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ORIGINAL ARTICLE

Surgeon Volume is Predictive of 5-Year Survival in Patients with Hepatocellular Carcinoma after Resection: A Population-Based Study

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Abstract

Background and Aim No study has examined associations between physician volume or hospital volume and survival in patients with liver malignancies in the hepatitis B virus-endemic areas such as Taiwan. This study was to examine the effect of hospital and surgeon volume on 5-year survival and to determine whether hospital or surgeon volume is the stronger predictor in patients with hepatocellular carcinoma after hepatic resection in Taiwan.

Methods Using the 1997–1999 Taiwan National Health Insurance Research Database and the 1997–2004 Cause of Death Data File, we identified 2,799 patients who underwent hepatic resection and 1,836 deaths during the 5-year follow-up period. The Cox proportional hazard regressions were performed to adjust for patient demographics, comorbidity, physician, and hospital characteristics when assessing the association of hospital and surgeon volume with 5-year survival.

Results When we examined the effect of physician and hospital volumes separately, both physician and hospital volumes significantly predicted 5-year survival after adjusting for characteristics of patient, surgeon, and hospital. However, after we adjusted for characteristics of physician and hospital, only physician volume remained a significant predictor of the 5-year survival.

Conclusions Physician volume is a stronger predictor of 5-year survival in hepatocellular carcinoma patients receiving hepatic resection.

Keywords Hepatocellular carcinoma · Survival · Hospital volume · Physician volume · Taiwan

Introduction

Hepatocellular carcinoma (HCC) is the most common cancer in Taiwan in terms of both incidence and mortality. HCC has been the second leading cause of cancer death in Taiwan.[1] The high-risk group for HCC in Taiwan includes patients chronically infected with hepatitis B virus (HBV) or hepatitis C virus (HCV) and liver cirrhosis or a family history of HCC, HBV, or HCV chronic infections, which are the two major etiologies for HCC in Taiwan.[2] The last three decades has seen remarkable advances in hepatic surgery.[3] Hepatic surgeries are now a safe and effective therapy and one of the curative therapies for liver cancer.[4,5]

One of the most important issues of surgical oncology is to identify prognostic factors that influence the length of survival for cancer patients. Associations between hospital or physician volume and patient outcomes have been established for many surgical and other invasive procedures, with lower mortality among patients treated at hospitals or by physicians with higher procedural volumes.[6–8] Improved overall long-term survival in patients with HCC has resulted in an increased number of liver resection being performed with an increasingly aggressive surgical approach.[9] However, no study has examined

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associations between physician volume or hospital volume and survival in patients with liver malignancies in the HBV-endemic areas such as Taiwan. Most of the hepatic resections for malignancies are performed on an elective, rather than emergent, basis. 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.[10] Identification of factors contributing to better survival will help clinicians or policy makers to develop effective strategies to improve the quality care of HCC and survival.

A rapid rise in mortality from HCC has been observed in Taiwan since 1991 in patients aged greater than 20 years. Important efforts have been made to improve the survival rates of patients with HCC. However, despite scientific advances and the implementation of measures for early HCC detection in patients at risk, patient survival has not improved during the last three decades.[11] The 5-year survival for asymptomatic small HCC is approximately 50% after surgical resection.[12] To determine whether surgeon and hospital volumes are independent predictors of 5-year survival after resection of HCC, we examined the association of both volume elements with 5-year survival in a national sample in Taiwan. We also investigated whether physician or hospital volume was more strongly associated with 5-year survival.

Materials and Methods

Database

Two databases were used in this study. First, the Taiwan National Health Insurance Research Database (NHIRD), published by the Taiwan National Health Research Institute, was used to obtain hospitalization data. The NHIRD is possibly one of the largest and most comprehensive databases; it covers 96% of the Taiwanese population of some 23 million. The NHIRD included medical claims for inpatient expenditures by admissions, details of inpatient orders, and registry for contracted medical facilities, board-certified specialists, medical personnel, and beneficiaries. One principal diagnosis and procedure based on the 'International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM)' code and up to four secondary diagnoses and procedures using ICD-9-CM codes are listed for each patient.

Second, the mortality date was obtained from the Cause of Death Data File published by Taiwan's Department of Health (DOH) covering the years 1997–2004. The Cause of Death file provides data on marital status, the date of birth and death, place of legal residence, underlying cause of death (ICD-9-CM code), and employment status. The data are believed to be very accurate and complete because of mandatory registration of all births and deaths in Taiwan. The NHIRD was linked to the Cause of Death Data File with the assistance of Taiwan's DOH.

