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Gastric cancer surgery in high volume university medical centers influences long-term survival

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ABSTRACT

Background: Short-term gastric cancer surgery outcomes depend greatly on hospital surgical volume, whereas long-term survival studies show conflicting results. This study evaluated the effect of surgical volume on the long-term survival of patients who underwent surgery for gastric cancer in Slovenia.

Methods: A retrospective cohort analysis was performed using the Slovenian Cancer Registry data. Patients diagnosed between 2016 and 2020 who underwent gastric cancer surgery were categorized into high- and low-volume centers. High-volume centers were defined, as the two University Medical Centers (Ljubljana and Maribor), which together treated 76.4 % of all patients during the study period. Survival analysis was conducted using Kaplan-Meier overall survival and Pohar-Perme net survival estimators, with predefined subgroup analysis. Cox proportional hazards models assessed the independent association between center volume and overall survival.

Results: Among the 652 patients, 498 (76.4 %) underwent surgery at high-volume centers (44,2–55,4 mean surgeries/year), which demonstrated higher median overall survival (4.9 vs. 3.2 years) and improved overall and net 1-, 3-, and 5-year survival rates compared with low-volume centers (0,2–6,2 mean surgeries/year). This differences persisted in stratified analyses by stage and neoadjuvant therapy but not by age. In multivariable Cox analysis the hazard ratio remained directionally favorable for high-volume centers but was not statistically significant.

Conclusions: Overall, high-volume centers were consistently associated with better long-term survival after gastric cancer surgery in Slovenia, supporting further evaluation of centralization strategies. Future policies should aim to balance the benefits of centralization while maintaining equitable access to timely and high-quality surgical treatment, regardless of location or socioeconomic status.

1. Introduction

Except in cases detected at the earliest stages, surgical resection remains the only curative treatment for gastric cancer (GC). Hospital surgical volume is believed to be an important predictor of surgical technical skills, potentially influencing both short- and long-term outcomes following surgery. Better outcomes in several types of cancer surgeries have been observed in several large population-based studies addressing both perioperative mortality and long-term survival [1–7]. The magnitude of this influence varies among different pathologies, as does the definition of the number of cases required to achieve the status of a high-volume center (HVC).

In GC surgery several studies show the benefit of surgery performed in HVC in terms of perioperative mortality [1,8–11]. In terms of long-term survival, the results are more heterogeneous. Several studies have shown improved 5-year survival in HVC, but the definitions of HVC and LVC varied, and the difference in survival was most apparent in LVCs with the lowest volumes [6,12–14]. However, several studies,

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including two Japan Clinical Oncology Group (JCOG) phase III trials, did not show a statistically significant long-term survival difference between HVC and LVC [15–19]. The potential influence on long-term survival thus remains controversial and is likely influenced by the specifics of individual healthcare systems and patient populations.

In Slovenia, there is no obligation to centralize gastric surgery. Despite this, the majority of patients with GC receive surgical treatment at two larger university hospitals, whereas other hospitals perform GC surgery only sporadically. To further elucidate the relationship between surgical volume and survival in GC surgery and obtain an up-to-date overview, we analyzed patients who underwent surgery for gastric adenocarcinoma diagnosed in Slovenia between 2016 and 2020.

2. Methods

2.1. Study design and population

In this retrospective cohort study, data from the Slovenian Cancer Registry (SCR) were used to evaluate the impact of surgical volume on the survival of patients diagnosed with gastric adenocarcinoma. The SCR, founded in 1950, is a nationwide population-based cancer registry. It is a member of the International Association of Cancer Registries and the European Network of Cancer Registries. Cancer reporting is mandated by law in Slovenia and is required of all physicians.

The study included patients who underwent GC surgery with curative intent and were diagnosed in Slovenia between 2016 and 2020. Patients were identified using the International Classification of Diseases 10th edition (ICD-10) code for GC (C16). Eligible patients were aged ≥18 years. Patients were excluded if they had GC other than adenocarcinoma, multiple cancers, underwent palliative surgery, had procedures for progression or recurrence, were operated outside Slovenia, or did not undergo surgical treatment. Patient and tumor characteristics, including age, sex, tumor stage, neoadjuvant therapy, systemic therapy, and radicality of surgery, were extracted from SCR.

