The Relationship Between Hospital Volume and Outcomes of Hepatic Resection for Hepatocellular Carcinoma

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Background: Volume-outcome relations have been established for several complex therapies. However, few studies have examined volume-outcome relations for high-risk procedures in general surgery, such as hepatectomy for hepatocellular carcinoma (HCC).

Objective: To evaluate the relation between hospital volume and outcome for patients undergoing hepatectomy for HCC.

Design: Retrospective cohort study.

Setting: All acute-care hospitals in California.

Patients: Hospital discharge data were analyzed for each patient in California who underwent major hepatic resection for HCC from January 1, 1990, through December 31, 1994. Hospitals were grouped according to number of hepatectomies performed at each center during the 5-year study.

Main Outcome Measures: Outcome measures included operative mortality and length of hospital stay. Regression analyses were used to adjust for differences in patient mix.

Results: Five hundred seven patients underwent hepatectomy for HCC during the study. Hepatic resections were performed in 138 hospitals, with an overall in-hospital mortality rate of 14.8%. Three quarters of patients were treated at hospitals that average 3 or fewer hepatic resections for HCC per year. These low-volume providers represent 97.1% of all hospitals treating patients with HCC statewide. Significant reductions in risk-adjusted operative mortality rates (22.7%-9.4%; \( P = .002 \), multiple logistic regression) and risk-adjusted length of stay (14.3-11.3 days; \( P = .03 \), multiple linear regression) were observed as hospital volume increased.

Conclusions: Low operative mortality and length of stay were associated with high-volume centers. These data support regionalization of high-risk procedures in general surgery, such as hepatectomy for HCC.

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Today’s changing health care environment is being driven, in part, by external pressures on providers to deliver economical, high-quality care. For some medical therapies, quality of care varies little among providers, making cost a primary focus. For other treatments, however, quality of care is not uniform. Such is the case with coronary angioplasty, coronary surgery, and bone marrow and solid organ transplantation. For these complex therapies, a volume-outcome relationship exists where poor patient outcome, such as in-hospital mortality, is related to low provider volume and inexperience. These volume-outcome relations serve as the basis for the argument that high-risk procedures should be regionalized to centers of excellence.

In the case of coronary angioplasty, coronary surgery, and transplantation, regionalization is beginning to occur as payers selectively contract with providers for these services. However, this is not the case with other complex therapies. In general surgical practice, standards for the minimum of experience necessary to perform highly complex and risky procedures, i.e., major hepatic, pancreatic, or esophageal resection for neoplasia, do not exist. The number of these complex operations performed each year is insufficient for all surgeons and hospitals to have experience. Most of these operations are performed on an elective rather than emergent basis. Thus, if centers with superior patient outcomes could be identified, these procedures could be regionalized as a means of providing the most efficacious and cost-effective care.

See Invited Critique at end of article
MATERIALS AND METHODS

DATA SOURCES

We retrospectively analyzed standardized patient discharge abstracts obtained from the California Office of Statewide Health Planning and Development (OSHPD), Sacramento. This database contains discharge data abstracts for every patient hospitalization from every acute-care facility in the state of California. Each abstract includes a variety of demographic, clinical, and hospitalization data that characterize a specific hospitalization. Each patient is assigned a principal diagnosis and procedure and up to 16 secondary diagnoses and procedures. The OSHPD database uses diagnostic and procedural codes derived from the International Classification of Diseases, Ninth Revision, Clinical Modification (4th ed) (ICD-9-CM), issued by the US Department of Health and Human Services.9

All discharge abstracts from January 1, 1990, through December 31, 1994, were included in the initial search of the OSHPD database. From these abstracts, all patients who underwent hepatic lobectomy (ICD-9-CM code 50.3) or partial hepatectomy (ICD-9-CM code 50.2) were examined. From this group, a subset of patients undergoing hepatic resection for HCC was selected (ICD-9-CM code 155.0). Hospitals were characterized with regard to the number of acute and intensive care beds, discharges and patient hospital days per year, yearly overall surgical volume and number of hepatic resections for benign and malignant neoplasia, presence of a liver transplantation program and general surgery residency program, university affiliation, and capability for other complex surgery, as determined by the presence of cardiac surgery services. These data were derived, in part, from the Licensed Services and Utilization Profiles: Annual Report of Hospitals for January 11, 1991, through December 31, 1991.10 Frequency distributions for the individual patient characteristics within the data set and hospital characteristics listed above were computed.

