Urolithiasis (2015) 43:527–533
DOI 10.1007/s00240-015-0796-y

ORIGINAL PAPER

Tubeless percutaneous nephrolithotomy with non-absorbable hemostatic sealant (Quikclot®) versus nephrostomy tube placement: a propensity score-matched analysis

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Received: 13 February 2015 / Accepted: 15 June 2015 / Published online: 30 June 2015

Abstract The purpose of this study was to determine the efficacy and safety of tubeless percutaneous nephrolithotomy (PNL) using a non-absorbable hemostatic sealant (Quikclot®) as an adjunct compared to nephrostomy tube placement in patients exhibiting significant parenchymal bleeding following PNL. We identified 113 PNL cases performed between May 2011 and October 2014. For patients with insignificant parenchymal bleeding following stone removal, defined as a clear visualization of the surgical field at full irrigation of the nephroscope, tubeless PNL was performed. For patients with significant parenchymal bleeding, we introduced the tubeless Quikclot® technique as of September 2013 and have performed it ever since. Formerly, nephrostomy placement PNL was performed. In this study, 40 Quikclot® applied PNL cases were matched with an equal number of nephrostomy placement cases by propensity scoring based on body mass index, stone size, and Guy's stone score. The mean postoperative drop in hematocrit was comparative between the Quikclot® group and the nephrostomy group on both postoperative days 1 ($p = 0.459$) and 2 ($p = 0.325$). Quikclot® application was associated with lower VAS scores throughout the postoperative period, lower cumulative analgesic requirement ($p = 0.025$), and with shorter hospitalization ($p = 0.002$). Complication rates were comparable with no need for blood transfusions in any patients. Tubeless Quikclot® PNL was safe and provided effective hemostasis of significant parenchymal bleeding. By avoiding nephrostomy placement, we were able to reduce postoperative pain, analgesic requirements, and hospitalization. Application of Quikclot® may be considered prior to nephrostomy placement in patients with significant parenchymal bleeding.

Keywords Hemostatic agents · Percutaneous nephrostomy · Tubeless

Introduction

Percutaneous nephrolithotomy (PNL) is the preferred option for the treatment of large and/or complex renal stones [1]. Although continuous technical refinements have been made, complications of hemorrhage and urine extravasation are areas of continuous innovation and debate. Postoperative nephrostomy tube placement may be performed to reduce such complications [2]. However, its efficacy is controversial, and nephrostomy drainage may increase risks of postoperative pain and morbidity [3]. Several alternative approaches including tubeless PNL have been established, with several randomized controlled trials and meta-analyses having proven its feasibility [4, 5].

Various hemostatic sealants have been developed and applied in the nephrostomy tract following tubeless PNL [6, 7]. The placement of hemostatic sealants has been proposed to be useful adjuncts to decrease hospital stay, without significant reduction of bleeding, transfusion and fever rates, and complications [8]. At the same time, hemostatic sealants have shown to increase the potential for infectious complications, allergic reactions, and most importantly, to pose risks of urinary drainage occlusion [8, 9]. In overall, recent meta-analyses have suggested that hemostatic sealants might not be necessary for tubeless PNL [8, 10].

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However, the hemostatic sealants associated with these adverse events were non-absorbable, permanent agents [8]. In this context, the use of non-absorbable hemostatic sealants appears to be a feasible alternative.

Quikclot® is a non-absorbable surgical gauze impregnated with kaolin [11]. Due to its unique efficacy in controlling both venous and arterial bleeding, it has widely been used in military action and percutaneous coronary procedures [11]. To our knowledge, it has never been tested as a hemostatic sealant for tubeless PNL. Using a propensity score-matched analysis, we compared the efficacy and safety of Quikclot® in tubeless PNL with nephrostomy placement PNL among patients with significant parenchymal bleeding.

