Volume and Surgical Outcomes in Gastric Cancer

Subjects: Health Policy & Services
Contributor: Luigi Marano

Gastric cancer is ranked as the fifth most frequently diagnosed type of cancer. Complete resection with adequate lymphadenectomy represents the goal of treatment with curative intent. Quality assurance is a crucial factor in the evaluation of oncological surgical care, and centralization of healthcare in referral hospitals has been proposed in several countries. However, an international agreement about the setting of "*high-volume hospitals*" as well as "*minimum volume standards*" has not yet been clearly established. Despite the clear postoperative mortality benefits that have been described for gastric cancer surgery conducted by high-volume surgeons in high-volume hospitals, many authors have highlighted the limitations of a non-composite variable to define the ideal postoperative period.

Keywords: gastric cancer ; gastrectomy ; hospital volume ; surgical volume

1. Predictors for Good Quality of Care

In Europe, the mortality rate after gastric cancer surgery ranges from 2% in specialized centers [1] to 10% in certain nationwide registries [2]. Quality assurance has been regarded as the current main challenge for surgeons [3], in order to pursue the so-called "*rescue phenomenon*", i.e., the ability to prevent minor postoperative events from developing into severe complications and death.

Standardized surgical therapy is supported in surgical oncology, due to the weak evidence of the surgical randomized control trials, especially those focusing on chemotherapy. Many international initiatives, such as the new platform SURGCARE, a collaborative project between the European Society of Surgical Oncology (ESSO) and the Japanese Clinical Oncology Group (JCOG) [4][5], invested their resources and promoted quality assurance. In gastric cancer, the pursuit of evidence-based medicine and the shift toward precision surgery [6] have advocated the standardization of gastric cancer treatment and the creation of a standard level of competence. This application includes multimodal aspects of treatment, surgical competence with particular attention to the application of minimally invasive approaches, the establishment of a registry of complications as well as a medical database including follow-up [7].

For this purpose, the risk-adjusted and case mix-adjusted American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) has been established, with the aim to collect data that provide an accurate, correct, and thorough analysis, in order to help surgeons and hospitals to better understand the quality of their care than similar hospitals with similar patients [8]. Each hospital assigns a trained Surgical Clinical Reviewer to collect 30-day perioperative data on a web-based platform. Blinded information is shared with participant hospitals, allowing them to nationally benchmark their complication rates and surgical outcomes [9].

Over the past years, several studies have investigated the effect of hospital volume on gastric cancer surgery outcomes, leading to the concept that centralization results in better outcomes, acting as a proxy measure for various processes and providing the advantages of a qualified multidisciplinary team and a comprehensive multidimensional assessment [10][11], easier access to sophisticated cancer imaging equipment, availability of skilled surgeons, and better postoperative care facilities [12][13][14][15][16]. In this regard, an experienced radiologist with dedicated skills in gastric cancer metastasis detection (i.e., gastric carcinomatosis) is fundamental to allow for better patient selection [17]. Similarly, it has been proven that intensive care units (ICUs) with dedicated board-certified staff are associated with a lower post-gastrectomy mortality rate [18][19]. Additionally, early diagnosis as well as successful and effective management of postoperative complications might be better in high-volume hospitals [20]. Moreover, in an attempt to guarantee high-quality oncologic care, the discussion of clinical cases within a regional multidisciplinary expert panel is advocated [21].

In addition, the existing research does not focus on the patients-perceived quality of care [22]. A Swedish analysis emphasized that patient satisfaction arises from well-functioning care pathways, individualized care plans, continuity of treatment with local providers, accessibility for contact and information, involvement in the care process, and limited waiting time. A dramatic disadvantage of centralization is an increase in travel demands. A recent experiment conducted in

England highlighted that patients were prepared to travel an average of 75 min longer to decrease their risk of complications by 1%, and over 5 h longer to reduce the risk of death by 1%, in line with the centralization trend [23]. Additionally, centralization should address real-life issues, such as postoperative continuity of care, long-term follow-up, and the possible need for urgent readmission [24]. The literature data suggested that most patients were prepared to travel long distances to receive specific care, but information on clinical outcomes of different hospitals is not widely available for the patients.

2. Hospital Volume

Despite the lack of unanimity [25][26], there is a growing recognition that multidisciplinary care in high hospital volume can improve postoperative mortality for gastrectomy [27][28][29].

Nelen SD et al. [30] reported a study aimed at investigating the outcomes of 250 gastric cancer patients after the centralization of surgery in the Netherlands since the introduction of the centralization policy in 2012. The treatment in high-volume hospitals resulted in an improvement in the percentage of patients treated with appropriate lymphadenectomy (21% vs. 93%, respectively), and a successful introduction of laparoscopic gastrectomies (6% vs. 40%, respectively). However, centralization did not realize an improvement in 30-day mortality as well as complication requiring a reintervention. More recently, the same Dutch study group reported the impact of centralization of gastric cancer surgery in a population-based setting. In this updated study comparing 3777 gastric cancer patients treated between 2009–2011 and 3427 between 2013–2015, the impact of the centralization was more evident in terms of improvement in surgical outcomes (lymph node retrieval and R0 resection rate), lower postoperative mortality and increased overall survival for all gastric cancer patients [31].

