-ratio in staging gastric cancer[7, 10]. In this retrospective study we investigated the amount of lymph nodes evaluated and N-ratio after surgery for gastric carcinoma, and its relationship to survival in the Southern part of the Netherlands.

Nodal evaluation

This region is served by 10 community hospitals, all draining on 6 departments of pathology; the median number of investigated lymph nodes between departments of pathology varied between 5 and 9 lymph nodes per patient, with a median number of 7 in the whole region. These results are confirmed by other studies, where the median number of lymph nodes examined also varied between different geographical regions[11, 12]. The region is characterised by the absence of an academic hospital in our region. Recent Dutch studies showed that hospital characteristics also influenced nodal yield in colon cancer; especially academic centres showed a higher median lymph node yield[13, 14]. Volume did not seem to have an effect. Also after adjustment in a multi-level analysis for these and other relevant factors, differences between departments of pathology remained, probably suggesting variation in diligence and effort put in these time-consuming examinations. Fat-clearing agents are not widely used in the Netherlands. Although a minimum number of at least 15 lymph nodes is considered mandatory for proper staging, more studies reported an insufficient number of investigated lymph nodes[11, 12]. Factors associated with a higher amount of lymph nodes in these studies were younger age, female gender, Asian race, and more radical surgery[11, 15]. Obesity has been suggested to be of influence as well[16]. In the present study, we did not find an effect of age or gender, but we did find an effect of more radical surgery. Obviously, in a total gastric resection more surrounding tissue is removed, resulting in more lymph nodes retrieved. Other factors associated with the amount of lymph nodes found were comorbidity, T- and N-category, and department of pathology. Practice of surgeons and pathologists can influence the amount of lymph nodes found. In the Netherlands, mostly a D1 resection is performed. Several prospective studies have proven no benefit of a D2 resection over a D1 resection with high postoperative morbidity and mortality[4, 5], although latest analyses showed lower gastric cancer related deaths and locoregional recurrence 15 years after a D2 dissection.[6] The

number of lymph nodes evaluated in our region reflects the type of lymph node dissection performed. Only in 21 patients a D2 resection was reported in the study period. Although the amount of harvested lymph nodes can partly be accounted to the type of surgery, patient characteristics can be of influence as well. In a D2 resection on cadavers a range from 17 to 44 lymph nodes per patient was reported[17]. Considering the inter-individual variation in nodal count, this might lead to an inadequate lymph node dissection among certain patients. Furthermore, as patients grow older the amount of lymph nodes decreases. Differences in immunologic reaction can play a role as well. The immune reaction against neoplastic cell products alters the shape and morphology of lymph nodes. An advanced T-category might as well stimulate immune reaction, but the larger size of the tumour also might stimulate surgeon and pathologist for more aggressive lymph node harvesting. In addition, in advanced T-category, the risk of lymph node metastases rises. Metastatic lymph nodes have a greater size, which makes harvesting and examining them easier. The positive association between N-category and the number of lymph nodes evaluated reflects this as well.

Besides treatment and patient- and tumour-related characteristics, inadequate lymph node harvesting might be related to the pathological examination. Different techniques of pathologic examination influences the total number of lymph nodes found. One retrospective study found more lymph node metastases when they retrospectively sectioned lymph nodes at three levels instead of one[18]. Using fat clearing technique instead of conventional techniques increased nodal yields[19]. As mentioned before, a previous report from the Eindhoven Cancer Registry, pathology practice was linked to the adequacy of nodal assessment in colon cancer[14]. However, the increasing median number of lymph nodes in 5 out of 6 departments of pathology in our study suggests a rise in awareness of the importance of an adequate nodal examination. There also is a role for the surgeon as well in improving quality of treatment by performing a more thorough lymph node dissection. In the end, it remains a joint responsibility of pathologist and surgeon, and communication and feedback are essential in increasing and maintaining quality of nodal assessment.