DATA ANALYSIS

Patients were grouped according to hospital identification number. Hospitals were then classified into quartile groups based on the number of hepatic resections performed in the study period. Crude operative mortality rate and length of hospital stay were calculated for each volume range. Operative mortality in this study was defined as patient death before hospital discharge. Because length of hospital stay is directly related to events within the postoperative course, patients with long hospital stays are most likely patients in whom significant perioperative complications develop. Thus, the percentage of patients with hospital stays longer than the 75th percentile (14 days) was calculated for each volume group. This measure served as a surrogate for postoperative complications, as other reliable objective measures of postoperative complications were not directly available within this database. To characterize a profile of hospitals within each volume group, the distribution of the various hospital characteristics was analyzed.

Regression modeling was used to evaluate the independent associations of patient and hospital characteristics with the primary outcomes of interest (ie, operative mortality and length of hospital stay). The patient was the unit of analysis, with hospital volume group defined as a patient characteristic. This allowed for a volume group effect to be assessed while controlling for the characteristics of individual patients. Multiple logistic regression was used to model the dichotomous outcome, in-hospital mortality, and multiple linear regression was used to model length of hospital stay.

The independent variables in these analyses included hospital volume, age group, sex, year of surgery, source of admission, type of resection (hepatic lobectomy or partial hepatectomy), presence of chronic liver disease, and presence of other preoperative comorbid illneses. Age was entered into the regression equations as the following sets of dummy variables: 45 to 60 years, 60 to 75 years, and older than 75 years, with younger than 45 years as the reference group. Significant preoperative comorbid illnesses within a given patient abstract were grouped into 1 dichotomous variable to minimize potential colinearities among the various comorbidities. For example, patients with a history of congestive heart failure are likely to also have coronary artery disease. We believed the following comorbidities to have a significant influence on operative risk: coronary artery disease (ICD-9-CM codes 412-414), chronic obstructive pulmonary disease (ICD-9-CM codes 490-496), diabetes mellitus (ICD-9-CM codes 250), congestive heart failure (ICD-9-CM code 428), nutritional deficiencies (ICD-9-CM codes 260-263), and preoperative intra-abdominal hemorrhage (ICD-9-CM code 499). The presence of chronic liver disease, including cirrhosis (ICD-9-CM code 571), was treated as a separate dichotomous variable, as it represents an independent factor associated with poor operative risk. The dependent variables for these analyses were operative mortality or death before discharge and length of hospital stay.

Adjusted means for operative mortality rate and length of hospital stay were calculated from regression equations that included all of the independent variables. A complete description of the process of adjustment is provided by Cohen and Cohen.11 An adjusted mean is an estimate based on the hypothetical situation that all hospital volume groups had the same mean values on each of the independent variables that were entered into the equation. In other words, the adjusted mean represents the estimated operative mortality rate or length of stay if each of the volume groups treated patients with similar patient characteristics. To further evaluate this volume-outcome relation, an additional analysis was performed, where hospital volume was defined by the total number of hepatic resections for benign and malignant neoplasia, including metastatic disease.

A key goal of any reorganization of health care delivery practices in the United States is to preserve or improve quality while reducing costs. Quality of a surgical procedure is measured by operative morbidity and mortality, outcome, effectiveness compared with alternate therapies, and patient satisfaction. It is an open question whether regionalization of high-risk procedures in general surgical practice is desirable or warranted from this standpoint. To help answer this question, we analyzed the relation between hospital volume and postoperative outcome in 1 high-risk, complex general surgical operation, major hepatic resection for hepatocellular carcinoma (HCC). We hypothesized that the risk, as measured by operative mortality, and the cost, as measured by length of hospital stay, are reduced when these patients...
During the study, 507 patients underwent major hepatic resection for HCC in the state of California. The number of resections performed each year was relatively constant, ranging from 117 in 1990 to 87 in 1993 (Table 1). A total of 138 hospitals reported to the database during the 5 years but, because a hepatic resection was not performed at all hospitals in each year, the yearly average number of hospitals in which a hepatic resection for HCC was performed was 53 (Table 1).

