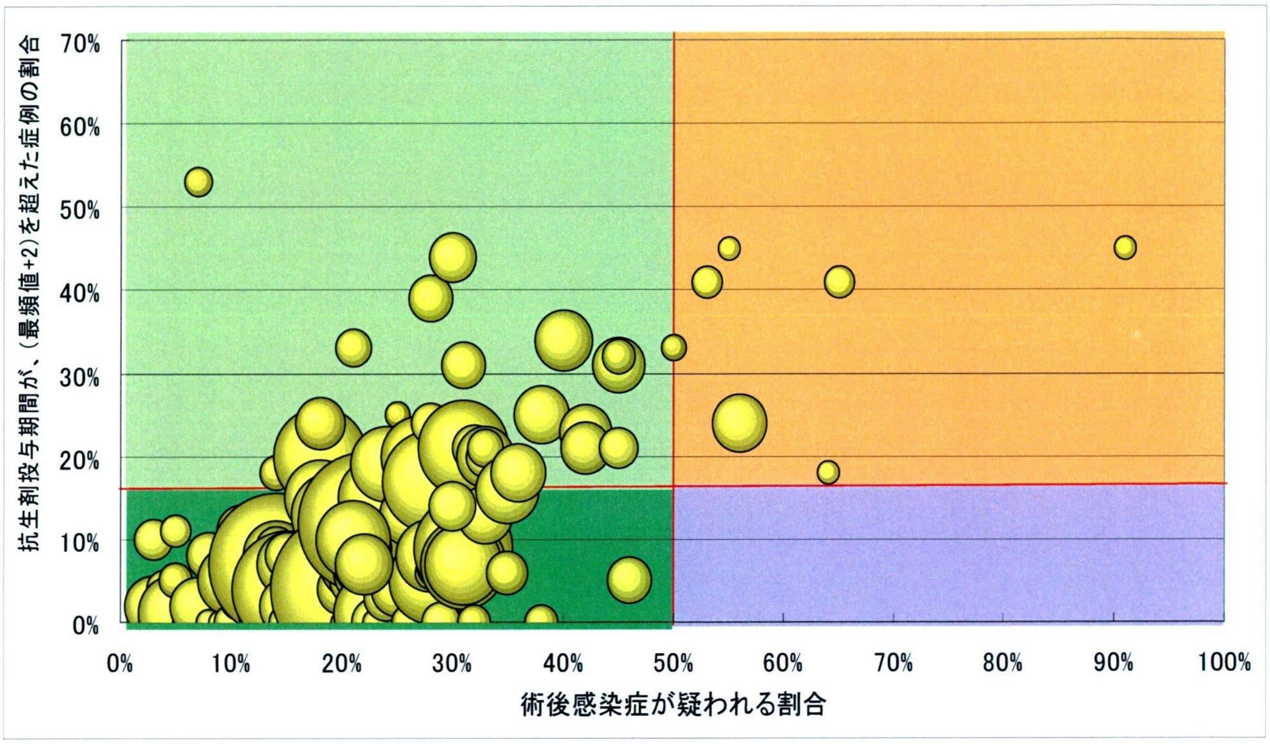
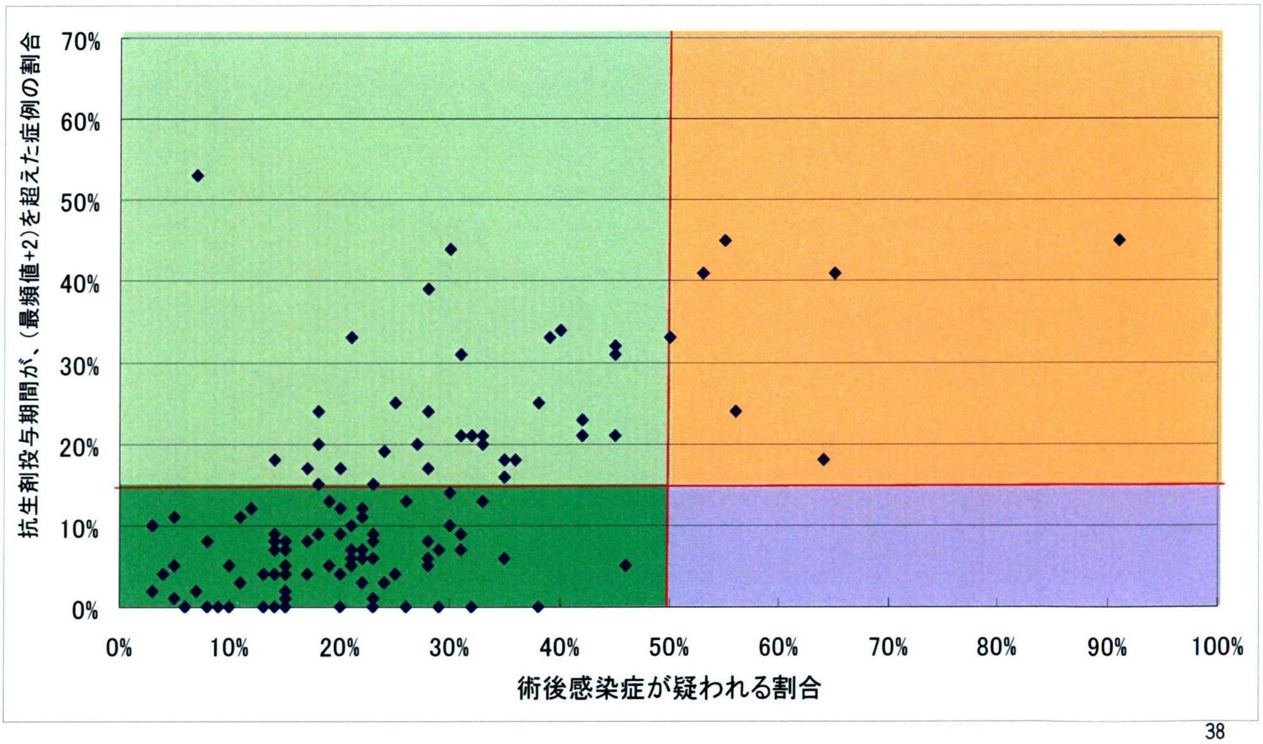
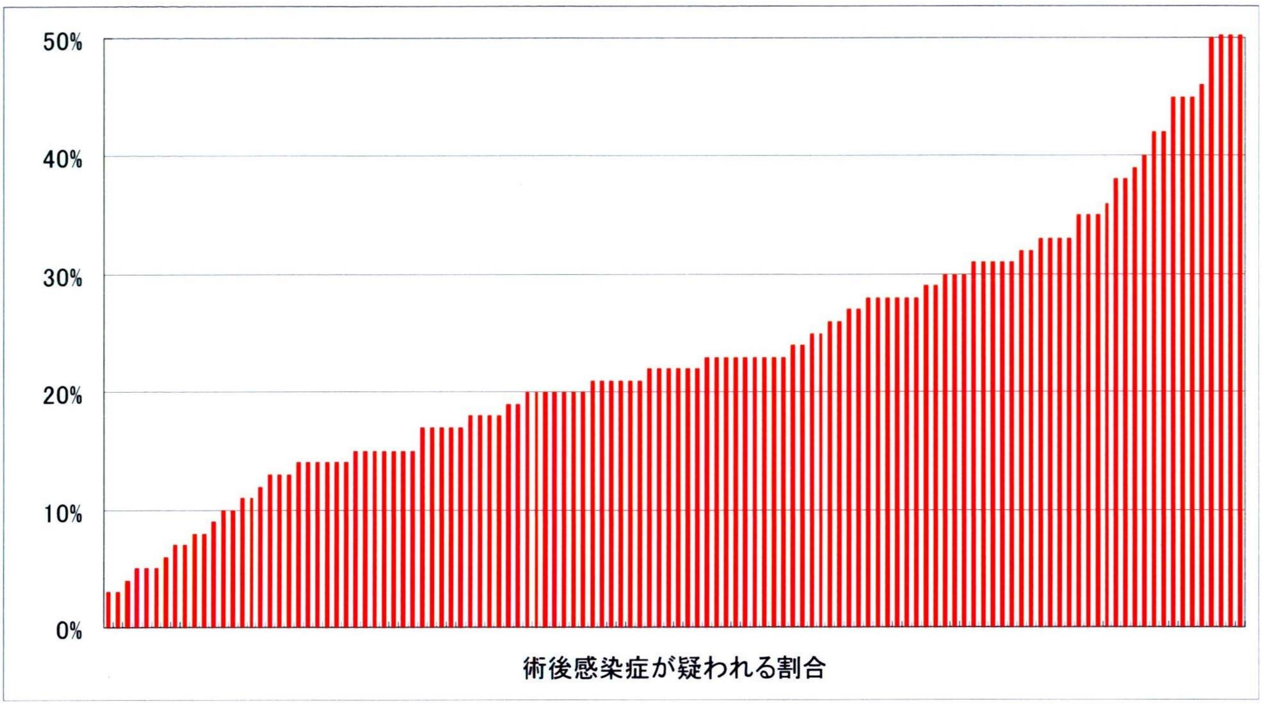
抗生剤投与期間が、(最頻値＋2日間)を超えた症例の割合と術後感染症が疑われる割合(100%まで)