Slovenia has a publicly funded universal healthcare system, primarily financed through mandatory health insurance administered by the Health Insurance Institute. All residents have access to comprehensive cancer care without direct out-of-pocket payments at the point of care. Patients are generally free to choose their treatment hospitals. Although referring physicians often direct complex oncologic surgeries to larger public institutions, this practice is not mandated by national guidelines or formally supported by the Health Insurance Institute or the Ministry of Health. Although private practice exists in Slovenia, it is not commonly involved in the management of gastric cancer, particularly in surgical treatment.

2.2. Grouping and categorization

The patients were stratified according to the annual surgical volume of their treatment centers. HVC were defined as two university hospitals that performed the majority of gastric resections in Slovenia. All other hospitals were categorized as LVC.

Subgroup analyses were conducted based on sex, age, tumor stage, neoadjuvant therapy, and systemic-therapy. Patients were divided into age groups that were adjusted to enable a balanced comparison. Age groups were defined as 18–54, 55–74, and ≥75 years. Tumor stage at diagnosis was classified using a standard three-tier system widely used by population-based cancer registries to ensure consistency in longitudinal data analysis. Tumors were categorized as localized, regional, or distant, depending on the extent of the disease at the time of diagnosis. The localized stage refers to cancer confined to the organ of origin, the regional stage indicates spread beyond the organ and/or involvement of regional lymph nodes, and the distant stage signifies metastasis to distant organs. For international comparability, these categories can be aligned with the 8th edition of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) TNM classification. Specifically, localized disease corresponds to T1–T2, N0, M0; regional disease to T3–T4, N0, M0 or any T, N1–N3, M0; and distant disease to any T, any N, M1. Systemic therapy was defined as pharmacological treatment administered for the primary management of gastric cancer, including chemotherapy and targeted agents. All patients receiving systemic therapy were treated with cytotoxic chemotherapy, and a small subgroup (n = 7) additionally received targeted therapy. Neoadjuvant therapy was defined as systemic therapy administered prior to surgical resection.

2.3. Statistical analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patient population. Categorical variables were compared between the HVC and LVC groups using the chi-square test.

Overall observed survival, the probability that a person is alive at a specific time after diagnosis, was calculated using the Kaplan-Meier estimator. To account for the mortality of the general population with the same demographic structure, net survival was calculated using the Pohar-Perme estimator and Slovenian life tables by sex, age, and year. Net survival is the survival that would be observed if the only cause of death was the disease being studied, that is, cause-specific survival. Differences in survival among the groups were assessed using the log-rank test (overall survival) and log-rank type test (net survival).

Separate survival analyses were performed for subgroups (HVC vs. LVC) according to sex, age, tumor stage, adjuvant therapy, and systemic therapy.

To account for potential confounding factors influencing long-term survival, we additionally performed Cox proportional hazards regression. Univariate models were first fitted for each covariate (treatment center volume (HVC vs. LVC), age, sex, tumor stage, neoadjuvant therapy, and systemic therapy). These same variables were then entered into a multivariable Cox model to adjust for potential confounding. The primary variable of interest was treatment center volume. Hazard ratios (HRs) were calculated for both univariate and multivariable analyses.

All analyses were performed using R program language (version 4.3.1), program RStudio (version 2023.06.1) and packages survival (version 3.5–5) and relsurv (2.2–9). Statistical significance was defined as $p < 0.05$.

3. Results

A total of 652 patients met the inclusion criteria. Two HVC were identified: University Medical Center Ljubljana (UMC Ljubljana) and University Medical Center Maribor (UMC Maribor). A total of 498 (76.4 %) patients were diagnosed and treated at HVC and 154 (23.6 %) at LVC (Table 1). The patient groups were comparable in terms of sex, age, and cancer stage; however, a significant difference was observed in the proportion of patients receiving systemic and neoadjuvant therapy, which was higher in the HVC group (Table 1).

The mean patient volume for HVC was 55.4 at UMC Ljubljana and 44.2 per year at UMC Maribor (Table 2). Eleven LVC were identified in Slovenia, with a mean GC patient volume varying from 0.2 to 6.5 (Table 2).

3.1. Survival analysis

3.1.1. Overall survival

The median overall survival for the entire cohort was 4.5 years, with 1-, 3-, and 5-year overall survival rates of 81.1 %, 55.8 %, and 46.9 %, respectively (Table 3).

