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RESEARCH ARTICLE

Re-Examining the Significance of Surgical Volume to Breast Cancer Survival and Recurrence versus Process Quality of Care in Taiwan

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Objective. This study explored the association of surgical volume versus process quality with breast cancer survival and recurrence.

Data Sources/Study Setting. Population-based cancer registration data and National Health Insurance claim data.

Study Design. This population-based study linked Taiwan's Cancer Database with Taiwan's National Health Insurance Database to collect data on all patients diagnosed with breast cancer in 2003–2004 who received surgical treatment.

Principal Findings. This study included 6,396 female breast cancer patients, reported by 26 hospitals. After controlling for patient and provider characteristics, Cox's regression models did not reveal any association between a physician's surgical volume and breast cancer recurrence or survival, although hospital volume was marginally associated with positive 5-year recurrence (HR: 1.001, 95%CI: 1.000, 1.001). After controlling for hospital or physician volume of surgery, we found a significant association between quality of care and both 5-year survival and recurrence. Random effects were also identified between patients and providers based on 5-year survival and 5-year recurrence.

Conclusions. Process quality of care was significantly more related to survival or recurrence than to surgical volume. The random effects found within hospital-patient clustered data indicated that the effect of the clustered feature of this data should be considered when performing volume-outcome related studies.

Key Words. Quality of care, volume-outcome relationship, breast cancer, multilevel analysis, survival analysis

Beginning with Luft et al. in 1979 (Luft, Bunker, and Enthoven 1979), researchers have expressed a great interest in and conducted a large number of studies on the relationship between the volume of procedures performed by hospitals or surgeons and care outcome, commonly referred to as volume-outcome. One of the findings of their study, which retrospectively collected data on hospital volume of 12 surgical procedures performed in 1,498 hospitals and mortality data, was that hospitals that performed a greater volume of procedures had lower related inhospital mortality rates (Luft, Bunker, and Enthoven 1979). Following that study, two hypotheses were proposed to explain and further explore this relationship: *practice makes perfect* and *selective referral* (Luft 1980; Luft, Hunt, and Maerki 1987; Farley and Ozminkowski 1992; Hannan et al. 1992). Today, the findings, methods, and proposals of that study continue to spark controversy, especially regarding the thresholds that have since been set for specific procedures as well as the causality between volume and outcome itself (Shahian and Normand 2003). Most studies interested in the relationship between volume and outcome for other procedures (Chowdhury, Dagash, and Pierro 2007; Henebiens et al. 2007; Holt et al. 2007), especially those used to treat cancer (Hillner, Smith, and Desch 2000; Hodgson, Fuchs, and Ayanian 2001; Halm, Lee, and Chassin 2002; Weitz et al. 2004; Hebert-Croteau, Roberge, and Brisson 2007), support Luft et al.'s conclusions. Following a study which reported that a volume threshold could predict the outcome after risk-adjustment (Hannan et al. 1991), the Leapfrog Group began to translate the academic discussions on volume-outcome relationship into policy practice and initiated its "evidence-based referrals" for coronary artery bypasses (Birkmeyer, Finlayson, and Birkmeyer 2001). Evidence-based referral, often referred to as regionalization, was then later recommended by the US National Cancer Policy Board and the Institute of Medicine for high-risk operations for cancer care (Hogan and Winter 2008).

Despite the preponderance of studies that support the relationship between volume and outcome, other studies have found the results of previous studies to be inconsistent and their study designs or statistical methods to be problematic (Halm, Lee, and Chassin 2002; McKee et al. 2002; Rathore et al. 2004; du Bois et al. 2005; Sioris et al. 2008) and began to challenge the wisdom of basing case referral policy on service volume criteria (Zacharias et al. 2005; Marcin et al. 2008). Those previous volume-outcome studies can be challenged from several perspectives (Shahian and Normand

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2003). For example, some of them argue that high volume cannot guarantee either high quality or good outcomes (Hogan and Winter 2008), and some have pointed out that there are great differences in the definition of high and low volume across the studies as well as biases caused by improper risk adjustment (Shacley et al. 2000; Hodgson, Fuchs, and Ayanian 2001; Chowdhury, Dagash, and Pierro 2007). Moreover, many studies have neglected to recognize the clustering characteristics of data and did not use multilevel models to estimate variation (Urbach and Austin 2005; Panageas et al. 2007). Finally, others suggested that volume is only one of several components of quality and not the only predictor of outcome (Hogan and Winter 2008).