Survival

Five-year survival was significantly higher when 7 or more lymph nodes were investigated among N0M0 patients. In most other studies, the threshold was set at 15 resected lymph nodes as in concordance with the UICC/AJCC guidelines, with hazard ratios of ~0.50 in favour of evaluation of more than 15 lymph nodes[12, 15, 20, 21]. In our region, only 12% of patients had > 15 investigated

lymph nodes, making evaluations at this cut-off point less reliable. Several hypotheses have been mentioned to explain the positive correlation between survival and the number of evaluated lymph nodes. One hypothesis is understaging. Understaging can be a result of a minimum amount of lymph nodes retrieved. Another hypothesis is reduction of tumour burden. With an extended lymphadenectomy, tumour burden is reduced. Even pN0 patients with a lymph node count of more than 15 are found to have better survival[7]. This can be attributed partly to the removal of lymph nodes with micrometastasis, which are difficult to detect in normal pathological evaluation[20]. The fact that in our study the number of lymph nodes examined had a larger influence on survival among node-negative than among node positive patients confirms this hypothesis. Where the effect of reduction of tumour burden becomes more important than understaging is not clear, although a prospective study of Siewert et al suggested a threshold around 15 to 20 lymph nodes[7]. This was confirmed by other, retrospective studies[12, 21]. Unfortunately we were not able to adjust for radicality of resection, since this item was not routinely collected during the whole study period. Also, we could not discriminate between resections with curative versus palliative intent. However, since we included only patients who were metastasis-free at time of diagnosis (M0), we assume that the proportion of patients undergoing a tumour resection with strict palliative intent was very low, and has therefore probably not influenced our results.

Lymph node ratio

To overcome the problem of inadequate nodal harvest in staging, the lymph node ratio (N-ratio) has been suggested. This is defined as the amount of positive lymph nodes divided by the total amount of retrieved lymph nodes. It gives information about the N-category and about the extent of lymph node dissection. In breast, colon and rectal cancer it has proven its superior prognostic information over N-category according to the TNM classification[22-25]. In all studies evaluating N-ratio in gastric cancer, as we know of, it has proven to be an important independent prognostic factor in multivariate analysis, as confirmed by the results of our study[7, 8, 10, 14, 26-28]. We found a 5-year survival of 50% in N-ratio group 1, while these patients would have been assigned to at least the N1 group using the traditional TNM classification (6th edition), with an expected 5-year survival of maximum 17%. These results suggest a higher prognostic value of the N-ratio system in comparison to the traditional TNM classification, although more analyses should be performed to confirm this. One of the drawbacks of the N-ratio is that there are no standardized categories in literature; N-ratio groups can therefore be fit

to the used dataset. Because of the low number of patients with a low N-ratio we used a higher cut-off point. This can bias our results and give a seemingly higher prognostic value than the TNM-classification; some authors have questioned the clinical usefulness in case of low numbers of nodes[29]. In the new AJCC/UICC TNM classification (7th edition; N1 category: 1-2 positive nodes, N2 category: 3-6 positive nodes, N3a 7-15 positive nodes, N3b >15 positive nodes) N-category is adjusted to overcome the lower prognostic value of the 6th edition (N1 category 1-6 positive nodes, N2 category 7-15 positive nodes, N3 >15 positive nodes). The role of staging according to N-ratio is therefore still not clear and should be further investigated. It should be mentioned that improvement in staging should primarily be done by adequate lymph node harvesting and assessment.

Conclusion

Even though lymph node count improved over time, improvement in nodal assessment is still mandatory. Five-year survival in N0M0 patients was positively correlated with lymph node count. Also in this series of patients with a relatively low number of evaluated lymph nodes, a high prognostic accuracy of N- was found.

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Figure captions

Figure 1a. Five-year crude survival of resected N0, M0 gastric cancer patients, according to number of nodes evaluated.