Patients and methods

Study sample

This study included 113 patients with renal calculi who underwent PNL performed by a single surgeon (CHH) from May 2011 to October 2014. The decision to perform PNL was made irrespective of stone number and size, hydronephrosis grade, anatomic abnormalities, and previous ipsilateral renal surgery. All patients were evaluated in terms of clinical history, complete blood cell count, serum creatinine, electrolytes, urinalysis, urine culture, plain X-rays of the kidney, ureters and bladder, and abdomino-pelvic computed tomography imaging. Stone burden was assessed as surface area calculated according to European Association of Urology guidelines [12]. In cases of multiple stones, the three largest stones were measured, and the stone burden was considered the sum of the three. All patients provided informed consent for all procedures and were informed about any complications.

For patients with insignificant parenchymal bleeding, defined as clear visualization of the surgical field at full irrigation of the nephroscope following stone removal, tubeless PNL was performed without using hemostatic sealants. Prior to August 2013, nephrostomy placement PNL was performed in cases with significant parenchymal bleeding, defined as unclear visualization of the intrarenal structures at full irrigation of the nephroscope. As of September 2013, we introduced the tubeless Quikclot® applied technique for patients with significant bleeding and have performed it ever since unless nephrostomy placement was indicated, i.e., those needing more than one nephrostomy tract or a second look procedure. With exclusion of 21 (18.6 %) patients who exhibited insignificant bleeding and received tubeless PNL, we compared perioperative outcomes of 40 (35.4 %) patients who received tubeless Quikclot® applied PNL and 52 (46.0 %) patients who received nephrostomy placement PNL. The study was carried out in lieu of a formal ethics committee and followed the principles of the Helsinki Declaration.

Intervention

Under general anesthesia, a 6F ureteral occlusion balloon catheter was placed in a transurethral manner. With the patient in a prone position, percutaneous access was achieved by a single-step procedure in the operating room under ultrasonographic and fluoroscopic guidance. The nephrostomy tract was dilated using a balloon dilator, and a 28F Amplantz sheath was positioned within the collecting system. Fragmentation of the calculi was performed using a rigid 26F nephroscope (Richard Wolf, Vernon Hills, IL, USA) and the StoneLight Holmium Laser System (American Medical Systems, San Jose, CA, USA). Stone removal was performed using foreign body forceps and a suction device, and visual examination was performed to confirm complete removal and to detect any significant mucosal damage or bleeding. A flexible cystoscope combined with fluoroscopy was utilized when necessary.

In the Quikclot® group, the subsequent procedure was to indwell a 6F Foley catheter via Amplantz sheath into the renal collecting system. Under fluoroscopic examination, 2–3 cc of contrast medium was insufflated into the Foley balloon. After placing the distal end of the Amplantz sheath outside the renal capsule, the Foley catheter balloon was retracted against the inner aspect of the nephrostomy tract, allowing visual confirmation of the full-thickness renal parenchyma. Then, Quikclot® gauze was rolled around the Foley catheter and introduced through the Amplantz sheath. A foreign body forceps was used to compress the Quikclot® against the renal parenchymal tract (Fig. 1), with simultaneous counter-retraction of the Foley catheter balloon (Figs. 2, 3). After 5 min, Quikclot® was removed, and hemostasis of the renal parenchyma was visually confirmed. If parenchymal bleeding was insignificant, the 6F Foley catheter and the Amplantz sheath were withdrawn. In cases of unclear visualization of the field, a 24F nephrostomy catheter was indwelled in the usual manner. The skin incision was sutured with a pressure dressing after all procedures. Finally, the ureteral occlusion balloon catheter was removed.