Therefore, in this study, we linked three population-based databases in Taiwan to evaluate whether *patient- and hospital-level process quality of care* could better explain the variation in the recurrence of breast cancer and survival than *volume* after controlling for age, disease severity, comorbidity, and other patient-level factors. The results were tested not only using the Cox regression model but also using a multilevel model, which may be better suited for clustered data.

METHODS

Data Source

This study links population-based data collected from three databases in Taiwan: the Taiwan Cancer Database, the National Health Insurance Claims Database, and the National Death Registry. The 2003–2004 Taiwan Cancer Database, which is maintained by Taiwan's Department of Health's Bureau of Health Promotion, collects cancer-specific data, including type of cancer, cancer stage, surgical margin, and details of the surgical procedures used. Only major cancer care providers in Taiwan are eligible to report to the Taiwan Cancer Database. The data were abstracted by trained cancer registrars at each hospital into a standard report form, submitted with supporting medical records, and passed through a computerized logic check. The Bureau of Health Promotion also carries out regular medical records reabstractions from a set of randomly selected cases to ensure data quality. Participating hospitals are accredited by the BHP and regularly receive quality reports. At present the database covers more than 80 percent of the newly diagnosed breast cancer patients in Taiwan. This study also used Taiwan's 2002–2007 National Health Insurance Claims Database to collect patient ID, date of the ambulatory or inpatient care, disease classification codes (i.e., the ICD-9-CM codes), physician ID, physician specialty, hospital ID, surgical and nonsurgical procedures performed, and medications prescribed for each case. The two databases were linked to measure process quality of care, which is defined as how closely physicians followed suggested treatment guidelines (Chung et al. 2008), and determine whether there was a recurrence of breast cancer. Taiwan's 2003–2008 National Death Registry was linked to the previous databases to calculate survival time. The IDs of the patients, physicians, and hospitals were all encrypted using the same encryption algorithm to cross-link the data while protecting privacy. The release of all data was approved by the Data Release Review Board of the Bureau of Health Promotion. The protocol for this study was approved by the IRB of the College of Public Health, National Taiwan University (protocol # 990205).

Study Sample

This study included all cases of woman breast cancer diagnosed between 2003 and 2004 and reported to Taiwan's Cancer Database. Excluded were patients who did not receive curative surgery, patients who received surgery more than 2 years after their first diagnosis, and patients in whose records the date of surgery was omitted. Also excluded were patients who received treatment at hospitals with fewer than 30 cases during the study period. The case list was then linked to the 2002–2007 National Health Insurance Database of claims data. Patients who received treatment not reported in this database or who paid out-of-pocket for their treatment were also excluded. The case list was then linked to the 2003–2008 Death Registry to determine survival status.

Measures

Process Quality Of Care. The process-dimensional quality of care measured in this article was primarily based on the core measure indicators cited by Chung et al. (2008), which originally consisted of fifteen indicators: two pretreatment, nine treatment-related, and four monitoring-related indicators. Because we focused on the process quality of the first course of treatment, we excluded the four monitoring-related indicators, as they are more related to post-treatment outcome than to treatment quality of care. We did not include one of the other original indicators because the databases we used did not collect information on it. We therefore separately measured a total of 10 indicators at the patient level (see Appendix). We then aggregated these scores to obtain the scores of the process quality, which were calculated as the total number of indicators related to each case divided by the actual number applying to that case. The result of the patient-level scores of the process quality was then aggregated to the physician- and hospital-levels to create physician- and hospital-level process quality scores.

Comorbidity. The individual comorbidity scale was estimated following the method first published by Klabunde et al. in 2000 and modified in 2006 (Klabunde, Harlan, and Warren 2006; Klabunde et al. 2000, 2007). This scale is also known as the "NCI comorbidity index." In this estimation, different comorbidities (ICD-9-CM diagnosis codes) listed on a case's insurance claims a year before first diagnosis are assigned specific scores and summed for each case. Comorbidities that appeared less than three times or within the same month were excluded.

Survival And Recurrence. The outcomes measured in this study were the overall survival and recurrence of the patients. The surgeries were performed between 2003 and 2005. Survival was derived by linking the Taiwan Cancer Database data to the Death Registry data. Cases listed in the Death Registry were defined as event cases in our survival analysis, and those not listed in the registry as of the end of 2008 were defined as censor cases. Recurrence in a patient was defined if the recurrence was directly reported along with recurrence information (type of recurrence, recurrence date) to the Taiwan Cancer Database. It was also defined if that patient subsequently received treatment after the last follow-up date recorded in that database. The type of therapies included surgeries, chemotherapy, radiotherapy, and palliative care. Chemotherapy data were excluded if the regimens were the same as used within 2 months before the last day of follow-up. The length of the follow-up was calculated as the number of days from the date of the initial diagnosis to the event date, censor date, or the end of 2008.