抗生剤投与期間が、(最頻値＋2日間)を超えた症例の割合と術後感染症が疑われる割合(100%まで)



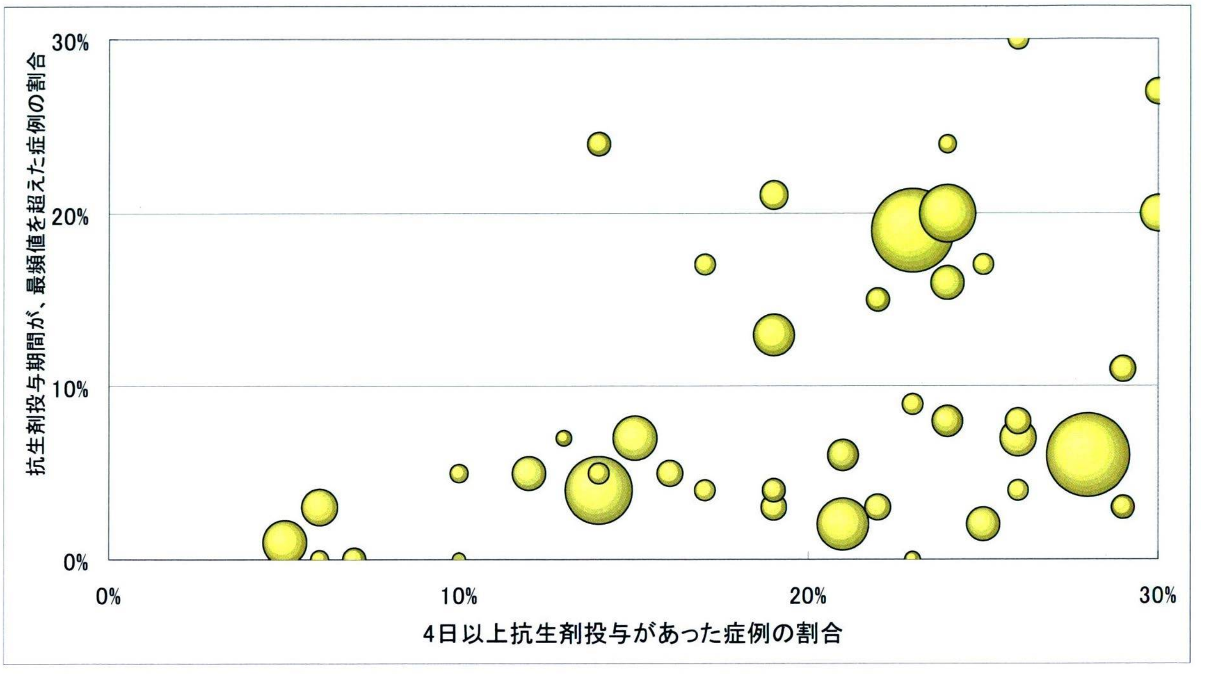
術後感染症が疑われる割合（100%まで）



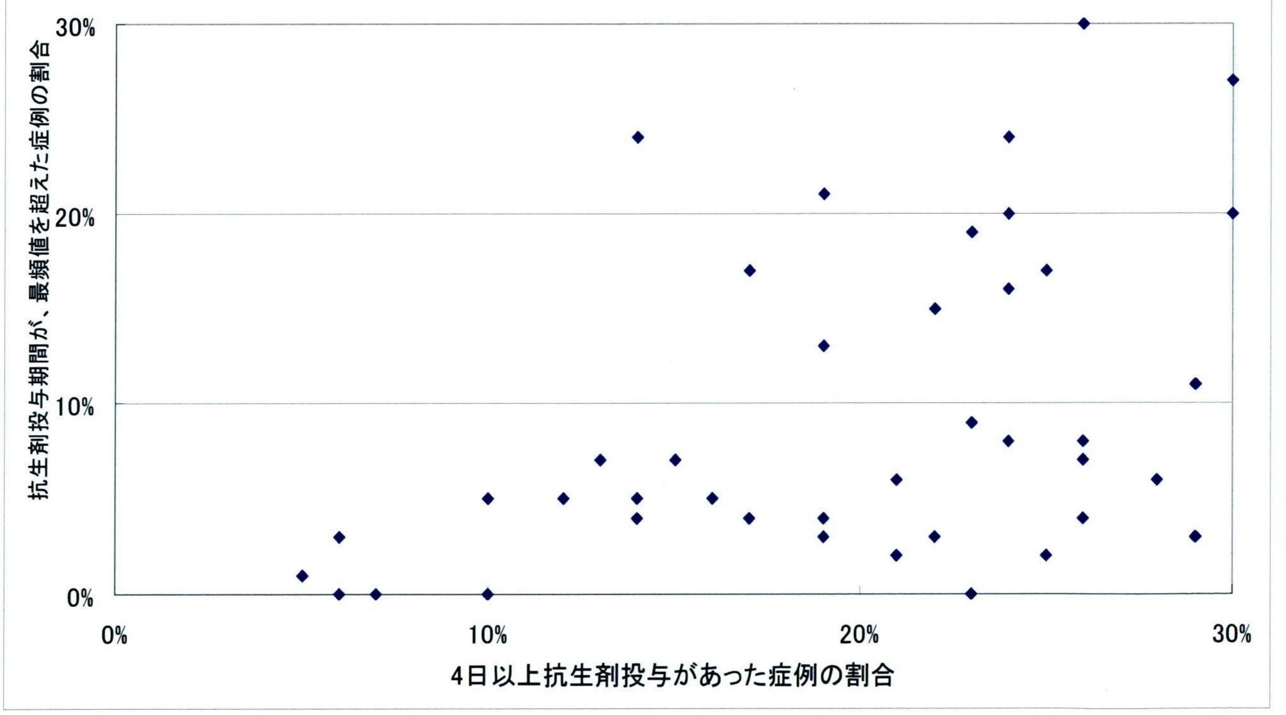
胃切除術患者

- 30%まで
  - 予防的投与が4日以上
    - 病院数：40病院
    - 症例数2,250人の患者さん
    - スライド9~11は、スライド２～４と同じデータで、30%まで切ったグラフになります。

