The Volume-Outcome Relationship in Cancer Surgery
A Hard Sell

Ingemar Ihse, MD

Since the first volume-outcome relationships in the medical care were reported by Luft in 1979,[1] there has been a persistent and sometimes emotional debate about whether certain sorts of complex, elective care should be restricted to high-volume medical centers. Over the past 2 decades, numerous studies have shown that higher hospital volume is associated with lower postoperative mortality and morbidity rates after a great number of different surgical procedures.[2–12] These include both high-risk operations and less complex procedures. There are also reports on improved survival after cancer surgery done in high-volume specialty centers as compared with low- and medium-volume units.[13–16] Still, the referral pattern has remained practically unchanged in most countries, and few if any signs of regionalization of complex procedures have been seen. In The Netherlands, 40% to 46% of pancreaticoduodenectomies continue to be done in low-volume units,[7] and such operations are practiced in 50% of Swedish hospitals, most of which do less than three operations annually.[17] Although relations between volume and outcome have long been recognized efforts to concentrate, selective procedures in high-volume hospitals are only now beginning to gain momentum. What explains the hesitation?

HOW COMPELLING IS THE EVIDENCE?

Opponents of the concept remind us that volume is not a formal indicator of quality but rather a structural characteristic. They also point out limitations of published analyses.

Besides case volume, a variety of other factors underlie differences in outcome: selection of patients, preoperative preparation, skills of interventional and diagnostic radiologists and of critical care specialists, postoperative care, nurse staff levels, surgical judgment and skill, and others. Thus, volume is not an exclusive indicator of outcome, I agree, but it certainly enhances the level of all the above-mentioned factors by increasing the experience of the interdisciplinary treatment teams. It is therefore plausible to assume that volume is often associated with quality.

It is true that several of the studies, especially the early ones, have some methodological limitations that should be considered. Still, convincing evidence from multiple analyses suggests that cancer patients enjoy superior outcomes when surgical resection is performed in hospitals with large case volumes. In a recent structured review of the literature, Dudley et al found lower hospital mortality at high-volume hospitals in 123 of 128 analyses involving 40 different procedures.[18] I will mention a few of them in this address and discuss their strengths as well as caveats.

In a large national study published last year by Birkmeyer et al, 14 types of procedures and 2.5 million patients were included.[9] Higher-volume hospitals had lower operative mortality for all types of procedures. The eight different, major cancer operations analyzed represented more than 520 000 operations: colectomy, gastrectomy, esophagectomy, pancreatic resection, nephrectomy, cystectomy, lung lobectomy, and pneumonectomy. Even if this is one of the best studies from a methodological point of view, it has the limitations, like the majority of studies, of relying on administrative data, thereby perhaps not accounting adequately for differences in case mix as such data are limited in their ability to differentiate patients according to severity of disease. I believe, though, that the results of the study reflect real differences because the effect is so large, the study population is so big, and the findings are so clinically plausible.

Begg et al used the Surveillance, Epidemiology and End Results (SEER) Medicare liked database, permitting them to adjust for case mix.[4] They included 5013 patients who underwent pancreatectomy, esophagectomy, pneumonectomy, liver resection, and pelvic exenteration. Main outcome measure was 30-day mortality in relation to procedure volume adjusted for comorbidity, patient age, and cancer stage. Higher volume was linked with lower mortality for all operations except pneumonectomy. Adjustment for case mix and other factors did not change the findings. Similar results have been reported by others[19,20] speaking against the suggestion that low-volume hospitals are treating "sicker" pa-

From the Department of Surgery, Lund University Hospital, Lund, Sweden.
The 10th meeting of the European Surgical Association, Paris 2003.
Reprints: Ingemar Ihse, MD, Lund University Hospital, Lund, Sweden S-99185.

0003-4932/03/23806-0777
DOI: 10.1097/01.sla.0000098616.19622.af

tients and that difference in case mix might explain the difference in outcome. Also, a recent structured review by the Institute of Medicine in the United States found no evidence that studies based on clinical data report weaker volume-outcome relationships than those based on administrative data.[21]

Few elective surgical procedures are associated with higher operative risk than pancreaticoduodenectomy. Numerous studies show a consistent trend toward hospital case volume predicting better outcome in pancreas surgery. These studies offer the most compelling support of the hospital case volume: better outcome concept because of their size and diversity of study design. I will therefore pay special attention to this patient group in my presentation.

