Centralization of Highly Complex Low-Volume Procedures in Upper Gastrointestinal Surgery. A Summary of Systematic Reviews and Meta-Analyses

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Key Words

Centralization • Volume • Mortality • Upper GI surgery • Systematic review

Abstract

Centralization of complex upper gastrointestinal (GI) surgery and the effect on postoperative outcomes, especially mortality, has been reported extensively in the literature. In this review the highest level of evidence on the volume outcome relationship is discussed together with other important aspects that can influence postoperative outcomes. Do high-volume centers and surgeons result in better outcomes after surgery for the different upper GI surgical procedures such as esophageal, gastric, liver and pancreatic tumors? Twelve systematic reviews including four meta-analyses described the effect of hospital and/or surgeon volume on mortality. The majority of reviews (>90%) showed a lower mortality in high-volume hospitals. This correlation was also reported when analyzing the different GI procedures separately for esophageal, gastric, hepatic and pancreatic tumors. The vol-

ume discussion has limitations and therefore the relationship between hospital structure and process of care in hospitals and the outcome of surgery has also been acknowledged. Besides surgeon expertise and skills, high-intensity intensive care units, 24/7 availability of interventional radiology, effective prevention and managing of complications and adequate patient selection will influence postoperative outcomes. These forms of hospital structures and process of care might even play a more important role in surgical outcomes.

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Introduction

During the past decade, regionalization, specialization and centralization of highly complex esophageal and hepato-pancreatico-biliary (HPB) surgery has been discussed extensively and led to numerous publications from different parts of the world about the impact of high hospital and surgeon volume [1–7]. Complex surgical procedures are still performed in low-volume (LV) hospi-

tals but generally need an extensive multidisciplinary approach. Different aspects of the hospital structures such as the intensive care unit (ICU), 24 × 7 interventional radiology, anesthesiology, experienced surgeons and gastroenterologist as well as the process of care are involved in the outcome of the treatment. Postoperative morbidity and mortality are directly influenced by these different aspects [8].

In this narrative review the impact of hospital volume and surgeon volume on mortality and survival of patients undergoing upper gastrointestinal (GI) surgery will be discussed. The aim was to review the literature on centralization of upper GI surgery by summarizing all systematic reviews investigating the relationship between volume and outcome. Do HV centers and HV surgeons result in better outcomes after surgery and is this reported in all different upper GI surgical procedures? A distinction was made between reviews that reported risk-adjusted studies and nonadjusted studies. Important hospital structures and process of care that can influence patient outcomes will also be briefly summarized.

Methods

A literature search was conducted of Medline, Embase and the Cochrane Library from 1980 to 2012, using the keywords 'hospital', 'surgeon', 'volume', and 'outcome'. Mesh terms were included. To ensure the highest quality of evidence, the search was limited to systematic reviews and meta-analyses. Only English language articles were selected. References of the included articles were checked to ensure no systematic review or meta-analysis was missed.

We included those studies that analyzed an association between hospital volume and/or surgeon volume and one of the next mentioned postoperative outcomes: mortality, morbidity, length of hospital stay or survival. Studies were only valuable for this review if they contained upper GI surgery, i.e. esophageal, gastric, hepatic or pancreatic surgery, and analyzed at least three articles on the subject. In systematic reviews describing more than one type of surgery, data were analyzed separately. All studies were analyzed independently for different criteria: study period, number of included patients, source of data, cutoff points for HVs and LVs and significant differences in postoperative outcomes between HV and LV hospitals and surgeons. Reviews discussing the same studies were not excluded.

The effect of HV on outcome parameters mortality and survival was analyzed separately for nonadjusted and adjusted reviews. Nonadjusted studies do not take the patient or disease characteristics into account and results can therefore differ from those seen in adjusted studies. If a review contained adjusted as well as nonadjusted studies, the data was analyzed separately. The complexity of an operation influences postoperative outcomes, though liver resections can vary widely from minor wedge resection to extended

hepatectomy. Therefore, variables used for risk adjustment were screened for type of operation.

Results were stated as mortality rates (percentages), median difference between mortality rates (percentages), odds ratios (OR), number needed to treat to prevent 1 death (NNT) and hazard ratios (HR).