Statistics

Cox's proportional hazard models were fitted to explore the association of surgical volume and quality of care on the 5-year recurrence and the overall survival of breast cancer patients while controlling for age, stage, comorbidity, and type of surgery. As our data are clustered at the provider level, the random effects of patient-level process quality on 5-year overall mortality and 5-year recurrence were also examined using multilevel modeling. Physician and hospital volume were treated differently depending upon the kind of analysis performed. To examine the association between process quality of care and survival or recurrence, volume was treated as a continuous variable in the Cox PH models. In the multilevel models, volume was classified according to the k-means clustering method, and all hospitals were grouped as high-, medium-, and low-volume hospitals. The multilevel modeling was performed using HLM 6.0 (Raudenbush et al. 2008). These multilevel models were estimated by maximum likelihood estimation (MLE), and the standard errors were estimated using EM Laplace iterations for accurate approximation to maximum likelihood (ML) estimates of all parameters. Except for multilevel modeling, all statistical operations were performed by *SAS* (version 9.1, SAS Institution Inc., Cary, NC, USA).

Results

Patient Characteristics

The original number of newly diagnosed breast cancer cases identified from the Taiwan Cancer Database was 6,618. From this number we excluded those who could not be linked to the National Health Insurance data (n = 42, 0.6%), duplicate reporting (n = 12, 0.2%), discontinued enrollment, or incomplete National Health Insurance data for the year prior to the day of breast cancer diagnosis (n = 105, 1.6%), as well as those for whom the quality indicators could not be fitted to (n = 63, 1.0%). After excluding the cases from 1 of the 27 hospitals because it had fewer than 30 cases, this study included 6,396 breast cancer patients (96.6%) ranging from 31 to 919 patients per hospital, with an average of 246.0 (SD = 231.0). As can be seen in Table 1,788 and 1,305 cases of a total of 6,396 cases in this study died or had a recurrence of cancer within 5 years. Compared to those who survived, the patients who died had a significantly higher comorbidity score (p = <.001), lower physician and hospital process quality scores (<.001 and < .001, respectively), and were treated by a physician and hospital with a lower surgical volume (.001 and .002, respectively). Compared to recurrence-free patients, those who had recurring breast cancer had significantly higher comorbidity (<.001), and significantly lower physician and hospital process quality scores (<.001 and <.001). However, although we found a significantly

Table 1: Distribution of Patients' Age, Comorbidity Score, Received Quality of Care, and Providers' Volume

	Grouped by 5-Year Mortality					*Grouped by 5-Year Recurrence*				
	Death (n = 788)		*Survive (n = 5,608)*			*Recurrence (n = 1,305)*		*Free (n = 5,069)*		
	Mean	*SD*	*Mean*	*SD*	*p-value*	*Mean*	*SD*	*Mean*	*SD*	*p-value*
Age	54	13.1	50.4	11.2	<.001	50.17	11.82	50.97	11.46	.025
NCI comorbidity index	0.419	0.703	0.2	0.41	<.001	0.278	0.508	0.215	0.45	<.001
Score of process quality	0.655	0.234	0.67	0.225	0.082	0.657	0.222	0.671	0.228	0.055
Physician's score of process quality	0.654	0.104	0.67	0.104	<.001	0.656	0.103	0.671	0.104	<.001
Hospital's score of process quality	0.658	0.085	0.67	0.089	<.001	0.658	0.086	0.671	0.089	<.001
Physician's volume	119.5	105.2	132.7	105.9	0.001	123.7	106.3	133	105.8	.005
(Q1, Q3), IQR	(32, 197)	165	(41, 235)	194		(35, 197)	162	(42, 235)	193	
Hospital's volume	375.3	217.6	400.7	234.3	0.002	390.3	226	400	234.3	.181
(Q1, Q3), IQR	(243, 471)	228	(243, 665)	422		(243, 665)	422	(243, 665)	422	

Table 2: Distribution of the Type of Surgery, Surgeon Specialty, Cancer Stage, and Status of Surgical Margin

