

Title:

“The impact of hospital resection-volume and service-capability on post-operative mortality following gastrectomy”

Short Title (running head): Mortality following gastrectomy

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Abstract

Background:

Improved post-operative mortality following gastrectomy for cancer in hospitals with higher resection-volumes has not been reported in Australia. Using a population-based study in Queensland, we aimed to compare post-operative mortality following gastrectomy between high and low-volume hospitals stratified by their service-capability.

Methods:

All patients undergoing gastrectomy for adenocarcinoma in Queensland between 2001 and 2015 were obtained from the Queensland Oncology Repository. Hospital service-capability was defined using the 2015 AIHW hospital peer groupings. Hospitals were grouped into 'high-volume' (≥ 5 gastrectomies annually), high service-capability; 'low-volume (< 5), high service-capability' and 'low-volume, low service-capability'. Negative binomial regression models were used to compare 30- and 90-day mortality between hospital groups adjusting for age, sex, socio-economic status, Charlson and ASA scores, treatment regimen, stage and time-period. Potential mediation of mortality differences between hospital groups due to differences in the type of gastrectomy performed was also examined.

Results:

Low-volume hospitals with low service-capability have higher adjusted 30-day (IRR= 2.97, 95% CI: 1.65-5.35) and 90-day (IRR= 1.95, 95% CI: 1.23- 3.09) mortality compared with high-volume, high service-capability hospitals. There is no significant difference in adjusted 30-day (IRR=1.16, 0.48 - 2.79) and 90-day (IRR=1.12, 0.59 – 2.13) mortality comparing low-volume, high service-capability hospitals with high volume, high service-capability hospitals. The type of gastrectomy performed did not significantly influence differences in mortality compared between hospital-groups .

Conclusion:

In the Australian environment, post-operative mortality following gastric cancer surgery may be optimised by centralising gastrectomy away from hospitals characterised by low volume and low service-capability.

Key words:

Hospital Mortality; Gastrectomy; Hospitals, High-volume; Hospitals, Low-Volume;

Introduction:

In 2018, gastric cancer was estimated to account for over 700,000 deaths globally ¹ and over 1000 deaths in Australia ². Surgical resection is the only curative treatment with 30-day post-operative mortality rates in western populations reported to be 1.6-16% ³⁻⁷.

Improved mortality has been reported following gastrectomy in high-volume centres which are defined by resection-volumes varying between 13 to over 21 procedures annually^{4, 8, 9} in population-level studies based in Europe and the USA^{4, 8, 10, 11}. By comparison, Australia is characterised by a smaller and geographically more dispersed population, a low incidence of gastric cancer and consequently lower hospital resection-volumes compared to other western populations⁶. In Australia, an association between higher volumes of resection and lower post-operative mortality, adjusted for case-mix, has not been reported¹². This may relate to factors including lower mortality rates reported by Australian centres performing gastrectomy ^{7, 12}, as well as some centres considered low-volume in Australia offering services including trained specialist surgeons, high-level intensive care, advanced gastroenterology and interventional radiology. These services are reported to be associated with improved post-operative mortality following other complex upper-GI surgery, such as pancreatic resection¹³. A high hospital service-capability, with appropriately trained surgeons, may explain why some Australian low-volume centres report post-operative mortality outcomes equivalent to those reported by centres with much higher resection volumes⁶.

Using a population-based study in Queensland, we aimed to assess 30- and 90-day post-operative mortality following gastric cancer surgery and compare mortality outcomes between high and low-volume hospitals stratified by their service-capability.