Postoperative care and follow-up

Complete blood cell count and serum chemistry measurements were obtained immediately after surgery and on postoperative days 1 and 2. To focus on the amount

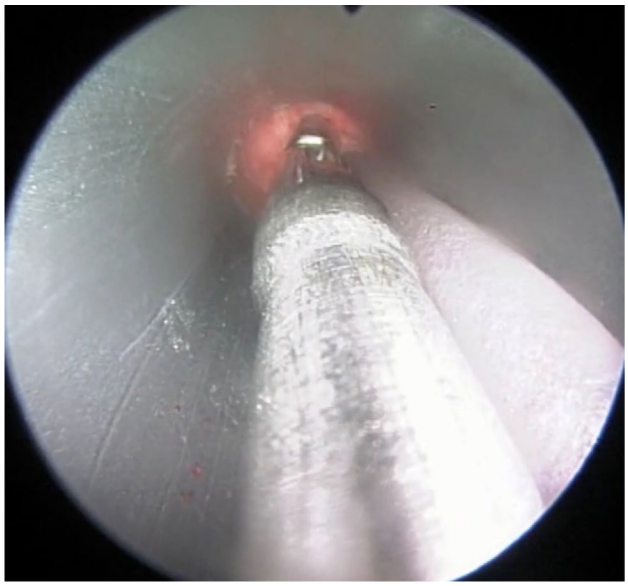

Fig. 1 Foreign body forceps is used to compress Quikclot® against the renal parenchymal defect under direct vision

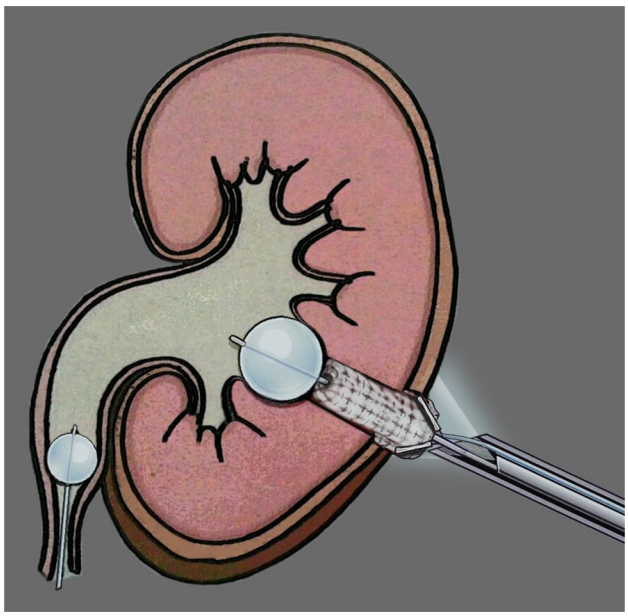

Fig. 2 Quikclot® is applied through the nephrostomy tract, and a foreign body forceps is used to compress the renal parenchyma with simultaneous counter-retraction of the Foley catheter balloon

of postoperative bleeding, blood cell counts obtained on postoperative days 1 and 2 were compared to measurements obtained immediately after surgery. A visual analog scale (VAS) was used to assess pain 6 h postoperatively as well as on postoperative days 1 and 2 (Fig. 4). Single intravenous injection of 50 mg tramadol hydrochloride was

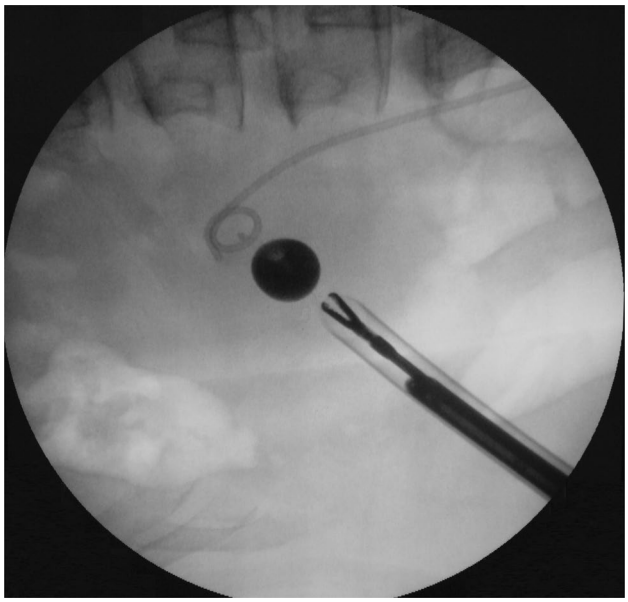

Fig. 3 Fluoroscopic guidance is used to ensure proper compression of Quikclot® onto the renal parenchyma

administered according to patient request. Prior to surgery, no patient had been given any periodic opioid-based analgesics that may influence perception of pain or analgesic requirements.

