Effect of diabetes on mortality and length of hospital stay in patients with renal or perinephric abscess

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OBJECTIVES: We compared the risk of in-hospital mortality and the length of hospital stay between diabetic and non-diabetic patients hospitalized for renal or perinephric abscess.

METHOD: The data analyzed in this study were retrieved from Taiwan's National Health Insurance claims. The risk of in-hospital mortality and the length of hospital stay were compared between 1,715 diabetic patients, hospitalized because of renal or perinephric abscess in Taiwan between 1997 and 2007, and a random sample of 477 non-diabetes patients with renal or perinephric abscess.

RESULTS: The in-hospital mortality rates from renal or perinephric abscess for the diabetic patients and the non-diabetic patients were not different, at 2.3% and 3.4%, respectively. However, diabetes was significantly associated with a longer length of hospital stay among patients with renal abscess, by 3.38 days (95% confidence interval [CI]: 1.59-5.17).

CONCLUSIONS: Diabetes does not increase the risk of in-hospital mortality from renal or perinephric abscess. Nevertheless, appropriate management of patients with diabetes and concurrent renal or perinephric abscess is essential to reduce the length of hospital stay.

KEYWORDS: Renal Abscess; Diabetes; Mortality; Length of Hospital Stay; Cohort Study.

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INTRODUCTION

Renal abscess (RA) and perinephric abscess are potentially lethal complications of urinary tract infections (UTIs). The insidious clinical course and variable symptoms and signs at the time of clinical evaluation can cause difficulty in the diagnosis of RA, thereby resulting in an increased case-fatality rate in RA patients (1,2). Although progress in imaging studies and the development of percutaneous drainage techniques for retroperitoneal abscesses have substantially decreased the case-fatality rate from RA (3,4), in-hospital mortality rates have remained high, with rates ranging from 5% to 15%, as reported in several recent studies, including findings from Taiwan (5,6).

Diabetes is one of the most common endocrine diseases, and its global prevalence for all age groups worldwide was estimated to be 2.8% in 2000 and is predicted to reach 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million by 2030 (7). Diabetes is a serious illness with multiple complications (8,9) and premature mortality, and it accounts for at least 10% of the total health care expenditure in many countries (10). Additionally, diabetes has frequently been found to increase the risk of developing RA (11).

Patients with diabetes are at increased risk for infections (12,13), particularly those originating in the urinary tract (8). Diabetes can also cause several changes in the host defense system, including defects in neutrophil function (14), increased bacterial adherence to the uroepithelial cells of diabetic patients (15) and decreased antibacterial activity as a result of glycosuria (16). As a result, diabetic patients tend to have a higher incidence and prevalence of bacteriuria (17), and they are at a higher risk for developing serious consequences, such as emphysematous cystitis, pyelonephritis, renal papillary necrosis, and abscess (18,19).

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With respect to the prognosis of diabetes-complicated infections, such as bacteremia, sepsis, or liver abscess, findings from previous studies have been inconsistent (20-23). An earlier study (11) used a nationally representative diabetic cohort, retrieved from the National Health Insurance (NHI) database, to investigate the relative risk of RA in diabetes, and found a significantly increased risk of RA in diabetic patients. Using the same dataset, the present study further explored whether RA patients with diabetes have an increased risk of in-hospital mortality and whether they experience an increased length of hospital stay (LOS) compared to RA patients without diabetes.

MATERIALS AND METHODS

The data analyzed in this study were obtained from our previous study, which investigated the risk of admission for RA in the diabetic population (11). The previous study, based on Taiwan's NHI claims, used a cohort study design and followed more than a half million diabetic patients and sex- and age-matched controls from 1997 to 2007.

Briefly, the diabetic cohort consisted of all individuals (n = 500,867) who had an initial diabetes-related diagnosis (ICD-9: 250 or A code 181) at any time in 1997 and who received one or more additional diagnoses within the subsequent 12 months. The control subjects (n = 500,365) were matched to the diabetic cohort according to sex and age and were identified from the registry of beneficiaries, after the data of the diabetic group were excluded. Using unique personal identification numbers, we linked the ambulatory claims data of the study subjects to inpatient claim records (1997-2007) to identify episodes of admission for RA (ICD-9: 590.2). Over 11 years of follow-up, 1,715 diabetic patients were admitted for RA, whereas 477 controls were admitted with the same diagnosis, representing cumulative incidences of 0.34% and 0.10%, respectively. After adjustment for confounders, diabetic patients had a significantly increased hazard ratio (HR) (3.81) of admission for RA (11).