On the other hand, Claassen YHM et al. [32] did not report differences in morbidity and mortality rates between the hospital volume categories, ranked as very low (1–10 gastrectomies/year), low (11–20), medium (21–30), and high (31 or more). They postulated that patients referring to medium and high-volume centers had major comorbidities (co-morbidity score ≥3) or more frequently underwent total gastrectomy surgery. Moreover, a retrospective review of the CRITICS trial reclassified hospitals as low-volume (1–20 gastrectomies/year) and high-volume (21 or more) finding higher overall survival and disease-free survival from high-volume hospitals [33].

Agnes A et al. argued that the high-volume status is referred to surgeons performing a high number of gastric resections and to other measurable and non-measurable variables, such as case mix (complexity of operation, comorbidities), well-organized perioperative process (ICU, trained anesthesiologist, radiologist, and nurses, availability of other specialists around the clock), timely management of postoperative complications (continuous assistance from experienced physicians, interventional radiology, digestive endoscopy) and appropriateness of the indication resulting from multidisciplinary cancer boards [34]. Most of these aspects could directly improve early postoperative outcomes and influence failure to rescue phenomenon [35].

The UK National Esophago-Gastric Cancer Audit registered a 90-day mortality of <5% and an anastomotic leakage rate of 6.3% in gastric cancer surgery. Moreover, after adjustment, lower 30-day mortality and anastomotic leak rate were observed in hospitals with higher volumes, while higher surgeon volume was associated with a lower anastomotic leak rate [36]. A German observational study revealed that treatment in a very high volume is associated with lower in-hospital mortality compared to low-volume hospitals [37]. Similar results arose from the Taiwan National Insurance Research Database [38]. Interestingly, postoperative mortality was low for each hospital volume category in a retrospective French study [39] that reported the impact of institution volume on 90-day postoperative mortality after gastric cancer surgery. Postoperative mortality rate ranged from 4.3 to 10.2% and resulted in 7.9% in very high-volume hospitals (at least 60 resections/year). Those data suggest the role of other factors, such as hospital facilities, or timely recognition of complications, in determining outcomes [12]. It could be argued that death or complication after surgery are imperfect measures of surgical quality.

On the other hand, a Japanese perspective on a total of 145,523 patients who underwent distal gastrectomy for gastric cancer by 11,914 surgeons at 2182 institutions has been recently published [40]. Hospital volumes were divided into 3 tertiles (low, 1–22 cases per year; medium, 23–51 and high, 52–404): An inversely proportional relationship between mortality rate and hospital volume was registered, resulting in the operative mortality of 1.9% in low-volume hospitals, 1.0% in medium and 0.5% in high ($p < 0.001$). Similarly, surgical complications such as anastomotic leakage, pneumonia, and surgical site infection were significantly higher in low-volume hospitals ($p < 0.001$) [40][41]. The same group recently analyzed a cohort of 71,307 patients undergoing total gastrectomy at 2051 institutions. Hospital volumes were divided into three tertiles: low, 0–11 cases per year; medium, 12–26, and high, 27–146. The peri-operative mortality rate passed from

3.1% in low-volume hospitals to 1.7% and 1.2% in medium and high volumes, respectively ($p < 0.001$). Surprisingly, the anastomotic leakage rate was not significantly different between low- and high-volume hospitals, while the rate of septic shock and medical complications of the nervous system were significantly higher in low-volume hospitals ($p < 0.001$) [42].

A South Korean study, using National Health Insurance Service (NHIS) Sampling Cohort data during 2004–2013, noted that if mortality decreased with increasing hospital volume, the risk of mortality increased again after reaching some level of surgery volume [43].

Another interesting topic is the assessment of procedure volume effect on patient outcomes after the perioperative period. Long-term outcomes could be strongly influenced by the appropriateness of patient selection for peri-operative therapies, the type of surgery, the technical skills of the surgeon, and the availability of a specialized pathologist to appropriate stage the disease. To date, only a limited number of studies investigating the relationship between hospital volume and long-term survival after gastrectomy have been published, with scarce and conflicting results [25][26][27][31][44]. Birkmeyer JD et al. [45] explored the relationship between hospital volume and late survival after different types of cancer resections, using the national Surveillance Epidemiology and End Results (SEER)–Medicare-linked database. They found a statistically significant association between 5-year survival and hospital volume, reporting a lower survival rate in low-volume compared with high-volume centers (25.6% vs. 32.0%, respectively), irrespective of differences in the use of adjuvant radiation and chemotherapy [45]. On the contrary, a prospective, population-based study of 3293 consecutive patients with esophageal or gastric cancer endorsed by the Scottish Audit of Gastric and Oesophageal Cancer (SAGOC) failed to demonstrate any correlation between hospital volume and postoperative morbidity or mortality, nor between survival and volume of patients neither for the hospital of diagnosis nor hospital of surgery [25].