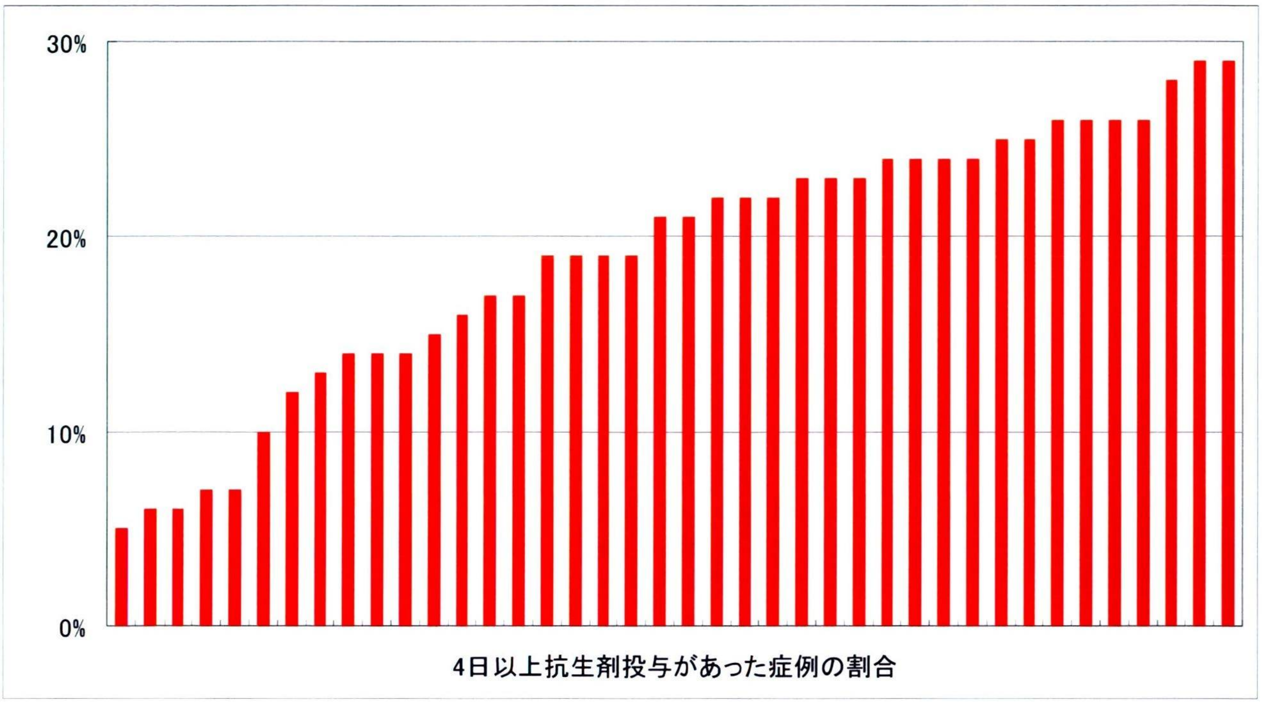
抗生剤投与期間が、最頻値を超えた症例の割合と4日以上抗生剤投与があった症例の割合（30%まで）



抗生剤投与期間が、最頻値を超えた症例の割合と4日以上抗生剤投与があった症例の割合（30%まで）



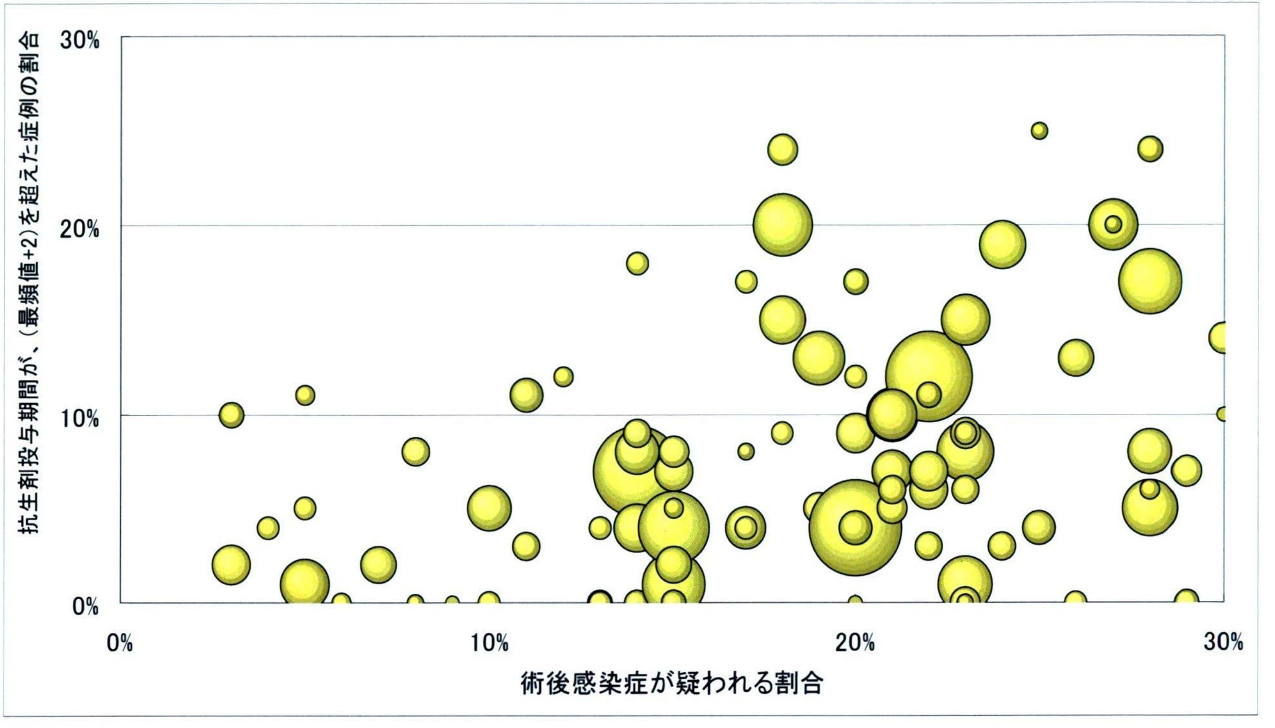
4日以上抗生剤投与があった症例の割合（30%まで）



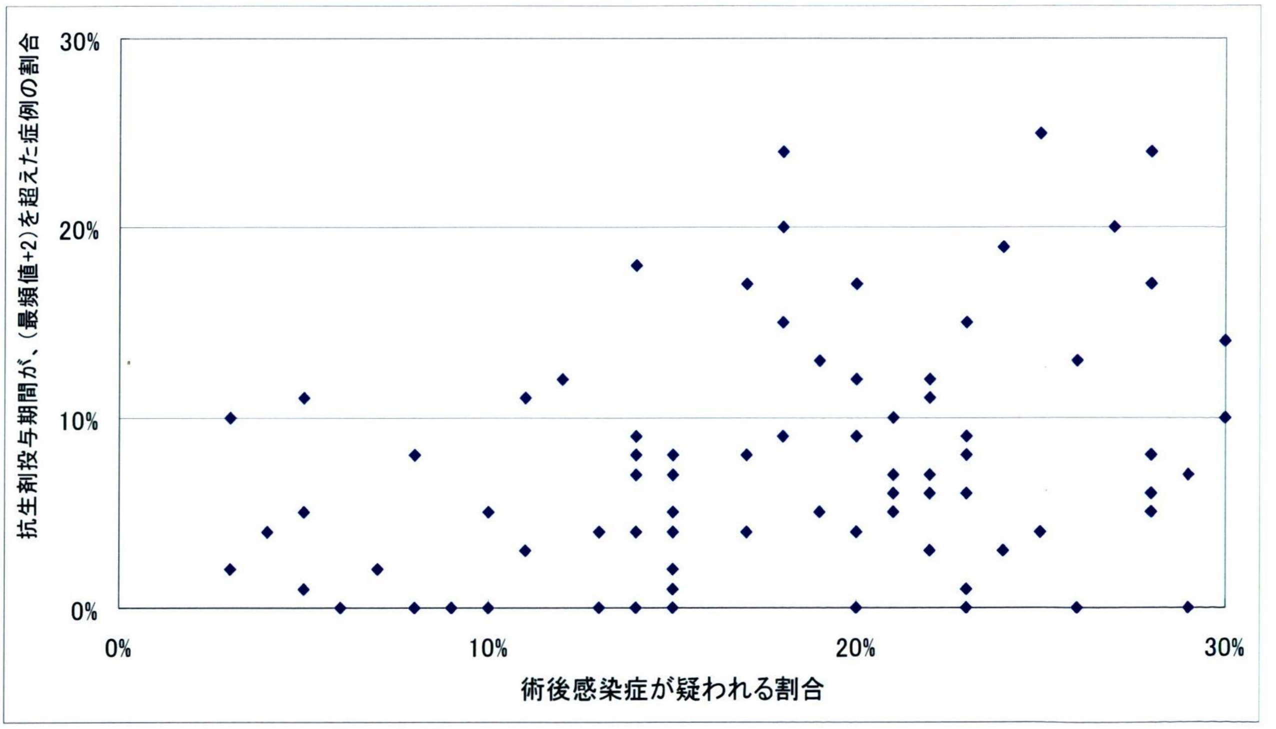
胃切除術患者

- 30%まで
  - 術後感染症が疑われた症例
    - 病院数：85病院
    - 症例数5,549人の患者さん
    - スライド13~15は、スライド5～7と同じデータで、30%まで切ったグラフになります。