Study Subjects

All hospitalized patients from the NHIRD covering the period 1997–1999 by a principal diagnosis of malignant neoplasm of liver and intrahepatic bile ducts (ICD-9-CM codes 155.XX) were selected as our study sample (n= 34,158). We limited the cases to those who underwent a liver lobectomy (ICD-9-CM procedure code 50.3) or partial hepatectomy (ICD-9-CM procedure code 50.22), and 3,159 cases were left. In addition, those patients who were also diagnosed with secondary and unspecified malignant neoplasm (ICD-9-CM codes 196.XX–199.XX), malignant neoplasm of intrahepatic bile ducts (ICD-9-CM code 155.1), or malignant neoplasm of liver, not specified as primary or secondary (ICD-9-CM code 155.2), were all excluded from the study sample. Ultimately, we were left with a sample of 2,799 eligible subjects with primary liver malignancy and underwent hepatectomies during the period of the study.

Five-year follow-up were subsequently undertaken in order to determine whether any of the sampled patients were dead within a 5-year period after hepatic resections. All cause mortality was used except those who died of accidents (ICD-9-CM codes E800–E869, E880–E928, and E950–E999). In total, 1,836 deaths were identified, regardless of time of occurrence, during the 5-year follow-up period.

Surgeon and Hospital Hepatectomy Volume Groups

Since unique physician and hospital identifiers are available within the NHIRD for each medical claim submitted, this enabled us to identify the same physician, or the same hospital, carrying out one or more hepatectomies during our 3-year study period. Surgeons and hospitals were sorted, in ascending order of their total volume of liver cancer resections, with the cutoff points (high, medium, and low) being determined by the volume that most closely sorted the sample patients into three groups, which were roughly equivalent in size. The sample of 2,799 patients was divided into three surgeon volume groups: ≤19 cases (hereafter referred to as low volume), 20–95 cases (medium volume), and ≥96 cases (high volume), while the three hospital volume groups were ≤87 cases (low volume), 88–298 cases (medium volume), and ≥299 cases (high volume).

Key Variables of Interest

The key dependent variable of interest was “5-year survival,” with “patient” as the unit of analysis, and the key independent variables were the “hepatectomy volume groups” for both surgeons and hospitals.

The characteristics of surgeon, hospital, and patient were taken into account in our study. Surgeon characteristics included the surgeon’s age (as a surrogate for practice experience) and gender; hospital characteristics included hospital ownership, hospital level, teaching status, and geographical location, with the hospital ownership variable being recorded as one of three types, “public,” “private not-for-profit” and “private for-profit” hospitals. Within the hospital level variable, each hospital was classified as a medical center (with a minimum of 500 beds), a regional hospital (minimum 250 beds), or a district hospital (minimum 20 beds); hospital level can therefore be used as a proxy for both hospital size and clinical service capabilities.

Patient characteristics comprised of age, gender, severity of illness, and type of operation. Age was not linearly associated with survival and was categorized into four groups (<50, 50–64, 65–74, and >74). Since no illness severity index is currently available in Taiwan, we used a modified Charlson’s index, the Deyo–Charlson index, to adjust for the patients’ clinical comorbidities; the Deyo–Charlson index has been used as a means of adjusting for the higher mortality risks associated with comorbidities and has been widely used since then for risk adjustment in administrative claims datasets. Higher scores on Charlson’s index indicate more illness severity. The “type of operation” comprised of partial hepatectomy and liver lobectomy.

Statistical Analysis

The SAS statistical package (SAS System for Windows, Version 8.2) was used to perform the statistical analysis of the data in this study. The distribution of characteristics of surgeon, hospital, and patient according to surgeon and hospital hepatectomy volume groups were examined by χ^2 or ANOVA test. Five-year cumulative survival estimates and survival curves were calculated using the Kaplan–Meier method and compared by means of the log-rank test by surgeon and hospital volume. Survival time was computed from the date of hepatectomy to the date of death within the 5-year follow-up period. In order to account for possible clustering effects within each surgeon or hospital panel, we used stratified Cox regression models to evaluate the contributions of surgeon and hospital volume to 5-year survival while adjusting for the characteristics of surgeon, hospital, and patient. Hazard ratios and 95% confidence intervals are presented. A two-sided p value of less than or equal to 0.05 was considered statistically significant.

Results

Table 1 describes the distribution of the characteristics of surgeons and patients by surgeon hepatectomy volume group. Hepatectomies were performed by 286 surgeons between January 1997 and December 1999, at a mean volume per surgeon of 9.8 operations. Of the total of 2,799 patients, 996 (35.6%) had undergone liver lobectomy, and the other 1,803 (64.4%) had partial hepatectomy. The surgeons in the high-volume group were more likely to be older ($p<0.001$). Patients in the low-volume group, on average, had higher Charlson Comorbidity Index Score than their counterparts in other groups ($p<0.001$).