This review was divided into different subheadings: centralization of esophageal surgery, gastric surgery, liver surgery and pancreatic surgery followed by a discussion on volume and other aspects of quality of care such as hospital structure and process that can affect postoperative outcomes.

Results

The search identified 28,326 studies; after limiting the search to systematic reviews and/or meta-analyses, 585 reviews remained. After screening titles and abstracts, 12 systematic reviews remained of use, a meta-analysis was performed in four reviews (table 1) [3, 14–24]. All eligible studies were in English.

The study period varied from 1957 till 2011. Per site of diagnosis a minimum of 3 and a maximum of 34 studies were included in the systematic reviews. The number of patients in the different reviews varied from 19,688 to 150,473, some did not state the number of patients. Nine reviews included studies that used administrative databases for patient information. The studies in two reviews used both administrative and clinical databases and in one review the source of information was not stated.

All reviews described the effect of hospital and/or surgeon volume on mortality and the effect of volume on patient survival was described in two reviews. Three reviews described postoperative morbidity and three the length of hospital stay. Four reviews solely described pancreatic surgery; three reviews described esophageal surgery and one liver surgery. The remaining four reviews described multiple oncological diagnoses. All reviews were heterogeneous; the studies included in the reviews varied widely in HV and LV definitions and case mix factors. Pooling of data in this paper was therefore not justified.

Centralization of Esophageal Surgery

Seven systematic reviews investigated the effect of volume on mortality after esophageal surgery (esophagus and cardia resection); hospital volume was analyzed in three reviews and hospital and surgeon volume in four

Table 1. Characteristics of included reviews describing the association between hospital or surgeon volume and mortality, morbidity, hospital stay or survival after esophageal, gastric, liver or pancreatic surgery

Reference (first author)	Study type	Study period	Site of diagnosis	Number of studies and patients	Data	Volume and outcome variable
Dudley 2000 [14]	Systematic review	1983–1998	Pancreas	8 studies	Administrative and clinical	Hospital volume, mortality
Halm 2002 [15]	Systematic review	1984–1997	Pancreas Esophagus Stomach	10 studies 3 studies 3 studies	Administrative	Hospital volume, mortality
Metzger 2004 [16]	Systematic review including a meta-analysis	1990–2003	Esophagus	13 studies, NS	NS	Hospital volume, mortality
Van Heek 2005 [3]	Systematic review	1966–2004	Pancreas	12 studies, n = 19,688	Administrative	Hospital volume, mortality
Killeen 2005 [17]	Systematic review	1984–2004	Pancreas Esophagus Stomach	11 studies, n = 41,306 10 studies, n = 22,734 5 studies, n = 54,445	Administrative and clinical	Hospital and surgeon volume, mortality
Burgers 2007 [18]	Systematic review	2000–2005	Pancreas Esophagus Stomach	7 studies 14 studies 8 studies	Administrative	Hospital and surgeon volume, mortality
Chowdhury 2007 [19]	Systematic review	1957–2002	Pancreas	20 studies	Administrative and clinical	Hospital and surgeon volume, mortality, morbidity, hospital stay
Garcea 2009 [20]	Systematic review	1984–2003	Liver	10 studies, n = 30,421	Administrative	Hospital volume, mortality, survival, morbidity, hospital stay
Gruen 2009 [21]	Systematic review including a meta-analysis	1966–2007	Pancreas Esophagus Stomach Liver	34 studies, n = 64,215 27 studies, n = 66,145 22 studies, n = NS 11 studies, n = NS	Administrative	Hospital and surgeon volume, mortality, survival ^a
Lauder 2010 [22]	Systematic review	1997–2006	Esophagus	27 studies, n = 68,882	Administrative	Hospital and surgeon volume, mortality, morbidity, hospital stay
Gooiker 2011 [23]	Systematic review including a meta-analysis	<2010	Pancreas	14 studies, n = 150,473	Administrative	Hospital and surgeon volume, mortality, survival
Markar 2012 [24]	Systematic review including a meta-analysis	1996–2011	Esophagus	9 studies, n = 27,843	Administrative	Hospital volume, mortality

^a Only analyzed in studies on pancreatic surgery.

[15–18, 21, 22, 24]. Two reviews with nonadjusted mortality rates are summarized in table 2a and five reviews with risk-adjusted studies in table 2b.