3. Surgeon Volume

The hospital volume and outcome relationship does not maintain its correlation at the individual surgeon level. As for hospital volume, similar attention was paid to the relationship between mortality rate and surgeon volume. Several reports have demonstrated an impact of surgeon activity on postoperative short- as well as long-term outcomes among patients undergoing gastric cancer surgery [40][46][47]. Even though 10-15 gastrectomies per year were suggested as a minimum surgeon volume for gastrectomy, [48][49], further evaluation in a large-scale cohort is needed [40].

Furthermore, it is hard to apply the same caseload threshold to clinical practice in different countries since the differences in epidemiology, biology, and treatment strategy can influence the cut-off value.

In the Western setting, the lower incidence of gastric cancer also resulted in a lower average volume, which ultimately led to poorer opportunities for surgical trainees. In terms of postoperative results, the learning curve is considered optimized once the minimum threshold of 15–25 cases is exceeded [50][51][52]. In the minimally invasive era, a significant reduction of the conversion rate and an increase in the lymph node yield was reported after the 10th case [53]. Moreover, comparing well-trained laparoscopic surgeons working in high- and low-volume hospitals, perioperative outcomes were not influenced, underlining that hospital volume is not a decisive factor [54].

In Japan, the National Clinical Database (NCD) was established in 2010 with the aim of recording all procedures performed by national surgeons. From this project, data on 11,300,000 Japanese patients with gastric cancer were extracted to discuss how surgical and hospital volume impact mortality following surgery for gastric cancer [40]. Interestingly, Iwatsuki M et al. disclosed a strong impact of hospital and surgeon volume on mortality and morbidity rates [40][42]. Particularly, dividing surgeon volume into four groups, S1 (0–2 cases per year), S2 (3–9 cases), S3 (10–25 cases), and S4 (>26 cases), the operative mortality rate after a total gastrectomy decreased from 2.5% in S1 to 0.6% in S4. By contrast, after proper statistical analysis adjusted by risk model variables (demographic factors, preoperative functional status, pre-existing comorbidities, operative factors, and preoperative laboratory data), only hospital volume showed a crucial role in improving outcomes compared with the surgeon volume. In other words, surgeons with low volumes could obtain lower morbidity and mortality rates compared to surgeons with high volumes and worse results.

Urbach DR et al. assumed that low-volume surgeons may have excellent outcomes because of experience or because they performed a high volume of similar operations requiring similar technical skills [55]. Interestingly, the best postoperative outcomes were obtained by high-volume surgeons in high-volume hospitals, followed by low-volume surgeons in high-volume hospitals [56]. These results may influence surgical training programs and the centralization of advanced surgical procedures.

However, a more precise standardization of surgical training is needed through dedicated fellowships or the establishment of a minimum skill–volume load for performing certain surgical procedures. If no doubt exists that the accreditation of

hospitals improves surgical quality and safety, surgeons' accreditation programs are currently lacking. The ESSO Core Curriculum, since its conception in 2013 by ESSO, the European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Medical Oncology (ESMO), has served as a guidance document for surgical oncologists to obtain the level of knowledge needed both for surgical oncology practice but also for the European Board of Surgery Qualification (EBSQ) in surgical oncology. In October 2021, an update on ESSO Core Curriculum was published [57], with the aim to give the candidate an idea of expectations and areas for in-depth study, in addition to the practical requirements to "*permit flexibility to suit the needs of the different regions of the world with their inherently diverse sociocultural, financial and cultural differences*"—Audisio R. In this way, the paradox of having a particular hospital accredited to perform several complex procedures without having qualified accredited surgeons can be avoided. It is time to shift from the pursuit of high-volume to high-quality centers.

On the other hand, the annual surgeon activity can only represent a surrogate marker for medical care quality [58], since it may not cover the complexity of this issue consisting of hospital volume, specialization, and mentorship opportunities [46]. Quality of care, in fact, consists of more than the performance of a single surgeon. Organizational effectiveness, perioperative care, anesthesia, ICU staffing, the experience of the nursery staff, nutritional evaluation, comprehensive geriatric assessment [10], and collaboration between different disciplines all contribute to the outcomes of the performed procedure [59].

4. Textbook Outcome

In 2017 the Dutch Upper Gastrointestinal Cancer Audit (DUCA) group designed the Textbook Outcome (TO), a multidimensional scale that provides an ideal route after esophagogastric cancer surgery [60]. It comprises ten perioperative quality-of-care parameters:

(1)Complete, potentially curative, resection as judged by the surgeon at the time of surgery;

(2)No intraoperative complication;

(3)Negative resection margin;

(4)Greater than 15 lymph nodes sampled;

(5)No severe postoperative complications (Clavien–Dindo grade II or higher);

(6)No re-intervention (surgical, endoscopic, or radiological) ≤30 days after surgery;

(7)No unplanned ICU or medium-care unit (MCU) admission ≤30 days after surgery;

(8)Duration of stay not exceeding 21 days;

(9)No 30-day readmission;

(10)No 30-day mortality following surgery.