	Grouped by 5-Year Mortality					*Grouped by 5-Year Recurrence*				
	Death (n = 788)		*Survive (n = 5,608)*			*Recurrence (n = 1,305)*		*Free (n = 5,069)*		
	n	*%*	*n*	*%*	*p-value*	*n*	*%*	*n*	*%*	*p-value*
Specialized surgeon										
Yes	764	12.1	5,569	87.9	<.001	1,286	20.4	5,025	79.6	.056
No	24	38.1	39	61.9		19	30.2	44	69.8	
Type of surgery										
BCS	138	7.1	1,818	92.9	<.001	327	16.7	1,626	83.3	<.001
Others	650	14.6	3,790	85.4		978	22.1	3,443	77.9	
Cancer stage										
0	12	2.1	564	97.9	<.001	38	6.6	537	93.4	<.001
1	66	3.7	1,709	96.3		198	11.2	1,574	88.8	
2	274	10	2,479	90		530	19.3	2,213	80.7	
3	351	30.8	789	69.2		474	41.7	663	58.3	
4	75	78.1	21	21.9		50	54.9	41	45.1	
N/A	10	17.9	46	82.1		15	26.8	41	73.2	
Surgical margin										
Negative	714	11.9	5,286	88.1	<.001	1,196	20	4,784	80	<.001
Positive or close	74	18.7	322	81.3		109	27.7	285	72.3	

lower physician volume (.005), we did not find a statistical difference in hospital volume (.181).

As can also be seen in Table 2, patients who were treated by specialized surgeons also had a lower mortality (<.001) or recurrence (.056) than those treated by surgeons who were not specialized in the treatment of their specific disease. In addition, those who had negative surgical margins, meaning no cancer cells at the outer edge of the tissue, and those who received breast conserving surgery tended to have low mortality and low recurrence rates (all, <.001).

Surgical Volume Versus Process Quality as Predictors of Outcome

As shown in Table 3, which summarizes the results of four Cox's PH models analyzing the effect of hospital surgical volume and process quality on 5-year overall survival and 5-year recurrence, age, cancer stage, and comorbidity were significantly associated with 5-year overall survival. Model 1, an analysis of 5-year survival in which process quality was not considered,

Table 3: Five-Year Overall Survival and Five-Year Recurrence for the Hospital's Surgical Volume and Process Quality

	5-Year Overall Survival								*5-Year Recurrence*							
	Model 1				*Model 2*				*Model 3*				*Model 4*			
	HR	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*
Age	1.011	1.005	1.018	.001	1.010	1.003	1.017	.003	.988	.983	.994	<.001	.987	.982	.993	<.001
Stage (0 as ref.)																
1	1.807	.976	3.343	.060	1.903	1.027	3.523	.041	1.721	1.215	2.436	.002	1.830	1.291	2.595	.001
2	4.661	2.610	8.324	<.001	4.656	2.606	8.318	<.001	3.118	2.239	4.342	<.001	3.182	2.283	4.434	<.001
3	15.840	8.874	28.276	<.001	17.439	9.742	31.219	<.001	8.386	6.000	11.721	<.001	9.456	6.730	13.286	<.001
4	73.619	39.788	136.216	<.001	80.540	43.491	149.149	<.001	20.368	13.245	31.321	<.001	23.237	15.057	35.863	<.001
n/a	8.851	3.812	20.553	<.001	8.218	3.536	19.096	<.001	3.925	2.151	7.161	<.001	3.671	2.011	6.701	<.001
Comorbidity	1.522	1.359	1.704	<.001	1.548	1.382	1.734	<.001	1.305	1.169	1.456	<.001	1.314	1.177	1.467	<.001
Surgical margin (Positive or closed as ref.)																
Negative	.799	.622	1.025	.077	.836	.650	1.074	.162	.810	.661	.993	.043	.849	.691	1.042	.118
Type of surgery (Other as ref.)																
BCS	.877	.721	1.066	.187	.916	.753	1.115	.383	1.078	.941	1.235	.280	1.178	1.023	1.356	.023
Date of diagnosis	1.000	1.000	1.000	.665	1.000	1.000	1.000	.940	1.000	1.000	1.000	.892	1.000	1.000	1.000	.659
Hospital's volume of surgery	1.000	1.000	1.000	.944	1.000	1.000	1.001	.762	1.001	1.000	1.001	.007	1.001	1.000	1.001	.003
Score of process quality					.576	.418	.793	.001					.548	.415	.724	<.001
Hospital's process quality					.474	.155	1.447	.190					.871	.354	2.143	.764
−2 Log Likelihood (*p*-value)	12,644.117	(<.001)			12,627.595	(<.001)			21,087.342	(<.001)			21,067.095	(<.001)		

Note. The mean survival time was 54.4 months (range, 0–73 months, SD: 12.4); the mean of the recurrence free time was 40.1 months (range, 0–78 months, SD: 13.4); *p*-values of −2 log likelihood for each model was compared with the former model. All models were also controlled for hospital characteristics (owner type, medical school affiliation, accreditation, and location).