Volume and Mortality (Nonadjusted Data)

The cutoff points for HV and LV varied markedly (table 2a). One systematic review did not state cutoff points but reported a significant decrease in mortality rates in the HV hospitals and HV surgeons [18]. The second review concluded that esophageal surgery in HV hospitals

had better outcomes compared with LV hospitals regarding mortality, without exact data [22].

Volume and Mortality (Adjusted Data)

Cutoff points varied widely in the five reviews containing adjusted data [15–17, 21, 24]. Only Metzger et al. [16] defined four different levels of volume: <5, 5–10, 11–20, and >20 resections per year. In their meta-analysis, HV hospitals showed lower mortality rates (OR = 0.43, 95% confidence interval (CI) 0.31–0.58). All studies in-

Table 2. Studies describing the association between volume and mortality after esophageal surgery**a** Non-adjusted data

Reference (first author)	Studies with significant results	Cutoff HV and LV ^a	Results: association between volume and mortality
Burgers, 2007 [18]	13/14	Not stated	Mortality rate HV hospital: 5.9% Mortality rate LV hospital: 15% Mortality rate HV surgeon: 3.3% Mortality rate LV surgeon: 9.6%
Lauder, 2010 [22]	20/27	Variable LV: 2–32 HV: 3–236	Upper GI surgery in HV hospitals have better outcomes compared with LV hospitals

b Adjusted data

Reference (first author)	Studies with adjusted data and significant results	Cutoff high and LV ^a	Results: association between volume and mortality ^b
Halm, 2002 [15]	3/3	Variable LV: 5–10 HV: 11–200	Median absolute difference in mortality between LV and HV hospital: 12%
Metzger, 2004 [16]	13/13	Very LV: <5 LV: >5 Medium volume: >10 HV: >20	Difference in median mortality rates: Very LV: 18% LV: 13.8% Medium volume: 11% HV: 4.9%, OR 0.43, 0.31–0.58
Killeen, 2005 [17]	9/10	Variable LV: 3–32 HV: 8–60	NNT to prevent 1 death: 7–9
Gruen, 2009[21]	21/26 ^c	LV: 1–4 ^d HV: >13	First study on the effect of volume on mortality: HV surgeon: OR 0.6, 0.36–0.99 Second study: HV surgeon: OR 1.8, 1.13–2.87 HV hospital: OR 1.67, 1.02–2.73
Markar, 2012 [24]	6/9	Variable LV: 1–22 HV: 4–81	In-hospital mortality is increased in LV hospital compared to HV hospital, OR 0.29, 0.16–0.53

^a Resections per year. ^b OR, 95% CI. ^c Two studies used for adjusted mortality risk. ^d Based on one study.

cluded by Halm et al. [15] reported a significant association between HV and LV mortality. A third review calculated the NNT and report that 7–9 resections need to be performed in a HV center to prevent 1 death [17]. Another review performed a meta-analysis of nonadjusted data and summarized the adjusted mortality data, significantly lower mortality was reported in HV hospitals and HV surgeons [21]. The last review also performed a meta-analysis and a significant association between HV and LV mortality was found (OR = 0.29, $p < 0.001$) [24].

No significant difference was found in length of hospital stay or in postoperative complications. Results are summarized in table 2b.

Volume and Survival

Although better postoperative outcomes are described in most HV hospitals, Gruen et al. [21] did not show a benefit in survival after esophagectomies in HV centers (HR = 1.01). However, high surgeon volume was associated with better survival (HR = 0.92, 95% CI 0.85–0.99).

Table 3. Study describing the association between volume and survival after esophageal surgery (adjusted data)

Reference (first author)	Included studies	Volume variable	Adjusted for	Results: association between volume and survival ^a
Gruen, 2009 [21]	1	Hospital volume Surgical volume	Age, stage of disease, comorbidities, hospital and surgeon volume and clustering effects	Hospital volume: HR = 1.01, 0.96–1.05 Surgical volume: HR = 0.92, 0.85–0.99

^a HR, 95% CI.**Table 4.** Studies describing the association between volume, mortality and survival after gastric surgery (adjusted data)