They demonstrated that the quality of surgical care for patients with gastric cancer is multidimensional, and it is possible to generate supplementary information when different outcome parameters are combined into a single comprehensive outcome measure. TO was achieved in 48.6% (569/1172 patients) of patients with gastric cancer, resulting in a good match of 30-day postoperative mortality (5.5%) and severe postoperative complications (11.7%) when compared with other contemporary results [59][61].

In van der Kaaij's RT series, TO was associated with long-term overall survival (OS) after surgery for gastric cancer. Patients with a TO had 1-, 2-, and 3-year overall survival rates of 85%, 70%, and 64%, respectively, versus 64%, 49%, and 42% for patients with no TO, respectively. Good patient selection, well-performed surgery, and optimal postoperative care can ensure a rapid discharge, optimize long-term outcomes, and reduce costs for the healthcare system. Interestingly, the DUCA group achieved TO in 23% of patients in hospitals performing 0 to 19 gastrectomies per year, 29% in hospitals performing 20 to 39 gastrectomies per year, and 27% in hospitals performing more than 40 gastrectomies per year [62][63].

The next update of the Population Registry of Esophageal and Stomach Tumors of Ontario (PRESTO) group did not include radical resection according to the surgeon and intraoperative complications (previously not unambiguously

differentiated from postoperative complications) [64]. Overall, the new TO definition included eight points in total and was achieved in 24.6% of patients with gastric cancer. First, the proportion achieving TO varied significantly by year of surgery and displayed a significant and positive trend (20.3% in 2004 and 29.3% in 2015, $p < 0.001$). Secondly, surgeons and hospitals were ranked into quintiles (Q): surgeon Q1 performing 0 gastrectomies per year to surgeon Q5 performing 3.5–9.5 gastrectomies per year, and hospital Q1 with 0–2 volume per year to hospital Q5 with 12–22 procedures. TO was achieved in a higher percentage of patients treated in the highest volume hospitals compared to the lowest volume ones (Hospital Q5 23.5% vs. Q1 16.2%), while similar TO results were obtained by the highest and lowest volume surgeons (Surgeon Q5 24.0% vs. Q1 20.8%). This discrepancy was due to the adequate lymph node sampling rate, the lower rate of unplanned ICU admissions, and lesser 30-day mortality. However, neither TO nor 30-day postoperative morbidity, readmission, and mortality were associated with surgeon or hospital volumes.

In 2022, the same group concluded that achieving TO is strongly associated with improved long-term survival in 1836 gastric cancer patients, with a 41% reduction in 3-year mortality ($p < 0.001$) [65].

According to Levy J et al., the volume–outcome relationship is analogous to practice-makes-perfect, whereas "*perfect practice makes perfect*" may be more effective [64]. Future policies should be focused more on meeting quality parameters than on absolute volume.

Anyway, new scientific evidence is shedding light on the grey zones of the management of gastric cancer, focusing researchers' efforts on new outcomes. This is the premise for setting a new TO for gastric cancer.