Based on the above-mentioned previous report (11), the present study employed a retrospective cohort design, in which all 1,715 newly diagnosed RA patients with histories of diabetes were recruited. The control group consisted of 477 newly diagnosed RA patients without a history of diabetes in 1997. We linked the diabetic and non-diabetic RA patients to the NHI inpatient claims between the time of their first-time admissions for RA and the last day of 2007 to examine whether they experienced in-hospital mortality. The information on the LOS of the study subjects was based on their first-time hospitalization for RA between 1997 and 2007.

To evaluate the effects of diabetes, sex, age, and treatment modality on the risk of in-hospital mortality in RA patients, we applied Cox's multivariate proportional hazard regression analysis, with time to in-hospital mortality as the dependent factor in the model. The index date of follow-up was the RA date of first-time admission between 1997 and 2007. The date of the end of follow-up was the date of discharge from the last hospitalization for individuals who died or the date of termination of the NHI policy or the last day of 2007 for individuals who were censored. The treatment modality included antimicrobials only, percutaneous drainage (International Classification of Disease, 9th version, Clinical Modification [ICD-9-CM], procedure codes: 55.03 or 55.92), surgical drainage (ICD-9-CM procedure codes: 55.01 or 55.02), and nephrectomy (ICD-9-CM procedure codes: 55.51).

We also performed multiple linear regressions to assess the difference in LOS between RA patients with and without diabetes. In addition to diabetic status, age, sex, and treatment modality, we also included geographic area and urbanization level in the multivariate model to account for possible geographic and urbanization variations in cancer incidence and mortality in Taiwan (24). All of the statistical analyses were performed using SAS (version 9.2; SAS institute, Cary, NC). $P<0.05$ was considered statistically significant. Access to the NHI claims was reviewed and approved by the National Health Research Institutes Review Committee.

RESULTS

The RA patients with diabetes were younger than the control patients (58.2 ± 12.4 *vs.* 64.5 ± 9.9 years old). Female patients dominated the samples in both groups. The distributions of geographic areas and urbanization levels were similar in both groups. The treatment modalities used were also similar in both groups (Table 1).

In-hospital mortality, in association with diabetes status, sex, age, and treatment modality, is presented in Table 2. The in-hospital mortality rates for the diabetic RA and non-diabetic RA groups were 2.3% and 3.4%, respectively, which represents a non-significantly reduced covariate-adjusted HR of 0.91 (95% CI: 0.49-1.69, $p = 0.759$) for RA patients with diabetes. Compared with the female RA patients, male RA patients had a significantly higher hazard rate of in-hospital mortality (adjusted HR = 2.03). Additionally, older age tended to be associated with a higher rate of in-hospital mortality, and the highest adjusted HR (3.86) was noted in the group >64 years old. With regard to treatment modalities, 74.8% of the RA patients received antimicrobial treatment alone, and the corresponding figures for percutaneous drainage, surgical drainage, and nephrectomy were 14.6%, 6.3%, and 4.3%, respectively. The in-hospital mortality rates for RA patients treated with antimicrobials alone, percutaneous drainage, surgical drainage, and nephrectomy ranged from 1.1% to 3.8%, but they were not significantly different across treatment modality.

Table 3 compares the LOS between the two study groups. The mean LOS for RA patients with and without diabetes was 18.89 and 16.19 days, respectively. The covariate-adjusted difference in LOS between the two groups (3.27 days) was statistically significant.

DISCUSSION

Urinary tract infections are among the most common bacterial infections. Renal abscess is a potentially lethal complication of UTIs. Some previous studies have reported the risk factors, clinical presentation, treatment modalities, and outcomes of RA; however, almost all of them were hospital-based (4,5,25,26). To our knowledge, our study is the first to employ a population-based design to investigate the risk of mortality from RA relative to diabetes.