Patient age were distributed as seen in the following tabulation:

<table>
<thead>
<tr>
<th>Age Range, y</th>
<th>No. (% of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>126 (24.8)</td>
</tr>
<tr>
<td>45-59</td>
<td>125 (24.6)</td>
</tr>
<tr>
<td>60-74</td>
<td>203 (40.0)</td>
</tr>
<tr>
<td>≥75</td>
<td>53 (10.4)</td>
</tr>
</tbody>
</table>

The median age was 60 to 64 years. Men outnumbered women by a ratio of nearly 3:2 (293 [57.8%] vs 214 [42.2%], respectively). The most common race of treated patients was white (263 [51.9%] of the study population), followed by Asian (135 [26.6%]), Hispanic (68 [13.4%]), other (21 [4.1%]), and African American (20 [3.9%]). Payer source is presented in the following tabulation:

<table>
<thead>
<tr>
<th>Source</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare</td>
<td>160 (31.6)</td>
</tr>
<tr>
<td>Medi-Cal</td>
<td>76 (15.0)</td>
</tr>
<tr>
<td>Blue Cross/Blue Shield</td>
<td>28 (5.5)</td>
</tr>
<tr>
<td>Private insurance</td>
<td>94 (18.5)</td>
</tr>
<tr>
<td>Health maintenance or preferred</td>
<td>128 (25.2)</td>
</tr>
<tr>
<td>health provider organization</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>21 (4.1)</td>
</tr>
</tbody>
</table>

Source of admission and presence of comorbid medical illnesses were analyzed as indicators of severity of illness. Patients transferred from other acute-care hospitals and those admitted on an elective basis for surgery far outnumbered patients admitted from the emergency department (453 [89.3%] vs 54 [10.6%]). Preoperative comorbidities included diabetes mellitus (46 [9.1%]), coronary artery disease (37 [7.3%]), chronic obstructive pulmonary disease (36 [7.1%]), chronic nutritional deficiencies (17 [3.4%]), congestive heart failure (9 [1.8%]), and chronic renal insufficiency (6 [1.2%]). Eight patients, or 1.6% of the total, presented emergently with a diagnosis of intra-abdominal hemorrhage. Six (11.1%) of the 54 patients admitted through the emergency department had a diagnosis of intra-abdominal hemorrhage, compared with 2 (0.4%) of the 453 patients admitted on a routine basis or transferred from another acute-care facility. The median number of significant comorbidities per patient was 0, with a mean ± SE of 0.70 ± 0.04.

Chronic liver disease, including cirrhosis, was present in 192 (37.9%) of patients overall. For patients with chronic liver disease, the crude operative mortality rate was 27.1% compared with 7.3% in patients without chronic liver disease (P<.001 by χ² analysis). Likewise, increasing number of comorbidities correlated with increased crude operative mortality. For patients with no comorbidities, the operative mortality was 5.0%. This rate increased significantly with increasing number of secondary diagnoses (P<.001 by linear regression analysis). For patients with 4 or more comorbidities, the operative mortality was 50.0%. Partial hepatectomy (ICD-9-CM code 50.22) was performed in 299 patients compared with 208 patients who underwent hepatic lobectomy (ICD-9-CM code 50.3).

Each of the 4 volume groups included approximately 127 patients (25.0% of the total number of patients). One half of all patients were treated at centers where 6 or fewer resections were performed during the study (Table 2). These centers accounted for 88.4% of all reporting hospitals. In contrast, the highest-volume centers averaged 37 patients each during the 5 years and accounted for only 2.9% of the reporting hospitals statewide.