References

1. Degiuli, M.; Sasako, M.; Ponti, A. Italian Gastric Cancer Study Group Morbidity and Mortality in the Italian Gastric Cancer Study Group Randomized Clinical Trial of D1 versus D2 Resection for Gastric Cancer. Br. J. Surg. 2010, 97, 643–649.
2. Lepage, C.; Sant, M.; Verdecchia, A.; Forman, D.; Esteve, J.; Faivre, J. Operative Mortality after Gastric Cancer Resection and Long-Term Survival Differences across Europe. Br. J. Surg. 2010, 97, 235–239.
3. Peeters, K.C.M.J.; van de Velde, C.J.H. Quality Assurance of Surgery in Gastric and Rectal Cancer. Crit. Rev. Oncol. Hematol. 2004, 51, 105–119.
4. Evrard, S.; Audisio, R.; Poston, G.; Caballero, C.; Kataoka, K.; Fontein, D.; Collette, L.; Nakamura, K.; Fukuda, H.; Lacombe, D. From a Comic Opera to Surcare an Open Letter to Whom Clinical Research in Surgery Is a Concern: Announcing the Launch of SURCARE. Ann. Surg. 2016, 264, 911–912.
5. Tanis, E.; Caballero, C.; Collette, L.; Verleye, L.; den Dulk, M.; Lacombe, D.; Schuhmacher, C.; Werutsky, G. The European Organization for Research and Treatment for Cancer (EORTC) Strategy for Quality Assurance in Surgical Clinical Research: Assessment of the Past and Moving towards the Future. Eur. J. Surg. Oncol. 2016, 42, 1115–1122.
6. Japanese Gastric Cancer Association, J.G.C. Japanese Gastric Cancer Treatment Guidelines 2014 (Ver. 4). Gastric Cancer 2017, 20, 1–19.
7. Zhang, K.C.; Chen, L. Emphasis on Standardization of Minimally Invasive Surgery for Gastric Cancer. Zhonghua Wai Ke Za Zhi 2018, 56, 262–264.
8. Papenfuss, W.A.; Kukar, M.; Oxenberg, J.; Attwood, K.; Nurkin, S.; Malhotra, U.; Wilkinson, N.W. Morbidity and Mortality Associated with Gastrectomy for Gastric Cancer. Ann. Surg. Oncol. 2014, 21, 3008–3014.
9. American College of Surgeons National Surgical Quality Improvement Program. Available online: https://www.facs.org/quality-programs/data-and-registries/acs-nsqip/ (accessed on 7 November 2022).
10. Boccardi, V.; Marano, L. The Geriatric Surgery: The Importance of Frailty Identification Beyond Chronological Age. Geriatrics 2020, 5, 12.
11. Marano, L.; Carbone, L.; Poto, G.E.; Gambelli, M.; Nguefack Noudem, L.L.; Grassi, G.; Manasci, F.; Curreri, G.; Giuliani, A.; Piagnerelli, R.; et al. Handgrip Strength Predicts Length of Hospital Stay in an Abdominal Surgical Setting: The Role of Frailty beyond Age. Aging Clin. Exp. Res. 2022, 34, 811–817.
12. Busweiler, L.A.D.; Dikken, J.L.; Henneman, D.; van Berge Henegouwen, M.I.; Ho, V.K.Y.; Tollenaar, R.A.E.M.; Wouters, M.W.J.M.; van Sandick, J.W. The Influence of a Composite Hospital Volume on Outcomes for Gastric Cancer Surgery: A Dutch Population-based Study. J. Surg. Oncol. 2017, 115, 738–745.
13. Siriwardena, A.K. Centralisation of Upper Gastrointestinal Cancer Surgery. Ann. R. Coll. Surg. Engl. 2007, 89, 335–336.

14. Mesman, R.; Westert, G.P.; Berden, B.J.M.M.; Faber, M.J. Why Do High-Volume Hospitals Achieve Better Outcomes? A Systematic Review about Intermediate Factors in Volume-Outcome Relationships. Health Policy 2015, 119, 1055–1067.

15. Halm, E.A.; Lee, C.; Chassin, M.R. Is Volume Related to Outcome in Health Care? A Systematic Review and Methodologic Critique of the Literature. Ann. Intern. Med. 2002, 137, 511–520.

16. Finlayson, S.R.G. The Volume-Outcome Debate Revisited. Am. Surg. 2006, 72, 1038–1042, discussion 1061–1069, 1133–1148.

17. Van Vliet, E.P.M.; Hermans, J.J.; De Wever, W.; Eijkemans, M.J.C.; Steyerberg, E.W.; Faasse, C.; van Helmond, E.P.M.; de Leeuw, A.M.; Sikkenk, A.C.; de Vries, A.R.; et al. Radiologist Experience and CT Examination Quality Determine Metastasis Detection in Patients with Esophageal or Gastric Cardia Cancer. Eur. Radiol. 2008, 18, 2475–2484.

18. Pronovost, P.J.; Angus, D.C.; Dorman, T.; Robinson, K.A.; Dremsizov, T.T.; Young, T.L. Physician Staffing Patterns and Clinical Outcomes in Critically Ill Patients: A Systematic Review. JAMA 2002, 288, 2151–2162.

19. Needleman, J.; Buerhaus, P.; Mattke, S.; Stewart, M.; Zelevinsky, K. Nurse-Staffing Levels and the Quality of Care in Hospitals. N. Engl. J. Med. 2002, 346, 1715–1722.

20. Ghaferi, A.A.; Birkmeyer, J.D.; Dimick, J.B. Hospital Volume and Failure to Rescue with High-Risk Surgery. Med. Care 2011, 49, 1076–1081.

21. Koëter, M.; van Steenbergen, L.N.; Lemmens, V.E.P.P.; Rutten, H.J.T.; Roukema, J.A.; Wijnhoven, B.P.L.; Nieuwenhuijzen, G.A.P. Hospital of Diagnosis and Probability to Receive a Curative Treatment for Oesophageal Cancer. Eur. J. Surg. Oncol. 2014, 40, 1338–1345.

22. Svederud, I.; Virhage, M.; Medin, E.; Grundström, J.; Friberg, S.; Ramsberg, J. Patient Perspectives on Centralisation of Low Volume, Highly Specialised Procedures in Sweden. Health Policy 2015, 119, 1068–1075.

23. Vallejo-Torres, L.; Melnychuk, M.; Vindrola-Padros, C.; Aitchison, M.; Clarke, C.S.; Fulop, N.J.; Hines, J.; Levermore, C.; Maddineni, S.B.; Perry, C.; et al. Discrete-Choice Experiment to Analyse Preferences for Centralizing Specialist Cancer Surgery Services. Br. J. Surg. 2018, 105, 587–596.