In 1995, Gordon et al published a retrospective study on 501 patients who underwent pancreatic resection at one of 39 hospitals in Maryland.[2] Hospital mortality rate was significantly less at the high-volume regional medical center compared with all other hospitals (2.2% vs. 13.5%).

Lieberman et al studied 2233 pancreaticoduodenectomies or total pancreatectomies performed in New York state from 1984 to 1991.[3] Hospital mortality rate was 19% in hospitals where less than 10 resections were done during the period, 12% where 10 to 50 resections were done, 13% where 51 to 80 operations were performed, and 6% in hospitals doing more than 80 operations. The authors found also higher operative mortality rate for low-volume surgeons (<9 resections; 16%) compared with high-volume surgeons (>41 resections, 5%). Glasgow and Mulvihill carried out a similar study when they used statewide hospital discharge records in California from 1950 to 1994.[19] Among the 298 hospitals, 88% treated an average of 2 or less patients per year with pancreatic resection. Centers with higher volume had better profiles in mortality. Birkmeyer et al performed a national cohort study of 7229 Medicare patients over 65 years of age undergoing pancreaticoduodenectomy between 1992 and 1995.[6] Hospitals performing 5 to 10 operations per year had higher in-hospital mortality rates than the 7 hospitals doing 10 to 20 operations or the 3 hospitals doing 20 or more procedures annually (6.2% vs. 2.5% vs. 1.7%, $P < 0.01$).

Simunovic et al reported a population-based retrospective analysis of 842 pancreatic resections for cancer performed in Ontario from 1988 to 1995.[22] This study differed from the above-mentioned U.S. studies by representing a publicly financed health care system. Again, case fatality was associated with hospital volume, being 14.4%, 12.8%, and 3.4%, respectively, for low-, medium-, and high-volume hospitals.

The first European study evaluating the higher volume-better outcome concept in pancreatic resection was done by Gouma et al from The Netherlands, where the medical registry included 1126 partial pancreatoduodenectomy patients between January 1994 and December 1998.[7] The annual hospital death rates ranged from 13.6% to 20% in low-volume hospitals and from 0% to 2.9% in high-volume hospitals (>25 operations per year).

In a study published this year based on 6652 patients, Ho and Heslin found that hospitals with more years of experience with pancreaticoduodenectomy had lower rates of hospital mortality.[23] However, higher procedure volume played a larger role than increased experience in reducing the mortality. Like almost all other authors who have studied the influence of hospital volume on outcome of pancreatic resection, Ho and Heslin recommend referral of patients to "centers of excellence."[23] In the single study by Wade et al, a positive volume-outcome relation was not obtained.[24] It is likely that this negative finding resulted form a lack of high-volume centers in the analysis.

An additional measure of surgical outcome is postoperative complication rate. Some of the studies on the volume-outcome association have included such information showing lower complication rate at high-volume hospitals after, eg, esophageal, pancreatic, prostatic, and thyroid surgery.[5,10,12,25,26] Another reflection of postoperative outcome is duration of hospital stay. Four studies reported shorter stay at high-volume centers after pancreaticoduodenectomy.[2,3,6,22] If complication rate is lower and hospital stay shorter, the costs should be reduced as well. This has been documented for at least four cancer operations: colorectal resection, esophagectomy, pancreatectomy, and total thyroidectomy.[2,5,20,26,27]

In addition to the influence of hospital volume on the early surgical outcome, there is an increasing bunch of evidence suggesting that patients live longer after operations at high-volume hospitals for cancer of, eg, the rectum, pancreas, and breast.[13,28–31] In an analysis of lung cancer, Bach et al found that patients treated at higher-volume hospitals were 25% more likely to be alive at 5 years compared with patients at very low volume hospitals.[16] Finlayson and Birkmeyer recently published a decision analysis where they assessed the impact of hospital volume on overall survival after surgery for pancreatic, lung, and colon cancer.[15] For all three cancers, life expectancy increased monotonically with hospital volume, meaning that life expectancy increased with each increase in hospital volume stratum. The authors incorporated both operative and late mortality in their model and found that the differences in life expectancy were largely attributable to differences in late mortality. The greatest gain for the individual patient was seen for pancreatic cancer. However, the potential number of life years gained from a population perspective was far greater for colon cancer surgery, which is the most common of the three procedures. The improved survival may, of course, not only be ascribed to better surgery but most probably also to better total management by the interdisciplinary treatment team.

