



Impact of disease biology and stage on outcomes for oesophageal and gastric adenocarcinoma (OGA) treated with neoadjuvant chemotherapy

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BACKGROUND

Oesophageal and gastric cancer are the eighth and fifth most common malignancies worldwide, respectively (1). After two UK MRC trials (MAGIC and OEO2) were published, neoadjuvant and peri-operative treatments became standard practice for OGA at the Royal Marsden Hospital (2,3). Following neoadjuvant treatment, the identification of factors to evaluate individual patient risk may be helpful for early identification of patients with poor prognosis. The aim of this analysis was to identify predictors of survival after surgical resection in patients treated with neoadjuvant approach.

METHODS

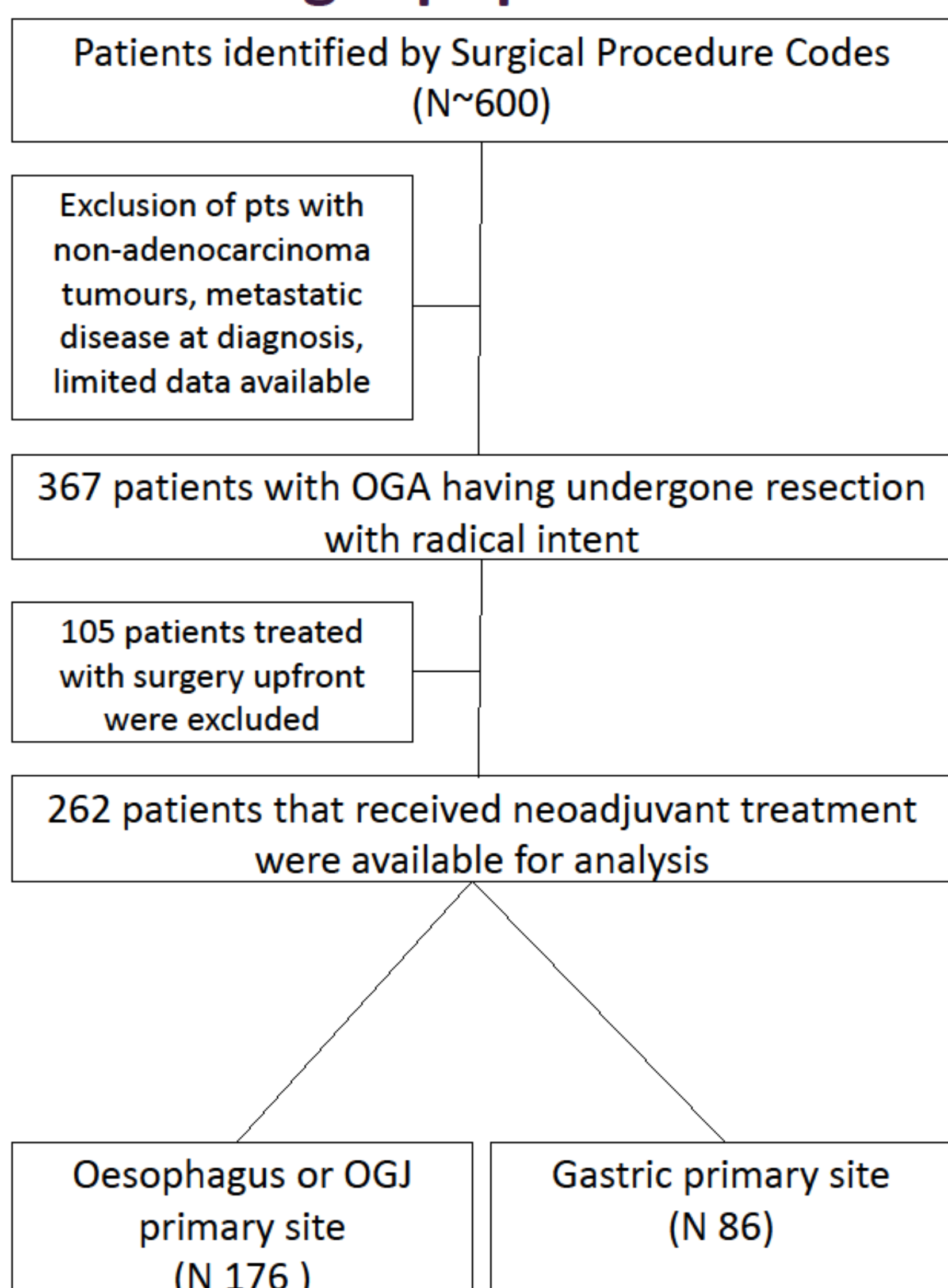
STUDY POPULATION

- Patients included had:
 - Adenocarcinoma of oesophagus (OES), oesophago-gastric junction (OGJ) or stomach.
 - Surgery with radical intent between January 2001 and December 2010 at the Royal Marsden Hospital, London, UK.
 - Neoadjuvant chemotherapy
- Patients who were followed up in a different hospital or for whom no data besides the date of surgery were available on the system were excluded.
- Approval for this project was obtained prior to study commencement from the institutional review board (Service Evaluation 3407).

STATISTICAL ANALYSIS

- Demographic, management, surgical outcomes and pathological findings were analysed using descriptive statistics.
