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Risk Factors for Perinephric Hematoma Formation After Shockwave Lithotripsy: A Matched Case-Control Analysis

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Abstract

Purpose: To determine the incidence of and evaluate the potential risk of a symptomatic perinephric hematoma (PNH) after shockwave lithotripsy (SWL) with the Storz Modulith SLX-F2 device.
Patients and Methods: Patient and treatment-related data from 6172 SWL treatments for proximal ureteral and kidney stones were collected prospectively from April 2006 to August 2010. Patients in whom signs or symptoms of a PNH developed after SWL were investigated with imaging studies. Each patient identified with a PNH was matched with four controls using sex, age (±5 years), shockwave rate, energy and number, and no SWL within the previous 6 months as the matching variables. The baseline characteristics of the 21 cases and 84 controls were compared using the Student *t* test. The independent variables of hypertension (intraoperative value >140/90 mm Hg), anticoagulant/antiplatelet drugs, obesity (body mass index ≥30), and diabetes were compared using a conditional logistic regression analysis. The dependent variable was hematoma.
Results: A PNH developed after SWL with the Storz Modulith SLX-F2 device in 21 (0.34%) adult patients (19 men, 2 women) with a mean age of 55.2 years. Significant risk factors identified included intraoperative hypertension (hazard ratio [HR] 3.302, 1.066–10.230, $P=0.0384$) and anticoagulant/antiplatelet medications (HR 4.198, 1.103–15.984, $P=0.0355$). Diabetes ($P=0.1043$) and obesity ($P=0.1021$) were not associated with PNH.
Conclusions: A clinical PNH occurred in less than 1% of our population. This is consistent with reports from earlier generation devices. Risk factors identified for hematoma formation were intraoperative hypertension and the use of anticoagulant/antiplatelet drugs.

Introduction

The introduction of shockwave lithotripsy (SWL) in the early 1980s revolutionized the treatment of patients with upper urinary tract calculi, leading to its current prominence as first-line therapy for the majority of uncomplicated upper tract stones. Although SWL is a relatively noninvasive treatment, perinephric hematoma (PNH) formation remains a potentially serious complication. The exact incidence of this adverse event is difficult to accurately determine with reports varying between 0.1 and 25%.[1–3] The disparity among reports is likely a reflection of whether hematomas were clinically apparent or asymptomatic, the imaging modalities used for detection, and the type of lithotripter.

Previous investigators have identified a number of potential risk factors for bleeding post-SWL, including hypertension, obesity, diabetes mellitus, coagulative disorders, shockwave frequency, number, and energy.[4–7] In a multivariate analysis, however, only advancing patient age was singled out as a significant risk factor.[8]

With evolution in lithotripter technology, concerns have been raised that the latest generation devices may be associated with a greater risk of renal bleeding, related to the narrower treatment focus and higher peak pressures generated at F2.[9] The Storz Modulith SLX-F2 (Storz Medical AG, Tagerwilen, Switzerland), a fourth generation lithotripter, has attracted concerns about a significantly higher rate of hemorrhagic complications. In a recent prospective comparison of the modified HM3 and the Storz Modulith SLX-F2, the perinephric hematoma rates were 1% and 3%, respectively.[10]

The goal of this study was to evaluate the incidence of clinically apparent renal or perinephric hematomas with the Storz SLX-F2 and the potential patient- and treatment-related risk factors at a high-volume lithotripsy unit. A matched case-control analysis was used for this purpose.

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Patients and Methods

Prospective data collection was performed on all adult patients undergoing SWL on the Storz Modulith SLX-F2 at St. Joseph's Health Care, London, Ontario, Canada, since its installation in April 2006. This database, reviewed retrospectively, served as the basis of this report. Our lithotripsy program is one of three in the province of Ontario serving a population of more than 13 million people, and approximately 1700 patients are treated in our unit annually.

The Storz Modulith SLX-F2 is the latest generation of lithotripter featuring an electromagnetic shockwave generator and stone localization options including both fluoroscopic imaging and in-line ultrasound. A novel feature of this lithotripter is the ability to switch between two different focal sizes—6×28 mm (standard) *vs* 9×50 mm (wide)—without significantly compromising energy delivery. The efficacy and general safety of this device has been previously reported by several authors.[11–13]

This study focused specifically on patients who were treated at our institution between April 2006 and August 2010 and in whom symptomatic renal or perinephric hematomas developed. Hematomas were identified when clinical suspicion was raised because of severe flank pain exceeding the normal postoperative experience or when unexplained tachycardia or hypotension with a concomitant drop in hemoglobin was observed. When clinical suspicion was raised, CT was performed to confirm the diagnosis.