3.1.2. Survival by center volume

Patients treated at HVC had a median overall survival of 4.9 years. Patients treated at LVC had a median overall survival of 3.2 years. Both

Table 1
Demographic and clinical characteristics of the patient population. A Chi-square test was performed to compare the key characteristics between the HVC and LVC.

	High-volume center		Low-volume center		
variable	Number of patients	%	Number of patients	%	p-value
Surgical volume	498	76.4	154	23.6	<0.001
Sex					
Male	318	63.9	94	61.0	0.591
Female	180	36.1	60	39.0	
Age					
15–54	84	16.9	18	11.7	0.183
55–74	272	54.6	83	53.9	
75+	142	28.5	53	34.4	
Stage					
Localized	119	23.9	40	26.0	0.547
Regional	324	65.1	94	61.0	
Distant	52	10.4	20	13.0	
Unknown	3	0.6	0		
Systemic therapy					
No	238	47.8	101	65.6	<0.001
Yes	260	52.2	53	34.4	
Neoadjuvant therapy					
No	304	61.0	128	83.1	<0.001
Yes	194	39.0	26	16.9	
Radicality of resection					
R0	435	87.3	119	77.3	0.238
R1	30	6.0	15	9.7	
R2	23	4.6	10	6.5	
unknown	10	2.0	10	6.5	

Table 2
Number of GC patients diagnosed in 2016–2020 at HVC and LVC in Slovenia.

Hospital	2016	2017	2018	2019	2020	Total	Mean (surgeries/year)
UMC Ljubljana	67	55	62	49	44	277	55.4
UMC Maribor	46	34	45	56	40	221	44.2
Low volume hospital 1	9	4	3	8	7	31	6.2
Low volume hospital 2	4	5	3	3	4	19	3.8
Low volume hospital 3	2	1	1	1	0	5	1.0
Low volume hospital 4	3	0	2	0	1	6	1.2
Low volume hospital 5	0	0	0	0	1	1	0.2
Low volume hospital 6	2	2	2	1	0	7	1.4
Low volume hospital 7	0	1	6	6	3	16	3.2
Low volume hospital 8	0	1	0	0	0	1	0.2
Low volume hospital 9	5	6	9	5	4	29	5.8
Low volume hospital 10	7	4	4	4	5	24	4.8
Low volume hospital 11	2	2	2	3	6	15	3.0
Total	**147**	**115**	**139**	**136**	**115**	**652**	**130.4**

overall and net survival analyses revealed higher 1-, 3-, and 5-year survival rates for HVC (Table 3). The difference in survival curves was statistically significant for overall survival (log-rank test for overall survival: chi-square = 4,490, df = 1, p = 0.034). There was a trend toward better net survival (Log-rank type test for net survival: test statistics = 3.283, df = 1, p = 0.07) (Fig. 1).

3.1.3. Survival by center volume and sex

The median overall survival for males was 4.6 years, while that for females was not reached within the study period. Both overall and net survival analyses revealed higher 1-, 3-, and 5-year survival rates for HVC than for LVC, adjusted for sex (Table 3). There was a trend towards improved overall survival for HVC (chi-square = 6.588, df = 3, p = 0.086), but not for net survival (test statistics = 3.969, df = 3, p = 0.265) (Fig. 1).

3.1.4. Survival by center volume and age group

Overall survival and net survival analyses revealed higher 1-, 3-, and 5-year survival rates for HVC than for LVC, adjusted for age group in the age groups 55–74 years and 75+ years age groups but not in the 15–54 years age group (Table 3). The analysis showed that overall and net survival were higher in the HVC group after adjusting for patient age. The difference was statistically significant for both overall survival (chi-square = 38.634, df = 5, $p < 0.001$) and net survival (test statistics = 18.311, df = 5, p = 0.003) (Fig. 1).

3.1.5. Survival by center volume and tumor stage

Overall and net survival analyses revealed higher 1-, 3-, and 5-year survival rates for HVC than for LVC, stratified by tumor stage except for 1-year and 5-year survival for localized tumors and 3-year net survival for distant tumors (Table 3). The analysis showed that overall and net survival were higher in the HVC group, stratified by tumor stage. The difference was statistically significant for both overall (chi-square = 156.962, df = 5, $p < 0.001$) and net survival analyses (chi-square = 152.905, df = 5, $p < 0.001$) (Fig. 1).