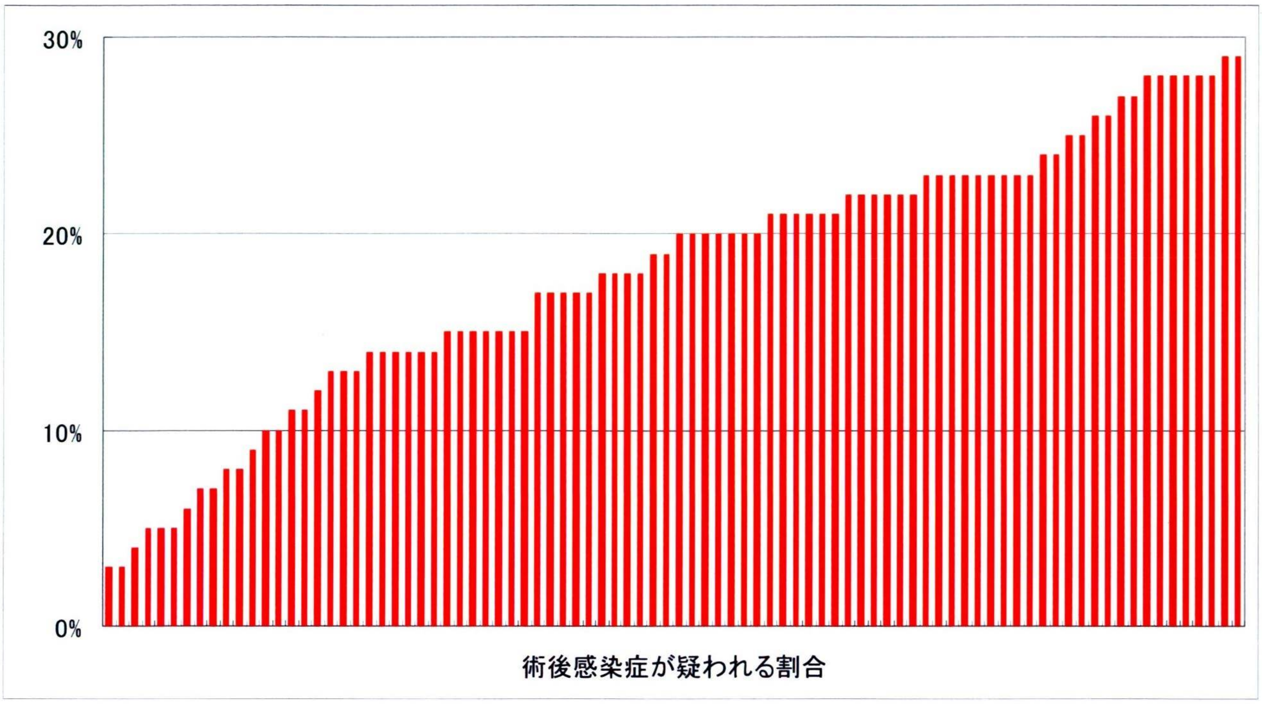
抗生剤投与期間が、(最頻値＋2日間)を超えた症例の割合と術後感染症が疑われる割合(30%まで)



抗生剤投与期間が、(最頻値＋2日間)を超えた症例の割合と術後感染症が疑われる割合(30%まで)



術後感染症が疑われる割合（30%まで）



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Risk-adjusted increases in medical resource utilization associated with health care-associated infections in gastrectomy patients

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Keywords
cross infections, medical resources, risk adjustment

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Abstract

Rationale, aims and objectives Quantifying the impact of health care-associated infections (HAIs) on medical resource utilization is necessary for payers and providers to appropriately allocate limited resources for interventions. However, previous studies tend to involve single institutions and do not take into account patient and practice variations between several hospitals. The objective of this study was to conduct a multi-institutional risk-adjusted comparison of HAI-associated impact on medical resources in gastrectomy patients in Japan.

Methods Health care-associated infections were identified using a combination of International Classification of Diseases-10 codes and antibiotic utilization patterns in 1058 gastrectomy patients from 10 Japanese hospitals. Multiple linear regression models and risk adjustment were used to analyse the impact of HAIs on: (1) total hospital costs; (2) antibiotic costs; and (3) post-surgical length of stay (LOS).

Results Overall HAI incidence for the database was 20.3%, with a range of 8.8–29.6% among the 10 hospitals. Regression models showed that HAIs were significantly associated with increases in all three indicators. Risk-adjusted comparisons revealed that HAIs were associated with an increase of US$2767 (range: US$1035–6513) in overall hospital cost, US$202 (US$98.8–764.6) antibiotic costs and 10.6 (4.7–24 days) post-surgical LOS days.

Conclusions Even after adjusting for patient characteristics and other variables, there was still a high degree of variation observed in the impact of HAIs on total hospital costs and antibiotic costs from a third-party payer's perspective and post-surgical LOS among the 10 hospitals. This information can increase the efficiency of allocation of resources for interventions to reduce HAIs.

Introduction

The control of health care-associated infections (HAIs) is a particularly important yet elusive goal for increasing the quality of health care. In addition to decreased quality of life [1,2] and increased morbidity and mortality [3], HAIs represent potentially preventable increases in medical resource utilization [4–7]. These increases in resource utilization must first be quantified in order for providers and payers to decide how to appropriately allocate limited resources for preventive measures.

While studies that estimate the impact of HAIs on resource utilization generally involve data from one or two hospitals [8–12], a multi-institutional comparison would provide a wider contextual backdrop in which to interpret the results of each hospital. However, risk adjustments must first be conducted in order to account for practice variations and patient characteristics before meaningful comparisons can be made. To the best of our knowledge, there is no current risk-adjusted multi-institutional comparison of the impact of HAIs on medical resource utilization in a Japanese setting.

The aforementioned studies generally involved chart reviews [8,9] or prospective studies [10–12]. However, these methods are extremely labour-intensive and tend to be self-limiting in terms of population sample size and study period duration. An alternative approach is the use of reimbursement data or administrative data, which provides a standardized and detailed database that can be used for multi-institution comparative studies. The hospital payment system in Japan uses an identical reimbursement schedule for all acute-care hospitals, and it is required for hospitals to produce data in similar formats. Therefore, these data are easily obtained, analysed and used to compare multiple institutions in a Japanese setting.

Infection identification using administrative data can be conducted by the use of International Classification of Diseases (ICD) codes. However, the use of these codes alone to identify HAIs has been found to have poor identification capability [13,14]. In order to improve identification capability, we chose to complement ICD code-based identification with the use of antibiotic utilization patterns as a clinically relevant indicator of infection incidence.

The objective of this study was to quantify increases in medical resource utilization associated with infections in gastrectomy patients from several Japanese hospitals, and to conduct a risk-adjusted comparison of performance between the hospitals.

Methods

Patient selection

Patient information was obtained from hospitals enrolled in the Quality Indicator/Improvement Project (QIP), a database of 16 Japanese hospitals (at the time of study) that consists of clinical and claims data on discharged patients. We selected patients with gastric cancer who were hospitalized for the purpose of gastrectomy as our target population as gastric cancer occurs with very high incidence in Japan [15]. By focusing on patients who had only undergone gastrectomies, we reduced the intrinsic variation associated with procedural differences.

Data were obtained on patients who were admitted from April 2004 to January 2007. Total and subtotal gastrectomies for gastric cancer performed were identified using the Diagnostic Procedure Combination coding system for reimbursement, a national fee schedule introduced into Japan in 2003. The sampled hospitals had a bed size ranging from 280 to 1106 beds, with a mean of 561 beds.

Patients were excluded if they fulfilled any of the following criteria: (1) patients who had died during admission; (2) patients who were given antibiotics before the day when gastrectomy was performed; (3) patients who had other surgeries before gastrectomy; (4) patients admitted directly from the emergency ward; and (5) patients with missing data with regards to antibiotic payments and anaesthesia time. Finally, hospitals with fewer than 30 cases were excluded from analysis.

Clinical diagnoses were conducted using ICD-10 (10th revision of ICD codes). Pre-existing co-morbidity conditions were analysed using the Charlson co-morbidity index (Dartmouth–Manitoba version) [16,17].