After discharge, there was follow-up for all patients at 1 week, 4–6 weeks, and 3 months postoperatively. In cases of remnant stone fragments, patients underwent ancillary treatments, namely shock wave lithotripsy or ureteroscopy.

Statistical analysis

To control for imbalances in preoperative factors that may affect surgical outcome among distinct study cohorts, propensity scores were calculated for each subject using multivariable logistic regression based upon the following covariates: body mass index, stone size, and Guy's stone score [13]. Individuals in the Quikclot® group were matched to patients in the nephrostomy group at a 1:1 ratio based on propensity scores.

Demographic characteristics of patients and tumors were compared with descriptive statistics. Appropriate comparative tests, such as the Mann–Whitney *U* test and Fisher's exact test, were used to compare continuous and categorical variables. The outcomes were compared using the two-tailed independent sample *T* test with the 95 % CI. Statistical analyses were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA), with statistical significance set at $p < 0.05$.

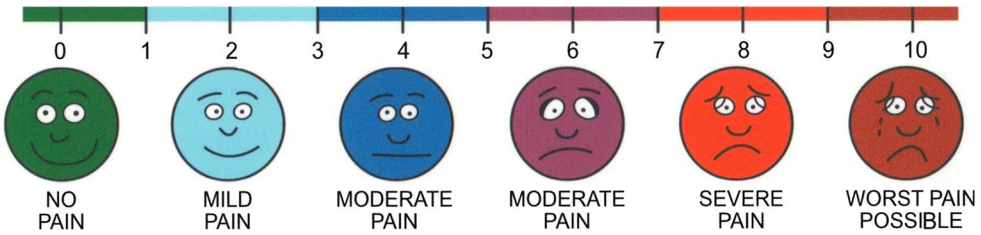

Fig. 4 The visual analog scale was used to assess postoperative pain

Table 1 Patient demographics

	Tubeless Quikclot® PNL	Nephrostomy PNL	*p*
Number	40	40	NS
Propensity-matched variables			
BMI (kg/m^2)	24.5 ± 3.4	24.2 ± 2.9	0.698
Stone burden (mm^2)	678.3 ± 674.6	619.2 ± 532.2	0.872
Guy's score			1.0
1	10 (25.0 %)	10 (25.0 %)	
2	12 (30.0 %)	12 (30.0 %)	
3	15 (37.5 %)	15 (37.5 %)	
4	3 (7.5 %)	3 (7.5 %)	
Unmatched variables			
Age (years)	56.3 ± 12.5	47.7 ± 13.4	0.007
Gender			0.824
Male	27 (67.5 %)	25 (59.5 %)	
Female	13 (32.5 %)	17 (40.5 %)	
Multiplicity of stones			0.564
Single	15 (37.5 %)	16 (38.1 %)	
Multiple	25 (62.5 %)	26 (61.9 %)	
Stone location			0.389
Pelvis	9 (22.5 %)	13 (30.9 %)	
Upper calyx	1 (2.5 %)	2 (4.7 %)	
Lower calyx	7 (17.5 %)	5 (11.9 %)	
Multiple calyx	23 (57.5 %)	22 (52.5 %)	

Data are mean (SD) and number (%)

BMI body mass index

Results

Patient demographics

One patient planned for tubeless Quikclot® PNL was converted to nephrostomy placement due to significant parenchymal bleeding despite Quikclot® compression. With exclusion of this patient, propensity-based matching resulted in 40 patients in each group. Patient demographics of matched and unmatched variables according to each specific PNL procedure are presented in Table 1. No significant differences existed between the two groups with respect to variables used for propensity score matching, stone multiplicity, and stone location. However, patients in the Quikclot® group tended to be older.