Diabetes and other risk factors for in-hospital mortality among patients hospitalized for RA

Recent hospital-based studies have reported in-hospital mortality rates associated with RA ranging from 0% to 15%

Table 1 - Characteristics of patients with renal or perinephric abscess according to diabetic status.

Variables[a]	RA[b] patients without diabetes		RA patients with diabetes	
	N	%	N	%
Sex				
Male	136	28.5	368	21.5
Female	341	71.5	1347	78.5
Age (years)				
<45	10	2.1	232	13.5
45-54	71	14.9	379	22.1
55-64	139	29.1	542	31.6
>64	257	53.9	562	32.8
Mean (SD)	64.5 (9.9)		58.2 (12.4)	
Geographic area				
North	159	34.0	607	35.9
Central	118	25.2	417	24.6
South	166	35.5	570	33.7
East	25	5.3	99	5.8
Urbanization level				
Metropolis	169	35.8	583	34.4
Satellite city	110	23.3	453	26.7
Rural area	193	40.9	658	38.9
Treatment modality				
Antimicrobials only	349	73.2	1291	75.3
Percutaneous drainage	78	16.3	242	14.1
Surgical drainage	28	5.9	109	6.3
Nephrectomy	22	4.6	73	4.3
Total	477	100.0	1715	100.0

[a]Inconsistency between total population and population summed from individual variables resulted from missing information.
[b]RA: renal or perinephric abscess.

(4,5,25,26). In our study, the overall in-hospital mortality rate was estimated at 2.6%, and diabetes did not increase the risk of in-hospital mortality from RA. Patients with diabetes often have abnormalities in both cell-mediated and humoral immune responses (27). Diabetic patients may have an increased risk of dying from an infectious disease, particularly serious bacterial infections (28). However, evidence obtained from previous studies has been inconsistent with regard to the prognosis of complicated infections associated with diabetes.

Table 2 - Hazard ratio of in-hospital mortality relative to diabetes, age, sex, and treatment modality in patients with renal or perinephric abscess (n = 2,192).

Variables	No. of patients admitted	In-hospital mortality		Relative risk estimates					
		N	%	HR[a]	95% CI[a]	*p*-value	AHR[a,b]	95% CI[b]	*p*-value
Diabetes									
No	477	16	3.4	1.00			1.00		
Yes	1,715	40	2.3	0.69	0.38-1.24	0.213	0.91	0.49-1.69	0.759
Sex									
Male	504	21	4.2	2.05*	1.18-3.56	0.010	2.03*	1.15-3.59	0.015
Female	1,688	35	2.1	1.00			1.00		
Age									
<45	242	3	1.2	1.00			1.00		
45-54	450	5	1.1	0.90	0.21-3.78	0.881	0.80	0.18-3.65	0.775
55-64	681	15	2.2	1.79	0.52-6.25	0.359	2.31	0.65-8.16	0.195
>64	819	33	4.0	3.34*	1.02-11.00	0.046	3.86*	1.15-12.98	0.029
Treatment modality									
Antimicrobials only	1,640	39	2.4	1.00			1.00		
Percutaneous drainage	320	12	3.8	1.60	0.83-3.09	0.162	1.30	0.63-2.66	0.478
Surgical drainage	137	4	2.9	1.24	0.44-3.51	0.692	1.51	0.52-4.39	0.448
Nephrectomy	95	1	1.1	0.44	0.06-3.21	0.416	0.45	0.06-3.40	0.442
Total	2192	56	2.6						

[a]HR = hazard ratio; CI = confidence interval; AHR = adjusted hazard ratio.
[b]Estimated from Cox's multivariate proportional hazard model, with diabetes, age, sex, treatment modality, geographic area, and urbanization level simultaneously included in the model.
*$p<0.05$.

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Table 3 - Comparison of length of hospital stay between renal or perinephric abscess patients according to their diabetic status (N = 2,192).

Variables	No. of patients admitted	LOS[a]		Difference in mean LOS					
		Mean	SD[a]	Crude â[a]	95% CI[a]	*p*-value	Adjusted â[a,b]	95% CI	*p*-value
Diabetes									
No (reference)	461	16.19	15.62						
Yes	1675	18.89	16.62	2.70*	1.01-4.40	0.002	3.27*	1.55-5.00	<0.0001

[a]LOS = length of hospital stay; SD = standard deviation; â = regression coefficient,CI = confidence interval.
[b]Estimated from multivariate linear regression model with adjustment for age, sex, treatment modality, geographic area, and urbanization level.
*$p<0.05$.