24. Choi, Y.Y.; Cheong, J.H. Beyond precision surgery: Molecularly motivated precision care for gastric cancer. Eur. J. Surg. Oncol. 2017, 43, 856–864.

25. Thompson, A.M.; Rapson, T.; Gilbert, F.J.; Park, K.G.M. Hospital Volume Does Not Influence Long-Term Survival of Patients Undergoing Surgery for Oesophageal or Gastric Cancer. Br. J. Surg. 2007, 94, 578–584.

26. Finlayson, E.V.A. Hospital Volume and Operative Mortality in Cancer Surgery. Arch. Surg. 2003, 138, 721.

27. Dikken, J.L.; Dassen, A.E.; Lemmens, V.E.P.; Putter, H.; Krijnen, P.; van der Geest, L.; Bosscha, K.; Verheij, M.; van de Velde, C.J.H.; Wouters, M.W.J.M. Effect of Hospital Volume on Postoperative Mortality and Survival after Oesophageal and Gastric Cancer Surgery in the Netherlands between 1989 and 2009. Eur. J. Cancer. 2012, 48, 1004–1013.

28. Learn, P.A.; Bach, P.B. A Decade of Mortality Reductions in Major Oncologic Surgery: The Impact of Centralization and Quality Improvement. Med. Care 2010, 48, 1041–1049.

29. Smith, J.K.; McPhee, J.T.; Hill, J.S.; Whalen, G.F.; Sullivan, M.E.; Litwin, D.E.; Anderson, F.A.; Tseng, J.F. National Outcomes after Gastric Resection for Neoplasm. Arch. Surg. 2007, 142, 387–393.

30. Nelen, S.D.; Heuthorst, L.; Verhoeven, R.H.A.; Polat, F.; Kruyt, P.M.; Reijnders, K.; Ferenschild, F.T.J.; Bonenkamp, J.J.; Rutter, J.E.; de Wilt, J.H.W.; et al. Impact of Centralizing Gastric Cancer Surgery on Treatment, Morbidity, and Mortality. J. Gastrointest. Surg. 2017, 21, 2000–2008.

31. Van Putten, M.; Nelen, S.D.; Lemmens, V.E.P.P.; Stoot, J.H.M.B.; Hartgrink, H.H.; Gisbertz, S.S.; Spillenaar Bilgen, E.J.; Heisterkamp, J.; Verhoeven, R.H.A.; Nieuwenhuijzen, G.A.P. Overall Survival before and after Centralization of Gastric Cancer Surgery in the Netherlands. Br. J. Surg. 2018, 105, 1807–1815.

32. Claassen, Y.H.M.; van Sandick, J.W.; Hartgrink, H.H.; Dikken, J.L.; De Steur, W.O.; van Grieken, N.C.T.; Boot, H.; Cats, A.; Trip, A.K.; Jansen, E.P.M.; et al. Association between Hospital Volume and Quality of Gastric Cancer Surgery in the CRITICS Trial. Br. J. Surg. 2018, 105, 728–735.

33. Claassen, Y.H.M.; van Amelsfoort, R.M.; Hartgrink, H.H.; Dikken, J.L.; de Steur, W.O.; van Sandick, J.W.; van Grieken, N.C.T.; Cats, A.; Boot, H.; Trip, A.K.; et al. Effect of Hospital Volume with Respect to Performing Gastric Cancer Resection on Recurrence and Survival. Ann. Surg. 2019, 270, 1096–1102.

34. Agnes, A.; Lorenzon, L.; Belia, F.; Biondi, A.; D'Ugo, D. Impact of Hospital and Surgeon Volume on the Outcomes of Gastric Cancer Surgery. In Gastric Cancer: The 25-Year R-Evolution; Springer: Berlin/Heidelberg, Germany, 2021; pp. 127–136. ISBN 978-3-030-73157-1.

35. Diers, J.; Baum, P.; Wagner, J.C.; Matthes, H.; Pietryga, S.; Baumann, N.; Uttinger, K.; Germer, C.-T.; Wiegering, A. Hospital Volume Following Major Surgery for Gastric Cancer Determines In-Hospital Mortality Rate and Failure to Rescue: A Nation-Wide Study Based on German Billing Data (2009–2017). Gastric Cancer 2021, 24, 959–969.

36. Fischer, C.; Lingsma, H.; Klazinga, N.; Hardwick, R.; Cromwell, D.; Steyerberg, E.; Groene, O. Volume-Outcome Revisited: The Effect of Hospital and Surgeon Volumes on Multiple Outcome Measures in Oesophago-Gastric Cancer Surgery. PLoS ONE 2017, 12, e0183955.

37. Nimptsch, U.; Haist, T.; Gockel, I.; Mansky, T.; Lorenz, D. Complex Gastric Surgery in Germany—Is Centralization Beneficial? Observational Study Using National Hospital Discharge Data. Langenbecks Arch. Surg. 2019, 404, 93–101.