Perioperative data and outcomes

Perioperative data and outcomes of the two groups are presented in Table 2. The mean drops in hemoglobin and hematocrit at postoperative days 1 and 2, respectively, were comparable between the two groups. Patients in the Quikclot® group were also associated with lower VAS scores, lower analgesia requirements (cumulative dosage of intravenous tramadol hydrochloride within the first 2 days after surgery), and shorter hospitalization. Minor (Clavien I–II) complication rates were comparable in the two groups with no need for blood transfusion in any patient. There were no evidences of hemodynamic or metabolic abnormalities, postoperative retroperitoneal urinoma, or hematoma during follow-up.

Discussion

Since its introduction by Bellman et al. in 1997 [3], tubeless PNL has been widely accepted as a safe and effective procedure, with the advantages of reducing analgesic requirements and early convalescence [14]. However, it has some limitations including possible postoperative urinary extravasation or delayed bleeding. To overcome these problems, various hemostatic sealants have been applied at the conclusion of tubeless PNL and have showed favorable postoperative outcomes [5]. The most common hemostatic agents used in tubeless PNL are fibrin glue, gelatin matrix, and oxidized cellulose, all of which are absorbable agents that have been evaluated in clinical studies [9, 11–15]. However, knowledge of their exact effects on renal drainage and reaction at contact with tissue or urine is limited, although such effects must be considered when applying these agents to clinical practice.

There are several studies showing limitations of absorbable hemostatic sealants, which may pose detrimental effects when applied to human renal units. Histological data from an in vivo study have shown absorbable hemostatic agents

Table 2 Perioperative data and complications

	Tubeless Quikclot® PNL	Nephrostomy PNL	*p*
Hb decrease (gm/dl)[a]			
POD 1	1.02 ± 0.85	1.25 ± 1.04	0.316
POD 2	1.84 ± 1.09	2.19 ± 1.16	0.197
Hct decrease (%)[a]			
POD 1	2.79 ± 2.22	3.25 ± 2.92	0.459
POD 2	4.72 ± 2.76	5.42 ± 3.21	0.325
VAS score			
Operative day	4.03 ± 1.74	5.59 ± 1.82	0.001
POD 1	3.06 ± 1.53	4.45 ± 1.92	0.002
POD 2	2.14 ± 1.44	3.29 ± 1.98	0.010
Analgesic requirement (mg tramadol)	230.5 ± 92.8	294.5 ± 117.9	0.025
Hospitalization duration (days)	2.52 ± 0.92	3.39 ± 0.94	0.002
Complications			1.0
Delayed hematuria	4 (10.0 %)	2 (4.8 %)	
Flank pain (return visit)	0 (0 %)	1 (2.4 %)	
Fever (>38 °C)	0 (0 %)	2 (4.8 %)	
Stone composition			NS
Calcium oxalate	18 (45.0 %)	16 (38.2 %)	
Calcium phosphate	6 (15.0 %)	8 (19.0 %)	
Struvite	2 (5.0 %)	0 (0 %)	
Uric acid	7 (17.5 %)	3 (7.1 %)	
Miscellaneous	7 (17.5 %)	15 (35.7 %)	

Data are mean (SD) and number (%)

VAS visual analog score, *Hb* hemoglobin, *Hct* hematocrit, *POD* postoperative day

[a] In relation to immediate postoperative values

to induce inflammatory reaction within the renal parenchyma, which may in turn induce adverse reactions such as fever, granuloma, abscesses or foreign body reactions, and risk of drainage occlusion [9]. Uribe, et al. observed that fibrin glue and oxidized regenerated cellulose formed a fine suspension of particles on contact with both normal and sanguineous urine in an in vitro experimental study [16]. This raised concerns about potential acute or subacute obstructions of the ureteropelvic junction and lithogenic effects caused by particles that may act as a nidus for future stone recurrence [16]. In a porcine model, the use of fibrin glue, specifically Tisseel®, caused obstruction of the collecting system, which did not resolve over a 5-day period, resulting in associated retroperitoneal urinoma [17]. In some cases, Tisseel® has been observed to persist in the percutaneous tract for up to 30 days, with reabsorption in the tract leading to fistulae and potential for delayed urinary leak [18].