- Disease-free (DFS) and overall survival (OS) were estimated using the Kaplan Meier method.
- Co-variables were compared using the log rank test and hazard ratios calculated using Cox regression model.
- Variables with more than 50% of data missing were excluded in the multivariate analysis (MVA).
- Based on variables which were significant in MVA, a prognostic index was created.

Target population



Patients and Treatments

Characteristics	Oesophagus + OGJ Population	Gastric Population
	No. of Patients (%)	No. of Patients (%)
Total patients	176	86
Age, years		
Median	61.8	65.2
SD	10.2	9.6
Range	33 - 81	39 - 82
Gender		
Male	159 (90.3)	54 (62.8)
Female	17 (9.7)	32 (37.2)
Performance Status (PS)		
0	48 (27.3)	28 (32.6)
1	61 (34.7)	32 (37.2)
2	1 (0.6)	1 (1.2)
Not recorded	66 (37.5)	25 (29.1)
Ethnicity		
Afrocaribbean	1 (0.6)	8 (9.3)
East Asia	1 (0.6)	4 (4.7)
Indian Subcontinent	1 (0.6)	6 (7)
Western	167 (94.9)	58 (67.4)
Not recorded	6 (3.4)	10 (11.6)
Surgery		
Oesophago-gastrectomy	146 (82.9)	3 (3.5)
Total gastrectomy	30 (17.1)	40 (39.5)
Sub-total gastrectomy	0	43 (57)
Neo-adjuvant chemotherapy		
Median No. of cycles	4 (range 2 - 8)	3 (range 1 - 8)
Doublet	69 (39.2)	13 (15.1)
Triplet	56 (31.8)	17 (19.8)
Peri-operative chemotherapy		
Median No. of cycles	6 (range 2 - 12)	6 (range 4 - 10)
Doublet	15 (8.5)	10 (11.6)
Triplet	36 (20.5)	46 (53.5)
Post-operative chemoradiotherapy		
Yes	18 (10.2)	1 (1.2)
No	158 (89.8)	85 (98.8)

