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Short Communication

Hemostatic sealant in tubeless percutaneous nephrolithotomy: a monocentric experience

M. Auciello[1], A. Mangiatordi[1], G. Stallone[2], G. Carrieri[1], A. Hoznek[3], L. Cormio[1]

[1] Urology and Renal Transplantation Unit, Department of Medical and Surgical Sciences, University of Foggia, Italy; [2] Nephrology, Dialysis and Transplantation Unit, Department of Medical and Surgical Sciences, University of Foggia, Italy; [3] Department of Urology, Henri Mondor Hospital, Créteil, France

Background and aims. Tubeless percutaneous nephrolithotomy is increasingly been used but the question remains on the wisdom of using an hemostatic agents to seal the tract and whether this decision should be based on tract size. We compared the outcome of standard (26-30Fr) tubeless percutaneous nephrolithotomy sealed with Tachosil® *vs* mini (17.5Fr) percutaneous nephrolithotomy with a tract left unsealed.
Methods. We analysed our prospectively maintained Internal Review Board-approved percutaneous nephrolithotomy database to compare outcomes of patients who had undergone tubeless percutaneous nephrolithotomy either sealed or unsealed.
Result. Among 491 eligible patients, 294 had a mini (17.5 Fr) unsealed (Group A) and 197 a standard (26-30 Fr) sealed procedure (Group B). Groups were similar for baseline characteristics but median surgical time was significantly shorter (60 *vs* 75 min; p = 0.0004) in unsealed rather than in sealed procedures. There was no difference in the overall complications rate (44.9 *vs* 39.1%, p = 0.2); median Hb loss was statistically lower (0.8 *vs* 1.0; p = 0.028) in unsealed procedures but there was no difference in blood transfusion rate (3.1 *vs* 3.6%; p = 0.8). Four patients required embolization, 3 (1%) in unsealed and 1 (0.5%) in sealed procedures; 4 had urinary leakage from the flank requiring ureteral stenting, 3 (1%) in unsealed and 1 (0.5%) in sealed procedures. Finally, there was no difference in mean postoperative hospital stay and stone-free rate.
Conclusions. Tubeless percutaneous nephrolithotomy were proved to be safe, but elderly patients deserve more attention. The use of sealants, while not always necessary, may be useful in optimizing results.

Key words: Percutaneous nephrolithotomy, Sealant, Urolithiasis

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the recommended treatment option for large or otherwise complex renal or proximal ureteral stones. Since first described by Fernstrom and Johannson [1], great efforts have been made to improve the outcomes of this surgical procedure by optimizing its surgical steps, including patient positioning, puncture of the collecting system, dilation and fragmentation modality, and exit strategy [2]. The latter remains an area of continuing innovation and debate due to its relevant impact on postoperative clinical outcome.

The practice of routine placement of a large bore (20 to 26Fr) nephrostomy tube (NT), traditionally recommended to achieve hemostasis, urinary drainage and access for a second look procedure, has been challenged since the early 1980s [3] but the concept of "tubeless" PCNL remained neglected until 1997, when Bellman et al. [4] demonstrated that placement of a Double-J stent instead of a NT was associated with less postoperative pain, decreased analgesia requirement, shorter hospital

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Correspondence: Beppe Calò, Urology and Renal Transplantation Unit, Department of Medical and Surgical Sciences, University of Foggia, viale Luigi Pinto 251, 71122 Foggia, Italy. Tel. +39 328 2136373. Fax +39 0881 732275. E-mail: beppecalo49@gmail.com

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stay and faster return to normal activities. Several studies subsequently confirmed the tubeless approach to be associated with reduced postoperative pain and hospital stay [5 6]. Nevertheless, the wisdom of tubeless PCNL continues to be challenged by studies demonstrating the advantages of early NT removal [7] or placement of small bore NTs [8] over the tubeless approach. Indeed, most endourologists continue to favor NT placement probably due to fear of bleeding or urinary leakage through a tract left open [9], particularly in the elderly population whereby the healing process is expected to be less effective.