Figure 1b. Five-year crude survival of resected N+, M0 gastric cancer patients, according to number of nodes evaluated.

Figure 1c. Five-year crude survival of resected M0 gastric cancer patients, according to nodal status.

Figure 1d. Five-year crude survival of resected M0 gastric cancer patients, according to lymph node ratio (ratio between number of metastatic and evaluated lymph nodes).

Table 1. General characteristics of all 880 patients who underwent resection for M0 gastric carcinoma, diagnosed between 1999 and 2007 in the southern Netherlands.

Age (years)		
Median (range)	69	(13-100)
Gender		
	N	(%)
Male	574	(65)
Female	306	(35)
Socio-economic status		
Low	234	(27)
Intermediate	320	(36)
High	282	(32)
Institutionalised	28	(3)
Unknown	16	(1)
Comorbidity		
No comorbidity	265	(30)
One comorbid condition	248	(28)
Two or more comorbid conditions	313	(36)
Unknown	54	(7)
Tumour site		
Cardia	168	(19)
Middle part	222	(25)
Antrum and pylorus	323	(37)
Overlapping, unknown	167	(19)
Stage		
IA	108	(12)
IB	226	(26)
II	280	(32)
IIIA	180	(20)
IIIB	27	(3)
IV ^a	40	(5)
Unknown	19	(2)
Tumour grade		
Moderately/well differentiated	269	(30)
Poorly differentiated	520	(56)
Unknown	91	(14)
Preoperative treatment		
Chemo- and/or radiotherapy	29	(3)
None	861	(97)
Type of resection		
Total gastrectomy	192	(21)
Subtotal gastrectomy	509	(58)
Oesophageal-cardiac resection	118	(13)
Multi-organ resection	29	(3)
Unspecified type of resection	32	(4)
No. of lymph nodes evaluated		
0	66	(7)
1-2	60	(7)
3-5	120	(14)
6-8	170	(19)
9-11	111	(13)
11-14	75	(9)
≥15	105	(12)
Exact number unknown	173	(20)

^a Excluding patients with distant metastases (M1)

Table 2. Median number of lymph nodes evaluated and proportion N0, according to department of pathology

Dep. of pathology	Median number of nodes evaluated	Range	Proportion of patients with unknown number of evaluated nodes		%N0
			Unknown whether any nodes have been evaluated	At least 1 node evaluated, but exact number not stated in medical file ^a	
1	9	0-31	0%	0%	15%
2	6	0-21	1%	28%	20%
3	7	0-35	1%	27%	20%
4	9	0-41	2%	12%	17%
5	7	0-36	1%	8%	20%
6	5	0-21	3%	45%	22%
total	7	0-41	1%	19%	19%

Difference of median numbers of lymph nodes evaluated across departments of pathology: Kruskal

Wallis test $p < 0.0001$

Differences in postoperative nodal status between departments of pathology: χ^2 test $p = 0.003$

^a Often stated in the pathology report as: 'a few', or 'a number of'.

Table 3. Odds of having 7 or more lymph nodes evaluated, calculated by means of a multivariable logistic regression analysis (model including all listed variables).