Univariate Analysis

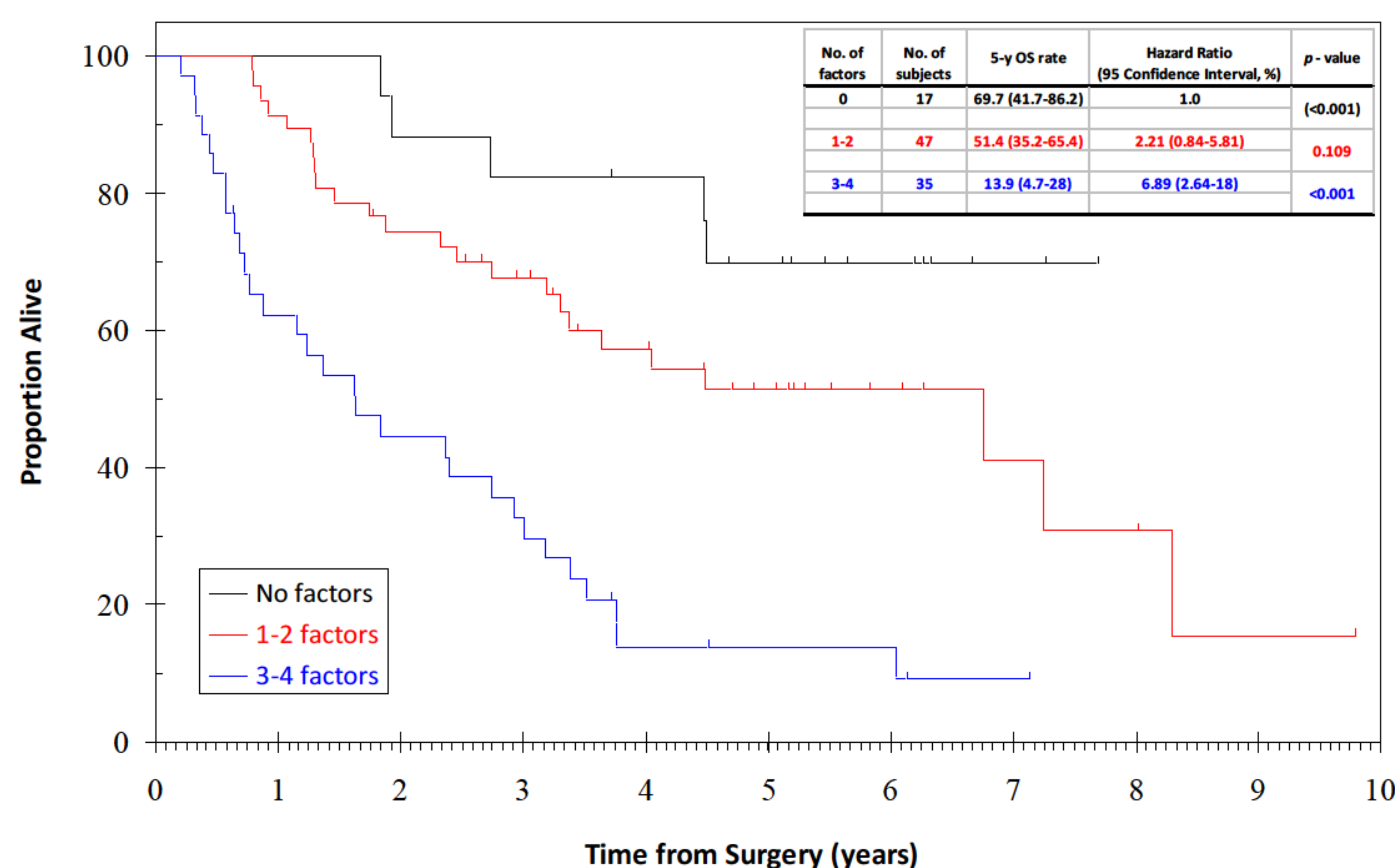
Characteristics	No. of Patients (%)	5-y DFS rate	5-y OS rate	Hazard Ratio (OS) (95% Confidence Interval)	p-value (OS)
Age					
≤ 65 years	146 (56)	39 (30.8-47.1)	47.9 (39.1-56.1)	1.0	
≥ 65 years	116 (44)	45.1 (35.7-54)	47.6 (38.5-56.6)	1.03 (0.74-1.44)	0.854
Gender					
Male	213 (81)	39.7 (32.9-46.4)	46 (38.8-52.9)	1.0	
Female	49 (19)	50.8 (36.1-63.7)	55.5 (40.2-68.4)	0.76 (0.49-1.18)	0.22
Site of Primary					
Gastric	176 (67)	54.6 (42.9-64.9)	57.5 (45.6-67.6)	1.0	
OES+OGJ	86 (33)	35.6 (28.4-42.7)	43.3 (35.6-50.7)	1.58 (1.08-2.29)	0.017
Elevated tumour markers(*)					
No	167 (64)	46.9 (38.9-54.5)	46.9 (39-54.5)	1.0	
Yes	74 (28)	31.2 (20.8-42.2)	31.2 (20.8-42.2)	1.70 (1.21-2.41)	0.003
Lymph nodes collected					
< 15	28 (11)	23.8 (10-40.9)	28.7 (12.6-47.1)	1.0	
≥ 15	225 (86)	44.2 (37.4-50.7)	50.2 (43.3-56.8)	0.71 (0.43-1.15)	0.159
Resection					
R0	210 (80)	48 (40.9-54.8)	53.8 (46.5-60.7)	1.0	
R+	45 (17)	16.6 (7.4-29)	23.3 (12.2-36.6)	2.61 (1.79-3.82)	<0.001
Grade					
Poor	154 (59)	34.2 (26.5-41.9)	38.9 (30.8-46.9)	1.0	
Moderated/Well	96 (37)	52.2 (41.5-61.8)	57.1 (46.1-66.6)	0.51 (0.35-0.73)	<0.001