Methods:

Demographic, hospital and clinical data on all patients undergoing gastrectomy for gastric adenocarcinoma in Queensland between January 1st, 2001 and December 31st, 2015 were obtained from the Queensland Oncology Repository (QOR). This is a secure data repository containing individual cancer patient demographic, treatment and outcome data from multiple administrative databases including population-based Queensland Cancer Registry, the state death registry, public and private pathology, public and private hospital clinical data systems and Queensland Oncology On-Line (QOOL). (Supplemental figure 1)

Three age groups were constructed: 0-49 years, 50-74 years and 75 or more years and three time-periods were defined: 2001-2005, 2006-2010 and 2011-2015. Area-level socio-economic status was defined using the 2011 Index of Relative Socio-economic Disadvantage (IRSD)¹⁴ and patients were categorized into “Disadvantaged”, “Middle” and “Affluent” groups. Patient comorbidity was derived using Charlson¹⁵ and American Society of Anaesthesiologists (ASA) scoring systems with the scores dichotomized: Charlson “0” and “1 or more”; ASA(1-2) “Normal or mild disease” and ASA (3-5) “Severe disease”. Patients were considered to have received chemotherapy or radiotherapy as part of curative treatment if delivered within four and a half months prior to or following surgical resection. Treatment variables were categorized into: Surgery alone; chemotherapy and Other (Neoadjuvant/adjuvant radiotherapy, neoadjuvant chemoradiotherapy). As well, the type of surgical procedure performed was recorded and categorised into “Partial” and “Total” gastrectomy. Cancer stage was manually collected for all patients from post-operative histology reports and standardized to UICC Edition 7¹⁶. Patients with stage IV disease were identified from post-operative histology reports and may include patients undergoing palliative resection of their gastric cancer.

High-volume hospitals were defined as performing five or more gastrectomies annually within the time-periods. This threshold was chosen using the lowest period-specific median annual average resection volume. As our threshold is lower than reported in other studies¹², we performed sensitivity analysis using a threshold of six gastrectomies annually to define high-volume centres. Hospitals were able to move between volume categories when comparing individual time-periods. Hospital service-capability was defined using the AIHW hospital peer groups¹⁷ with hospitals considered to have high service-capability if classified as Principle Referral Hospitals or Private Group A hospitals. Both these peer groups are defined by the presence of 24-hour emergency departments, accredited intensive care units and specialized units. In Queensland, these hospitals provide interventional radiology, advanced endoscopic and gastroenterology services as well as dedicated units staffed by surgeons with specialised expertise in upper gastro-intestinal surgery. Within the Private Group A hospitals, the surgeons performing gastrectomy were typically the same as those in the Principle Referral Hospitals. All other peer groups were defined as low service-capability for the purposes of this study. No high-volume hospitals met low service-capability criteria and hospitals were therefore grouped into three volume-service (VS) categories: High-volume, high service-capability (HVHS); low-volume, low service-capability (LVLS) and low-volume, high service-capability (LVHS).

Crude 30-day and 90-day death rates were calculated using the total number of deaths within 30 or 90 days, from any cause, following gastrectomy divided by the total number of gastrectomies performed in individual VS categories. Patient demographic, tumour and treatment characteristics were compared between hospital categories using Chi squared tests of significance set at a two-sided alpha of ≤ 0.05 . Directed acyclic graphs were used to select confounding variables for multivariate comparison of 30-day and 90-day mortality between hospital groups. For this comparison, we used negative binomial regression models adjusted

for age-group, sex, socio-economic status, Charlson and ASA dichotomized scores, post-operative cancer stage, period and treatment variables. This method was chosen due to evidence of overdispersion with Poisson regression analysis. Results from these models are presented as incidence rate ratios (IRR) with 95% confidence intervals.

To assess for mediation of mortality differences between hospital groups due to the type of gastrectomy performed, we compared the 30-day and 90-day mortality IRR estimates from the models above to those of negative binomial regression models of 30-day and 90-day mortality adjusted for covariates listed above, in addition to the type of gastrectomy performed.

Of note, adjusted IRR's comparing 30-day and 90-day mortality between patients with stage 0 with stage 1 cancer could not be modelled due to a lack of deaths in these groups. For similar reasons, we were unable to calculate the adjusted IRR's comparing 30-day and 90-day mortality between patients receiving "other" treatment regimens with those undergoing "Surgery alone".

Ethical approval for this study was granted by the Metro South Health Human Research Ethics Committee (HREC/18/QPAH/303).