3.1.6. Survival by center volume and systemic therapy

Overall and net survival rates were higher for HVC than for LVC in patients who received and those who did not receive systemic therapy. This was true for all subgroups, except for 1-year survival in patients who received systemic therapy, in which survival was higher in the LVC group (Table 3). The difference was not statistically significant both for overall (chi-square = 5.656, df = 3, p = 0.130) and net survival analysis (chi-square = 3.342, df = 3, p = 0.342) (Fig. 1).

3.1.7. Survival by center volume and neoadjuvant therapy

Overall and net survival rates were higher for HVC than for LVC in patients who received and those who did not receive neoadjuvant therapy. This was true for all subgroups, except for 1-year survival in patients who received neoadjuvant therapy, in which survival was higher in the LVC group (Table 3). The difference was statistically significant for overall survival (chi-square = 8.713, df = 3, p = 0.033) but not for the net survival analysis (chi-square = 5.192, df = 3, p = 0.158) (Fig. 1).

3.2. Cox proportional hazards analysis

In the univariate Cox model, treatment at a LVC was associated with lower overall survival compared to treatment at a HVC (HR 1.28, p = 0.042). Older age (≥75 years: HR 2.09, $p < 0.001$) and higher tumor stage (regional: HR 4.72, $p < 0.001$; distant: HR 11.58, $p < 0.001$) were also associated with reduced survival. Sex, systemic therapy, and neoadjuvant therapy were not significant in the univariate analysis (Table 4).

In the multivariable model including all variables, the association between center volume and survival was attenuated and was no longer statistically significant (HR 1.14, p = 0.282). Tumor stage (regional: HR 6.94, $p < 0.001$; distant: HR 18.19, $p < 0.001$) and age ≥75 years (HR 1.47, p = 0.057) remained the strongest predictors of survival. Sex (p = 0.069), systemic therapy (p = 0.091), and neoadjuvant therapy (p =

Table 3
Overall and net survival of GC patients diagnosed between 2016 and 2020 in Slovenia. [a]The observed survival did not drop below 0.5 during the follow-up period. [b]The upper limit of the confidence interval for observed survival did not fall below 0.5 during the follow-up period.[c] Fewer than 10 individuals were at risk.