Hospital volume groups varied widely with regard to hospital characteristics (Table 3). The highest-volume providers were larger, with more acute and intensive care unit beds and more discharges and patient days per year. They also were more likely to be university hospitals with a general surgery residency training program. In addition to a higher overall surgical volume per year, the highest-volume providers were more likely to perform other complex operations (ie, coronary artery bypass) and to have a higher overall volume of hepatic resections for benign and malignant neoplasia. Three of the 4 highest-volume providers had a liver transplantation program, indicating an institutional interest in hepatology and hepatic surgery. In contrast, none of the lowest-volume providers performed liver transplantation.

The overall mortality rate for the study population was 14.8%. Crude operative mortality rates decreased with increasing hospital volume, from 24.4% in the lowest-volume centers to 6.2% in the highest-volume centers (Table 4). This inverse relationship between decreasing operative mortality rate and increasing hospital volume is summarized in the Figure. This relationship was highly significant (P<.001).
survived (18.4 ± 2.24 vs 12.0 ± 0.42 days). When patients who died was longer than that for patients who
complicated postoperative courses than patients treated at high-
lowest-volume providers were twice as likely to have com-
this significant volume-outcome relationship persisted (Table 4).
the length of hospital stay for each volume group was ad-
had a mean length of stay of 14.7 days compared with 10.8
days in the highest-volume providers (Table 4). In addition, lowest-volume providers were more
\[ \text{Mean (±SEM) length of stay for each volume group} = \text{adjusted to account for differences in patient characteristics,} \]
by logistic regression analysis). When the crude mortality rates for each volume group were adjusted to account for
differences in patient characteristics, this highly significant
volume-outcome relationship persisted (Table 4).
A similar volume-outcome relationship was observed when length of hospital stay was analyzed. The mean
crude mortality rates for each volume group were adjusted to account for differences in patient characteristics, this highly significant
volume-outcome relationship persisted (Table 4).

### Table 3. Hospital Characteristics by Hospital Volume Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All</th>
<th>1-2</th>
<th>3-6</th>
<th>7-16</th>
<th>≥17</th>
</tr>
</thead>
<tbody>
<tr>
<td>University hospital, %</td>
<td>6.5</td>
<td>0.0</td>
<td>12.5</td>
<td>25.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Liver transplantation program, %</td>
<td>8.0</td>
<td>0.0</td>
<td>12.5</td>
<td>33.3</td>
<td>75.0</td>
</tr>
<tr>
<td>Residency training center, %</td>
<td>18.7</td>
<td>7.0</td>
<td>37.5</td>
<td>33.3</td>
<td>75.0</td>
</tr>
<tr>
<td>No. of acute-care beds, mean ± SEM*</td>
<td>302 ± 18</td>
<td>243 ± 20</td>
<td>337 ± 32</td>
<td>493 ± 53</td>
<td>734 ± 92</td>
</tr>
<tr>
<td>No. of discharges/y, mean ± SEM*</td>
<td>63 877 ± 4130</td>
<td>47 548 ± 4224</td>
<td>74 753 ± 6684</td>
<td>114 606 ± 11 242</td>
<td>171 701 ± 19 472</td>
</tr>
<tr>
<td>No. of intensive care unit beds, mean ± SEM*</td>
<td>11 906 ± 738</td>
<td>9498 ± 789</td>
<td>12 643 ± 0.2</td>
<td>21 273 ± 2099</td>
<td>29 056 ± 3637</td>
</tr>
<tr>
<td>No. of operations/y, mean ± SEM*</td>
<td>21.3 ± 1.7</td>
<td>14.4 ± 1.7</td>
<td>28.2 ± 2.9</td>
<td>39.8 ± 4.7</td>
<td>56.7 ± 8.1</td>
</tr>
<tr>
<td>No. of hepatotomies for neoplasia in 1990 through 1994, mean ± SEM†</td>
<td>7356 ± 482</td>
<td>5808 ± 532</td>
<td>8022 ± 862</td>
<td>13 456 ± 1408</td>
<td>16 245 ± 2439</td>
</tr>
<tr>
<td>Cardiac surgery center, %‡</td>
<td>54</td>
<td>45.6</td>
<td>62.5</td>
<td>83.3</td>
<td>100</td>
</tr>
</tbody>
</table>

*P < .001 by analysis of variance, linear regression analysis.
† Indicates January 1, 1990, through December 31, 1994.
‡P < .01 by analysis of variance, logistic regression analysis.