Results:

In Queensland, between 2001 and 2015, 48 hospitals performed a gastrectomy for cancer on a total of 1266 patients. Of these: 781 (62%) had surgery in eight hospitals with high volume and high service-capability(HVHS); 157(12%) had surgery in eight low-volume, high service-capability centres(LVHS); and 328 (26%) had surgery in thirty-four low-volume, low service-capability centres (LVLS). Comparing the period between 2001-2005 with the period 2011-2015, there was an increase in the proportion of patients having surgery in HVHS (53%

to 71%) and LVHS (10% to 15%) hospitals and a decrease in the proportion of patients having surgery in LVLS hospitals (37% to 14%).(Table 1).

Patient demographic, tumour and treatment characteristics compared between hospital-groups are shown in Table 1. There was no difference between hospital-groups with respect to patient age, sex, Charlson scores, post-operative cancer stage or treatment regimen. Compared with LVLS centres, HVHS hospitals had a higher proportion of patients from affluent socio-economic areas but also had a higher proportion of patients with ASA scores between three and five. As well, HVHS centres performed fewer partial gastrectomies and more total gastrectomies compared with LVHS and LVLS centres (p=0.02).

The overall 30 and 90-day mortality rates following gastrectomy in our cohort were 4.5% and 7.3% respectively. For HVHS hospitals the 30 and 90-day mortality rates were 3.6% and 6.3% respectively; while for LVHS hospitals the rates were 4.5% and 7.6% and for LVLS hospitals were 6.7% and 9.4% respectively. (Table 2)

In multivariate analysis of 30-day mortality, LVLS hospitals had significantly higher adjusted mortality compared to HVHS hospitals (IRR=2.97, 95% CI: 1.65 – 5.35) while no difference in 30-day mortality was seen when LVHS hospitals were compared to HVHS hospitals (IRR = 1.16, 95% CI: 0.48 – 2.79). (Table 2). The 30-day mortality was also higher in men compared with women and in patients undergoing surgery alone compared with those receiving chemotherapy in addition to surgery. As well, approximately double the rate of 30-day mortality was seen in patients with Charlson scores of one or more compared to those with a score of zero and there was a tendency towards higher 30-day mortality in patients with ASA scores from three to five compared with scores of one and two, but this failed to reach statistical significance. There was no significant difference in crude and adjusted 30-day mortality compared between time periods.

Results for multivariate analysis of 90-day mortality were similar and in the same directions as for 30-day mortality (Table 2) when compared by hospital group, patient sex, Charlson scores and treatment regimen. Patients with ASA scores between three and five had more than double the rate of 90-day mortality compared with patients with scores of one and two. As well, patients living in middle class areas had significantly higher 90-day mortality compared with those living in disadvantaged areas and higher 90-day mortality was also seen in patients with stage III and stage IV cancer compared with patients with stage I cancer. Of note, there was no difference in the distribution of 90-day deaths in patients with stage IV disease when compared between hospital-groups ($p=0.39$). There was a reduction in the crude 90-day mortality rates from 9.8% in period between 2001-2005 to 5.6% in 2011-2015 but this difference was not statistically significant after adjusting for hospital category and other factors.

In sensitivity analysis, raising the high-volume threshold to six annual gastrectomies did not significantly alter the adjusted mortality differences between hospital groups. Adjustment for differences in type of gastrectomy performed did not significantly alter the differences in adjusted IRR estimates for 30-day (LVHS = 1.35, 95%CI: 0.56-3.26; LVLS = 3.09, 95%CI: 1.67-5.69) and 90-day mortality (LVHS = 1.30, 95%CI: 0.68-2.47; LVLS = 1.99, 95%CI: 1.23-3.21) when compared between hospital groups. There was no statistically significant difference in the crude thirty-day or ninety-day mortality rates compared between hospitals within each hospital group.