					N at risk			Overall survival (%)			Net survival (%)		
	Variable	Volume	Sample size	Media survival [months] (overall survival)	1-year	3-year	5-year	1-year	3-year	5-year	1-year	3-year	5-year
All	2016–2020		652	53.7 [42.7–62.5]	528	363	204	81.1 [78.2–84.2]	55.8 [52.1–59.7]	46.9 [43.0–51.0]	83.1 [80.1–86.3]	59.8 [55.8–64.1]	52.9 [48.4–57.8]
Center	High volume	High volume	498	58.9 [49.6-][b]	408	285	164	82.1 [78.8–85.5]	57.4 [53.2–61.9]	48.9 [44.5–53.7]	84.1 [80.7–87.6]	61.4 [56.8–66.3]	55.2 [50.1–60.8]
	Low volume	Low volume	154	38.8 [29.3–59]	120	78	40	77.9 [71.6–84.8]	50.6 [43.3–59.2]	40.2 [32.8–49.2]	80.0 [73.5–86.9]	54.7 [46.8–64.0]	45.4 [36.6–56.3]
Sex	Male	High volume	318	54.7 [36.4–77.3]	258	175	97	81.4 [77.3–85.8]	55.2 [50.0–61.0]	46.9 [41.5–53.0]	83.6 [79.3–88.1]	59.8 [54.1–66.1]	54.4 [48.0–61.6]
	Female		180	[51.6-][a,b]	150	110	67	83.3 [78.1–89.0]	61.1 [54.4–68.7]	52.4 [45.4–60.6]	84.9 [79.5–90.7]	64.1 [56.9–72.2]	56.7 [48.9–65.9]
	Male	Low volume	94	36.3 [24–59]	76	47	23	80.9 [73.3–89.2]	50.0 [40.8–61.2]	36.7 [27.7–48.6]	82.8 [75.1–91.3]	54.4 [44.4–66.6]	41.1 [30.3–55.9]
	Female		60	42 [18.8-]	44	31	17	73.3 [63.0–85.4]	51.7 [40.5–66.0]	45.8 [34.6–60.6]	74.9 [64.4–87.0]	55.1 [43.2–70.3]	51.8 [39.2–68.6]
Age group	15–54	High volume	84	77.3 [50.7-][b]	74	52	29	89.2 [82.8–96.1]	62.7 [53.1–74.0]	54.8 [44.6–67.3]	89.4 [83.1–96.3]	63.2 [53.6–74.5]	55.6 [45.4–68.2]
	55–74		272	[59.2-][a,b]	228	168	104	83.8 [79.6–88.3]	61.8 [56.3–67.8]	54.7 [49.0–61.2]	85.0 [80.6–89.5]	64.5 [58.8–70.8]	59.3 [53.0–66.3]
	75+		142	29.9 [21.2–51.6]	106	65	31	74.6 [67.8–82.2]	45.8 [38.3–54.7]	34.1 [26.8–43.5]	79.1 [71.9–87.1]	53.9 [44.9–64.8]	46.9 [36.7–60.0]
	15–54	Low volume	18	[-][a,b]	17	16	10	94.4 [84.4–100]	88.9 [75.5–100]	82.5 [66.3–100]	94.7 [84.9–100]	89.7 [76.6–100]	84.0 [68.0–100]
	55–74		83	34.6 [23.8–64.3]	66	41	22	79.5 [71.3–88.7]	49.4 [39.7–61.4]	41.5 [31.8–54.3]	80.7 [72.4–90.0]	51.9 [41.8–64.4]	45.6 [35.0–59.4]
	75+		53	22.2 [16.2–45]	37	21	8[c]	69.8 [58.5–83.3]	39.6 [28.4–55.2]	24.3 [14.7–40.1]	73.1 [61.4–87.0]	46.9 [33.7–65.1]	32.3 [19.2–54.6]