Once patients in whom PNH developed were identified, each was then matched with four control subjects. Control patients were those who had undergone SWL during the same time period without development of symptomatic renal bleeding. The controls were matched for age (± 5 years), sex, shockwave number, energy, and rate. Control patients were excluded if they had undergone SWL in the previous 6 months, or if the treated stone(s) was in the mid or distal ureter. The charts and imaging studies of all case and control patients were retrospectively reviewed.

Noncategorical variables were compared between the cases and controls using the Student t test (two-tailed, $P \leq 0.05$). Patient variables assessed included patient age, body mass index (BMI), use of antiplatelet agents, diabetes mellitus, and intraoperative hypertension. Treatment variables included stone size, shockwave number, energy level, and rate of shockwave delivery. Conditional logistic regression analysis was performed to assess possible patient-related risk factors for PNH, using SPSS version 9.2. PNH formation was chosen as the dependent variable.

Independent variables assessed were intraoperative hypertension, diabetes, antiplatelet agent use, and obesity (BMI $\geq 30\ kg/m^2$). Hypertension was defined as a peak intraoperative blood pressure exceeding 140/90 mm Hg.[14] Antiplatelet agent use was defined at the time of patient referral; these medications may or may not have been held before the SWL treatment, in accordance with our institution's practice as described below. A P value ≤ 0.05 was considered significant.

To calculate the incidence of PNH formation post-SWL, only those treatments targeting stones in the proximal ureter or kidney were included to determine the denominator. The rationale for this assertion was that PNH formation was unlikely to be associated with shockwave treatments of stones in the mid or distal ureter because the geometry of this particular device would not have resulted in a blast path traversing the renal parenchyma.

All patients who are treated at our center undergo a standard preoperative assessment that includes a complete history with attention to potential bleeding risk factors, physical examination, urinalysis with culture, and complete blood cell count. Our institution's long-standing policy has been to counsel patients to stop warfarin, dipyridamole, and ticlopidine 5 days preoperatively, and clopidogrel 7 days before SWL. Acetylsalicylic acid (ASA) (81 mg), meloxicam, naproxen, and ketorolac are not routinely discontinued if it is thought that it is in the patients' best interest to remain on these medications. Pre-SWL imaging included CT or plain film radiography of the kidneys, ureters, and bladder (KUB) $\pm$ renal ultrasonography.

SWL was administered as an outpatient procedure under intravenous neurolept anesthesia in the majority of patients. Decisions on power setting, number of shock waves delivered, shockwave frequency, and focus size were at the discretion of the treating urologist but consistent with the guidelines provided by the manufacturer. Eight different urologists were involved in treatments during this study period. During the time interval encompassed by this study, a shockwave rate of 2 Hz, a maximum energy level of 8. and a maximum of 3000 shocks to the kidney were the parameters used. It is our usual protocol to use a gradual increase in energy up until 1000 shocks. It is not our usual practice to use a tissue-sparing delay or pause. The standard focus was used almost exclusively, with the wide focus reserved for the treatment of larger stones once fragmentation was noted. Use of the wide focus occurs in fewer than 20% of our cases. The study was approved by Western University's Health Sciences Research Ethics Board.

Results

Between April 2006 and August 2010, 6732 SWL procedures were performed with 6172 of the targeted stones in the kidney or proximal ureter. Among this group, 21 patients were identified with symptomatic PNH during the study interval. Fifteen patients presented with symptomatic bleeding before discharge from our unit on the day of treatment and were subsequently treated at our center. The remainder were recognized, investigated, and treated by the referring urologist. The incidence of clinically apparent PNH post-SWL in this series was 0.34% (21/6172).

Symptoms at presentation included severe flank or abdominal pain in 18 (86%), greater than expected flank bruising in 1 (5%), and hemodynamic changes such as tachycardia and/or hypotension in 2 (9%). Three patients needed blood transfusion (one, three, and four units). All patients were treated conservatively with fluid resuscitation and bed rest. No patient needed angioembolization or surgical intervention. The mean length of hospital stay was 3.6 ± 2.5 (standard deviation) days. Eight of 21 patients had undergone previous shockwave treatment. Of these, two were within 6 months (2, 4) of the session that resulted in a PNH.