Hemostatic agents appear to be an attractive means of sealing the tract without using a tube; again, this option could be most useful in the elderly. Indeed, sealed tubeless PCNL has been suggested to reduce patient discomfort and urinary leakage compared to unsealed tubeless PCNL [10 11] or NT placement [12 13] but if [14] and which [15] agent should be used remain controversial.

We demonstrated that TachoSil® [16] Sealed Tubeless PCNL provided better tract control and a shorter hospital stay than NT placement in patient having undergone standard PCNL (30Fr Amplatz sheath). Others [17] suggested the use of sealants also when using a smaller percutaneous access (mini-PCNL) but the minimal invasivity and, consequently, the theoretically minimal parenchymal trauma of mini-PCNL would question the need for sealants during PCNL.

The present study aimed to compare the outcome of standard (26-30Fr) tubeless percutaneous nephrolithotomy sealed with TachoSil® *vs* mini (17.5Fr) percutaneous nephrolithotomy with a tract left unsealed. Special attention was given to the elderly population.

PATIENTS AND METHODS

Data of patients scheduled for PCNL at our Department were prospectively entered into our Internal Review Board approved dedicated database.

Preoperatively, all patients underwent abdominal computed tomography scanning and urine culture. Antibiotic prophylaxis was carried out according to current recommendations [18]. All procedures were carried out in our supine antero-lateral position or in the Galdakao-modified supine position [19-21]. Until the end of 2014, standard anesthesia was general whereas, from the beginning of 2015, it was spinal. Renal collecting system was punctured under fluoroscopic guidance using an 18G needle. The percutaneous tract was dilated to 26-30F (standard PCNL) or, by the beginning of 2014, to 17.5F (mini-PCNL). Following stone/s fragmentation/extraction, flexible ureteroscopy and/or nephroscopy was carried out to check for stone clearance. Whenever possible, the procedure was closed placing a mono-J ureteral stent and a Foley catheter, thus were tubeless or TachoSil®-sealed tubeless procedures [2 16]. Whenever deemed necessary, we used a double-J stent instead of the mono-J ureteral catheter or a nephrostomy tube [22]. All procedures were carried out by one of us (LC).

All patients underwent abdomen X-ray and renal ultrasound (US) at 1 month postoperatively to assess stone free rate (SFR). Abdominal CT was used as needed. Patients with residual fragments ≤ 4 mm were considered stone-free [23]. Perioperative complications were assessed using the Clavien classification system adjusted for PCNL [24]. Infective complications were defined fever > 38°C or SIRS lasting > 24h, and/or infection of urine of blood.

Statistical analysis

The Mann-Whitney U-test was used for continuous variables, whereas the Chi-square test was used for categorical variables. Data were analysed by Stata 14 (StataCorp LP, College Station, TX, USA). All tests were 2-sided with a significance level set at $p < 0.05$.

RESULTS

Between April 2005 and March 2018, a total of 491 patients underwent tubeless PCNL at our Institution. Among them, 294 had a mini (17.5 Fr) unsealed (Group A) and 197 a standard (26-30 Fr) sealed procedure (Group B). Patients baseline characteristics are summarized in Table I. Basically, there was no difference in age, gender, body mass index (BMI), American Society of Anesthesiologists Classification (ASA score), positive preoperative urine culture rate, and stone features. However, mean stone size in patients with single or multiple stones was smaller in Group A.

Median surgical time was significantly shorter in unsealed than in sealed PCNLs (60.0 [IR 50.0, 90.0] *vs* 75.0 [IR 60.0, 100.0], respectively; $p = 0.0004$). There was no difference in the positive stone culture rate (10.8 *vs* 17.6%; $p = 0.1$).

Table II summarizes outcomes. There was no difference in the overall complications rate (44.9% *vs* 39.1%, $p = 0.2$) nor in the different grades of Clavien scores. Median Hb loss was statistically lower (0.8 *vs* 1.0; $p = 0.028$) in unsealed than in sealed procedures, but there was no difference in blood transfusion rate (3.1 *vs* 3.6%; $p = 0.8$). Indeed, 4 patients required embolization due to postoperative bleeding, 3 (1%) in the unsealed and 1 (0.5%) in the sealed procedures. Urinary leakage from the flank lasting > 12h, thus requiring placement of a double-J stent, occurred in 4 patients, 3 (1%) in the unsealed and 1 (0.5%) in the sealed procedures. Finally,

Table I. Patients characteristics.