38. Wu, J.-M.; Ho, T.-W.; Tien, Y.-W. Correlation Between the Increased Hospital Volume and Decreased Overall Perioperative Mortality in One Universal Health Care System. World J. Surg. 2019, 43, 2194–2202.

39. Pasquer, A.; Renaud, F.; Hec, F.; Gandon, A.; Vanderbeken, M.; Drubay, V.; Caranhac, G.; Piessen, G.; Mariette, C. FREGAT Working GroupFRENCH Is Centralization Needed for Esophageal and Gastric Cancer Patients with Low Operative Risk? Ann. Surg. 2016, 264, 823–830.

40. Iwatsuki, M.; Yamamoto, H.; Miyata, H.; Kakeji, Y.; Yoshida, K.; Konno, H.; Seto, Y.; Baba, H. Effect of Hospital and Surgeon Volume on Postoperative Outcomes after Distal Gastrectomy for Gastric Cancer Based on Data from 145,523 Japanese Patients Collected from a Nationwide Web-Based Data Entry System. Gastric Cancer 2019, 22, 190–201.

41. Marano, L.; Carbone, L.; Poto, G.E.; Calomino, N.; Neri, A.; Piagnerelli, R.; Fontani, A.; Verre, L.; Savelli, V.; Roviello, F.; et al. Antimicrobial Prophylaxis Reduces the Rate of Surgical Site Infection in Upper Gastrointestinal Surgery: A Systematic Review. Antibiotics 2022, 11, 230.

42. Iwatsuki, M.; Yamamoto, H.; Miyata, H.; Kakeji, Y.; Yoshida, K.; Konno, H.; Seto, Y.; Baba, H. Association of Surgeon and Hospital Volume with Postoperative Mortality after Total Gastrectomy for Gastric Cancer: Data from 71,307 Japanese Patients Collected from a Nationwide Web-Based Data Entry System. Gastric Cancer 2021, 24, 526–534.

43. Choi, H.; Yang, S.-Y.; Cho, H.-S.; Kim, W.; Park, E.-C.; Han, K.-T. Mortality Differences by Surgical Volume among Patients with Stomach Cancer: A Threshold for a Favorable Volume-Outcome Relationship. World J. Surg. Oncol. 2017, 15, 134.

44. Hannan, E.L.; Radzyner, M.; Rubin, D.; Dougherty, J.; Brennan, M.F. The Influence of Hospital and Surgeon Volume on In-Hospital Mortality for Colectomy, Gastrectomy, and Lung Lobectomy in Patients with Cancer. Surgery 2002, 131, 6–15.

45. Birkmeyer, J.D.; Sun, Y.; Wong, S.L.; Stukel, T.A. Hospital Volume and Late Survival after Cancer Surgery. Ann. Surg. 2007, 245, 777–783.

46. Mehta, A.; Efron, D.T.; Canner, J.K.; Dultz, L.; Xu, T.; Jones, C.; Haut, E.R.; Higgins, R.S.D.; Sakran, J.V. Effect of Surgeon and Hospital Volume on Emergency General Surgery Outcomes. J. Am. Coll. Surg. 2017, 225, 666–675.e2.

47. Liang, Y.; Wu, L.; Wang, X.; Ding, X.; Liang, H. The Positive Impact of Surgeon Specialization on Survival for Gastric Cancer Patients after Surgery with Curative Intent. Gastric Cancer 2015, 18, 859–867.

48. Mamidanna, R.; Ni, Z.; Anderson, O.; Spiegelhalter, S.D.; Bottle, A.; Aylin, P.; Faiz, O.; Hanna, G.B. Surgeon Volume and Cancer Esophagectomy, Gastrectomy, and Pancreatectomy: A Population-Based Study in England. Ann. Surg. 2016, 263, 727–732.

49. Bachmann, M.O.; Alderson, D.; Edwards, D.; Wotton, S.; Bedford, C.; Peters, T.J.; Harvey, I.M. Cohort Study in South and West England of the Influence of Specialization on the Management and Outcome of Patients with Oesophageal and Gastric Cancers. Br. J. Surg. 2002, 89, 914–922.

50. Parikh, D.; Johnson, M.; Chagla, L.; Lowe, D.; McCulloch, P. D2 Gastrectomy: Lessons from a Prospective Audit of the Learning Curve. Br. J. Surg. 2005, 83, 1595–1599.

51. Degiuli, M.; Sasako, M.; Calgaro, M.; Garino, M.; Rebecchi, F.; Mineccia, M.; Scaglione, D.; Andreone, D.; Ponti, A.; Calvo, F. Morbidity and Mortality after D1 and D2 Gastrectomy for Cancer: Interim Analysis of the Italian Gastric Cancer Study Group (IGCSG) Randomised Surgical Trial. Eur. J. Surg. Oncol. (EJSO) 2004, 30, 303–308.