Identification of post-surgical HAI

Antibiotic utilization patterns were discerned using daily drug claims data, which allowed us to identify antibiotic administration, type of antibiotic and dosage on a day-to-day basis. We used antibiotic utilization patterns that would not occur in the simple pre-surgical prophylaxis observed in uninfected patients. Patients were deemed to have HAIs if they fell into any of the following categories: (1) post-admission complications with ICD-10 codes indicating HAI, adapted from the Pennsylvania Health Care Cost Containment Council (PHC4) [13]; (2) the use of three or more different types of antibiotics during their hospital stay; (3) the use of two types of antibiotics in which a second antibiotic type was added or changed midway through the course; (4) more than 1 day of antibiotics given in a separate time frame in which no surgery was conducted; and (5) the use of more than 3 days of antibiotics starting from the day of surgery. The final sample size (*N*) used for analysis was 1058 patients from 10 hospitals.

Resource utilization indicators

Total hospital costs and antibiotic costs from a third-party payer's perspective, as well as post-surgical length of stay (LOS), were used as indicators of medical resource utilization.

Statistical analysis

Analyses were performed using Dr. SPSS VER. II 11.0.1J (SPSS Inc., Chicago, IL, USA); *P*-values reported were two-tailed and the level of significance was set at $P < 0.05$.

Multiple linear regression models were developed to estimate the impact of HAIs on medical resource utilization. Total hospital costs, antibiotic costs and post-surgical LOS were natural logarithm transformed before being used as dependent variables in the regression models. The independent variables used were age (equal to and above 70 years), gender, post-surgical infection, co-morbidities, pre-surgical LOS, type of gastrectomy (total or partial), number of surgeries, surgery duration and hospital stratification. The age of 70 years was selected as preliminary analysis showed that the proportions of patients above and below this age were approximately equal, and univariate analysis showed highly significant association with HAI presence/absence (data not shown). Anaesthesia time (minutes) was used as a proxy indicator for surgery duration.

Hierarchal regression models were developed, with covariates grouped into patient characteristics, co-morbidities and surgery-associated factors. The first model for each dependent variable excluded the use of hospitals as dummy variables, while the second model included hospital stratification.

Risk-adjusted values were obtained using the first regression models as described previously, but with hospital stratification and post-surgical infection status excluded as variables. These regression models were then used to produce predicted values for each of the three medical resource utilization indicators. As the dependent variables were logarithmic transformed before analysis, the exponentials of the predicted values were calculated in order to obtain expected values with units of Japanese Yen and days. Duan's smearing coefficient was applied to correct for retransformation bias [18,19]. Risk adjustment was conducted by dividing each hospital's mean observed value (O) by the mean expected value (E), and multiplying the result by the mean value of the entire data set.

Final estimates were adjusted for inflation using the Japanese consumer price index (to adjust all values to the 2007 Yen value) and then converted to US dollars using Purchasing Power Parities (Japanese 100 Yen = US$0.85; April 2007) [20].

Results

The distribution of patient characteristics and gastrectomy type are presented in Table 1. The population was skewed towards an older patient population, with 47.9% of the subjects equal to or more than 70 years of age. In all, 9.7% of the study population suffered from diabetes, and 9.5% exhibited metastatic cancer. There were more patients (64.2%) who underwent subtotal gastrectomies than those who underwent total gastrectomies.

Figure 1 shows HAI incidence in total and at the hospital level. In general, there was an infection incidence of 20.3% (215 cases) in our sample population, and a range from 8.8% (Hospital A) to 29.6% (Hospital E). A breakdown of infection cases by identification method shows that the use of ICD-10 codes resulted in 85 cases (8.03%) identified. In all, 72 of these cases were also identified by antibiotic utilization. Of the cases identified by ICD codes, 70% were 'unspecified infections following a procedure', 20% were specified as 'surgical site infections' (SSIs), and the remaining 10% consisted of unspecified pneumonia, septicaemia and urinary tract infections. There were an additional 130 patients identified by antibiotic utilization alone.

Furthermore, while 'the use of >3 days of antibiotics starting from the day of surgery' was included as a criterion for infection identification, all of the cases that were identified as infected patients by this particular criterion were also identified by at least one of the other four criteria.

The regression models used are shown in Table 2. Cases with post-surgical HAIs showed highly significant association in all three indicators of increased medical resource utilization ($P < 0.001$) in all of the six models constructed.

The first regression model constructed was able to account for 60.7% of variation observed in total hospital costs. With hospital stratification, the model accounted for 64.3% of variation. Age and all surgery-associated factors were significantly associated with total hospital costs, while gender was not. Congestive heart failure was the only co-morbid condition that was consistently significant in both models for total hospital costs, and diabetes showed significance when hospital stratification was included in analysis.

Table 1 Distribution of patients, patient characteristics and type of gastrectomy by hospital and in total

Hospital	A	B	C	D	E	F	G	H	I	J	Total	%
N	57	31	85	222	81	37	93	220	159	73	1058	100
Patient characteristics												
Female	16	8	30	61	28	12	31	74	59	24	343	32.4
Age (≥70 years)	24	16	52	102	41	15	30	102	92	33	507	47.9
Acute myocardial infarction	2	0	1	0	4	0	1	2	5	0	15	1.4
Congestive heart failure	0	1	0	0	1	1	0	0	4	0	7	0.7
Peripheral vascular disease	1	0	0	1	0	0	0	1	0	1	4	0.4
Cerebral vascular disease	3	1	3	7	7	0	3	3	6	2	35	3.3
Pulmonary disease	2	1	4	13	3	1	1	6	8	1	40	3.8
Peptic ulcer	3	2	8	7	2	1	0	9	13	9	54	5.1
Liver disease	0	0	0	3	1	0	0	1	1	0	6	0.6
Diabetes	10	4	10	30	3	2	4	16	21	3	103	9.7
Diabetes w/complications	0	1	0	1	7	0	0	1	2	0	12	1.1
Renal disease	2	0	0	2	1	0	2	1	7	1	16	1.5
Metastatic cancer	8	3	5	15	1	13	1	38	12	4	100	9.5
Gastrectomy type												
Subtotal	37	19	42	153	54	23	69	148	99	35	679	64.2

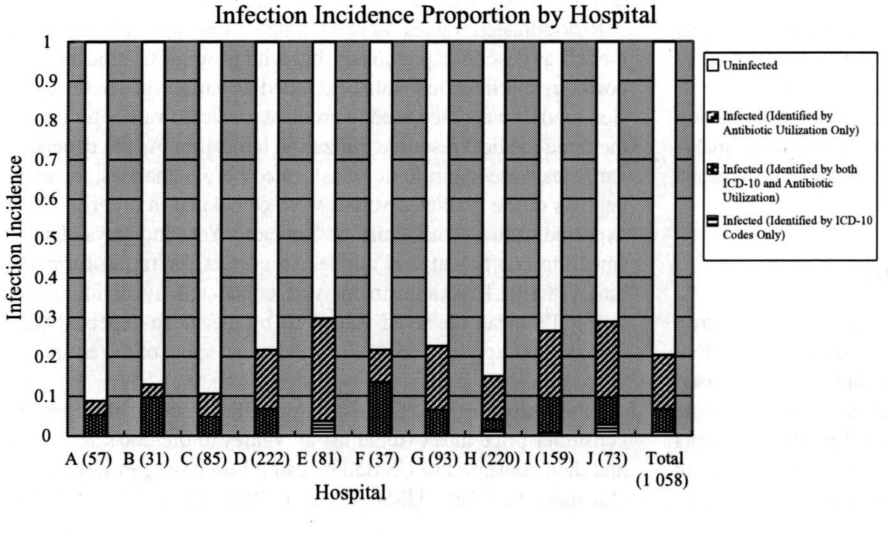

Figure 1 Infection incidence proportion by hospital and in total. White sections represent patients uninfected with HAIs; sections with diagonal lines represent infected patients identified by antibiotic utilization only; sections with dots represent infected patients identified by both International Classification of Diseases (ICD)-10 codes and antibiotic utilization; sections with horizontal lines represent infected patients identified by ICD-10 codes only (only in Hospitals E, H, I and J).