Reference (first author)	Studies with adjusted data and significant results	Cutoff HV and LV ^a	Results: association between volume and mortality ^b
Halm, 2002 [15]	2/3	Variable LV: 5–15 HV: 15–201	Median absolute difference in mortality between LV and HV hospital: 6.5% LV and HV surgeon: 4%
Killeen, 2005 [17]	3/5	Variable LV: 5–26 HV: 9–67	Mortality reduction of 1–6% NNT to prevent 1 death: 20–100 patients
Gruen, 2009 [21]	14/20 ^c	LV: 1–54 ^d HV: 55–496	First study Effect of volume on mortality: HV surgeon: OR 0.59, 0.32–1.07 Effect of volume on survival: HV hospital: HR 0.93, 0.89–0.98 Second study: Hospital volume low-high: 11.3–3.7%, $p < 0.001$ Surgeon volume low-high: 12.3–3.2%, $p < 0.001$

^a Resections per year. ^b OR, 95% CI; HR, 95% CI. ^c Two studies used for adjusted mortality risk. ^d Based on one study.

No other reviews discussed survival as an outcome measure (table 3).

Centralization of Gastric Surgery

The impact of volume on mortality after gastric surgery was reported in four systematic reviews [15, 17, 18, 21]. Hospital volume and surgeon volume was analyzed in all reviews, survival was also reported as an outcome in one review. Type of resection was not specified. The reviews described a total of 38 studies of which 24 reported a significant correlation between volume and outcome. Over 70% of the studies with significant outcomes analyzed hospital volume only.

Volume and Mortality (Nonadjusted Data)

One systematic review presented nonadjusted data, an overall decrease of 7% mortality in HV centers was reported, no association was found between mortality and surgeon volume [18].

Volume and Mortality and Survival (Adjusted Data)

Three reviews with adjusted data are stated in table 4 [15, 17, 21]. Two systematic reviews report a significant effect of high hospital and surgeon volume on mortality [15, 17]. The third review includes two studies which were used to calculate the volume effect on mortality and survival [21]. The first study did not reveal a significant relationship between volume and mortality, they did however report a better survival rate (HV hospitals HR =

Table 5. Studies describing the association between volume and mortality after liver surgery (adjusted data)

Reference (first author)	Studies with adjusted data and significant results	Cutoff HV and LV ^a	Results: association between volume and mortality ^b
Garcea, 2009 [20]	5/10	Variable LV: 1–60 HV: 10–201	Mortality rate HV hospital: 1.5–9.4% Mortality rate LV hospital: 5.8–22.7%
Gruen, 2009 [21]	11/11	Variable ^c LV: 1–5 HV: >34	Effect of volume on mortality: OR = 0.77 (0.72–0.83 95% CI) ^d NNT of 11

^a Resections per year. ^b OR, 95% CI. ^c Based on ten studies. ^d Based on nonadjusted data.

0.93). The second study reported a significant decrease of mortality in HV centers.

Centralization of Liver Surgery

Volume, Mortality and Survival (Adjusted Data)

Two systematic reviews report the association between volume and postoperative outcome after liver surgery (table 5) [20, 21]. Both reviews reported risk-adjusted data and have variable HV and LV cutoff definitions. In the first review, 50% of the included studies showed a significant effect of HV on mortality rates. Mortality rates were adjusted for patient characteristics, not for type of operation. Partial hepatectomy and lobectomy were performed in most patients. All studies in the second review report an association between high hospital volume and lower mortality. Type of resection was not specified in this review. None of the reviews discussed survival as an outcome measure.

Centralization of Pancreatic Surgery

Eight systematic reviews investigated the effect of volume on mortality after pancreatic surgery; hospital volume was analyzed in three reviews and hospital and surgeon volume in five [3, 14, 15, 17–19, 21, 23]. Type of resection was not specified in most reviews. The reviews with nonadjusted mortality rates are summarized in table 6a and risk-adjusted studies in table 6b.

Volume and Mortality (Nonadjusted Data)

The cutoff points for LV and HV varied markedly between the reviews. Only van Heek et al. [3] used four cutoff points: 2, 5, 10 and 20 resections per year. All reviews

reported a significant decrease in mortality rates in HV hospitals or surgeons. Decreased mortality rates, reduced relative risk or NNT to prevent 1 death were stated to indicate the effect of HV versus LV (table 6a).

Volume and Mortality (Adjusted Data)

Three systematic reviews reported adjusted mortality rates (table 6b) [14, 21, 23]. Dudley et al. [14] report one adjusted study with mortality rates of 14.1% in LV hospitals (1–5 resections per year) and 3.5% in HV hospitals (>50 resections per year) ($p < 0.001$).