Tumour T-Stage					
T0-2	154 (59)	52.6 (44.1-60.5)	58 (49.3-65.8)	1.0	
T3-4	105 (40)	26.9 (18.7-35.7)	33 (23.9-42.3)	2.15 (1.54-3)	<0.001
Tumour N-Stage					
N0	127 (48)	58.4 (49-66.6)	64.5 (55-72.5)	1.0	
N1-3	135 (51)	26.5 (19.2-34.3)	32.4 (24.3-40.7)	2.50 (1.77-3.55)	<0.001
Tumour Regression Grade(¥)					
1-3	27 (10)	57.7 (36.4-74.1)	56.5 (32.4-74.9)	1.0	
4-5	52 (20)	44.2 (30.6-57.1)	49.3 (34.3-62.6)	1.42 (0.68-2.97)	0.345
Histological Subtype					
Intestinal	79 (30)	48.2 (36.6-58.9)	52.6 (40.3-63.5)	1.0	
Non-intestinal	53 (20)	24.2 (13.1-37.1)	33 (20.3-46.2)	2.09 (1.33-3.29)	0.001
Lymphatic invasion					
Absent	93 (35)	56.3 (45.1-66)	65.8 (54.8-74.8)	1.0	
Present	125 (48)	26.6 (19.1-34.7)	30 (21.9-38.6)	2.65 (1.79-3.92)	<0.001
Neural invasion					
Absent	12 (5)	58.3 (27-80.1)	52.9 (20.5-77.4)	1.0	
Present	68 (26)	21.8 (12.8-32.2)	23 (13.5-34)	2.51 (1-6.29)	0.05
Vascular invasion					
Absent	147 (56)	49.9 (41.3-57.8)	58.7 (50-66.4)	1.0	
Present	60 (23)	18.3 (9.8-29)	18.6 (9.8-29.6)	2.55 (1.76-3.69)	<0.001
Lymphocytic Infiltrates					
Absent	5 (2)	40 (5.2-75.3)	40 (5.2-75.3)	1.0	
Present	87 (33)	50.7 (40-60.8)	57.8 (46.2-67.7)	0.71 (0.25-1.98)	0.508