	n	Odds ratio	95% CL
Age (yrs)			
<70 ^a	447	1.0	
70+	433	0.8	0.6-1.1
Gender			
Males ^a	574	1.0	
Females	306	1.3	0.9-1.8
Comorbidity^a			
No comorbidity ^a	265	1.0	
One comorbid condition	248	0.7	0.5-1.2
Two or more comorbid conditions	313	0.5	0.3-0.7
Unknown	54	1.3	0.6-2.9
T-category			
T1	132	0.4	0.2-0.7
T2 ^a	488	1.0	
T3	205	0.9	0.6-1.5
T4	35	0.4	0.2-0.9
N-category			
N0 ^a	449	1.0	
N+	431	2.3	1.6-3.2
Tumor site			
Cardia	168	1.6	0.8-3.3
Middle part	222	1.1	0.7-1.7
Pyloric part ^a	323	1.0	
Overlapping/unknown	167	1.1	0.7-1.9
Tumour grade			
Moderately/well differentiated ^a	269	1.0	
Poorly differentiated	520	1.3	0.9-2.0
Unknown	91	0.8	0.4-1.5
Neoadjuvant treatment			
No ^a	851	1.0	
Yes	29	0.8	0.3-1.7
Type of resection			
Total gastrectomy	192	1.9	0.1-3.0
Subtotal gastrectomy ^a	509	1.0	
Oesophageal-cardiac resection	118	1.3	0.6-2.8
Multi-organ resection	29	5.0	1.4-14.5
Department of pathology			
1	78	1.0	0.6-1.9
2	185	0.3	0.2-0.5
3	108	0.9	0.5-1.5
4	178	1.5	0.9-2.3
5 ^a	238	1.0	
6	93	0.5	0.3-1.1
Period of diagnosis			
1999-2003 ^a	426	1.0	
2004-2007	454	1.4	1.0-1.9

^a Reference category

CL=confidence limits

Table 4. Multivariable proportional hazard regression analysis for patients who underwent resection for gastric cancer between 1999 and 2006 in the south of the Netherlands (model including all listed variables).

	Model including N-category and number of evaluated lymph nodes separately		Model including N-ratio	
	Hazard ratio	95% CL	Hazard ratio	95% CL
Age (yrs)				
<70 ^a	1.0		1.0	
70+	1.1	0.9-1.3	1.1	0.9-1.4
Gender				
Males ^a	1.0		1.0	
Females	0.9	0.7-1.1	0.9	0.7-1.1
Comorbidity^a				
No comorbidity ^a	1.0		1.0	
One comorbid condition	1.1	0.9-1.4	1.1	0.9-1.4
Two or more comorbid conditions	1.3	1.0-1.7	1.3	1.0-1.7
Unknown	0.9	0.6-1.5	0.9	0.5-1.4
T-category				
T1	0.6	0.4-0.8	0.6	0.4-0.9
T2 ^a	1.0		1.0	
T3	1.1	0.9-1.5	1.2	0.9-1.5
T4	1.7	1.0-2.7	1.8	1.0-2.9
N-category				
N0 ^a	1.0		<i>n.a.</i>	
N1	2.9	2.2-3.6		
N2/3	4.5	3.1-6.2		
Number of evaluated lymph nodes				
<7 ^a	1.0		<i>n.a.</i>	
≥7	0.7	0.6-0.9		
N-ratio				
Ratio 0 (0%) ^a	<i>n.a.</i>		1.0	
Ratio 1 (0.1-19%)			1.5	1.0-2.2
Ratio 2 (20-29%)			3.1	2.0-4.6
Ratio 3 (≥30%)			3.8	2.9-4.9
Tumor site				
Cardia	0.9	0.6-1.4	0.9	0.6-1.3
Middle part	0.9	0.7-1.2	0.9	0.7-1.2
Pyloric part ^a	1.0		1.0	
Other/unknown	1.4	1.0-1.9	1.3	1.0-1.8
Tumour grade				
Moderately/well differentiated ^a	1.0		1.0	
Poorly differentiated	1.0	0.8-1.3	0.9	0.7-1.2
Unknown	1.0	0.7-1.6	0.9	0.7-1.5
Neoadjuvant treatment				
No ^a	1.0		1.0	
Yes	0.8	0.4-1.4	0.9	0.5-1.6
Type of resection				
Total gastrectomy	1.2	0.9-1.6	1.2	0.9-1.7
Subtotal gastrectomy ^a	1.0		1.0	
Oesophageal-cardiac resection	1.0	0.7-1.6	1.0	0.6-1.6
Multi-organ resection	1.4	0.7-2.6	1.4	0.7-2.6
Department of pathology				
1	0.8	0.6-1.1	0.8	0.6-1.1
2	1.1	0.8-1.5	1.1	0.8-1.4
3	0.9	0.6-1.2	0.9	0.6-1.2
4	1.0	0.7-1.3	1.0	0.7-1.3
5 ^a	1.0		1.0	
6	0.9	0.6-1.4	1.0	0.6-1.5
Period of diagnosis				
1999-2002 ^a	1.0		1.0	
2003-2006	1.0	0.8-1.3	1.0	0.8-1.3