In a National Health Service report from the United Kingdom on 2294 patients treated at 23 hospitals, it was

found that the risk of death among esophageal cancer patients, during the study period of 16 to 34 months from the time of the first presentation to the hospital, was 31% lower for those treated in hospitals that dealt with one new case per week than for those managed in hospitals seeing one new case a month.[14] The corresponding values for gastric and pancreatic cancer were 23% and 36%, respectively. Based on their own data and on the available international literature, the National Health Service in a recent report recommends that specialist treatment teams should be established at appropriate cancer centers or units.[32] Esophagogastric cancer teams should aim to draw patients from populations of more than 1 million; pancreatic cancer teams should aim to draw patients from populations of 2 to 4 million. Against the above backdrop, my answer to the question asked in the headline of this section is: yes, the evidence is enough compelling for the medical community and the health care providers to move ahead. Now, if the outcome is better at high-volume hospitals, why is it so?

WHAT EXPLAINS THE HIGHER VOLUME: BETTER OUTCOME ASSOCIATION?

To answer this question, one has to consider that the volume-outcome relationship usually is stronger for hospital volume than for surgeon volume. This has been ascribed to the "experience effect" of the whole team taking care of the patient.[20] Medical care is becoming more and more diagnosis based instead of discipline based as it has been up to now.

Two competing explanations for the observed association between volume and outcome have been advanced. The first ("practice makes perfect") hypothesizes that hospitals have better outcome because their case load and experience allow then to improve their systems and techniques. This is valid for the whole treatment team as well as for the surgeon alone. The second ("selective referral") hypothesizes that hospitals with better outcomes have larger volumes because their excellence is known and thus more patients come to be cared for in these hospitals. Which hypothesis is correct has not been established. I think, though, we all agree that specialization in surgery has led to improved results. Concentration of certain infrequent patient groups is per se a basis for specialization by allowing the surgeon and the treatment team to achieve large experience in specific areas.

ARGUMENTS FOR AND AGAINST THE HIGH-VOLUME CONCEPT

I should rather admit that I am a believer of the "practice makes better" concept even if I am well aware that individual quality and talent are needed in addition to experience for surgeons to reach optimal achievements. This emphasizes the importance of proper selection of residents for the various specialties. Normally, however, more experience leads to safer, better, and more complete cancer operations and better perioperative care. Furthermore, patients receiving their care in high-volumes centers are more likely to undergo adjuvant chemotherapy and/or radiation treatment.[32] If there is a specific interest in a particular patient group in a hospital, proper follow-up is more likely to be performed and clinical research requires a minimal critical patient mass to be meaningful. Furthermore, where should future cancer surgeons be trained? Well, of course, in centers with sufficient case load and experienced teachers, which you preferably find in high-volume hospitals. This training aspect is especially worrying in small countries with heavily decentralized health care system like Sweden where we today unfortunately are missing high-volume centers for more than one cancer diagnosis. Finally, it is well accepted that big costs in surgery to a great extent refer to operative complications.

There are, of course, also arguments against far-reaching concentration of certain patient groups to specialty centers. As I already have mentioned, several studies supporting the volume-outcome relationship harbor methodological limitations from a strict theoretical point of view, which antagonists have a tendency to overemphasize. Taken together the evidence of the volume effect on early surgical outcome is compelling and I feel confident that this will be true also for long-term survival in a few years.

Long travel distances can be a problem to some patients and their families. Many hospitals are already financially stressed, and losing patients will make it worse. Therefore, there is an opposition from many hospitals at risk. However, the most important obstacle is to my opinion the surgeon's ego and selfishness, and personal financial interests not to forget.

HOW FEW IS ENOUGH?