(*) Either CEA or Ca 19.9 or both at presentation
(¥) According to Mandard classification

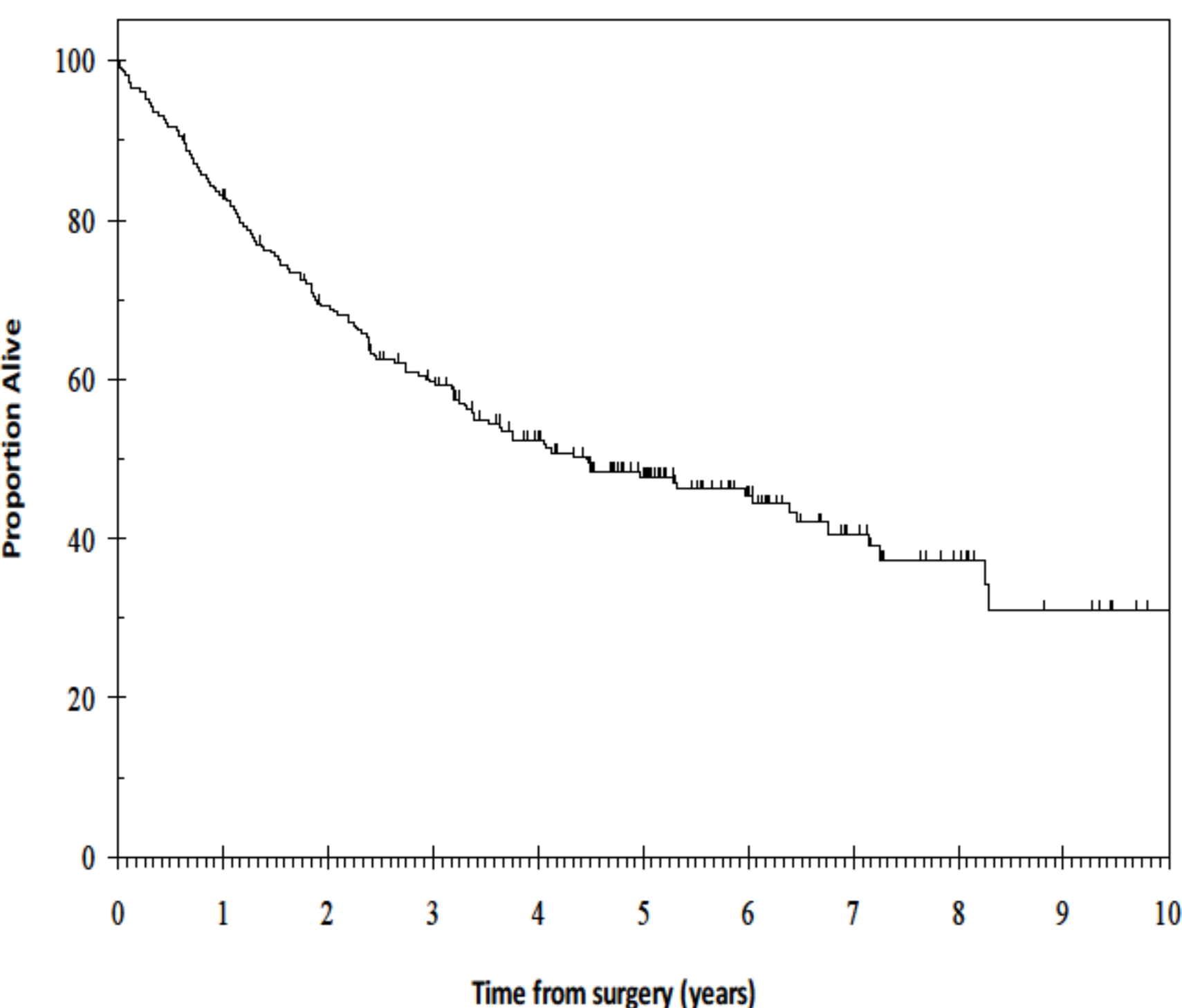
Overall Survival and Multivariate Analysis

After a median follow-up of 66.1 months (95% CI, 61.3 -72), median DFS and OS were 31.7 (95% CI, 23.9-43.6) and 53.5 (95% CI, 39.8-77.7) months respectively. Ninety-nine patients with all variables available were included in MVA.

Prognostic Index – Overall Survival



Overall Survival



Characteristics	Hazard Ratio (95% Confidence Interval, %)	p-value
Site of Primary		
Gastric	1.0	
OES+OGJ	2.11 (1.19-3.72)	0.01
Tumour T-Stage		
T0-2	1.0	
T3-4	1.89 (1.09-3.29)	0.024
Tumour N-Stage		
N0	1.0	
N1-3	1.95 (1.11-3.42)	0.02
Histological Subtype		
Intestinal	1.0	
Non-intestinal	2.29 (1.36-3.88)	0.002

CONCLUSIONS

This analysis was conducted using a large single-institution cohort of patients affected by adenocarcinoma of the oesophagus, junction or stomach who were treated in a uniform fashion with neoadjuvant chemotherapy followed by surgery performed in a high volume cancer centre.

- Our results are in line with those previously reported, where site of primary tumour, T and N pathological stage and histological subtype are independent prognostic factors of overall survival (4,5).
- A prognostic index was established in order to identify patients with different prognoses by the use of four variables described above.
- Future clinical trials may stratify patients according to these characteristics in order to optimise post-operative treatment.

References

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