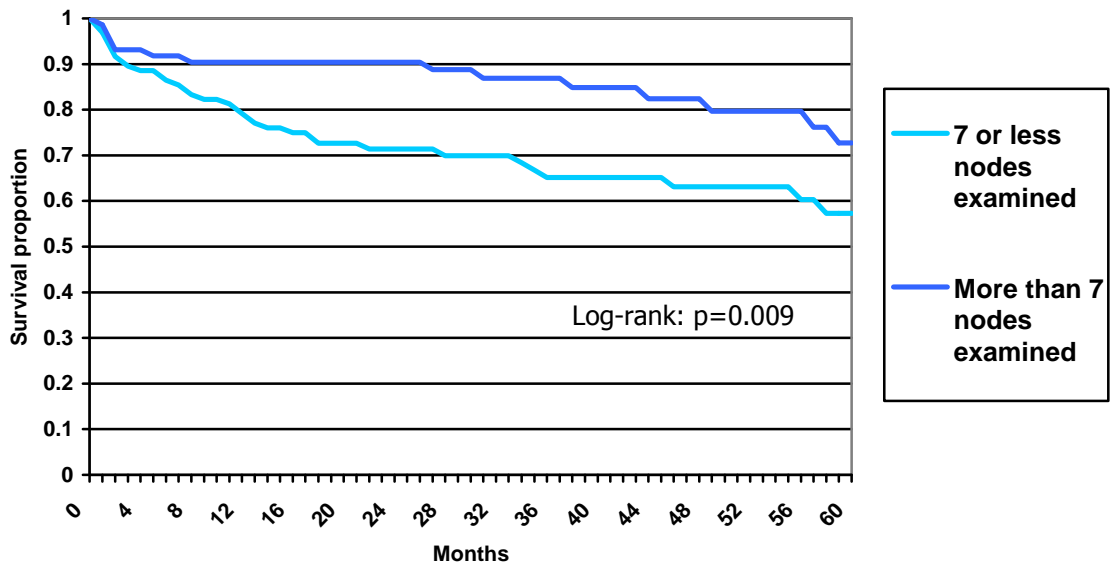
^a Reference category

n.a. = not applicable

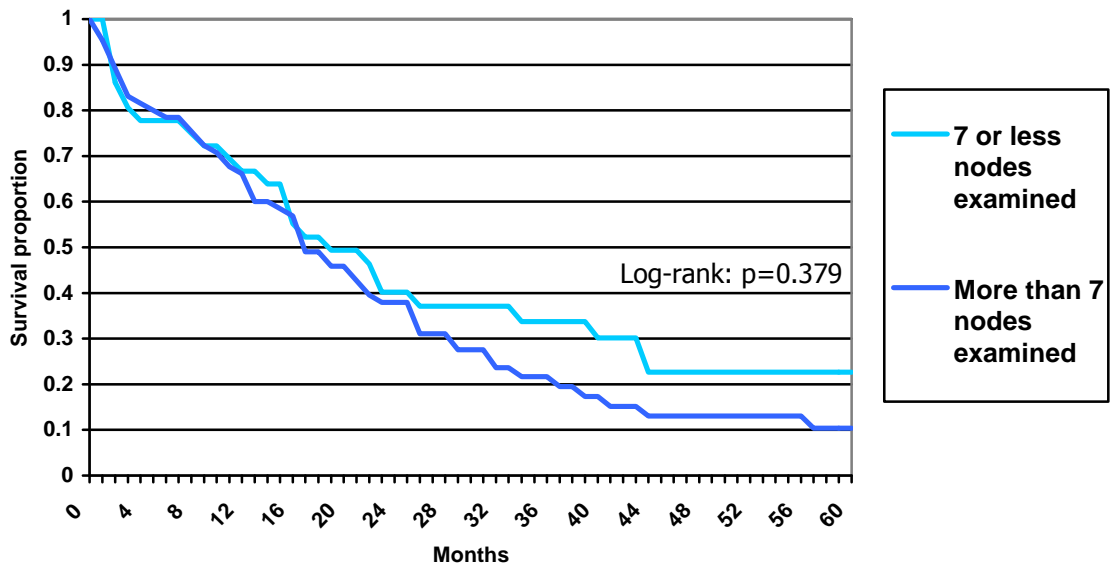
CL=confidence limits

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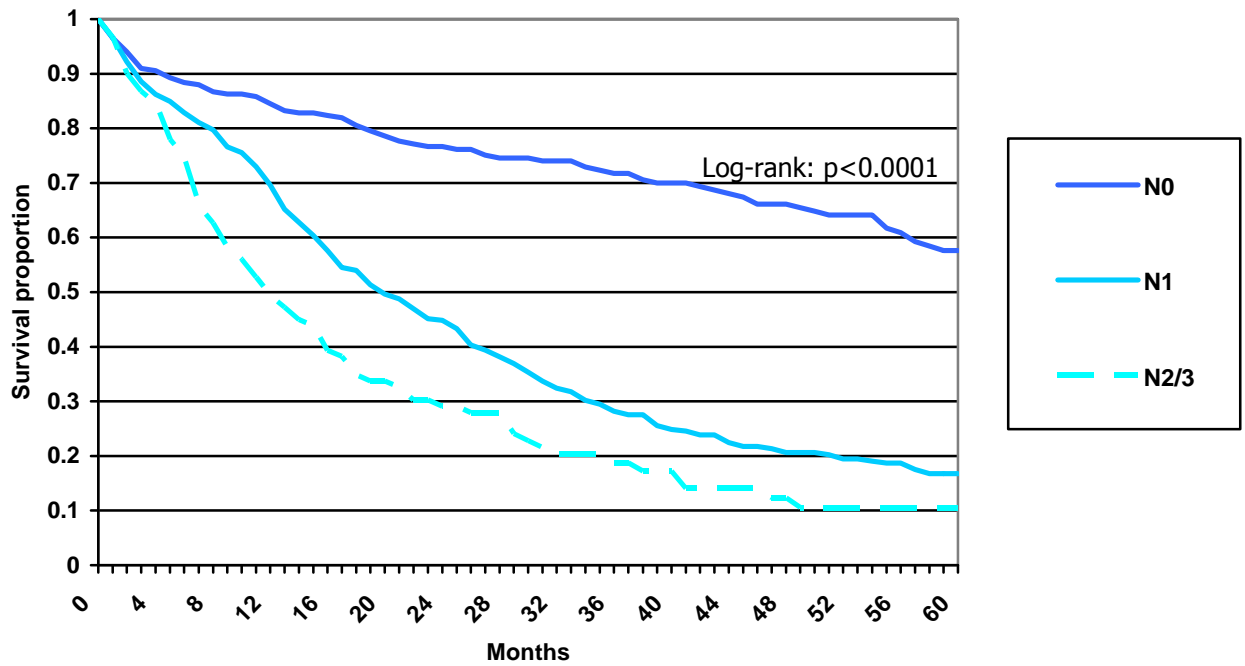
5-year survival of resected N0, M0 gastric cancer patients (N=321)



5-year survival of resected N+, M0 gastric cancer patients (N=559)



5-year survival of resected M0 gastric cancer patients (N=880)



5-year survival of resected M0 gastric cancer patients (N=880)