### Table 4. Crude and Adjusted Operative Mortality Rates by Hospital Volume Groups

<table>
<thead>
<tr>
<th>Hospital Volume Group, No. of Operations/5 y</th>
<th>Crude Operative Mortality Rate, Mean %*</th>
<th>Risk-Adjusted Operative Mortality Rate, Mean %†‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>24.4</td>
<td>22.7</td>
</tr>
<tr>
<td>3-6</td>
<td>16.2</td>
<td>13.3</td>
</tr>
<tr>
<td>7-16</td>
<td>14.7</td>
<td>15.4</td>
</tr>
<tr>
<td>≥17</td>
<td>6.2‡</td>
<td>9.4</td>
</tr>
<tr>
<td>All</td>
<td>14.8</td>
<td>. . .</td>
</tr>
</tbody>
</table>

* P < .001, using logistic regression analysis.
† Indicates risk-adjusted using multiple logistic regression analysis for sex, age, year of operation, source of admission, type of resection, presence of chronic liver disease, and presence of significant comorbid illnesses.
‡P < .05, hospitals with 17 or more operations vs those with 1 to 2, 3 to 6, and 7 to 16; hospitals with 1 to 2 operations vs those with 3 to 6, 7 to 16, and ≥17; and hospitals with ≥17 operations vs those with 1 to 2, using multiple logistic regression analysis.
§P < .05, hospitals with ≥17 operations vs those with 1 to 2, 3 to 6, and 7 to 16, using χ² analysis.
†Not applicable.

who died were excluded from the length-of-stay analysis, a significant volume outcome relationship persisted.

When hospital volume was defined as total number of hepatic resections for benign and malignant neoplasia, these significant volume-outcome relations persisted. In 2004 patients, the overall operative mortality rate was 6.9%, ranging from 9.3% in the lowest-volume providers to 4.1% in the highest-volume providers.

**COMMENT**

In an era of limited resources, increased attention is being paid in the United States to the most efficient delivery of health care services. The desired goal is to provide the highest quality of care while using the fewest resources. Volume-outcome analyses have shown that for certain complex surgical procedures, including heart transplantation and coronary artery bypass, the results of treatment are directly linked to experience. These observations have led to the suggestion that these complex, high-risk procedures should be regionalized to high-volume centers of excellence. To determine if similar volume-outcome relations exist in general surgical practice, we examined the relation between hospital volume
and operative outcome in 1 complex, high-risk procedure, hepatic resection for HCC.

Hepatic resection was selected for this analysis because it represents a technically challenging, resource-intensive procedure. Hepatic resection may be performed at any hospital, as there are no certificate-of-need requirements or other measures in place to regulate where such operations are performed. Similar to other complex, high-risk operations in general surgery, most hepatic resections are performed on an elective basis, making it possible for such cases to be regionalized to high-volume centers of excellence. Furthermore, hepatectomy for HCC is an infrequently performed procedure for which the average surgeon or hospital is not likely to have substantial experience. Hepatocellular carcinoma was selected as a model in this study, because it is a diagnosis for which major hepatic resection would be considered and represents a disease entity associated with significantly higher rates of operative morbidity and mortality compared with hepatic resection for other indications.\textsuperscript{12-14}

Our main finding was a highly significant relationship between hospital volume and operative outcome for patients undergoing hepatic resection for HCC in California during the 5-year study. The sample size was large, encompassing 507 patients treated at 138 hospitals. The effect of hospital volume on operative mortality was substantial, with a 4-fold difference in mortality between the lowest- and highest-volume groups. In addition to reduced operative mortality rates, high-volume centers were found to have shorter average lengths of hospital stay. These findings suggest that the highest-volume hospitals not only treat patients undergoing hepatic resection for HCC with substantially lower operative mortality, but also accomplish this by using fewer resources.