How few is enough? Do closely related procedures count? How should the effects of surgeon volume and hospital volume be combined? How should optimal thresholds be set and by whom? I have, unfortunately, no good answers to these questions. The only comment I can make is that the threshold is different for each and every operation and that the thresholds not only should consider the surgeon's perspective but also the team aspects and issues related to proper (compulsory?) reporting of results, to clinical research, to surgical teaching and training, and to procurement of specialized facilities and equipment. At the meeting this year of the American Surgical Association in Washington, DC, a promising method, in fact, was presented by which appropriate thresholds may be calculated.[33] The interaction between surgeon and hospital volume has been studied for colorectal cancer, and it was found that high hospital volume had a favorable impact on the outcomes of lower volume surgeons, raising their results to the level of high-volume surgeons.[26] A rule of thumb which I prefer is that to be allowed to practice a certain type of procedure so many of them must be done

annually that proper analysis of the results can be done and registered by the hospital.

PREEMPTIVE SURGERY: AN INCREASING CHALLENGE TO SURGICAL PERFECTION

Brennan has called our attention to the demands for technical perfection that will follow the increasing use of what he calls preemptive surgery, which is prophylactic operations for genetically predestined malignant disease.[34] This refocuses on the volume-outcome relationship and the request for risk-free operations. One can expect that more and more prophylactic operations will be accounted for by centralized and specialist units the more discoveries the geneticists are doing.

HOW TO PROMOTE THE USE OF HIGH-VOLUME CENTERS

The answer of this question is to some degree depending on what kind of health care system you have in your country. Irrespective of system, however, educating and informing patients and referring doctors on hospital volumes and outcomes for different procedures are usable. Public dissemination of performance data is already under way in some countries. More intrusive, regulatory means, eg, by national authorities or institutions, should be practicable in a country like Sweden with publicly financed health care. But also in the United States, such steps have been taken by the Leapfrog Group, a consortium of more than 100 large employers, purchasing coalitions, and states that collectively provide health insurance to more than 33 million people.[35] The group has set arbitrary volume thresholds for five different procedures. Other ways of financial incentives should be tested as well.

CONCLUSION

Data are, thus, accumulating that reasonable hospital volume is a plausible predictor of outcome after surgery for cancer. Even if the skill of the individual surgeon is important, it seems to be even more crucial that the multidisciplinary treatment team develops substantial experience in the management of the patients. It is becoming more and more difficult for the general surgeons to defend their preserves and to persist in undertaking cancer procedures once in a while. It is high time for us to pay regard to the higher volume-better outcome association for cancer surgery and cancer treatment. The changes are inevitable. It seems highly likely that regionalization of cancer surgery will be adopted in all countries with advanced health care systems. For the sake of the patients, surgical leaders in such countries should lead the way and unselfishly put the volume-output concept into practice.