Discussion:

In Queensland, between 2001 and 2015, nearly 40% of gastrectomies were performed in low-volume centres and 26% were performed in centres that were both low-volume and had low service-capability. We have shown that after multivariate adjustment, LVLS hospitals have

nearly three times the rate of 30-day mortality and double the rate of 90-day mortality following gastrectomy compared with HVHS hospitals. There was no difference in the adjusted mortality compared between high service-capability hospitals irrespective of their resection-volume. These relationships were not significantly altered following adjustment for differences in the type of gastrectomy performed between hospital groups. Between 2001 and 2015, there was an increase in the proportion of patients undergoing gastrectomy in high-volume centres, with a reduction in the rates of crude 90-day mortality in the periods following 2001-2005. This may reflect improved mortality with partial centralization of gastrectomy as well as advances in surgical technique and post-operative care. However, the reduction in 90-day mortality in the latter periods failed to reach statistical significance on multivariate analysis and there was no difference in crude or adjusted 30-day mortality rates when comparing time-periods.

Hospital service-capability has been reported to influence post-operative mortality outcomes following other complex surgery. For example, following pancreatic resection, strong hospital clinical support systems, including appropriate ICU staffing, presence of interventional radiology services and delivery of surgical and advanced gastroenterology training programs have been reported, in an American study, to be associated with a two-thirds reduction in post-operative mortality independent of hospital resection volume¹³. For gastrectomy, a Dutch study reported a 50% reduction in the hazard of three-month mortality following surgery performed in university teaching hospitals compared with non-university teaching hospitals after adjustment for hospital-volume. However, the study did not specify how the two hospital categories differed in terms of available services¹⁸. To date, no population level study, comparing post-operative mortality between high and low-volume centres, following gastrectomy, has specifically accounted for the hospital service-capability within hospital volume-groups. This may contribute to the conflicting associations between

post-operative mortality following gastrectomy and hospital-volume reported in the literature^{4, 9, 10, 12, 19-22}. Our results confirm the importance of a high hospital service-capability in improving the risk of post-operative 30- and 90-day mortality following gastrectomy and suggests that, among Australian hospitals with a high service-capability, high surgical-volume may not bring additional improvement in mortality rates following gastrectomy. However, we acknowledge that only 12% of our study cohort had surgery in hospitals with low-volume and high service-capability and worse mortality in these centres may be reported in future studies conducted over a longer period. As well, it should be noted that, amongst hospitals with low service-capability, surgical volume may play an important role, but we were unable to assess this in our study as all high-volume hospitals in our sample also had high service-capability.

It is likely that the results of our study are relevant to other regions characterized by low gastric cancer incidence, small populations and generally low hospital resection-volumes where many hospitals treating gastric cancer are less likely to achieve the volume thresholds that are reported to be associated with improved post-operative mortality in regions characterised by large populations and resection-volumes^{4, 8, 10, 11}. As well, in countries and regions with large land-masses and a dispersed population, such as Australia and, more specifically, the state of Queensland, centralization of gastric cancer surgery on a purely volume-based approach may risk reducing access to cancer surgery for the significant proportion of the population that live outside major cities. These patients could be subjected to travelling large distances to receive cancer care with a resultant increase in personal financial costs^{23, 24} which may serve as an important barrier to accessing curative cancer treatment^{25, 26}. Consideration of hospital service-capability broadens the pool of hospitals suitable for centralization of gastric cancer surgery and may improve accessibility to

treatment for many patients who would otherwise need to travel large distances to high-volume hospitals.

Our study has several strengths including being population based and assessing a large number of patients, as well as adjusting for a wide variety of factors that may confound the relationships between hospital-volume and service-capability with post-operative mortality. The limitations include the lower numbers of gastric resections and deaths compared with other published series^{3, 22}, which has resulted in wide confidence intervals around the IRR for some comparisons. Data on individual patient socio-economic status was not available within our dataset and the proxy measure of area-level socio-economic disadvantage may have misclassified some patients which may account for the unexpectedly higher 90-day mortality seen in patients with “Middle” socio-economic status. As well, pathological stage and data on ASA scores were not available for 20% of the study population and we were unable to identify patients undergoing treatment for gastro-oesophageal junction cancers as data on the site around the gastro-oesophageal junction are not captured in the QOR. We were unable to adjust for the influence of the extent of lymph node resection on post-operative mortality as this data is not recorded on a population-level in Queensland. However, to the best of our knowledge, the extent of nodal resection and its impact on post-operative mortality has not been reported in any population-level study, to date, that examines the influence of hospital characteristics on mortality following gastrectomy, suggesting that this parameter is not commonly recorded within population level datasets.