There are 3 possible explanations for these results. First, the data may have been flawed, and systematic reporting or coding errors may have favored the highest-volume providers. In previous studies of population database reliability, a 10% to 30% error rate in diagnosis and procedure coding has been reported.\textsuperscript{15-17} In our study, concordance between diagnosis and procedure codes was required for each patient as part of the inclusion criteria, thereby reducing the number of erroneously coded patient discharge abstracts from further analysis. An error rate of only 1% has been identified in the reporting of the end point of patient mortality when the OSHPD database has been reconciled to primary data from individual patient medical records.\textsuperscript{15} This error rate is not sufficiently large to explain the differences in operative mortality found between low- and high-volume hospitals in this study.

Second, differences in patient characteristics could account for the observed variations in patient outcome. We controlled for these differences in 2 ways. First, the data were pooled by hospital volume such that the number of patients in each volume group was sufficiently large to offset small differences in patient mix at any one hospital. Second, we used multivariate statistical techniques to adjust mortality rates and length of hospital stay for differences in patient characteristics. This risk adjustment did not alter the primary finding of a highly significant association between hospital volume and patient outcome. Additional risks may have been present but not identifiable in the OSHPD database, and the distribution of patients with these unknown risk factors may have been skewed toward hospitals with low volume, but this seems unlikely.

Finally, our findings probably represent true differences in outcome related to variations in patient care in hospitals of various volume groups. Supporting evidence suggests that this interpretation of the data is correct. First, the overall operative mortality rate of 14.8% and the rates for the lower-volume hospital groups in this study are comparable to previously reported operative mortality rates for this procedure in other large-population studies, including the nationwide Veterans Administration experience.\textsuperscript{14} Second, the operative mortality rates of the highest-volume centers in our study mirror the recently published results of other high-volume centers around the world.\textsuperscript{12,18-21} Therefore, the recently cited improvements in operative outcome in patients undergoing hepatectomy for HCC may apply only to high-volume centers and not more generally to the medical community. Finally, when the analysis in our study was extended to hepatic resection for all benign and malignant neoplasia, the volume-outcome relation persisted.

Only a limited insight into potential differences in patient care leading to lower operative mortality in the high-volume centers could be gleaned from the available data. High-volume centers were larger hospitals with higher overall surgical volume and university and residency program affiliation. They were more likely to perform other complex operations, such as cardiac surgery. The highest-volume providers performed a greater overall number of hepatic resections per year, and 3 of 4 had active liver transplantation programs, compared with none of the lowest-volume providers. Furthermore, a greater percentage of patients treated at low-volume providers had extended hospital stays, suggesting complicated postoperative courses. Patients treated at high-volume centers were less likely to have postoperative complications, or these centers have developed the means to better manage these complications should they arise. Thus, the improved in-hospital mortality rates and shorter lengths of hospital stay for patients with HCC at high-volume cen-
The article from Glasgow et al for the first time describes the relationship between high volume and outcome after liver resection for HCC. The authors clearly demonstrate lower postoperative mortality rates and a shorter hospital stay for resections. These results are not surprising, as Gordon et al have already shown lower postoperative morbidity and mortality rates for other intricate oncological operations in visceral surgery: the early results after the Whipple operation were distinctly better in high-volume centers. Similar results have been published for orthopedic and traumatological operations, cardiac and vascular surgery, and gynecological operations. This proves that not only specific surgical technical skills but the combination of a well-equipped center with potent intensive care and experienced anesthesiologists as well as a general training for large operations are important for successful therapy. In conclusion, we merely learn a truism.

In oncological surgery, however, the late results after 5 or 10 years, depending on tumor stage, additional therapies, and the surgeon, are crucial. To our knowledge, only Anderson et al in a prospective study and Hermanek et al in a multicenter observation have proven that the surgeon actually can be a bigger risk factor for the prognosis of the patient than the tumor stage. Recently, similar results for breast cancer have been reported from a multicenter study in Denmark.

The study by Glasgow et al is a step in the right direction; however, further studies for longer observation periods focusing on surgeon and center should be encouraged, as only these can sufficiently prove the success or failure of different surgical oncological concepts. In his programmatic presentation of the future work of the American College of Surgeons, Wells showed perspectives that we must follow. Similar concepts also exist in several centers in Europe; we hope that new focused knowledge will be generated here through the European unification process.

REFERENCES