Gruen et al. [21] described one adjusted study with no significant association between operative mortality and hospital or surgeon volume and another study in which surgical mortality was independently associated with hospital volume and surgeon volume, OR = 2.34 and 2.31 respectively. The third review performed a meta-analysis and reported a significant association between surgical mortality and hospital volume (OR = 0.32), no association was found between mortality and surgeon volume [23].

Volume and Survival

Two systematic reviews also assessed the effect of volume on both mortality and patient survival (table 7) [21, 23]. Risk adjustment criteria are summarized in the table. Both reviews showed a significant better survival rate in HV hospitals, no association was found between survival and surgeon volume.

Discussion

This extensive summary of systematic reviews and meta-analyses on the impact of high hospital and surgeon volume of complex upper GI surgery on postoperative

Table 6. Studies describing the association between volume and mortality after pancreatic surgery**a** Non-adjusted data

Reference (first author)	Studies with significant results	Cutoff HV and LV ^a	Results: association between volume and mortality
Halm, 2002 [15]	9/10	Variable LV: 1–22 HV: 3–200	Median absolute difference in mortality between LV and HV hospital: 13% LV and HV surgeon: 7%
Van Heek, 2005 [3]	9/12	4 cutoff points: 2, 5, 10, 20	Relative risk HV hospital: 0.07–0.15
Killeen, 2005 [17]	11/11	Variable LV: 1–22 HV: 4–81	NNT in HV hospital to prevent 1 death: 10–15
Burgers, 2007 [18]	6/7	Not stated	Mortality rate HV hospital: 5.4% Mortality rate LV hospital: 13.8% Mortality rate LV surgeon: 9% Mortality rate HV surgeon: 10.1%
Chowdhury, 2007 [19]	17/20	Variable LV: 1–21 HV: 5–50	NNT to achieve better outcomes: 50

b Adjusted data

Reference (first author)	Studies with adjusted data and significant results	Cutoff HV and LV ^a	Results: association between volume and mortality ^b
Dudley, 2000 [14]	1/8	LV: 1–6 ^c	1/year: OR = 5.00, 2.54–9.84 5–6/year: OR = 3.08, 1.66–5.70
Gruen, 2009 [21]	23/30 ^d	LV: 1–3 ^c HV: 4–13	First study on the effect of volume on mortality: HV hospital: OR = 1.1, 0.54–2.59 HV surgeon: OR = 0.9, 0.31–2.37 Second study: HV hospital: OR = 2.34, 1.38–3.99 HV surgeon: OR = 2.31, 1.43–3.72
Gooiker, 2011 [23]	9/14	Variable LV: 1–5 HV: 7–89	Pooled data Effect of volume on mortality: HV hospital: OR = 0.32, 0.16–0.64 HV surgeon: OR = 0.46, 0.17–1.26

^a Resections per year. ^b OR, 95% CI. ^c Based on one study. ^d Two studies used for adjusted mortality risk.

outcome clearly showed that hospital volume and surgeon volume are the most recognized variables to be correlated with hospital mortality and survival. The majority of reviews on upper GI surgery (>90%) and HV versus LV hospitals showed a lower mortality in HV hospitals. Some reviews included the same studies, but despite this overlap the volume-outcome relationship was also found analyzing the different GI procedures separately: esophageal, gastric, liver and pancreatic surgery. Although het-

erogeneity is seen in HV and LV definitions between the included reviews, the vast difference between the categories HV and LV in every review is similar. This explains the similar results and conclusions in the reviews.

The older studies were criticized for using clinical data without risk adjustment but after evaluating studies using risk adjustment, significant lower mortality in HV hospitals was found [23]. An important aspect for post-operative outcomes is the type of operation and its com-

Table 7. Studies describing the association between volume and survival after pancreatic surgery (adjusted data)

Reference (first author)	Included studies	Volume variable	Adjusted for	Results: association between volume and survival ^a
Gruen, 2009 [21]	1	Hospital volume Surgical volume	Age, stage of disease, comorbidities, hospital and surgeon volume and clustering effects	HV hospital: HR = 0.88, 0.83–0.93 HV surgeon: HR = 1.03, 0.91–1.17
Gooiker, 2011 [23]	2	Hospital volume	Comorbidities, stage of disease, admission acuity	Pooled data HV hospital: HR = 0.79, 0.70–0.89
^a HR, 95% CI.				

plexity. Esophageal and pancreatic resections are generally complex but liver surgery varies from small wedge resections to extended hemihepatectomies. Therefore, type of operation should be taken into account when calculating mortality rates, though often it is not stated and not included in the risk adjustment. A study from the USA already showed that the hospitals' ranking by mortality rates might change enormously when using risk-adjusted mortality rates compared to nonadjusted rates [25], so currently analysis of risk-adjusted data should become the standard.