	Group A = unsealed (n = 294)	Group B = sealed (n = 197)	P-value
*Age, years	54.5 (44.3, 63.6)	54.8 (41.5, 63.2)	0.4
Female gender, n (%)	157 (53.4%)	105 (53.3%)	1
*BMI	26.0 (24.0, 30.0)	26.0 (25.0, 31.0)	0.4
ASA score, n (%) 1 2 3 4	 27 (9.2%) 244 (83.0%) 23 (7.8%) 0 (0.0%)	 23 (11.7%) 148 (75.1%) 25 (12.7%) 1 (0.5%)	 0.11
Positive preop. urine culture, n (%)	33 (11.9%)	19 (10.9%)	0.7
Stone features, n (%)			
Single Multiple Staghorn	154 (52.4%) 89 (30.3%) 51 (17.3%)	99 (50.3%) 69 (35.0%) 29 (14.7%)	0.6 0.27 0.45
*Stone size", mm	20.0 (17.0, 30.0)	25.0 (20.0, 30.0)	0.026

*Data are expressed as median (Interquartile Range) "only for single and multiple stones".

Table II. Clinical outcomes.

	Group A = unsealed (n = 294)	Group B = sealed (n = 197)	P-value
Clavien, n (%)			
0	162 (55.1%)	120 (60.9%)	0.3
I	98 (33.3%)	52 (26.4%)	
II	16 (5.4%)	12 (6.1%)	
IIIa	15 (5.1%)	12 (6.1%)	
IIIb	3 (1.0%)	0 (0.0%)	
V	0 (0.0%)	1 (0.5%)	
*Hb loss, g/dl	-0.8 (-1.9, 0.2)	-1.0 (-2.6, 0.1)	0.028
Blood transfusions, n (%)	9 (3.1%)	7 (3.6%)	0.8
Embolization, n (%)	3 (1%)	1 (0.5%)	0.65
Urinary leakage, n (%)	3 (1%)	1 (0.5%)	0.65
*Postop. Hosp Stay, days	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)	0.3
Infective complications, n (%)	8 (2.7%)	10 (5.1%)	0.2
Stone free, n (%)	215 (74.7%)	137 (69.9%)	0.2

*Data are expressed as median (Interquartile Range).

there was no difference in mean postoperative hospital stay, infective complication and stone-free rate.

Table III reports the outcomes of patients > 70y. There was no difference in the overall complications rate nor in the different grades of Clavien scores. Specifically, there was no difference in blood transfusion rate (7.1 *vs* 4%) nor in the infective complications rate (7.1 *vs* 12%). Having said this, it is worth mentioning that the blood transfusion rate of elderly patients who had an unsealed procedure was double that of their younger counterpart (7.1 *vs* 3.1%; p = 0.1790). Also the infective complications rate was higher in the elderly as opposed to their younger counterpart (7.1 *vs* 2.7% for unsealed procedures, p = 0.1466; 5.1 *vs* 12% for sealed procedures, p = 0.1685).

DISCUSSION

TachoSil® is a sterile, ready to use absorbable patch consisting of an equine collagen matrix coated with fibrin glue components, human fibrinogen and human thrombin, thus combining the assets of a pliable patch material with the hemostatic and adhesive properties of the coagulation factors. Its efficacy and safety have been demonstrated in several surgical procedures leading to product approval in Europe as a supportive hemostatic treatment for intraoperative topical application. We previously demonstrated [16] that TachoSil® sealed tubeless PCNL provided better tract control and a shorter hospital stay than NT placement in patient having undergone standard PCNL (30Fr Amplatz sheath).

Table III. Outcomes in elderly (> 70y) patients.