Conclusion:

To ensure optimal operative mortality rates following gastrectomy for cancer within the Australian environment, centralisation of surgery away from low-volume, low service-capability centres should be considered. Future studies conducted over a longer time-period

are needed to evaluate the impact of resection volume on outcomes in hospitals with a high-service capability.

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List of supporting information:

Supplemental figure 1: Flow-chart of study data sources, patient selection and allocation to hospital-groups

Table 1: Demographic, tumour and treatment characteristics of patients undergoing gastrectomy for cancer compared between hospitals grouped by resection-volume and service-capability^a

	HVHS	LVHS	LVLS	P*
Age group				
<50 years	66 (8.5%)	9 (5.7%)	26 (7.9%)	0.8
50-74 years	408 (52.2%)	83 (52.9%)	168 (51.2%)	
75 + years	307 (39.3%)	65 (41.4%)	134 (40.9%)	
Sex				
Male	490(62.7%)	101 (64.3%)	222 (67.7%)	0.3
Female	291 (37.3%)	56 (35.7%)	106 (32.3%)	
Socio-economic status				
Disadvantaged	156(20%)	22 (14.0%)	99(21.9%)	<0.01
Middle	436(55.8%)	116 (73.9%)	211 (64.3%)	
Affluent	189 (24.2%)	19 (12.1%)	18 (5.5%)	
Charlson				
0	384 (49.2%)	66 (42.3%)	144 (44.2%)	0.1
1 or more	397 (50.8%)	90 (57.7%)	182 (55.8%)	
ASA				
Normal/Mild disease (ASA 1-2)	266(34.1%)	40 (25.5%)	101(32.1%)	<0.01
Severe disease (ASA 3-5)	348 (44.6%)	82 (52.2%)	110 (33.5%)	
Unknown	167 (21.4%)	35 (22.3%)	117 (35.7%)	
Stage				
0	3(0.4%)	0 (0%)	3 (0.9%)	0.2
I	188 (24.1%)	31 (19.7%)	60 (18.3%)	
II	179 (22.9%)	38(24.2%)	84 (25.6%)	
III	248 (31.7%)	48 (30.6%)	93 (28.3%)	
IV	31(4.0%)	7 (4.5%)	12 (3.7%)	
Unknown	132 (16.9%)	33 (21.0%)	76 (23.2%)	
Treatment				
Surgery alone	596 (76.3%)	111(70.7%)	254(77.4%)	0.2
Chemotherapy	178(22.8)	46(29.3%)	73(22.3%)	
Other	7(0.9%)	0(0%)	1(0.3%)	
Type of procedure				
Partial Gastrectomy	493(63.1%)	115(72.2%)	227(69.2%)	0.02
Total Gastrectomy	288(36.9%)	42(26.8%)	101(34.0%)	
Period ^b				
2001-2005	242 (52.7%)	47 (10.2%)	170 (37.0%)	<0.01
2006-2010	262 (62.8%)	51 (12.2%)	104 (24.9%)	
2011-2015	277 (71.0%)	59 (15.1%)	54 (13.9%)	

^aData are proportions of patients within combined volume service categories: number (column %); * Chi Squared test of significance
^b Period data = Number of patients in period (row %)
HVHS= High volume with high service-capability; LVHS= low volume with high service-capability; LVLS: Low-volume with low service-capability; Other = Neoadjuvant/adjuvant radiotherapy, neoadjuvant chemoradiotherapy,

Table 2: Post-operative mortality following gastrectomy for cancer compared between hospitals grouped by resection- volume and service-capability, Queensland, 2001-2015