It might be questioned if volume is the only or most important factor for reduction of mortality.

A recent study evaluated hospital mortality for five different groups of hospitals, assigned according to quintiles of hospital mortality varying from 3.5 to 6.9%, and analyzed the rates of all complications, major complications and death in these five categories. No significant difference in total and major complications was shown in those hospitals, but significant differences in mortality of patients with major complications were found ranging from 12.5% up to 21.4% due to more adequate management of these complications [26]. This is an argument that, besides surgeons' experience, the basic hospital resources and hospital processes might play an important role in postoperative outcomes.

Hospital Volume versus Aspects of the Hospital Structure and Process of Care

Birkmeyer and colleagues [8, 26] already reported extensively about the conceptual model of the relationship between the structure and process of care in hospitals and the outcome of surgery. An adapted model with extra attention for the role of the multidisciplinary approach in different parts of the care process together with the gen-

erally accepted outcome score of postoperative complications in the Netherlands [27] is summarized in figure 1.

The different 'hospital resources' are not only important for management of complications in GI surgery, but also for prevention of complications. In particular for patients undergoing high-risk surgery, who will need more complex perioperative care as well as complex management of severe life-threatening complications. For example it has been shown that the relative risk for hospital mortality with high-intensity ICU staffing is lower 0.71 (95% CI 0.62–0.82) compared with low-intensity ICU staffing [28]. The same has been shown for nursing staffing and up-to-date technology and equipment on ICU and surgical wards [29]. The importance of other hospital specialties such as interventional radiologists, interventional endoscopists, anesthesiologists, cardiology services, pain management team, etc., have been reported previously [30]. The structure and adequate resources of a hospital are crucial as the facilitating factor for an optimal process of care.

The process of care reflects different aspects starting with patient selection, screening and evaluation before a surgical procedure. In fact, there should be a clear general accepted (evidence-based) guideline for preoperative work-up of these patients and well-defined criteria to accept patients for a surgical procedure. Discussing all patients in a multidisciplinary meeting for the indication of surgery also prevents bias in selection due to 'surgeon-related aspects' and gives another opportunity to evaluate all imaging studies and screen for different anatomical variations important for the surgical procedure [31].

All patients should have a pre-assessment by the anesthesiologist before the patient is accepted for surgery and a checklist should be used to control the completeness of the different preoperative aspects [32, 33]. Another im-

Fig. 1. Relation between structure and process of care and outcome in terms of complications and mortality. Adapted from Birkmeyer and Dimick [8] and according to the National Surgical Complication Registry in The Netherlands [27].

portant factor to prevent complications is to reach a certain standard for the peri- and intraoperative care and the surgical procedure. There is a wide variation of measures ranging from prophylaxis for venous thromboembolism, continuous use of cardiac medication, antibiotic prophylaxis, nutritional support, etc. Other measurements should also include aspects of the organization, such as preoperative control of instruments, counting gauzes, etc. Currently the checklist, including timeout procedure, is introduced routinely in the Netherlands to facilitate this process [33].

The multidisciplinary approach is also important during ward rounds for optimal interaction with general medical staff for medication, bacteriologists for antibiotic intervention and anesthesiologists for pain management. Finally, the potential relation between HV hospitals and the structure and process of care in those hospitals might influence the volume-outcome relationship in the above-summarized studies.

In conclusion, this extensive summary of systematic reviews and meta-analyses on the impact of hospital volume on outcome after complex upper GI surgery clearly showed that hospital volume and surgeon volume are the most recognized variables to be correlated with mortality.

Other aspects besides hospital volume and surgeons' experience such as the basic hospital resources/structure and hospital processes might even play a more important role in outcome and mortality.

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