Table 2 presents the characteristics of hospital and patients, classified by three hospital hepatectomy volume group. Hepatectomies were carried out by 90 hospitals between 1997 and 1999, at a mean volume of 31.2 resections per hospital. The vast majority of the hospitals (92.2%) fell into the low-volume group; these hospitals were generally located in the northern part of Taiwan. All hospitals in the medium- and high-volume groups are medical centers and teaching hospitals. Patients treated by surgeons in low-volume group were more likely to undergo liver lobectomies ($p<0.001$).

Figures 1 and 2 illustrate the unadjusted 5-year survival of patients by surgeon and hospital volume. The log-rank tests show that patients treated by high-volume surgeons or hospitals had significantly greater 5-year survival (both $p<0.001$).

Table 3 provides the 5-year survival rate, crude hazard ratios and adjusted hazard ratios by hospital and surgeon volume group. Five-year survival rate increased with increasing surgeon volume group; it was 33.7%, 40.8%, and 46.8% for sampled patients in low-, medium-, and high-volume groups, respectively, while the 5-year survival rate was 34.0%, 45.1%, and 43.1% for sampled patients in low-, medium-, and high-volume hospital groups, respectively. Cox proportional hazard regressions show that patients treated by low-volume surgeons had a 51.6% higher risk of death than those treated by high-volume surgeons ($p<0.001$). Similarly, the risk of death for patients receiving resections in low-volume hospitals was 1.335 times as high as the risk of their counterparts in high-volume hospitals ($p<0.001$).

After adjusting for characteristics of patient, surgeon, and hospital and clustering effects of surgeon or hospital, the relationships between 5-year survival and surgeon volume group remains; the stratified Cox regression models

Table 1 Surgeon and Patient Characteristics in Taiwan, by Surgeon Liver Cancer Resection Volume Groups, 1997–1999

Variable	Surgeon liver cancer resection volume groups												*p* value
	Low (1–19)				Medium (20–95)				High (>95)				
	Number	Percent	Mean	SD	Number	Percent	Mean	SD	Number	Percent	Mean	SD	
Surgeon characteristics (*n*=286)													
Total number of surgeons	263				18				5				
Liver cancer resection volume			3.5	3.8			49.3	23.5			247.0	132.5	–
Age			40.8	7.6			42.7	7.0			43.6	4.1	–
Gender													
Male	258	98.1			18	100.0			5	100.0			0.805
Female	5	1.9			–	–			–	–			
Physician age													
<40	141	53.6			8	44.4			1	20.0			0.3424
41–50	96	36.5			8	44.4			4	80.0			
>51	26	9.9			2	11.2			–	–			
Patient characteristics (*n*=2,799)													
Total number of patients	910				887				1,002				
Patient age													
<50	249	27.4			255	28.8			305	30.4			0.0066
50–64	304	33.4			316	35.6			369	36.8			
65–74	264	29.0			263	29.7			259	25.9			
>74	93	10.2			53	6.0			69	6.9			
Patient gender													
Male	681	74.8			695	78.3			817	81.5			0.0018
Female	229	25.2			192	21.7			185	18.5			
Charlson Comorbidity Index score													
3	457	50.2			434	48.9			58	54.7			<0.001
4	279	30.7			336	37.9			360	35.9			
5 or more	174	19.1			117	13.2			94	9.4			
Surgery type													
Lobectomy	363	39.9			291	32.8			342	34.1			0.0036
Partial hepatectomy	547	60.1			596	67.2			660	65.9			

show that adjusted risk of death for patients operated by low-volume surgeons was 41.1% higher than those by high-volume surgeons ($p<0.001$). However, hospital case volume alone is not a significant predictor of 5-year survival for hepatectomies.

Discussion

The volume–outcome relationship has been rarely explored in liver cancer. Although few studies have examined the relationship between volume and outcomes of hepatic resection for HCC in the USA, these studies examined only in-hospital mortality and examined effects of hospital volume only. These studies did not examine effects of hospital and physician volume simultaneously.[10,13,14] This is the first study using population-based data to investigate whether physician or hospital volume was more strongly associated with long-term survival of hepatic resection for HCC.