Table 2 Regression models showing association between patient characteristics, co-morbid conditions, surgery associated factors and hospital stratification on total hospital costs, antibiotic costs, and post-surgical length of stay

Models	Total hospital costs 1			Total hospital costs 2			Antibiotic costs 1			Antibiotic costs 2			Post-surgical length of stay 1			Post-surgical length of stay 2		
	0.607			0.643			0.349			0.661			0.282			0.322		
R^2	Beta	*B*	*P*-value	Beta	*B*	*P*-value	Beta	*B*	*P*-value	Beta	*B*	*P*-value	Beta	*B*	*P*-value	Beta	*B*	*P*-value
Patient characteristics																		
Age (≥70 years)	0.061	0.032	0.002	0.064	0.034	0.001	0.009	0.023	0.713	0.008	0.020	0.662	0.083	0.078	0.002	0.072	0.068	0.007
Gender	0.006	0.003	0.779	−0.002	−0.001	0.929	−0.015	−0.039	0.546	−0.004	−0.010	0.835	0.053	0.053	0.049	0.045	0.046	0.084
Post-surgical infection	0.325	0.216	<0.001	0.315	0.209	<0.001	0.580	1.716	<0.001	0.593	1.755	<0.001	0.404	0.473	<0.001	0.401	0.469	<0.001
Co-morbid conditions																		
Acute myocardial infarction	0.022	0.050	0.252	0.010	0.022	0.597	−0.050	−0.502	0.047	−0.023	−0.232	0.208	0.025	0.099	0.343	0.013	0.051	0.619
Congestive heart failure	0.057	0.189	0.004	0.055	0.182	0.004	−0.027	−0.397	0.286	0.021	0.311	0.253	0.047	0.276	0.075	0.043	0.247	0.103
Peripheral vascular disease	−0.008	−0.035	0.679	−0.007	−0.029	0.720	0.013	0.256	0.596	0.014	0.280	0.425	0.009	0.072	0.719	0.013	0.099	0.614
Cerebral vascular accident	0.014	0.022	0.462	0.008	0.011	0.682	0.000	0.003	0.984	0.016	0.105	0.389	−0.004	−0.010	0.882	−0.009	−0.025	0.716
Pulmonary disease	−0.023	−0.032	0.246	−0.014	−0.020	0.447	0.013	0.081	0.606	0.000	−0.002	0.986	0.005	0.013	0.842	0.009	0.022	0.724
Peptic ulcer	−0.002	−0.003	0.905	0.000	0.000	0.988	−0.034	−0.181	0.184	−0.024	−0.127	0.202	−0.004	−0.009	0.881	−0.006	−0.014	0.808
Liver disease	0.016	0.056	0.420	0.021	0.075	0.254	0.002	0.033	0.933	−0.002	−0.024	0.933	0.021	0.132	0.423	0.023	0.141	0.378
Diabetes	0.024	0.021	0.228	0.037	0.034	0.046	0.020	0.079	0.436	0.000	−0.001	0.989	0.026	0.042	0.318	0.034	0.054	0.187
Diabetes w/complications	0.035	0.089	0.073	0.024	0.061	0.206	−0.021	−0.234	0.410	0.034	0.387	0.064	0.060	0.265	0.024	0.038	0.168	0.151
Renal disease	0.032	0.071	0.097	0.025	0.054	0.191	−0.046	−0.453	0.065	−0.043	−0.418	0.019	0.012	0.045	0.658	0.007	0.025	0.799
Metastatic cancer	0.007	0.006	0.723	0.036	0.033	0.064	0.036	0.145	0.164	0.051	0.209	0.007	0.010	0.016	0.718	0.031	0.050	0.243
Surgery associated factors																		
Pre-surgical LOS	0.333	0.019	<0.001	0.325	0.019	<0.001	0.069	0.018	0.006	−0.026	−0.007	0.175	0.090	0.009	0.001	0.065	0.006	0.018
Gastrectomy type	0.359	0.200	<0.001	0.352	0.196	<0.001	0.061	0.152	0.020	0.058	0.145	0.003	0.144	0.142	<0.001	0.132	0.129	<0.001
No. of surgeries	0.194	0.071	<0.001	0.221	0.081	<0.001	−0.039	−0.064	0.144	0.031	0.051	0.154	0.070	0.046	0.012	0.121	0.079	<0.001
Surgery duration	0.148	0.000	<0.001	0.136	0.000	<0.001	0.010	0.000	0.707	0.043	0.001	0.040	0.091	0.000	0.001	0.070	0.000	0.018
Hospitals																		
B				0.023	0.036	0.316				−0.255	−1.801	<0.001				0.118	0.329	<0.001
C				0.030	0.029	0.309				0.218	0.954	<0.001				0.058	0.100	0.153
D				−0.075	−0.049	0.043				0.256	0.749	<0.001				−0.016	−0.018	0.758
E				0.067	0.067	0.019				−0.161	−0.719	<0.001				0.119	0.211	0.002
F				−0.068	−0.099	0.006				−0.212	−1.372	<0.001				−0.103	−0.265	0.003
G				0.137	0.129	<0.001				0.126	0.529	<0.001				0.069	0.115	0.082
H				−0.014	−0.009	0.700				0.238	0.698	<0.001				0.096	0.111	0.057
I				0.050	0.038	0.139				0.065	0.215	0.051				0.123	0.162	0.009
J				0.036	0.038	0.195				−0.105	−0.493	<0.001				0.030	0.055	0.434

Beta refers to standardized coefficients and B refers to unstandardized coefficients.

Table 3 Observed and risk-adjusted means of total hospital costs, antibiotic costs, post-surgical length of stay in total and by hospital

	Total hospital costs (US$)				Antibiotic costs (US$)				Post-surgical length of stay (days)			
	Uninfected		Infected		Uninfected		Infected		Uninfected		Infected	
	Observed	Adjusted	Observed	Adjusted	Observed	Adjusted	Observed	Adjusted	Observed	Adjusted	Observed	Adjusted
Total	11 252.9	11 543.6	15 676.3	14 310.6	42.9	45.9	277.9	248.3	16.1	17.5	29.2	28.1
A	11 041.2	11 334.7	19 919.8	17 848.0	28.9	31.0	838.9	795.6	15.1	16.6	38.4	40.6
B	11 597.7	12 205.9	16 785.4	13 897.1	7.9	8.9	161.2	114.4	21.1	23.0	31.3	27.7
C	13 270.0	11 740.7	14 981.6	12 776.0	69.6	67.7	208.8	196.7	17.7	17.4	24.8	23.1
D	10 314.6	10 783.7	14 271.6	13 696.7	56.8	59.7	335.4	313.2	14.6	16.0	24.6	24.9
E	12 407.0	12 205.4	15 937.8	14 001.7	14.8	15.5	124.4	114.2	18.8	19.5	28.5	25.7
F	10 736.8	10 644.5	12 601.3	11 811.6	8.3	9.3	218.9	207.2	12.5	13.2	18.0	18.1
G	11 541.3	12 759.4	16 375.3	17 681.3	42.5	50.7	250.7	275.0	14.9	17.6	33.3	38.2
H	10 771.2	11 421.2	14 687.9	13 602.8	51.2	56.9	289.2	247.4	15.7	18.1	27.2	27.0
I	11 476.4	11 745.3	16 937.2	14 230.7	37.1	38.3	302.9	254.9	17.4	18.3	33.6	29.5
J	11 329.9	11 750.8	17 167.6	15 266.5	23.0	24.8	222.1	175.7	16.2	17.5	34.0	31.1

In the case of antibiotic costs, the regression model was able to account for 34.9% of variation observed, and 66.3% with hospital stratification included. Age and gender were not significant with antibiotic costs in both models. When hospitals were not included in analysis, pre-surgical LOS and gastrectomy type were significantly associated with antibiotic costs. When hospitals were included, only gastrectomy type remained significant, and surgery duration gained significance.

The regression models developed were able to account for 28.2% of variations in post-surgical LOS, and 32.2% after taking into account hospital stratification. Age showed significant association in both models, while gender showed association only when hospitals were not included in analysis. The only co-morbid condition significantly associated with post-surgical LOS was diabetes with complications in the first model. Furthermore, pre-surgical LOS, gastrectomy type and number of surgeries were significant factors associated with post-surgical LOS.

The risk-adjusted differences for all three medical resource utilization indicators between infected and uninfected patients at hospital level were shown in Table 3. Risk adjustment resulted in reducing the variation between infected and uninfected patients. Infected patients showed a risk-adjusted increase in US$2767, or approximately 24% for total hospital costs (and a pre-adjusted increase of US$4423.4). At the hospital level, there was a range of adjusted infection-based increases in total hospital costs from US$1035 (Hospital C) to US$6513 (Hospital A).