We introduced the use of Quikclot® as an attempt to avoid permanent instillation of such hemostatic sealants. Quikclot® is a non-woven surgical gauze impregnated with kaolin, an inert mineral that promotes clotting via contact activation [11]. Kaolin directly interacts with Factor XII, the first protein of the intrinsic pathway of the clotting cascade, and shows unique efficacy in controlling both venous and arterial bleeding [19]. Quikclot® may function in PNL as a non-absorbable hemostatic sealant to minimize the potential for adverse tissue reaction and urinary obstruction. Unlike other procedures using hemostatic sealants, our counter-retraction technique with the 6F Foley catheter balloon under direct vision enabled efficient compression of the renal parenchyma. Most importantly, a 'real-time' visual confirmation of the parenchymal hemostasis was obtained after Quikclot® removal, which allowed the flexibility in decision to insert a nephrostomy. Another advantage of Quikclot® is its cost (US $43), which is substantially lower than those of other commercially used hemostatic agents. While most patients experience bleeding after tubeless PNL, the instillation of hemostatic agents should be avoided if possible and used economically only for significant hemorrhage. However, owing to the low cost of Quikclot®, surgeons may follow relatively lenient criteria for its use. Overall, our procedures combined the advantages of tubeless PNL and Quikclot® and showed that, compared to nephrostomy placement PNL, Quikclot® in tubeless PNL led to significant reductions in pain and analgesic requirements, without increased risks of postoperative bleeding and complications.

The strength of the Quikclot® sealant is the potential to be applied to all patients regardless of the degree of parenchymal bleeding following stone removal. Unlike absorbable hemostatic agents that are selectively applied to those with low risk of urine leakage and lesser degree of bleeding, Quikclot® sealants are removed after compression, and bleeding control is visually confirmed prior to deciding upon tubeless technique or a nephrostomy placement. As of September 2013, our criterion for conventional nephrostomy placement was significant parenchymal bleeding despite the application of Quikclot®. In overall, 40 (97.6 %) patients in whom tubeless Quikclot® PNL were planned achieved efficient parenchymal bleeding control and one (2.4 %) patient required nephrostomy placement. To emphasize the feasibility of this technique, we also highlight that we obtained good results even without excluding staghorn stones, anatomic abnormalities, and previous ipsilateral PNL.

Based on our experience, the current protocol at our institution is to apply Quikclot® for all future patients undergoing PNL who exhibit significant bleeding following stone removal. Our report adds to the literature regarding the safety of tubeless PNL and suggests that Quikclot® application is an effective way of limiting patient morbidity due to hemorrhage, pain, or prolonged hospitalization. However, our study has limitations: (1) our patients were retrospectively collected at a single center, and a randomized-control study design was not implemented; (2) the results may be sensitive to selection bias. For example, a discrepancy existed in age distribution between the two study groups, while age itself is a confounder that may affect postoperative perception of pain and readiness for discharge. However, no significant correlations were noted between age and both VAS scores and length of hospitalization in our overall cohort; (3) another potential selection biases may arise from the lack of a standard definition for significant parenchymal bleeding. Therefore, a physician preference may have existed regarding the implementation of tubeless Quikclot® or nephrostomy placement PNLs. Nevertheless, we believe that this effect is inherent in any similar study and may reflect the reality of clinical practice; (4) as an histologic assessment is not realistic in this setting, we were unable to provide supportive evidence that Kaolin is free from tissue inflammation; and (5) the follow-up period was short, and the preventive effect of Quikclot® on future stone recurrence was not fully evaluated.

Conclusions

We demonstrated that the use of Quikclot® was safe and provided effective hemostasis of significant parenchymal bleeding. By avoiding nephrostomy placement, we were able to reduce postoperative pain, analgesic requirements, and length of hospital stay. Application of Quikclot® may be considered prior to nephrostomy placement in patients with significant parenchymal bleeding.

Conflict of interest None of the contributing authors have any conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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