A number of studies have correlated perioperative outcome to hospital volume or physician volume for some certain types of surgical procedures, including cardiac, vascular, and general surgeries.[15–18] These volume–outcome relationships serve as the basis for the argument that high-risk procedures should be regionalized to centers of excellence.[10,19–21] However, it is relatively unknown whether long-term survival after hepatic resections may be altered by such regionalization. These data in this current study further support regionalization of high-risk

Table 2 Hospital and Patient Characteristics in Taiwan, by Hospital Liver Cancer Operation Volume Groups, 1997–1999

Variable	Hospital Liver Cancer Resection Volume Groups												p value
	Low (1–87)				Medium (88–298)				High (>298)				
	Number	Percent	Mean	SD	Number	Percent	Mean	SD	Number	Percent	Mean	SD	
Hospital characteristics (n=90)													
Total number of hospitals	83				5				2				
Liver cancer operation volume			11.4	18.3			173.8	75.7			495.5	111.0	
Hospital level													
Medical center	7	8.4			5	100.0			2	100.0			<0.001
Regional hospital	46	55.4			–	–			–	–			
District hospital	30	36.1			–	–			–	–			
Hospital ownership													
Public	23	27.7			4	80.0			1	50.0			0.1336
Private (not-for-profit)	36	43.4			1	20.0			1	50.0			
Private (for-profit)	24	28.9			–	–			–	–			
Hospital location													
Northern	34	41.0			1	20.0			2	100.0			0.5404
Central	21	25.3			1	20.0			–	–			
Southern	25	30.1			3	60.0			–	–			
Eastern	3	3.6			–	–			–	–			
Teaching status													
Yes	75	90.4			5	100			2	100.0			0.69096
No	8	9.6			–	–			–	–			
Patient characteristics (n=2,799)													
Total number of patients	939				869				991				
Age													
<50	264	28.1			240	27.6			305	30.8			0.0013
50–64	335	35.7			276	31.8			378	38.1			
65–74	261	27.8			273	31.4			252	25.4			
>74	79	8.4			80	9.2			56	5.7			
Gender													
Male	722	76.9			707	81.4			764	77.1			0.0345
Female	217	23.1			162	18.6			227	22.9			
Charlson Comorbidity Index score													
3	426	45.4			487	56.1			526	53.1			<0.001
4	341	36.3			268	30.8			366	36.9			
5 or more	172	18.3			114	13.1			99	10.0			

Table 2 (continued)

Variable	Hospital Liver Cancer Resection Volume Groups												p value
	Low (1–87)				Medium (88–298)				High (>298)				
	Number	Percent	Mean	SD	Number	Percent	Mean	SD	Number	Percent	Mean	SD	
Surgery type													<0.001
Lobectomy	413	44.0			288	33.1			295	29.8			
Partial hepatectomy	526	56.0			581	66.9			696	70.2			

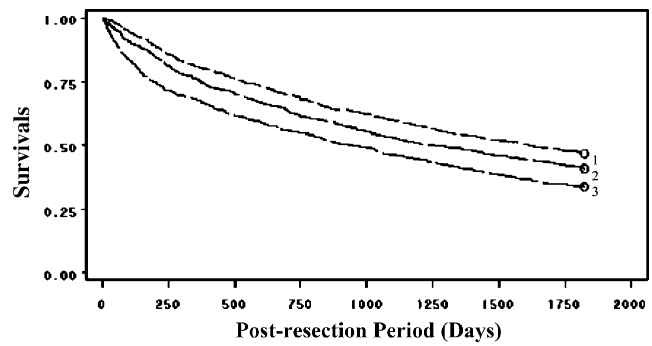

Figure 1 Liver cancer resection survival rates for patients hospitalized in Taiwan, by surgeon volume, 1997–1999. *Asterisk* Surgeon volume was defined as the number of liver cancer surgeries between the years 1997 and 1999 as follows: *1* high, *2* medium, and *3* low.

procedures, such as hepatectomy for HCC, in Taiwan. In the current study, we confirmed a relationship of long-term survival with hospital volume for liver resections using a large national database in Taiwan. If centers with superior patient outcomes, i.e., long-term survival, could be identified, the procedure of resection of HCC could be regionalized as a means of providing the most cost-effective care with optimal quality.