found no association between hospital surgical volume and overall survival. Model 2, which adds patient-level process quality and hospital-level process quality to the survival analysis, found a significant relationship between patient-level process quality and survival (HR: 0.576, $p < .001$) but not for hospital-level process quality. Model fitting was improved significantly after entering these quality scores ($p < .001$). Model 3, an analysis of 5-year recurrence which did not control for process quality, found a significant association between high hospital surgical volume and increased recurrence (HR: 1.001, $p = .007$), although the hazard ratio was marginal. Model 4, which adds process quality to the 5-year recurrence analysis, found a significant relationship between patient-level process quality and decreased recurrence (HR: 0.548, $p < .001$) but not hospital-level process quality. Again, model fitting was also improved significantly after entering the quality scores in the model.

Unlike Table 3, which analyzes hospital-level variables, Table 4 summarizes the results of the four Cox's PH models analyzing the relationship between physician's surgical volume and physician- and patient-level process quality and 5-year overall survival and 5-year recurrence. After controlling for stage of cancer, comorbidity, and other patient-level and hospital-level characteristics, Model 1, an analysis of 5-year survival, found no association between physician surgical volume and survival. Model 2, which adds physician- and patient-level process quality to the analysis, found a significant association between patient-level process quality and survival (HR: 0.560, $p = .001$) but not for physician-level process quality. As before, model fitting was improved significantly after entering the process quality scores.

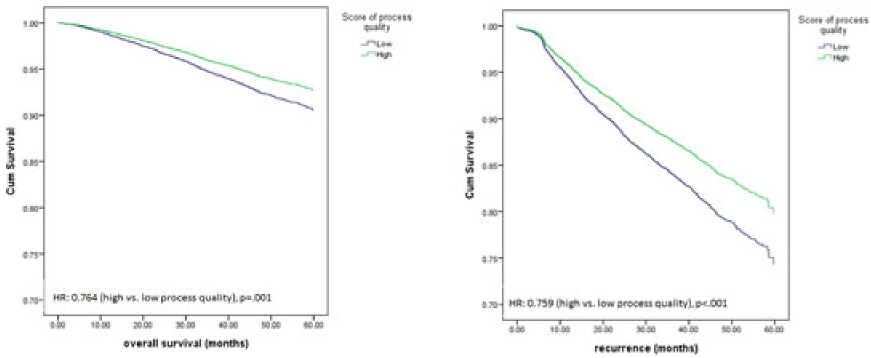
Models 3 and 4 analyzed the 5-year recurrence with physician level surgical volume, with the latter adding process quality variables. In both models there was no association between physician surgical volume and 5-year recurrence, after controlling for possible confounders. The results of Model 4 showed a significant association between patient-level process quality and decreased recurrence (HR: 0.560, $p < .001$) but not for physician level. It is interesting to note that in Model 4 there was a significant association between breast conserving surgery and increased risk of recurrence, but there was no significant difference between recurrence rates regardless of surgeon specialty. The adjusted Cox survival and freedom from recurrence curves presented in the Appendix (Figure 1) also show that after controlling for other factors, patients who received high quality of care were associated with better survival and a lower risk of recurrence.

Table 4: Five-Year Overall Survival and Five-Year Recurrence for the Physician's Surgical Volume and Process Quality