One population-based epidemiological study suggested that diabetes is an important prognostic factor for severe Gram-negative infections, including bacteremia, and the authors concluded that among patients with bacteremia, diabetes was also associated with a poorer prognosis. We speculated that latent diabetic organ disease would render patients with diabetes particularly vulnerable to multiorgan failure associated with Gram-negative sepsis. Protracted multiorgan failure promoted by diabetic organ disease could play a role in the higher mortality among diabetic patients (20). Another study on the association of diabetes with liver abscess-related mortality also reported a higher 30-day post-discharge mortality rate in patients with diabetes. We argue that the harmful effects of hyperglycemia, general diabetic angiopathy, and decreased immunity may be possible pathophysiological mechanisms (21).

In contrast, Foo et al. (22) demonstrated that in patients with pyogenic liver abscesses, diabetes was not a predictor of case fatality. We argue that because the growth of pyogenic liver abscess occurred mostly in immunocompromised patients, other etiologies of immunodeficiency should be more prevalent in the non-diabetic group (22). Stegenga et al. (23) also reported that the outcome of severe sepsis was not influenced by the presence of diabetes. We found no strong influence of diabetes on the host response to severe sepsis, possibly because sepsis and diabetes both induced a pro-coagulant state and both interfered with an adequate inflammatory reaction. The modest effect of pre-existing diabetes on the host response to sepsis may result from disturbances of the coagulation system and the inflammatory responses caused by severe sepsis being stronger and more important for outcomes than the relatively smaller derangements attributable to coexistent diabetes (23). Along with our earlier report (11), the present data indicate that diabetes is associated with a significantly elevated risk of RA, but diabetes does not increase the risk of in-hospital mortality from RA.

In our study, 74.8% of patients with RA received antimicrobial treatment alone. We found no differences in the risk of in-hospital mortality among the different treatment modalities. Previous studies have reported that renal abscess can be treated with antimicrobials alone, whereas drainage procedures have always been necessary for perinephric abscess or mixed abscess (5,25,26). Some other studies have also reported that small perinephric abscesses with a diameter <3 cm in clinically stable patients could be treated successfully with antimicrobials alone (4,29). Compared with previous studies, most of which were conducted in tertiary teaching hospitals or in referral centers, our study found a higher proportion of patients receiving antimicrobials alone as a treatment modality for RA. Patients admitted to tertiary teaching hospitals or referral centers tend to be more severely ill, so drainage procedures are expected to be performed more frequently in such patients. However, our study found no association of treatment modality with the risk of in-hospital mortality, which suggests that the clinical management delivered to RA patients in Taiwan is appropriate.

Although there was no significant association of diabetes or treatment modality with in-hospital mortality from RA, this study did find that male patients and older (>64 years) patients had a significantly higher risk of in-hospital mortality. Yen et al. (25) reported an in-hospital mortality rate of 14% from RA and found that older age, elevated blood urea nitrogen, and lethargy were all significant risk factors for mortality. Lin et al. reported an in-hospital mortality rate of 8% and noted that age >64 years, thrombocytopenia, and abscess without drainage were risk factors for poor outcome (nephrectomy or mortality); they also found that the patients in the delayed diagnosis group were older than the patients in the early diagnosis group. Delayed diagnosis and co-morbidity in the older patients were found to be responsible for the increased risk of case-fatality from RA (6).

It is generally agreed that men with UTIs require thorough urological evaluations to identify predisposing structural or functional abnormalities, which are common in men with UTIs (30,31). Although the pathogens in men with community-acquired febrile UTIs were similar to those in women, with a predominance of *Escherichia coli (E. coli)*, and the distributions of *E. coli* serotypes were similar between men and women, the distributions of virulence properties are quite different between men and women (32). Studies have found a higher proportion of hemolytic strains but a lower frequency of P-fimbriated and aerobactin-producing strains in women, which suggests different host-parasite relationships in the male and female urinary tracts (32). Associated urinary tract abnormalities and different host-parasite relationships may be responsible for the increased mortality risk from RA in male patients.