	Group A = unsealed (n = 42)	Group B = sealed (n = 25)	P-value
Clavien, n (%)			
0	18 (42.9%)	14 (56.0%)	0.14
I	15 (35.7%)	4 (16.0%)	
II	4 (9.5%)	1 (4.0%)	
IIIa	3 (7.1%)	5 (20.0%)	
IIIb	2 (4.8%)	0 (0.0%)	
V	0 (0.0%)	1 (4.0%)	
Blood transfusions, n (%)	3 (7.1%)	1 (4%)	0.6
Infective complications, n (%)	3 (7.1%)	3 (12.0%)	0.5
*Postop. Hosp Stay, days	3.0 (2.0, 5.0)	3.0 (3.0, 7.0)	0.2
Stone free, n (%)	33 (80.5%)	15 (60.0%)	0.7

*Data are expressed as median (interquartile range).

In a recent systematic review and meta-analysis, Yu et al. [25] addressed the use of hemostatic agents for tract closure after tubeless PCNL. Eight studies including six RCTs showed that use of hemostatic agents was safe. Hemostatic agents showed short hospital stay. There were no difference between hemostatic agents and common methods on blood loss, transfusion rate, fever rate, and complication rate. Another recent systematic review and meta-analysis addressing the use of hemostatic agents for tract closure after tubeless PCNL [26] analyzed 7 studies involving 351 patients. Again, hospital stay was shorted in sealed patients than in controls ($p < 0.05$). There were no statistically significant difference in terms of Hb drop, analgesic requirements, and blood transfusion rate. In spite of the advantage in hospital stay, the study concluded that, in view of their cost, hemostatic agents might not be necessary in tubeless PCNL.

The present study pointed out no difference in the overall complications rate. There was a statistically but certainly not clinically significant difference in Hb loss in favor of unsealed procedures; indeed, blood transfusion rate was similar in the two groups. Embolization and urinary leakage requiring placement of a double-J stent were slightly more common (1 *vs* 0.5% for both events) in unsealed than in sealed procedures. While the first event is probably related to puncture/dilation, urinary leakage is probably related to tract handling. Case volume is too small to draw any definite conclusion [27] but findings would suggest that, in terms of urinary leakage, sealing the tract with TachoSil® performs better than NT placement, as shown in our previous study [16], as well as than just leaving the tract unsealed. If we join findings from our previous study [16] together with those from the present one, it comes out that our rate of urinary leakage requiring stenting is 6% for standard PCNL with NT placement, as shown in the previous study, 1% for unsealed mini-PCNL and 0.5% for TachoSil®-sealed standard PCNL, somehow pointing out a minimal advantage in sealing the tract.

While potentially advantageous, hemostatics rise concerns about their safety, particularly about their potential antigenicity exposing to the risk of local foreign-body reactions, such as granuloma or abscess formation [28], and/or systemic hypersensitivity/anaphylactic reactions. Clinical studies seem to rule out the risk of systemic reactions, but little is known regarding local reactions, as the only two studies addressing this issue were both carried out on animal models [28 29]. This issue would deserve further attention.

Differently from the above-mentioned meta-analyses, we found no difference in hospital stay. This may be due to the fact that we adopted the same protocol in sealed and unsealed PCNL and we had quite similar outcome.

An interesting and novel information coming from our study was the sub-analysis of elderly (> 70y) patients outcomes. While there was no substantial difference between sealed and unsealed procedures also in this subset of patients, it should be noted that the overall complications rate was higher compared to their younger counterpart. Specifically, the blood transfusion rate of elderly patients who had an unsealed procedure was double than the one of their younger counterpart; the same applied for the infective complications rate, which was higher in the elderly patients independently on whether they had a sealed or an unsealed procedure. Though findings did not reach statistical significance, they suggest the elderly patient to be a bit more frail in this respect.

This study is not without limitations. One is its retrospective nature, but data were prospectively collected. Another aspect is difference in Amplatz sheath size, but this provided furthers insights on its impact on urinary leakage. Further studies addressing the role of TachoSil® when using the same sheath size are awaited.

In conclusion, tubeless PCNL, both sealed and unsealed, provided a safe and effective means of handling the tract. While the use of an hemostatic agent is not always necessary, it may sometimes be useful in optimizing results thus justifying costs. Due to their slightly higher risk of complications, elderly patients deserve greater attention.

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Conflict of Interest

The authors declare no conflict of interest.

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