Stage	Localized	High volume	119	[-][a,b]	111	107	69	93.3 [88.9–97.9]	89.9 [84.7–95.5]	82.9 [76.1–90.3]	94.3 [89.9–99.0]	96.2 [90.2–100]	94.8 [86.2–100]
	Regional		324	40.8 [30.1–57.9]	265	167	86	82.1 [78.0–86.4]	51.7 [46.5–57.5]	41.3 [36.0–47.4]	84.0 [79.8–88.4]	55.1 [49.5–61.3]	46.3 [40.3–53.3]
	Distant		52	13.2 [10.2–21.7]	29	8[c]	6[c]	55.8 [43.8–71.0]	15.4 [8.1–29.1]	13.5 [6.8–26.8]	57.1 [45.0–72.4]	16.1 [8.7–29.9]	14.3 [7.3–28.0]
	Unknown		3										
	Localized	Low volume	40	[-][a,b]	38	34	20	95.0 [88.5–100.0]	85.0 [74.6–96.8]	85.0 [74.6–96.8]	96.7 [90.0–100]	90.7 [79.1–100]	97.3 [84.8–100]
	Regional		94	29.7 [19.3–42.5]	72	41	19	76.6 [68.5–85.7]	43.6 [34.7–54.9]	29.8 [21.5–41.3]	78.8 [70.5–88.0]	47.3 [37.6–59.5]	32.9 [23.0–46.9]
	Distant		20	10.9 [7.3–32.6]	10	3[c]	1[c]	50.0 [32.3–77.5]	15.0 [5.3–42.6]	5.0 [0.7–33.8]	50.8 [33.4–77.5]	16.2 [6.3–41.7]	5.3 [1.1–25.5]
	Unknown		0										
Systemic therapy	No	High volume	238	58 [37.6-][b]	183	136	72	76.9 [71.7–82.4]	57.1 [51.2–63.8]	48.5 [42.2–55.6]	79.7 [74.3–85.5]	62.6 [55.9–70.2]	57.5 [49.7–66.5]
	Yes		260	59.2 [40.8-][b]	225	149	92	86.9 [82.9–91.1]	57.5 [51.8–63.9]	49.2 [43.3–55.9]	88.0 [83.9–92.3]	59.9 [54.0–66.6]	53.0 [46.6–60.2]
	No	Low volume	101	32.3 [18.7-][b]	71	50	23	70.3 [61.9–79.8]	49.5 [40.7–60.3]	39.1 [30.2–50.7]	72.2 [63.7–81.9]	54.2 [44.4–66.1]	45.4 [34.2–60.2]
	Yes		53	42.5 [29.6–64.3]	49	28	17	92.5 [85.6–99.8]	52.8 [41.0–68.1]	41.9 [30.3–58.1]	93.9 [87.1–100]	55.0 [42.7–70.9]	45.1 [32.6–62.4]
Neoadjuvant therapy	No	High volume	304	52.8 [34.2–65.4]	238	167	90	78.3 [73.8–83.1]	54.9 [49.6–60.8]	45.0 [39.5–51.3]	80.8 [76.1–85.7]	59.9 [53.9–66.4]	52.5 [45.9–60.1]
	Yes		194	[53.4-][a,b]	170	118	74	88.1 [83.7–92.8]	61.2 [54.6–68.4]	54.9 [48.2–62.6]	89.2 [84.7–94.0]	63.7 [56.9–71.3]	59.2 [52.0–67.5]
	No	Low volume	128	38.8 [24–59]	96	65	32	75.0 [67.9–82.9]	50.8 [42.8–60.2]	39.9 [31.8–49.9]	77.1 [69.8–85.2]	55.2 [46.5–65.6]	45.3 [35.6–57.7]
	Yes		26	37.1 [22-][b]	24	13	8c	92.3 [82.6–100]	50.0 [34.0–73.4]	41.2 [25.8–65.9]	93.8 [84.3–100]	52.4 [36.1–76.1]	44.4 [28.3–69.6]