Diabetes-associated length of hospital stay in RA patients

Notably, we found that diabetes increased the LOS by 3.27 days in patients with RA. As the most common endocrine disease, diabetes was also incorporated into the Charlson Comorbidity Index (CCI), which takes into account 19 predetermined clinical conditions and is a strong predictor of various clinical adverse outcomes (33). Yang et al. (34) reported that a higher grade of co-morbidity was

significantly associated with sepsis and therefore with a longer LOS. The longer LOS may have reflected clinical difficulty in caring for RA patients with diabetes.

Strengths and limitations

Our study had several methodological strengths. First, we used NHI data, which reduced selection or recall bias, and there was little likelihood of non-response and loss to follow-up among the cohort members. Second, the large number of study subjects also made it possible for us to conduct analyses of certain variables of interest, including age, sex, and treatment modality. Third, the advantage of using insurance claims data in clinical research is easy access to longitudinal records for a large sample of geographically dispersed patients, which greatly increases the representativeness of the study sample. Fourth, although we identified RA patients from inpatient claims, most cases of RA in Taiwan are diagnosed by imaging studies, including ultrasound, computed tomography, or magnetic resonance imaging; percutaneous aspiration; and surgical exploration (6,25), which supports the validity of the RA diagnoses.

Several limitations of our study should be noted. First, exclusive reliance on claim data may have resulted in potential misclassification bias in our study. The accuracy of a single diabetes diagnosis in the NHI claims data in 2000 was reported to be 74.6% (35). However, we used at least two diabetes-related diagnoses with the first and last visits more than 30 days apart, which would have largely reduced the likelihood of disease misclassification. Second, we could not differentiate between type 1 and type 2 diabetes among the diabetic population included in our study. In Taiwan, type 1 diabetes constitutes only 1.8% of all types of diabetes (36), and the ratio of newly diagnosed type 2 to type 1 diabetes among school children aged 6 to 18 years old is approximately six to one (37). Therefore, the majority of our young diabetic patients tended to be type 2 diabetes patients. Third, the study subjects recruited for the current analysis were originally selected for the investigation of diabetes in predicting RA risk; therefore, the RA patients analyzed may not be representative of the entire RA population diagnosed during the study period. To address this issue, we compared characteristics between our study RA patients and other RA patients hospitalized during the study period. It should be noted that our study RA patients were older (59.6 *vs*. 45.4 years). This difference is attributable to our study RA patients having been selected from the diabetic population and the age- and sex-matched non-diabetic beneficiaries being older than the general population in general. The in-hospital mortality and length of hospital stay estimated from our study RA patients were therefore likely to be over-estimated. Thus, the findings of our analysis should be generalized with caution. Fourth, Taiwan's NHI claims data do not include laboratory test results, which prevented us from further evaluating the potential effects of bacterial virulence on the risk of mortality in RA patients. One study in Taiwan reported that, among the 111 pathogens isolated from abscesses or from urine samples from RA patients, *E. coli* was the most common organism (36%), followed by *Klebsiella pneumoniae* (20%). Previous studies have also found that the pathogens of RA are independent of diabetic status, and the RA pathogens did not influence the risk of mortality (25).

Finally, as is the case with most observational studies using linked administrative data, confounding may be a source of concern. We could not determine a comprehensive list of potential risk factors for mortality and LOS in the study subjects, which may also have confounded the study results.

In conclusion, our data show that RA patients with diabetes in Taiwan do not have an elevated risk of in-hospital mortality. However, among the patients hospitalized for RA, male patients and older (>64 years old) patients were at significantly higher risks for in-hospital mortality. Additionally, diabetes may increase the average LOS in RA patients. Given the longer LOS noted in RA patients with diabetes, appropriate clinical management of these patients during their hospital stay is essential to reduce the LOS.

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■ AUTHOR CONTRIBUTIONS

Ko MC, Chiu AWH, Yu LK, and Li CY conceived and designed the study and were responsible for data acquisition, analysis, and interpretation, and for drafting the manuscript. Liu CC and Liu CK drafted the article and revised it critically for important intellectual content. Woung LC, Yu LK, and Li CY critically reviewed the manuscript and provided statistical consultation. All of the authors approved the final version of the manuscript.

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