	5-Year Overall Survival								*5-Year Recurrence*							
	Model 1				*Model 2*				*Model 3*				*Model 4*			
	HR	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*	*HR*	*95% CI (LL, UL)*		*p-value*
Age	1.012	1.005	1.018	.001	1.010	1.004	1.017	.002	.988	.983	.994	<.001	.988	.982	.993	<.001
Stage (0 as ref.)																
1	1.807	.977	3.343	.060	1.893	1.022	3.506	.042	1.722	1.216	2.438	.002	1.825	1.287	2.588	.001
2	4.619	2.586	8.250	<.001	4.613	2.582	8.242	<.001	3.092	2.220	4.306	<.001	3.151	2.261	4.392	<.001
3	15.717	8.804	28.057	<.001	17.290	9.654	30.966	<.001	8.361	5.982	11.686	<.001	9.373	6.670	13.173	<.001
4	69.252	37.374	128.320	<.001	75.127	40.504	139.343	<.001	19.348	12.558	29.809	<.001	21.968	14.201	33.983	<.001
n/a	8.902	3.832	20.678	<.001	8.251	3.549	19.180	<.001	3.866	2.118	7.057	<.001	3.627	1.986	6.622	<.001
Comorbidity	1.513	1.351	1.693	<.001	1.533	1.369	1.716	<.001	1.291	1.156	1.441	<.001	1.300	1.164	1.451	<.001
Surgical margin (Positive or closed as ref.)																
Negative	.813	.633	1.043	.103	.842	.655	1.082	.179	.833	.680	1.020	.077	.869	.708	1.067	.179
Type of surgery (Other as ref.)																
BCS	.869	.715	1.058	.162	.905	.744	1.102	.321	1.086	.948	1.245	.235	1.181	1.026	1.361	.021
Date of diagnosis	1.000	1.000	1.000	.642	1.000	1.000	1.000	.964	1.000	1.000	1.000	.799	1.000	1.000	1.000	.757
Physician's specialty	.423	.277	.647	<.001	.443	.288	.680	<.001	.686	.431	1.091	.111	.730	.457	1.167	.189
Physician's volume of surgery	1.000	.999	1.001	.933	1.000	.999	1.001	.917	1.000	.999	1.000	.567	1.000	.999	1.000	.638
Score of process quality					.560	.398	.788	.001					.560	.419	.748	<.001
Physician's process quality					.962	.436	2.120	.923					1.013	.507	2.024	.972
−2 Log likelihood (p-value)	12,629.515	(<.001)			12,616.099	(.001)			21,090.519	(<.001)			21,072.661	(<.001)		

Note. The mean survival time was 54.4 months (range, 0–73 months, SD: 12.4); the mean of the recurrence free time was 40.1 months (range, 0–78 months, SD: 13.4); p-values of −2 log likelihood for each model were compared with the former model or null model. All models were also controlled for hospital characteristics (owner type, medical school affiliation, accreditation, and location).

Figure 1: Adjusted Cox Survival and Freedom from Recurrence Curves



Multilevel Mixed Effect Models

Considering that our data are clustered at the provider level, we also examined the random effects of patient-level process quality on 5-year overall mortality and 5-year recurrence while controlling for patient and hospital characteristics. Table 5 summarizes the results of our multilevel mixed effect models. Model 1 found no association between hospital volume and 5-year overall mortality, although random intercept was found to be significant (p = .004). Model 2 was performed to investigate a possible moderating effect of hospital volume and patient-level process quality on mortality. We found no moderating effect between the two variables. However, the random effect on the score of process quality was found to be significant (p < .001), suggesting that a hospital-patient clustered structure must be considered when exploring the association between hospital-level factors and 5-year overall mortality.

Models 3 and 4 analyzed the multilevel mixed effects for 5-year recurrence controlling for patient and hospital characteristics. Model 3 found no association between hospital surgical volume and 5-year recurrence, although random intercept was significant (p < .001). Model 4 was performed to investigate a possible moderating effect of hospital volume and patient-level process quality on 5-year recurrence. We found the random effect of patient-level process quality to be significant (p = .003). In summary, the random effects in Models 2 and 4 were found to be significant, indicating the importance of considering the clustering characteristics of the data when analyzing the association between surgical volume and outcome.

Table 5: Multilevel Mixed Effect Models for Five-Year Overall Mortality and Five-Year Recurrence