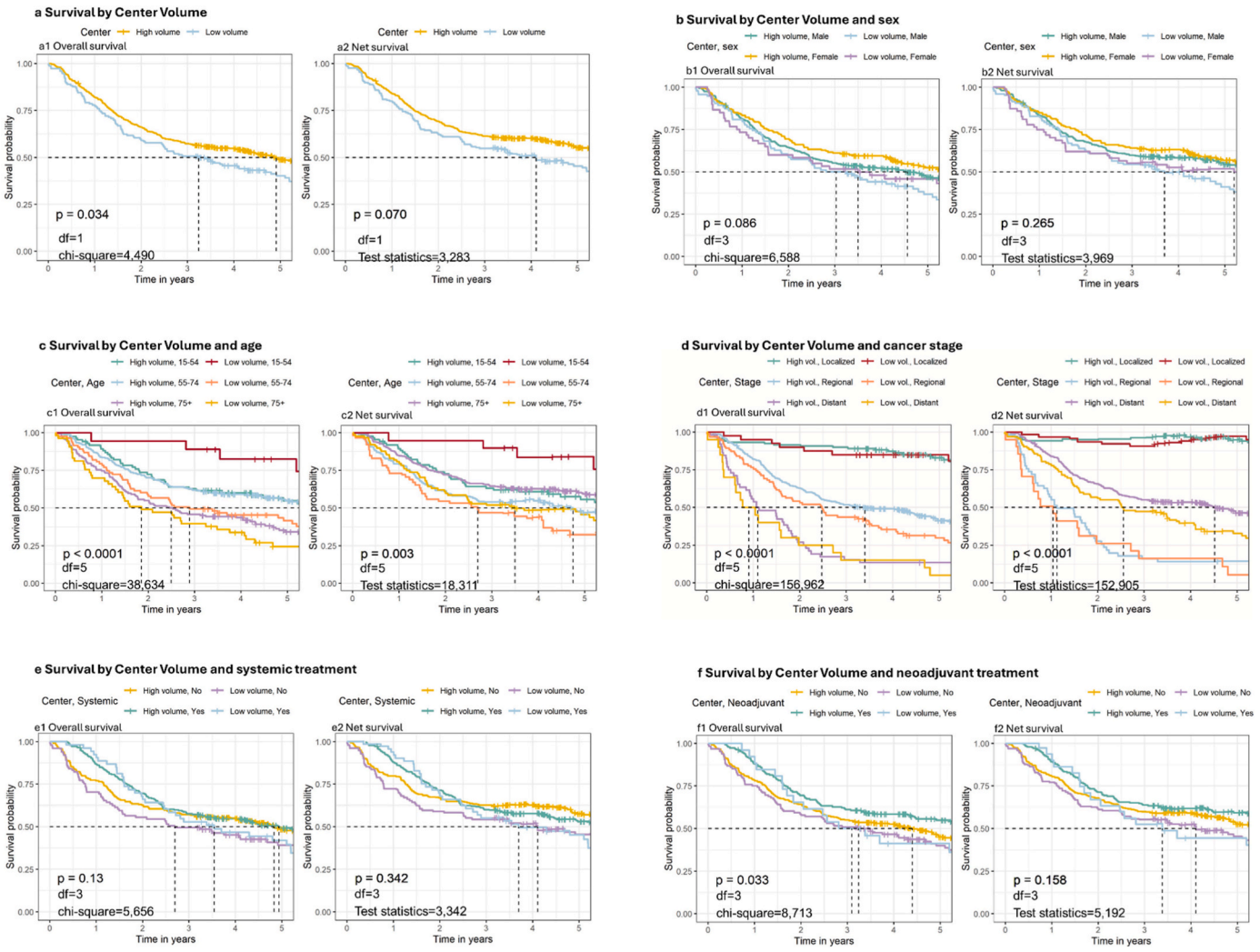

Fig. 1. Overall survival (Kaplan-Meier survival analysis with Log-rank test group comparison result) and net survival (Pohar-Perme net survival analysis with Log-rank type test group comparison result). df (degrees of freedom).

Table 4
Univariate and multivariable Cox proportional hazards models for overall survival.

		Univariate Cox model		Multivariable Cox model	
Variable	Category	HR	p-value	HR	p-value
Center volume	High volume	ref	–	ref	–
	Low volume	1.28	0.042	1.14	0.282
Sex	Male	ref	–	ref	–
	Female	0.86	0.184	0.81	0.069
Age group	15–54	ref	–	ref	–
	55–74	1.26	0.184	1.18	0.347
	≥75	2.09	<0.001	1.47	0.057
Tumor stage	Localized	ref	–	ref	–
	Regional	4.72	<0.001	6.94	<0.001
	Distant	11.58	<0.001	18.19	<0.001
Systemic therapy	No	ref	–	ref	–
	Yes	0.88	0.229	0.54	0.091
Neoadjuvant therapy	No	ref	–	ref	–
	Yes	0.78	0.033	0.83	0.221

0.221) were not significant in the adjusted model (Table 4).

4. Discussion

In recent decades, there has been a significant push toward centralizing complex cancer surgeries to HVC, driven by a growing body of evidence linking hospital surgical volume to improved outcomes [5,20]. Most studies on GC show a significant relationship between hospital volume and postoperative mortality, whereas the relationship with long-term survival is more heterogeneous [21]. Conflicting results on the influence of surgical volume on long term survival are further complicated by a wide range of definitions of HVC [6,12,13,16,17].

Besides survival, factors such as patient travel distance, treatment delays, and institutional capacity must also be considered, as they may impact access, patient comfort, and outcomes [5,14,22,23].

Our survival analysis demonstrated a significant positive relationship between hospital volume and long-term survival rates in GC patients, with a 2.1-year increase in median survival observed in HVC (5.8 years) compared to LVC (3.7 years). To complement the Kaplan–Meier and Pohar-Perme survival analyses, we performed Cox proportional hazards modelling. In the univariate model, treatment at a HVC was associated with significantly better overall survival. However, in the multivariate model this association was attenuated and is no longer statistically significant. We conclude, that this shift is primarily due to

the higher survival rates of patients in the 15–54 age group who were treated in LVC compared to patients treated in HVC. However, clear conclusions cannot be drawn since the number of patients in this age group is quite small. The adjusted hazard ratio nevertheless remained directionally favorable for high-volume centers, consistent with the survival differences observed in the non-adjusted analyses. In the multivariable model, age and tumor stage were by far the strongest predictors of survival, while neoadjuvant and systemic therapy did not reach statistical significance. Given the magnitude of the effects of age and stage, and their strong correlation with treatment pathways, it is plausible that these dominant prognostic factors mask smaller, jet still clinically relevant differences between HVC and LVC, as well as the effects of systemic and neoadjuvant treatment.

Several factors make Slovenia well-suited for interpreting the volume-outcome relationship while observing the characteristics of the local healthcare system. As a small country with a population of roughly two million, it has a compact healthcare system covered by two large university clinical centers no further than 150 km from any point in the country. The two centers performed 76.4 % of all GC surgeries, which reduced the variation in treatment in the system. This shows that centralization in Slovenia has, to an extent, occurred without guidance from healthcare providers. This drive towards centralization can be explained by better results and surgeon preference, as small-volume centers increasingly cease to perform surgeries in which they are not comfortable and do not achieve optimal results [5].