In this study, when we examined the effect of physician volume and hospital volume separately, both physician volume and hospital volume significantly associated with 5-year survival. However, after we adjusted for characteristics of physician and hospital, only physician volume remained a significant predictor to the 5-year survival. In those very few studies, which sought to identify the simultaneous contribution of hospital and physician volume to outcomes, they have generated similar results, i.e., physician volume is more significant than hospital volume on the relationship between volume and mortality. Halm et al.[22] conducted

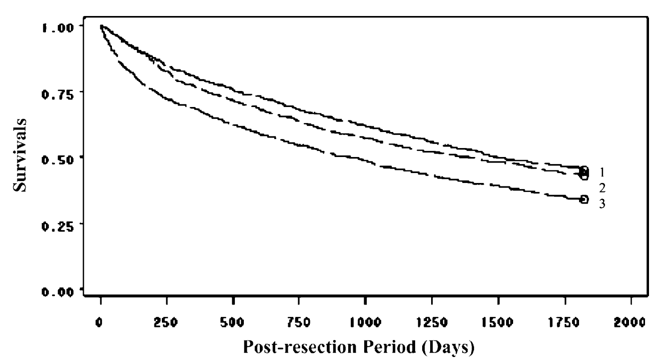

Figure 2 Liver cancer resection survival rates for patients hospitalized in Taiwan, by hospital volume, 1997–1999.*Asterisk* Hospital volume was defined as the number of liver cancer surgeries between the years 1997 and 1999 as follows: *1* high, *2* medium, and *3* low.

Table 3 Relative 5-Year Survival and Hazard Ratios by Surgeon and Hospital Liver Cancer Resection Volume Groups

Variables	Relative 5-year survival (%)	Crude hazard ratio/95% CI	Adjust hazard ratio[a]/95% CI
Surgeon hepatectomy volume			
≤19	33.7	1.516 (1.349–1.704)***	1.411 (1.232–1.617)***
20–95	40.8	1.203 (1.066–1.357)**	1.189 (0.871–1.620)
>95	46.8	1.000	1.000
Hospital hepatectomy volume			
≤87	34.0	1.335 (1.191–1.496)***	1.211 (0.832–1.751)
88–298	45.1	0.925 (0.819–1.045)	1.110 (0.834–1.452)
>298	43.1	1.000	1.000

Total sample No.=2,799

** $p<0.01$; *** $p<0.001$

[a] Odds ratios are adjusted for patient's age, gender, type of operation, the Charlson Comorbidity Index, and surgeon's age and gender and hospital characteristics including hospital ownership, hospital level, teaching status and geographical location and clustering effect of surgeon or hospital (by stratified Cox regression model)

a systematic review on volume–outcome relationship in health care and concluded that the surgeon seemed to be a more important determinant of outcomes than hospital volume in the case of coronary artery bypass surgeries, carotid endartectomy, surgery for ruptured abdominal aortic aneurysm, and surgery for colorectal cancer. Similarly, Hu et al.[23] found that hospital volume is not significantly associated with outcomes after adjusting for physician volume in male patients who underwent radical prostatectomy. Moreover, Hannan et al.[24] found that physician volume is more significant than hospital volume on the relationship between volume and mortality for coronary artery bypass surgeries, resection of abdominal aortic aneurysms, partial gastrectomies, and colectomies. Therefore, it appears that physician volume could be the mechanism that underlines the relationship between hospital volume and survival rates. More research efforts are needed to continue to clarify the impact of both hospital and surgeon volume on mortality rates simultaneously as well as the impact of the interaction of these two volume measures on mortality rates.

As documented in the literature, our results support the notion that high volume is often associated with better outcomes. Two major hypotheses have been proposed to explain these relationships.[22,25–28] First, "practice makes perfect," i.e., physicians and hospitals develop more effective skills if they treat more patients. Second is "selective referral", i.e., physicians and hospitals achieving better outcomes receive more referrals and thus accrue larger volumes. However, the relative contribution of physician versus hospital volume still remains unknown because there have been very few studies that examined both types of volume measures simultaneously.[22]

Although a compelling volume–outcome relationship was supported in our study, several limitations existed in this study. First, this study was adjusted for patient co-morbidities; nevertheless, the National Database lacked data on the severity of HCC, e.g., on MELD or Child scores, to account for differences in the severity of HCC among patients. Moreover, other variables that possibly affect patients' long-term survival rates were not comprehensively collected in the database, and therefore, we were not able to incorporate these possible confounding variables in the analyses. Lastly, this study used a cross-sectional design. We were not able to reveal the consequential relationship between volume and outcomes. Further longitudinal studies may be needed to explore whether hospitals or physicians with better outcomes would consequently acquire greater volume of patients.

In conclusion, this is the first population-based study examining associations between both physician volume and hospital volume and long-term survival in patients with liver malignancies in the HBV-endemic areas, Taiwan. We have demonstrated that higher volumes are associated with better long-term survival rates. Moreover, physician volume is more significant than hospital volume in predicting 5-year survival rates in HCC patients. If physicians or 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. Furthermore, it is important to find out why some providers have substantially better outcomes than others, and the government should make systematic efforts to transfer this capability to all providers in order to improve the care and treatment outcome for all HCC patients.

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