Table 1 compares the baseline characteristics, stone size, and treatment parameters between the case (PNH) and control subjects. There were no statistically significant differences between the groups. Of the 21 PNH cases, 19 (90%) were male

Table 1. Comparison of Baseline Characteristics, Stone Size, and Treatment Parameters Between Case and Control Patients

Parameter (means ± SD)	*Cases*	*Controls*	P *value*
Age (years)	55.2 ± 15.4	55.3 ± 14.9	0.98
BMI	28.8 ± 4.9	28.0 ± 4.82	0.2635
Stone size (mm^2)	77.1 ± 52.1	91.7 ± 83.0	0.4445
Number of shocks delivered	2743 ± 473	2814 ± 391	0.4775
Maximum energy level of shockwave	5.7 ± 1.1	5.7 ± 1.0	0.4235
Shock rate (Hz)	1.94 ± 0.17	1.98 ± 0.09	0.1654

SD = standard deviation; BMI = body mass index.

and 2 (10%) female. Although male sex was a risk factor on univariate analysis ($P = 0.0093$), higher mean energy levels were used among male patients. The results of the conditional logistic regression analysis assessing the potential risk factors for PNH development are presented in Table 2. From this analysis, only intraoperative hypertension and use of antiplatelet agents were identified as independent risk factors for PNH development after adjusting for other patient variables.

We reviewed the incidence of PNH at different time points in our series and despite the potential impact of a learning curve, there was no evidence of a heightened risk of PNH early in the series. Despite the involvement of eight different urologists in treatments during this study period, there was no significant difference in the rate of PNH between surgeons.

Discussion

Although a rare adverse event, SWL-induced renal or perinephric bleeding remains a potentially devastating complication. Studies assessing occurrence after treatments with the Dornier HM3 lithotripter (Dornier Medical Systems, Marietta, GA) reported an incidence of 0.2% to 1.5%.[1,15–18] With the evolution in SWL technology and the trend to manufacture devices with smaller focal zones and higher peak energy delivery, concerns have been raised about even greater risks of PNH development.[8,9] To date, no significant difference has been demonstrated in rates of hemorrhagic complications in two large comparative trials.[19,20]

Dhar and colleagues[8] reported a 4.1% incidence of symptomatic and asymptomatic PNH formation with the Storx SLX Lithotriper in a small series in which postoperative radiographic screening was performed on all treated patients.[8] Zehnder and associates[10] conducted a prospective comparison of the modified HM3 and the Storz Modulith SLX-F2 and noted a threefold higher rate of PNH in patients who were treated with the SLX-F2. Of note, however, a median energy level of 9 for those patients treated with the Storz device was reported, which exceeds the manufacturer's recommendation.

Table 2. Results of Conditional Logistic Regression Analysis Using Hematoma Development as the Dependent Variable

Independent variable	*HR*	*95% CI*	P *value*
Hypertension (intraoperative)	3.302	1.066–10.230	0.0384
Diabetes	0.329	0.059–1.829	0.1043
Drugs (antiplatelet)	4.198	1.103–15.984	0.0355
Obesity	2.540	0.843–7.659	0.1021

HR = hazard ratio; CI = confidence interval.

Various patient- and treatment-related risk factors for PNH formation have been evaluated with conflicting results. Hypertension, diabetes mellitus, obesity, coronary artery disease, and age have been suggested as potential factors.[8,16,17,21]

Uncorrected coagulopathy is generally considered an absolute contraindication to SWL. Life-threatening hemorrhages have been reported in patients undergoing SWL who continued their antiplatelet agent.[22] Zanetti and coworkers[7] found no post-SWL hematomas in 23 high-risk patients who were bridged with unfractionated heparin while their antiplatelet agents were held for 8 days before SWL.

The management of patients receiving antiplatelet agents who need SWL has become more pertinent than ever with the increasing use of these agents. A recent review of SWL in patients needing anticoagulation or antiplatelet agents attempted to provide clarity on this issue.[23] Unfortunately, there are no prospective randomized trials assessing patients undergoing SWL needing the concomitant use of anticoagulants. Guidelines on the optimal time for cessation of these agents specifically as it relates to lithotripsy are based on expert opinion.

Our lithotripsy unit's long-standing practice has been to discontinue patients' use of warfarin, heparin, dipyridamole, clopidogrel, and ticlopidine before treatment at a time interval consistent with the specific drug's half-life. Low dose ASA and nonsteroidal anti-inflammatory drugs (NSAIDs), on the other hand, are not routinely discontinued if it is thought that the risk of discontinuation might be harmful to the patients. As such, some patients are treated while continuing to take these agents. In a recent audit of our current practice, it was noted that approximately 30% of all patients are treated while on low-dose ASA or NSAIDs. Eight of 21 patients with symptomatic PNH were taking ASA or an NSAID at the time of SWL, as compared with 17 of the 84 controls. Using a matched case-control analysis, we demonstrated that the use of antiplatelet agents at the time of patient referral was associated with an increased risk of PNH post-SWL with a hazard ratio of 4.198 (95% confidence interval 1.103–15.984).