As both centers perform a significantly larger number of GC surgeries, this also provides a natural cutoff for the definition of HVC. While many studies select volume cut points to provide evenly sized groups, this may not reflect the optimum cut point from a performance perspective. As local characteristics and study designs differ HVC definitions cover a wide range from 7 to more than 119 surgeries/year [6,12-17,24,25]. We believe this reinforces the need for a local investigation of the role of HVC in improving long-term GC surgery results rather than a uniform standard of HVC.

Along with surgery, systemic therapy plays a central role in GC management. The success of systemic therapy is influenced by variations in medical oncology clinical experience, which has been shown to cause heterogeneity in disease survival [19]. An important limitation of our study is the lack of specific data concerning the precise regimen of systemic therapy. However, we believe that this is partially mitigated by the fact that all systemic therapy in Slovenia takes place in just two cancer centers, ensuring a high degree of treatment standardization and consistency. This is further supported by our results, which showed improved survival in HVC patients who were and were not treated with systemic or neoadjuvant treatment.

Several other limitations should be addressed. Surgical radicality was not statistically different between the groups, but the R0 resection rate was greater in the HVC group, potentially contributing to survival differences. We also failed to adjust for the possible influence of the emergency setting of surgery and minimally invasive surgery (MIS), although data supporting the oncologic equivalency of MIS suggests that MIS may not significantly affect long-term survival [26,27]. Perhaps most critically, we could not directly adjust for the experience of surgeons in both groups. In a study of volume-outcome relationships, Xirasagar et al. found that the influence of surgeons case volume and increasing age on survival was greater than that of hospital volume [16]. However, they found that more experienced surgeons tended to operate on younger patients, making it difficult to isolate these effects and suggesting that several factors need to be considered in the assessment of the volume-outcome relationship. While these data are not available in our study, we believe that the difference in hospital volumes may serve as a surrogate marker of surgical experience and case volume.

We also acknowledge that we were unable to adjust for important confounders such as comorbidities and socioeconomic status, which may influence the results [28,29]. Comorbidities, an important risk factors for postoperative morbidity and mortality, are a common indication for referral to a tertiary center which are better equipped in their management [11,28,30].

Although the association between center volume and survival was not statistically significant in the adjusted Cox model, the overall pattern of findings, including differences in median survival, Kaplan–Meier and Pohar–Perme estimates, and the directionally favorable hazard ratio consistently points toward better long-term outcomes for patients treated in high-volume centers in Slovenia, supporting continued consideration of centralization as a strategy to improve gastric cancer outcomes.

Nevertheless, universal centralization may be unrealistic due to factors such as patient preference, geography, and provider incentives for surgery. For this reason, we need to further understand the mechanism through which a volume-related influence on survival is mediated.

Future studies in Slovenia and abroad should adopt a more clinically oriented and prospective design, enabling the inclusion of detailed variables such as surgeon experience and case volume, patient performance status and comorbidity, comprehensive systemic and neoadjuvant therapy data, complications and their management, and progression-related outcomes. This will enable a tailored approach to improving GC outcomes by increasing referrals to HVC and enhancing care in LVC.

While our definition of HVC corresponds well to the local characteristics of the Slovenian healthcare system, these results are limitedly applicable to nations or regions with similar situations to Slovenia. Nevertheless, our study results support further studies on the volume-outcome relationship tailored to the local characteristics of individual healthcare systems. Such studies can support decision-makers in developing centralization strategies based on proven benefits while maintaining equitable access to timely and high-quality surgical treatment regardless of location or socioeconomic status.

Statements

All procedures followed were in accordance with the ethical standards of the Slovenian National Medical Ethics Committee (Komisija Republike Slovenije za medicinsko etiko, approval number 0120–251/2025-2711-3) on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

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All authors read and approved the final version of the manuscript.

Declaration of AI and AI-assisted technologies in the writing process

This manuscript was edited for language and clarity using AI-assisted tools (ChatGPT and Paperpal). These tools were employed solely to improve grammar, wording, and readability; they were not used for content generation, data analysis, or substantive contribution to the intellectual content of the work. After using these tools, the authors

reviewed and edited the content as needed and take full responsibility for the content of the publication.

Conflict of interest

The authors declare no conflicts of interest.

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