	Total patients Number (column %)	30-day deaths Number (row %)	30-day Adjusted IRR* (95% CI)	90-day deaths Number (row %)	90-day Adjusted IRR* (95% CI)
<i>Combined Volume & Service-capability</i>					
High Volume, High Service (HVHS)	781 (61.7%)	28(3.6%)	1	49(6.3%)	1
Low Volume, High Service (LVHS)	157 (12.4%)	7(4.5%)	1.16(0.48-2.79)	12(7.6%)	1.12(0.59-2.13)
Low Volume, Low Service (LVLS)	328 (25.9%)	22(6.7%)	2.97(1.65-5.35)	31(9.4%)	1.95(1.23-3.09)
<i>Age-group</i>					
< 50 years	101(8.0%)	1(1%)	1	2(2.0%)	1
50-74 years	659 (52.0%)	12(1.8%)	1.47(0.19-11.28)	24(3.6%)	1.39(0.34-5.64)
75+ years	506 (40.0%)	44(8.7%)	4.96(0.68-36.05)	66(13.0%)	3.44(0.87-13.63)
<i>Sex</i>					
Male	813 (64.2%)	42(5.2%)	1	65(8.0%)	1
Female	453 (35.8%)	15(3.3%)	0.55(0.31-0.99)	27(6.0%)	0.62(0.40-0.96)
<i>Total Charlson score</i>					
0	594 (47.0%)	15(2.5%)	1	25(4.2%)	1
1 or more	669 (53.0%)	41(6.1%)	2.19(1.25-3.84)	65(9.7%)	2.09(1.37-3.19)
<i>Post-operative stage</i>					
0	6 (0.5%)	0(0%)	-	0(0%)	-
I	279 (22.0%)	9(3.2%)	1	15(5.4%)	1
II	301 (23.8%)	13(4.3%)	1.38(0.57-3.32)	17(5.7%)	0.99(0.51-1.93)
III	389 (30.7%)	19(4.9%)	2.12(0.91-4.94)	33(8.5%)	1.96(1.07-3.58)
IV	50 (4.0%)	3(6.0%)	2.00(0.54-7.46)	8(16%)	2.53(1.21-5.29)
Missing/Cannot be assessed	241 (19.0%)	13(5.4%)	1.87 (0.77-4.53)	19(7.9%)	1.50(0.76-2.96)
<i>Socio-economic status</i>					
Disadvantaged	277 (21.9%)	9(3.2%)	1	16(5.8%)	1
Middle	763 (60.4%)	34(4.5%)	1.72(0.80-3.71)	59(7.7%)	1.81(1.05-3.14)
Affluent	226 (17.9%)	14(6.2%)	2.42 (1.00- 5.83)	17(7.5%)	1.62(0.82-3.18)
<i>ASA score</i>					
Normal/Mild disease (ASA 1-2)	407 (32.1%)	10(2.5%)	1	14(3.4%)	1
Severe disease (ASA 3-5)	540 (42.7%)	33(6.1%)	1.94(0.98-3.83)	56(10.4%)	2.59(1.50-4.47)
Unknown	319 (25.2%)	14(4.4%)	1.29 (0.59-2.84)	22(6.9%)	1.28(0.67-2.43)
<i>Treatment</i>					
Surgery alone	961 (75.9%)	56(5.8%)	1	90(9.4%)	1
Chemotherapy	297 (23.5%)	1(0.34%)	0.08(0.01-0.60)	2(0.67%)	0.10(0.02-0.41)
Other ^a	8(0.6%)	0(0%)	-	0(0%)	-
<i>Time-period</i>					
2001-2005	459 (32.3%)	23(5.0%)	1	45(9.8%)	1
2006-2010	417(32.9%)	17(4.1%)	1.0 (0.53-1.89)	25(6.0%)	0.71(0.43-1.15)
2011-2015	390 (30.8%)	17(4.4%)	1.36 (0.73-2.57)	22(5.6%)	0.76(0.47-1.25)
*Multivariate Negative Binomial regression adjusted for age, sex, area-level socioeconomic status, Charlson and ASA scores, hospital volume and service capability, post-operative cancer stage, treatment regimen, and period.					
^a Other = Neoadjuvant/adjuvant radiotherapy, neoadjuvant chemoradiotherapy					