	5-Year Overall Mortality						5-Year Recurrence					
	Model 1*			Model 2†			Model 3*			Model 4†		
(n = 6,396)	Exp(β)	95% CI (LL, UL)	p-value	Exp(β)	95% CI (LL, UL)	p-value	Exp(β)	95% CI (LL, UL)	p-value	Exp(β)	95% CI (LL, UL)	p-value
Fixed effect												
Hospital's volume of surgery (HV) (≤ 177 as ref.)												
178–337	1.118	(0.750, 1.667)	0.563				1.071	(0.775, 1.481)	.660			
≥ 338	1.005	(0.688, 1.470)	0.977				1.181	(0.819, 1.703)	.352			
Score of process quality (SPQ)				0.351	(0.181, 0.682)	.004				0.333	(0.193, 0.575)	<.001
SPQ × HV (moderating effect)												
178–337				1.242	(0.790, 1.953)	.333				1.188	(0.850, 1.661)	.300
≥ 338				1.114	(0.763, 1.627)	.560				1.444	(0.972, 2.144)	.067
Age	1.011	(1.003, 1.019)	.005	1.009	(1.002, 1.016)	.013	0.984	(0.979, 0.989)	<.001	0.982	(0.977, 0.987)	<.001
Comorbidity	1.885	(1.612, 2.204)	<.001	1.875	(1.575, 2.232)	<.001	1.413	(1.200, 1.663)	<.001	1.406	(1.200, 1.647)	<.001
Stage (0 as ref.)												
1	1.903	(1.013, 3.573)	.045	1.991	(1.142, 3.471)	.015	1.796	(1.422, 2.267)	<.001	1.913	(1.551, 2.359)	<.001
2	5.087	(2.807, 9.218)	<.001	4.918	(2.963, 8.164)	<.001	3.516	(2.631, 4.697)	<.001	3.512	(2.712, 4.549)	<.001
3	19.802	(10.892, 36.001)	<.001	22.599	(13.128, 38.905)	<.001	10.679	(7.895, 14.445)	<.001	12.413	(9.611, 16.031)	<.001
4	170.210	(79.406, 364.849)	<.001	197.767	(120.463, 324.677)	<.001	18.561	(12.318, 27.967)	<.001	21.024	(13.707, 32.248)	<.001
n/a	10.051	(4.041, 24.999)	<.001	8.228	(3.057, 22.144)	<.001	4.440	(2.338, 8.429)	<.001	3.948	(2.056, 7.581)	<.001
Random effect (SD, X^2, p-value)												
Intercept	0.131	36.492	.004	0.875	58.133	<.001	0.161	52.810	<.001	0.644	54.218	<.001
Score of process quality (SPQ)				1.182	55.268	<.001				0.788	46.744	.003

Note. All models were also controlled for surgical margin, type of surgery, and hospital characteristics (owner type, medical school affiliation, accreditation, and location).

*The hospital volume was entered as an explanatory variable against the outcome in Model 1 and Model 3.

†The hospital volume was entered as a moderating effect for patient's quality score (i.e., as 2nd-level predictors) in Model 2 and Model 4.

Discussion

In this study, which explored the associations between process quality of care and surgical volume and 5-year survival and 5-year recurrence in breast cancer, our multilevel analysis found no relationship between surgical volume and either mortality or recurrence. Our Cox's PH models and multilevel models indicated that process quality of care was more significantly correlated with survival/mortality and recurrence than with hospital surgical volume. In addition, we found significant random effects within hospital-patient clustered data, indicating that it was necessary to perform a multilevel analysis to obtain unbiased results in our study.

This study found no association between hospital surgical volume or physician surgical volume and breast cancer treatment outcomes after controlling for stage of cancer and comorbidity. We initially used a k-means cluster method to distinguish between high and low volume to accentuate the difference between high-volume and low-volume providers. However, our multilevel models found no association between hospital volume and mortality or recurrence in either case. We conducted a sensitivity analysis classifying volume by different approaches (e.g., the thirtiles) to confirm the results of our multilevel models. Still we found no volume-outcome association in our subjects with breast cancer (data not shown). Similarly, Harcourt el al. found no correlation between hospital case volume and survival (Harcourt and Hicks 2003). Although we found a marginal relationship between hospital surgical volume and 5-year recurrence in a Cox model (Table 2 Model 4), the hazard ratio was close to one and could be considered marginal when compared with the hazard ratio of process quality. This finding might be due to the fact that process quality of care has a stronger relationship with survival and recurrence, and volume is just one component related to quality (Halm, Lee, and Chassin 2002; Douek and Taylor 2003; Kraus, Buchler, and Herfarth 2005; Hogan and Winter 2008; Joseph et al. 2009).

Our study found no association between surgical volume and outcome, which is in disagreement with several studies. One study of 13,360 breast cancer resection patients in Taiwan, reporting a significant correlation between surgeon or hospital surgical volume and patient outcomes, suggests that surgical volume can be used as an overall indicator of treatment quality (Chen et al. 2008). However, that study did not provide cancer staging data and probably did not adjust for disease severity, which would bias their findings.

We conducted a sensitivity analysis using that study's definition of high- and low-volume hospitals but still found no association between surgical volume and 5-year survival after controlling for stage of cancer was found (data not shown). The result of our supplementary study was consistent with Shacley et al., who found that the relationship between outcome and volume was weakened after adjusting for case mix (Shacley et al. 2000). Some of their evidence suggested that positive volume-outcome relationships may be biased by a lack of adjustment for case mix or arbitrary definitions of volume and poor quality of studies. Halm et al. also pointed out that studies that performed more sophisticated risk adjustment using clinical data were less likely to report an association between hospital volume and outcome (Halm, Lee, and Chassin 2002).