52. Luna, A.; Rebasa, P.; Montmany, S.; Navarro, S. Learning Curve for D2 Lymphadenectomy in Gastric Cancer. ISRN Surg. 2013, 2013, 508719.

53. Brenkman, H.J.F.; Ruurda, J.P.; Verhoeven, R.H.A.; van Hillegersberg, R. Safety and Feasibility of Minimally Invasive Gastrectomy during the Early Introduction in the Netherlands: Short-Term Oncological Outcomes Comparable to Open Gastrectomy. Gastric Cancer 2017, 20, 853–860.

54. Lee, H.H.; Son, S.-Y.; Lee, J.H.; Kim, M.G.; Hur, H.; Park, D.J. Surgeon's Experience Overrides the Effect of Hospital Volume for Postoperative Outcomes of Laparoscopic Surgery in Gastric Cancer: Multi-Institutional Study. Ann. Surg. Oncol. 2017, 24, 1010–1017.

55. Urbach, D.R.; Baxter, N.N. Does It Matter What a Hospital Is “High Volume” for? Specificity of Hospital Volume-Outcome Associations for Surgical Procedures: Analysis of Administrative Data. BMJ 2004, 328, 737–740.
56. Ji, J.; Shi, L.; Ying, X.; Lu, X.; Shan, F. Associations of Annual Hospital and Surgeon Volume with Patient Outcomes After Gastrectomy: A Systematic Review and Meta-analysis. Ann. Surg. Oncol. 2022, 29, 8276–8297.
57. Van der Hage, J.; Sandrucci, S.; Audisio, R.; Wyld, L.; Søreide, K.; Amaral, T.; Audisio, R.; Bahadoer, V.; Beets, G.; Benstead, K.; et al. The ESSO Core Curriculum Committee Update on Surgical Oncology. Eur. J. Surg. Oncol. 2021, 47, e1–e30.
58. Jha, A.K. Back to the Future: Volume as a Quality Metric. JAMA 2015, 314, 214–215.
59. Dikken, J.L.; Stiekema, J.; van de Velde, C.J.H.; Verheij, M.; Cats, A.; Wouters, M.W.J.M.; van Sandick, J.W. Quality of Care Indicators for the Surgical Treatment of Gastric Cancer: A Systematic Review. Ann. Surg. Oncol. 2013, 20, 381–398.
60. Busweiler, L.A.D.; Schouwenburg, M.G.; van Berge Henegouwen, M.I.; Kolfschoten, N.E.; de Jong, P.C.; Rozema, T.; Wijnhoven, B.P.L.; van Hillegersberg, R.; Wouters, M.W.J.M.; van Sandick, J.W.; et al. Textbook Outcome as a Composite Measure in Oesophagogastric Cancer Surgery. Br. J. Surg. 2017, 104, 742–750.
61. Messager, M.; de Steur, W.O.; van Sandick, J.W.; Reynolds, J.; Pera, M.; Mariette, C.; Hardwick, R.H.; Bastiaannet, E.; Boelens, P.G.; van deVelde, C.J.H.; et al. Variations among 5 European Countries for Curative Treatment of Resectable Oesophageal and Gastric Cancer: A Survey from the EURECCA Upper GI Group (EUropean REgistration of Cancer CAre). Eur. J. Surg. Oncol. 2016, 42, 116–122.
62. Van der Kaaij, R.T.; de Rooij, M.V.; van Coevorden, F.; Voncken, F.E.M.; Snaebjornsson, P.; Boot, H.; van Sandick, J.W. Using Textbook Outcome as a Measure of Quality of Care in Oesophagogastric Cancer Surgery. Br. J. Surg. 2018, 105, 561–569.
63. Van der Werf, L.R.; Wijnhoven, B.P.L.; Fransen, L.F.C.; van Sandick, J.W.; Nieuwenhuijzen, G.A.P.; Busweiler, L.A.D.; van Hillegersberg, R.; Wouters, M.W.J.M.; Luyer, M.D.P.; van Berge Henegouwen, M.I. A National Cohort Study Evaluating the Association Between Short-Term Outcomes and Long-Term Survival After Esophageal and Gastric Cancer Surgery. Ann. Surg. 2019, 270, 868–876.
64. Levy, J.; Gupta, V.; Amirazodi, E.; Allen-Ayodabo, C.; Jivraj, N.; Jeong, Y.; Davis, L.E.; Mahar, A.L.; De Mestral, C.; Saarela, O.; et al. Gastrectomy Case Volume and Textbook Outcome: An Analysis of the Population Registry of Esophageal and Stomach Tumours of Ontario (PRESTO). Gastric Cancer 2020, 23, 391–402.
65. Levy, J.; Gupta, V.; Amirazodi, E.; Allen-Ayodabo, C.; Jivraj, N.; Jeong, Y.; Davis, L.E.; Mahar, A.L.; De Mestral, C.; Saarela, O.; et al. Textbook Outcome and Survival in Patients with Gastric Cancer. Ann. Surg. 2022, 275, 140–148.
