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Shock wave lithotripsy for renal stones is not associated with development of hypertension in Taiwan's Chinese population

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ABSTRACT

Objective: Shock wave lithotripsy (SWL) is widely available due to its ease of use and noninvasive nature, and it is highly effective for fragmentation of stones. After SWL became widely used, a number of urinary tract complications, such as hematuria, infection, and pain due to difficulty passing fragmented stones, were also reported. Long-term complications, such as hypertension and diabetes mellitus, were also raised by the previous reports. The association between SWL and development of new hypertension has become a matter of debate due to the publication of controversial data. In the present study, we aimed to determine whether SWL led to the development of hypertension.

Methods: Data were sourced from the Longitudinal Health Insurance Database (LHID2000) of Taiwan, Republic of China, compiled by Taiwan National Health Insurance (NHI) from 1996 to 2010. Patients who underwent SWL were compared with controls matched for age, sex, obesity, diabetes mellitus, and hyperlipidemia using the Taiwan NHI database.

Results: There was no difference in the incidence of new hypertension between SWL and comparison groups. Interestingly, the average new hypertension onset time was faster in the SWL group than in the control groups.

Conclusion: On the basis of our results, SWL is a safe procedure for properly managed nephrolithiasis patients.

1. Introduction

Shock wave lithotripsy (SWL) was first introduced in the 1980s and soon became the primary treatment modality for urolithiasis.[1] Although there are several limitations, such as larger stones (> 1.5 cm), hard composition stones, radiolucent stones, and stones in the lower pole calyx or lower ureter, SWL is still widely available due to its ease of use and noninvasive nature and is highly effective for fragmentation of stones.[2] After SWL became widely performed, numerous urinary tract complications were also reported.[3] Hematuria, infection, and pain due to difficulty passing fragmented stones are the most common immediate complications. Although the exact physical mechanisms of tissue injury are not well understood, the destructive forces generated by lithotripters may cause trauma to thin-walled vessels in the kidneys and adjacent tissues, resulting in hemorrhage, inflammatory responses, and organ injury.[3] Since the first observation by Peterson et al[4] reporting three patients with increased blood pressure or worsening hypertension immediately following SWL, the association between SWL and development of new hypertension has become a matter of debate due to the publication of controversial data.[2,4–13] Patients with urolithiasis reportedly have an independent clinical association between the occurrence of urolithiasis and hypertension.[14–16] It is difficult to determine whether SWL or the renal stones themselves induce hypertension. Therefore, hypertension caused by SWL alone remains debatable. Limitations of previous reports include the lack of a standardized diagnosis of hypertension, absence of an appropriate control group consisting of patients with nephrolithiasis history without other treatment, and inadequate long-term follow-up data. A prospective randomized study is

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difficult to perform due to ethical issues. Furthermore, previous studies almost exclusively focused on Caucasian populations, and there is still a paucity of studies on Asian populations. In the present study, we aimed to determine whether SWL led to the development of hypertension, with controls matched for age, sex, obesity, diabetes mellitus, and hyperlipidemia, using the Taiwan National Health Insurance (NHI) database.

2. Materials and methods

Data were sourced from the Longitudinal Health Insurance Database (LHID2000) of Taiwan, Republic of China, compiled by NHI from 1996 to 2010. In Taiwan, < 2% of the population is not covered by this insurance system ($n = 23.7$ million); therefore, the database was presumed to include over 98% of admission records. LHID2000 includes medical records for 1,000,000 individuals randomly sampled from all enrollees in NHI. Many researchers in Taiwan use LHID2000 for scientific studies. The present study was supervised by the review board of Kaohsiung Medical University Hospital, Kaohsiung, Taiwan. De-identified secondary data from LHID2000 were released to the researchers for study purposes.

This retrospective study consisted of a study group and a comparison group. Cases of renal stones were defined by two criteria: (1) the ICD-9-CM (The International Classification of Diseases, Ninth Revision, Clinical Modification) diagnostic code 592 and (2) the code was assigned by urologists. Patients with new onset of hypertension were defined by ICD-9 diagnostic codes 401 to 405 and use of hypertension medication (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, beta-blockers, diuretics, and other antihypertensive agents). Patients who underwent SWL were defined by the first procedure code 50023B. Patients younger than 18 years, patients with hypertension diagnosed before the index stone date, those with incomplete demographic data, those who had < 90 days of follow-up, or those with hypertension occurring within 90 days after the first stone episode were excluded. The reason for excluding patients with ureteral stones who underwent SWL was to focus on the potential effect on the kidney. For the remaining patients with renal stones, we defined the index date as the first ambulatory care visit for SWL. For the study group, we only included renal patients who underwent SWL; patients with the diagnosis of renal stones who underwent either percutaneous nephrolithotomy (PCNL; procedure code: 76016B) or ureterorenoscopic lithotripsy (URSL; procedure code: 77026B, 77027B, 77028B) were excluded from our cohort. For the control group, we included patients diagnosed with renal stones but who did not receive SWL, PCNL, or URSL. We defined the first ambulatory care visit index stone date as the date of the first stone diagnosed in the NHI database from 2000 to 2006.