In general, infections were associated with an increase in US$202.4 in mean antibiotic costs. Prior to adjustment, the difference in antibiotic costs between infected and uninfected patients was US$235. Hospital E showed the least amount of increase at a risk-adjusted mean of US$98.8. The highest increase in antibiotic costs as a result of infections was seen in Hospital A, at US$764.6. In addition, Hospitals B, E and F presented very low antibiotic costs for their respective uninfected populations, at less than US$15.

Hospital stay was extended by an adjusted average of 10.6 days post surgery, as a result of infection. While most hospitals managed to control the extended LOS to approximately 10 days or less, Hospitals A and G had large increases of 24 days and 20.7 days, respectively. Hospital B showed the lowest increase in mean post-surgical LOS in infected patients at only 4.7 days.

Discussion

In this study, we used a combination of ICD codes and antibiotic utilization patterns in order to identify HAIs in gastrectomy surgery patients admitted into 10 hospitals in Japan. Regression analysis was conducted to estimate the impact of medical resource utilization increases involved with infections, with resource utilization measured in three indicators – total hospital costs, antibiotic costs and post-surgical LOS. Finally, we conducted risk-adjusted performance comparisons within the 10 hospitals.

Previous studies have shown that the use of ICD codes to identify HAIs has poor sensitivity and positive predictive value [13,14]. Furthermore, using claims data alone to derive secondary diagnoses has been found to lack distinguishing ability between pre-existing conditions and conditions that occur post admission [21]. In response to these issues, we complemented ICD code identification with antibiotic utilization data and adjusted selection criteria to reduce misidentification of pre-existing conditions. The use of ICD codes alone would have resulted in an infection incidence of approximately 8%. ICD codes alone may have been limited to the more serious infections, while antibiotic utilization allowed us to include less severe infections in our calculations that were not reflected in ICD codes.

Evidence-based medicine supports that even with gastrectomy surgeries, a single dose of cefazolin before surgery is sufficient prophylaxis [22,23]. However, the Japanese Society for Chemotherapy produced guidelines that recommended 3–4 days of prophylaxis for clean-contaminated surgeries such as gastrectomy. Furthermore, a previous study [24] showed that the mean prophylaxis given to gastrectomy patients was approximately 3–4 days. Taking this into account, we adjusted for this over-utilization of antibiotics by allowing for a 3-day prophylactic period post surgery, and identifying cases with 4 or more days of antibiotic utilization as infections. The failure to do so may have resulted in mistakenly identifying antibiotic over-utilization as infections. However, there would be an uncertainty as to the validity of cases identified as infected by this criterion alone, as cases with 4 or more days of antibiotic utilization may simply represent antibiotic administration practice variation. Despite this, all cases that were identified by this criterion were further confirmed by at least one other identification criterion.

A previous study of a single hospital in Japan showed a 13.8% incidence of SSIs associated with gastrectomy [25], while the sample population here presented a 20.3% incidence proportion of infections that included other infections in addition to SSIs, such as bloodstream infections and pneumonia.

In all six regression models that we used, post-surgical HAIs were significantly associated with increases in total hospital costs, antibiotic costs and post-surgical LOS. Among the independent variables, comparisons of standardized coefficients (Table 2) showed that HAIs had the third highest magnitude of impact on total hospital costs (after type of gastrectomy and pre-surgical LOS), and the highest magnitude of impact on antibiotic costs and post-surgical LOS. Total hospital costs and post-surgical LOS were sensitive to all surgery-associated factors, but antibiotic costs were unsurprisingly less sensitive to this group of variables.

Post-surgical LOS showed significant associations with both age and gender, with elderly (≥70 years) male patients associated with longer hospital stays. This was consistent with previous studies that showed longer LOS periods associated with elderly [26] and male patients [27]. The problems of increases in post-surgical LOS associated with HAIs are further exacerbated by the already-lengthy hospital stay durations in Japan [28].

Pre-existing co-morbid conditions did not seem to show consistent or strong influences on increases in medical resource utilization based on our models, which may be due to the low volume of cases with co-morbidity scores. The two most common co-morbidities (that occurred in approximately 10% of the dataset population) were diabetes and metastatic cancer, which showed significant association with total hospital costs and antibiotic costs, respectively.

Even after risk adjustment, we observed large degrees of variation in HAI-associated increases in all three indicators. The difference between mean total hospital costs uninfected and infected patients ranged as much as from US$1035 in Hospital C to US$6513 in Hospital A. Hospital A had approximately 2.4 times the overall mean of increased total hospital costs associated with HAI, and had the largest observed difference between infected and uninfected patients with regards to post-surgical LOS. A more detailed inspection of the cases in Hospital A revealed that two of the five had methicillin-resistant *Staphylococcus aureus* (MRSA) infections, which may have accounted for the increased medical resource utilization reflected.

The overall risk-adjusted mean of increased antibiotic costs associated with HAIs was US$202. Table 2 showed that the R^2 value for the regression model using antibiotic costs as the dependent variable that had included hospital stratification was much higher than that of the model that did not. Furthermore, when hospital stratification was included in analysis, most of the hospitals showed significant association, implying high variation in antibiotic use at the hospital level. Hospital B showed the lowest adjusted antibiotic costs for uninfected patients at US$8.9, while Hospitals E and F also had very low values in this category. An analysis of the cases in these hospitals revealed that all uninfected cases were given the appropriate 1-day-only prophylaxis method as prescribed by evidence-based medicine. In addition to these laudable achievements, Hospitals B and E managed to control the increase in antibiotic costs in infected patients to US$99 and US$105, respectively. Increases in antibiotic costs in Hospital F were closer to the overall average at US$198. This could imply that there may be stringent antibiotic utilization guidelines in place at Hospitals B and E, and that they are strictly adhered to even in infected cases. The other seven hospitals had higher adjusted antibiotic costs in their uninfected cases, and an analysis of these hospitals showed that the majority of cases were given approximately 2–3 days of prophylaxis. This unfavourable utilization rates for uninfected cases reflected the results reported previously [25], and resulted in unnecessary cost as well as increase the risk of developing resistant bacteria.

With regards to limitations of this study, the sampled hospitals were part of a database known as the QIP. These hospitals had voluntarily entered this project in order to improve health care quality and management, and as such, may not represent the general situation of hospitals in Japan. Therefore, there may be a degree of selection bias and resulting generalizability issues.

We believe the method presented here can be similarly applied to analysing patients with other diseases and procedures. We have used this technique to quantify the increases in medical resource utilization associated with post-surgical HAIs, and also shown that even after adjusting for variations in patient characteristics and other variables, a large degree of variation still exists between hospitals in terms of resource utilization. In this study, we observed both good performers in terms of controlling infection incidence and the resulting resource utilization, as well as hospitals that did not perform as well. The results of this study were reported back to the participating hospitals in order to commend and encourage further good practice in good performers, as well as to bring attention to problem areas in the other hospitals. This information is highly useful for the hospitals involved as they represent not only information about their own hospitals, but provide a context of other hospitals in which to compare their own performance.

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Title Page

Title:
Healthcare-associated infections in acute ischemic stroke patients from 36 Japanese hospitals: risk-adjusted economic and clinical outcomes

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Abstract

Background

Healthcare-associated infections (HAIs) are a major cause for worsening in ischemic stroke patients. In addition to increased morbidity and mortality, HAIs also result in a potentially preventable increase in economic costs.

Aims

The aim of this study was to identify HAI incidence in ischemic stroke patients in Japanese hospitals, and to conduct a risk-adjusted analysis of the associated economic and clinical outcomes.

Methods

HAIs were identified in 36 Japanese hospitals using an administrative database. Identification was carried out using a combination of International Classification of Diseases (ICD-10) codes and antibiotic utilization patterns that indicated the presence of an infection. Risk-adjusted hospital charges and length of stay were calculated using multiple linear regression analyses correcting for patient and hospital factors. A logistic regression model was used to analyze the association between HAI infection and mortality.

Results

There was an overall HAI incidence of 16.4 %, with an inter-hospital range of 4.7% to 28.3%. After risk-adjustment, infected cases paid an additional US$3,067 per admission (inter-hospital range US$434 – US$7,151) and were hospitalized for an additional 16.3 days (Inter-hospital range: 5.1 days – 25.1 days) when compared to uninfected patients. HAIs also had a strongly significant association with increased mortality (OR=23.2, 95%; CI: 12.5 – 43.2).