Uncontrolled preoperative hypertension has been shown in two previous cases studies to be associated with an increased risk of post-SWL bleeding.[16,17] In a multivariate analysis, however, Dhar and associates[8] did not identify hypertension as a risk. In our study, intraoperative hypertension was assessed rather than a preexisting diagnosis of hypertension. Intraoperative hypertension was defined as a peak intraoperative blood pressure exceeding 140/90 mm Hg. Using this conservative definition, hypertension remained a risk factor in the conditional logistic regression analysis, further strengthening the notion that hypertension may increase the risk of bleeding. Because of the binomial nature of the conditional logistic regression analysis, it was not possible to assess the linear relationship between absolute blood pressure and the magnitude of increased risk.

Previous studies have demonstrated that specific SWL parameters affect the risk of PNH formation. A slow escalation in energy delivery, using slower SW frequency, and using

the lowest energy levels possible are all strategies to reduce renal injury and maximize effectiveness in human and animal studies.[24–29]

By matching the control patients to the PNH cases based on shockwave number, energy level, and rate, the contributory effects of the SWL treatment parameters are neutralized so that the patient-related risk factors can be assessed independently. The SLX-F2 lithotripter is equipped with a dual focus option. While it was tempting for us to try to evaluate the potential effect of the different focal zones on PNH formation, the relative infrequency of use of the wide focus in our practice relative to the standard focus made such a comparison invalid.

Strengths of this study include the large sample size and case-control methodology used with a strict definition of the cases and controls. A prospective study of the effect of modifying patient- and treatment-related parameters would be ideal; however, given the low incidence of PNH and the large sample size needed, this is impractical. Addressing the risk of PNH at a single site using uniform pretreatment evaluation and treatment parameters also helped minimize the effects of confounding variables. Because the focus of our assessment was only on symptomatic hematomas, the results have clinical applicability.

Several limitations of this study exist. The calculated incidence of PNH in our population may be an underestimate, given the referral pattern at our center. Most patients with PNH present within hours post-treatment and, as such, are still at our center for evaluation and treatment. Of the 21 patients with hematomas, 6 patients, however, presented to their community hospital and were treated by the referring urologist. Despite routinely soliciting feedback from our referring urologists about patients who presented with symptomatic PNH, it is possible that there were more patients with PNH of whom we are not aware. Even if the incidence is an underestimate, the assessment of the patient-related risk factors would unlikely be affected, because there is no reason to believe that any cases missed by underreporting would be systematically different from the known cases. The conditional logistic regression analysis allowed only binomial analysis of each risk factor, so the linear relationship between each parameter and the risk of PNH could not be assessed. Also, more precise guidance on the use of antiplatelet agents cannot be attained.

In addition, we recognize the possibility that when occurring in combination, ASA use and intraoperative hypertension may have additive effects. Because of the limited number of patients with the event (PNH) and those who had both ASA use and intraoperative hypertension, we were unable to perform a test of interaction.

Despite these limitations, this matched case-control analysis enabled a focused assessment of patient-related risk factors for PNH formation. To our knowledge, this study is based on the largest known series of patients treated on the latest generation lithotripter.

Based on our findings, we would continue to recommend optimizing blood pressure control preoperatively for those patients with renal stones treated by SWL. Should intraoperative hypertension develop, pharmacologic efforts to reduce the blood pressure might be considered; however, it is unknown whether this maneuver will reduce bleeding risks. The more prudent action may be to discontinue SWL and consider alternative treatment in the event of significant intraoperative hypertension. We would also recommend that low-dose ASA and NSAIDs be discontinued preoperatively. While these agents were associated with an increase of PNH formation, the magnitude of risk remains unclear. As mentioned, a significant number of our patient population who are receiving these agents are treated without clinical PNH development.

Conclusions

In this single center experience, the incidence of clinically apparent PNH after SWL with the Storz Modulith SLX-F2 was 0.34%. In a matched case-control analysis, risk factors included intraoperative hypertension and the use of antiplatelet agents, while the presence of diabetes and obesity were not.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

ASA = acetylsalicylic acid
BMI = body mass index
CT = computed tomography
NSAIDs = nonsteroidal anti-inflammatory drugs
PNH = perinephric hematoma
SWL = shockwave lithotripsy