REFERENCES

1. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med*. 1979;301:1364–1369.
2. Gordon TA, Burleyson GP, Tielsch JM, et al. The effects of regionalization on cost and outcome for one general high-risk surgical procedure. *Ann Surg*. 1995;221:43–49.
3. Lieberman MD, Kilburn H, Lindsey M, et al. Relation of perioperative deaths to hospital volume among patients undergoing pancreatic resection for malignancy. *Ann Surg*. 1995;222:638–645.
4. Begg CB, Cramer LD, Hoskin WJ, et al. Impact of hospital volume on operative mortality for major cancer surgery. *JAMA*. 1998;280:1747–1751.
5. Sosa JA, Bowman HM, Tielsch JA, et al. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. *Ann Surg*. 1998;228:320–330.
6. Birkmeyer JD, Finlayson SRG, Tosteson ANA, et al. Effect of hospital volume on in-hospital mortality with pancreaticoduodenectomy. *Surgery*. 1999;125:250–256.
7. Gouma DJ, van Geenen RCJ, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. *Ann Surg*. 2000;232:786–795.
8. Hannan EL, Radzyner M, Rubin D, et al. 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.
9. Birkmeyer JD, Siewers AE, Finlayson EVA, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med*. 2002;346:1128–1137.
10. Begg CB, Riedel ER, Bach PB, et al. Variations in morbidity after radical prostatectomy. *N Engl J Med*. 2002;346:1138–1144.
11. Schrag D, Panageas KS, Riedel E, et al. Hospital and surgeon procedure volume as predictors of outcome following rectal cancer resection. *Ann Surg*. 2002;236:583–592.
12. Dimick JB, Pronovost PJ, Cowan JA, et al. Surgical volume and quality of care for esophageal resection: do high-volume hospitals have fewer complications? *Ann Thorac Surg*. 2003;75:337–341.
13. Birkmeyer JD, Warshaw AL, Finlayson SRG, et al. Relationship between hospital volume and late survival after pancreaticoduodenectomy. *Surgery*. 1999;126:178–183.
14. Bachmann M, Alderson D, Peters T. Survival, clinical practice and costs in patients with pancreatic, esophageal and gastric cancers. In: *Influences of Doctor and Hospital Volumes*. Bristol: Departments of Social Medicine and Surgery, University of Bristol, 1999.
15. Finlayson EVA, Birkmeyer JD. Effects of hospital volume on life expectancy after selected cancer operations in older adults: a decision analysis. *J Am Coll Surg*. 2003;196:410–417.
16. Bach PB, Cramer LD, Schrag D, et al. The influence of hospital volume on survival after resection for lung cancer. *N Engl J Med*. 2001;345:181–188.
17. Ihse I. The association between higher volume and better outcome for pancreaticoduodenectomy. *HPB* 2001;3:153–155.
18. Dudley RA, Johansen KL, Brand R, et al. Selective referral to high-volume hospitals: estimating potentially avoidable deaths. *JAMA*. 2000;283:1159–1166.
19. Glasgow RE, Mulvihill SJ. Hospital volume influences outcome in patients undergoing pancreatic resection for cancer. *West J Med*. 1996;165:294–300.
20. Sosa JS, Bowman HM, Gordon TA, et al. Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg*. 1998;228:429–438.
21. Halm EA, Lee C, Chassin MR. Is volume related to quality in health care. A systematic review and methodologic critique of the research literature. *Ann Intern Med*. 2002;137:511–520.
22. Simunovic M, To T, Theriault M, et al. Relation between hospital surgical volume and outcome for pancreatic resection for neoplasm in a publicly funded health care system. *CMAJ*. 1999;160:643–648.
23. Ho V, Heslin MJ. Effect of hospital volume and experience on in-hospital mortality for pancreaticoduodenectomy. *Ann Surg*. 2003;237:509–514.
24. Wade TP, Halaby IA, Stapleton DR, et al. Population-based analysis of

treatment of pancreatic cancer and Whipple resection: Department of Defense Hospitals, 1989–1994. *Surgery*. 1996;120:680–687.
25. Edge SB, Schmieg RE Jr, Rosenlof LK, et al. Pancreas cancer resection outcome in American university centers in 1989–1990. *Cancer*. 1993; 71:3502–3508.
26. Swisher SG, Deford L, Merriman KW, et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. *J Thorac Cardiovasc Surg*. 2000;119:1126–1132.
27. Harmon JW, Tang DG, Gordon TA, et al. Hospital volume can serve as a surrogate for surgeon volume for achieving excellent outcome in colorectal resection. *Ann Surg*. 1999;230:404–413.
28. Porter GA, Soskolne CL, Yakimets WW, et al. Surgeon-related factors and outcome in rectal cancer. *Ann Surg*. 1998;227:157–167.
29. Sainsbury R, Haward B, Rider L, et al. Influence of clinician workload and patterns of treatment on survival from breast cancer. *Lancet*. 1995; 345:1265–1270.
30. Gillis CR, Hole DJ. Survival outcome of care by specialist surgeons in breast cancer: a study 3786 patients in the west of Scotland. *Br Med J*. 1996;312:145–153.
31. Roohan PJ, Bickell NA, Baptiste MS, et al. Hospital volume differences and five-year survival from breast cancer. *Am J Public Health*. 1998; 88:454–457.
32. Management of upper gastrointestinal cancer. Effective Health Care 2000;6:1–16. NHS Centre for Reviews and Dissemination.
33. Christian CK, Zinner MJ, Gustafson ML, et al. The Leapfrog volume criteria may fall short in identifying high quality surgical centers [abstract]. American Surgical Association Meeting, Washington DC, 2003.
34. Brennan MF. Pre-emptive surgery and increasing demands for technical perfection. *Br J Surg*. 2003;90:3–4.
35. Birkmeyer JD, Finlayson EVA, Birkmeyer CM. Volume standards for high-risk surgery: potential benefits of the Leapfrog initiative. *Surgery*. 2001;130:415–422.