This study found process quality of care to be relevant to breast cancer survival and recurrence, a finding in agreement with Cheng et al., who examined the association between adherence to quality indicators and breast cancer survival in 1,378 breast cancer patients treated in a cancer center (Cheng et al. 2009). Cheng et al. stated that their study was limited due to the improper control for comorbidity which they thought might bias their estimation of the real effect of indicator adherence. This study, however, did control carefully for comorbidity and came to similar conclusions as theirs. Our study also found that when patient-level process measure adherence is controlled, physician or hospital-level process quality is not associated with the patient's survival or recurrence-free time (Tables 3 and 4). This shows that seeking care from a health care provider who performs well overall does not guarantee a better outcome for specific patients who do not get optimal care. The comparison for process quality based on scoring at physician- or hospital-level could be misleading if a health care provider has greater variation than others.

It has been suggested that issues concerning the improper level of unit used can be avoided by applying a multilevel modeling (Carey and Burgess 1999). Our study found significant random effects in all of our multilevel models, suggesting the necessity for using multilevel modeling for exploring volume-outcome association. Panageas et al. advocated the importance of analyzing cluster-correlated data to obtain unbiased assessments of volume-outcome relationships (Panageas et al. 2007). Urbach and Austin also pointed out that many volume-outcome studies may have problems with using inappropriate statistical methods (Urbach and Austin 2005).

In the United States, health insurers often refer cancer patients to higher volume hospitals, as recommended by US National Cancer Policy

Board and the Institute of Medicine (Hogan and Winter 2008). In Taiwan, there is no referral policy based on surgical volume or case load. However, the Department of Health in Taiwan focuses on monitoring quality of care not volume of procedures to accredit hospitals as cancer centers. One recent study in Japan found no significant relationship between volume and outcomes for cancer care and questioned the effectiveness of regionalizing cancer surgery to high-volume centers (Yasunaga, Matsuyama, and Ohe 2009). Wouters et al. also criticized the use of “volume” as a proxy for quality of care because it overlooks the hospital outcomes in favor of volume when choosing future referral centers (Wouters et al. 2009).

Another concern would be that for those physicians who are more likely to recommend and perform surgery than others, their performance measured in this study could be biased. Although this care pattern (or preference for treatment choices) might affect their surgical volume, it is very difficult to conclude from this that the evaluation of the quality of care provided to the patient may be biased by the physician’s preference of treatment. Ideally, regardless if the physician is more likely to recommend surgery or not, the process quality of care should be guaranteed once the decision has been made that surgery is to be performed. It is the same reason why this study examined the significance of surgical volume and process quality of care on the outcome of breast cancer care: previous studies have reported that the surgical volume of breast cancer might have a positive relationship with the patient’s survival rate. However, most studies that explored the relationship between surgical volume and outcome in breast cancer care did not consider the effect of quality of care (Chen et al. 2008; Hebert-Croteau et al. 2005; Hebert-Croteau, Roberge, and Brisson 2007). To overcome the potential bias due to a physicians’ preferences for treatment choices when measuring their performance, future researches are suggested that they incorporate more information regarding the patients’ health status and severity of their disease(s).

This study has several limitations. It only used data from hospitals reporting to the Taiwan’s Cancer Database. Those hospitals all treat a high volume of cancer patients (at least 500 cases of any type of cancer annually). This may limit the generalizability to these hospitals alone. Although these hospitals treat more than 80 percent of the breast cancer patients in Taiwan, there are low-volume regional or community hospitals whose staging data are not included in Taiwan’s Cancer Database. Second, this study is based on 26 hospitals, which may raise questions on the fit of multilevel models to our study. Although the number is low, a robust estimation for standard error was chosen for this study and the regression coefficients were estimated without bias (Maas and Hox 2005). Third, the fact that this study does not include patients who did not receive curative surgeries may limit the generalizability of our findings to all breast cancer patients. The curative surgeries for those patients are more standardized and the outcome is expected to be more correlated with the quality of care. Patients who did not receive curative surgeries as their first course of treatment also limit the number of indicators that are applied for measuring the process quality of care. Another limitation is that our study observation period only covers a 5-year period. Because expected survival times for breast cancer exceed this time period for early stage breast cancer patients, future investigations may consider having longer observation periods.

Conclusion

This study found process quality of care, not surgical volume, to be significantly associated with survival and recurrence. We found significant random effects within hospital-patient clustered data, underscoring the necessity of performing multilevel analysis to ensure that our results are unbiased. The findings suggest that there may be possible bias in past studies and provide further evidence of the importance of using multilevel analysis for any outcome study based on hierarchical data.

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Appendix SA1: Author Matrix.

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