Conclusions

We observed a wide range of HAI incidence between the hospitals. HAIs were found to be significantly associated with increased hospital charges, LOS and mortality. Furthermore, the use of risk-adjusted multi-institutional comparisons allowed us to analyze individual performance levels in both infection and cost control.

(247 words)

Introduction

Healthcare-associated infections (HAIs) have previously been identified as having a significant impact in the worsening of ischemic stroke patients[1-4]. In addition to increased morbidity and mortality, the resulting extension in hospital stay results in increased costs to patients and 3rd party payers, as well as a reduction in potential bed-space for healthcare providers.

HAIs have been estimated to develop in over one-third of patients with acute stroke, with the most common infections being lung infections and urinary tract infections[1-2]. Studies have reported HAI incidences of 41.5%[5], stroke-associated pneumonia incidences ranging from 10% to 30.9%[3-4,6-8], and even incidences of significant bacteriuria alone reaching 39.1%[9]. Reported extensions in length of hospital stay ranged from 6 days[6] to 23 days[7]. Risk factors found to be associated with HAIs in stroke patients have include mechanical ventilation, dysphagia, age, parenteral nutrition, post-stroke disability, and urinary catheterization[6, 10-11]. In addition, the Barthel Index has been shown to be significantly associated with infections in acute ischemic stroke patients[12-13].

Quantifying the increases in hospital charges and length of stay (LOS) associated with HAIs would be useful for healthcare providers and 3rd party payers when considering the cost-effectiveness of interventions aimed at reducing HAIs. While some studies have attempted to quantify the outcomes associated with HAIs in stroke patients at the hospital level[6-7], a multi-institutional analysis that takes into account patient and hospital-related variations would allow for a more meaningful interpretation of each hospital's results.

There are currently no studies to our knowledge that have analyzed HAI incidence in stroke patients in Japanese hospitals, and no studies that have attempted to quantify the economic impact and mortality associated with HAIs at a multi-institutional level.

Aims

The objective of this study was to utilize an administrative database from multiple Japanese hospitals in order to identify HAI incidence in patients admitted for acute ischemic stroke, and to quantify risk-adjusted economic and clinical outcomes associated with HAIs.

Methods

Hospital and Patient Selection

The original sample population consisted of 16,886 ischemic stroke patients admitted during the period of April 1998 to April 2008 into 40 general hospitals *(designated H1 to H40)* enrolled in the Quality Indicator/Improvement Project (QIP), a database of Japanese hospitals that consists of clinical and claims data. Hospitals in the QIP voluntarily join the project and provide claims and administrative data in standardized formats for analysis with the objective of improving the quality and efficiency of healthcare provision. The hospitals included in this study were drawn from this database and represent a variety of public and private, teaching and non-teaching hospitals with different casemixes and specialties.

Clinical diagnoses were identified using ICD10 codes. Pre-existing comorbidity conditions were analyzed using the Charlson comorbidity index (Dartmouth-Manitoba version) [14-15].

Patients who had infections occurring within 48 hours were identified as having community-acquired infections and thus excluded from this study. Other exclusion criteria included minors (below 20 years), and cases with missing data in charge information, age and Japan Coma Scale (JCS)[16] score. For the linear regression models used for hospital charges and LOS, and the logistic regression model used for mortality, cases with standardized residuals greater than 3 standard deviations from the mean were considered outliers and excluded from analysis. In the regression models for hospital charges and LOS, patients who died during the hospitalization period were also excluded.

The JCS is the most widely used clinical tool for evaluating consciousness level in Japanese emergency care, and consists of a scale categorized into four levels: (i) alert; (ii) JCS levels 1~3 (disoriented: awake without stimulation); (iii) JCS levels 10~30 (somnolent: arousable only in the presence of stimulation); and (iv) JCS levels 100~300 (comatose: unarousable despite stimulation). [17]

Healthcare-Associated Infection Identification

HAIs were first identified using hospital-reported ICD10 codes adapted from the Pennsylvania Health Care Cost Containment Council (PHC4)[18]. However, previous studies have shown that the use of ICD codes alone is insufficient for HAI identification[18-19]. Therefore, HAIs were also identified through the use of antibiotic utilization patterns obtained from daily drug claims data, based on a technique adapted from our previous study[20].

Infections were identified where antibiotic utilization did not conform to surgical prophylaxis patterns in patients who had surgeries performed. Patients were identified as having HAIs if, in addition to reported ICD codes, they fell into any of the following categories: (1) Antibiotic utilization episodes with durations of 4 or more days that did not overlap a day in which surgery requiring prophylaxis was performed (2) Three or more antibiotic types used within a single episode of antibiotic utilization (3) Antibiotic types changed or a 2nd antibiotic type added midway during an antibiotic utilization episode (4) Prophylactic antibiotic utilization episodes of 5 or more days in which the start of the episode corresponds to a day where surgery was performed.

Clinical and Economic Outcome Indicators

Total hospital charges (Japanese Yen) and LOS (days) were used as indicators for economic outcome, while mortality was used as the clinical outcome measure.

Statistical Analysis:

Analyses were performed using Dr. SPSS VER. II 11.0.1J. Significance for P-values was set at $P < 0.05$(two-tailed).

Risk-Adjustment

Total hospital charges and LOS were natural logarithmically transformed before used as dependent variables in multiple linear regression analysis (Stepwise). Two models were developed for each dependent variable; one in which hospital stratification was included in the independent variables, and another in which hospital stratification was excluded. The former was used to calculate overall risk-adjusted hospital charges and LOS after taking hospital variations into account. The latter model was used in the calculation of hospital-level risk-adjusted hospital charges and LOS, which enabled inter-hospital comparisons.

The models for hospital charges included the following independent variables: age, sex, Barthel index, atherothrombotic stroke, cardioembolic stroke; Charlson score, LOS, surgeries performed, central venous catheter (CVC) use, mechanical ventilation, dysphagia, ICU stay, and JCS score upon admission. The models for LOS included the following independent variables: age, sex, Barthel index, atherothrombotic stroke, cardioembolic stroke; Charlson score, surgeries performed, central venous catheter (CVC) use, mechanical ventilation, dysphagia, ICU stay, and JCS score upon admission. The first model for each dependent variable also included hospital stratification while the second model did not. Apart from atherothrombotic and cardioembolic strokes, patients with other types of stroke were used as a reference for the regression models. The Barthel index used by the hospitals in this sample was the 20-point Collin scoring version[21].

Exponentials of the predicted values from the regression models were calculated in order to obtain expected values in units of Japanese Yen and days, and Duan's smearing coefficient[22-23] was applied to correct for retransformation bias. Risk adjustment was then conducted by dividing each hospital's mean observed value by the mean expected value, and the result was multiplied by the mean value of the entire dataset. Final estimates of hospital charges were adjusted for inflation using the Japanese consumer price index (adjusting all values to the 2008 yen value) and then converted to US dollars using Purchasing Power Parities (JPN 100 Yen = US$0.80[21]).

Mortality was used as the dependent variable in the logistic regression model, and adjusted with the following independent variables: HAI status, age, sex, Barthel index, atherothrombotic stroke, cardioembolic stroke; Charlson score, surgeries performed, CVC use, mechanical ventilation, dysphagia, ICU stay, LOS, JCS score upon admission, and hospital stratification. Calibration was evaluated with a Hosmer-Lemeshow statistical analysis[25], while discrimination was evaluated with a Receiver Operating Characteristic (ROC) curve.

Results

Patient and Hospital Characteristics

After excluding cases that fulfilled the aforementioned exclusion criteria, our final sample for analysis consisted of 8,861 patients from 36 hospitals, with four hospitals exclude due to a lack of patients.

General characteristics of the patients in our sample are shown in Table 1. Elderly patients were heavily represented in the study population, with almost half of the patients older than 75 years of age. There were more men than women at 58.3% versus 41.7%. Of the patients in our sample, 68% were originally admitted to either neurosurgery or neurology departments, 17.3% were admitted to internal medicine departments and the remainder in various other departments. The Barthel Index showed that upon admission, 20.1% of the patients had no form of disabilities, while 43.3% had relatively severe disabilities. Over 21% of the patients were classified as having an atherothrombotic stroke, 10.3% of the patients had a cardioembolic stroke, and 68.5% had strokes which did not fall into either of the above 2 categories. Almost 70% of the patients were completely lucid upon