2.1. Statistical analysis

Differences between categorical parameters were assessed using the χ^2 or Fisher's exact test. Basic social demographic data, such as age, sex, urbanization level, monthly income, and selected comorbidities, were considered as risk factors for the new onset of hypertension. We included diabetes mellitus and hyperlipidemia as selected comorbidities due to the potential risk for hypertension. Therefore, these potential confounders were adjusted in our study cohort. Propensity score matching was used to reduce the bias of confounding variables that could be found in the treatment effect obtained from simply comparing outcomes among units that received SWL versus those that did not. Kaplan–Meier analysis was applied to estimate the effect of SWL on hypertension-free rates. Follow-up was terminated with the last NHI record, death, or the diagnosis of hypertension. SWL was studied as a time-dependent covariate in a Cox proportional hazard model to estimate the hazard ratio and 95% confidence intervals for the effect of hypertension after SWL. Statistical significance was set at $p < 0.05$. SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

3. Results

LHID2000 in the 2000-sample population showed 50,538 patients diagnosed with renal stones from January 1, 2001 to December 31, 2005. First, we excluded patients aged > 18 years ($n = 647$) because of the relatively low prevalence and the possibility of congenital or nutritional problems in this age group. Next, we excluded patients who had a history of hypertension prior to their index date ($n = 10,127$). Furthermore, we excluded patients with incomplete demographic data ($n = 197$) and those with new onset of hypertension < 90 days ($n = 408$) after the first stone episode. Propensity score matching (SWL: Comparison with a ratio of 1:3) was performed; we included 940 patients with SWL and 2820 patients for comparison. Table 1 shows the basic characteristics and comorbidities in SWL and control groups. There were no differences in age, sex, urbanization level, monthly income, and comorbidities between the two groups. Table 2 shows that there was no difference in the incidence of new hypertension between SWL and comparison groups. The incidence rate of new hypertension during the follow-up period was 26.9 per 1000 person-years and 25.0 per 1000 person-years for the SWL and comparison groups, respectively. We further evaluated these findings using a Kaplan–Meier survival analysis on SWL patients free of new hypertension. Figure 1 shows that there were no differences between the two curves using the log-rank test ($p = 0.186$). The average follow-up times for SWL and control groups were 5.05 ± 1.19 years and 7.20 ± 2.58 years, respectively. The average new hypertension onset times after an index stone were 2.69 ± 1.43 years and 3.68 ± 2.34 years in SWL and control groups, respectively. The average time in the SWL group was shorter than that in the control group ($p < 0.001$). Interestingly, the average new hypertension onset time was faster in the SWL group than that in the control groups (Table 3).

4. Discussion

The advantages of SWL include its ease of use and noninvasive nature; it is highly effective for fragmentation of stones and is well

Table 1
Basic characteristics between SWL and comparison groups ($n = 3,760$).[a]

Variables	Comparison group ($n = 2820$)		SWL group ($n = 940$)		p
Age (y)					
< 40	1036	36.7	346	36.8	0.978
40–59	1514	53.7	502	53.4	
≥ 60	270	9.6	92	9.8	
Mean ± SD	44.04 ± 12.33		44.08 ± 12.01		0.931
Sex					
Female	657	23.3	217	23.1	0.894
Male	2163	76.7	723	76.9	
Urbanization level					
Urban & suburban	2170	77.0	721	76.7	0.876
Rural	650	23.0	219	23.3	
Insurance range					
< NT 14,999	766	27.2	253	26.9	0.984
NT 15,000–29,999	1344	47.7	448	47.7	
≥ NT 30,000	710	25.2	239	25.4	
Comorbidities					
Diabetes	128	4.5	43	4.6	0.964
Hyperlipidemia	263	9.3	91	9.7	0.747

Data are presented as n (%), unless otherwise indicated.
SD = standard deviation.
[a] The average exchange rate in 2016 was US$1 to New Taiwan (NT)$ 32.

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