Asian Journal of Urology (2020) 7, 116–121

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajur

Review

Definition, treatment and outcome of residual fragments in staghorn stones

Osman Ermis [a,*], Bhaskar Somani [b], Thomas Reeves [b], Selcuk Guven [a], Pilar Laguna Pes [a], Arun Chawla [c], Padmaraj Hegde [c], Jean de la Rosette [a]

[a] *Istanbul Medipol University, School of Medicine, Department of Urology, Istanbul, Turkey*
[b] *University Hospital Southampton NHS Trust, Department of Urology, Southampton, UK*
[c] *Kasturba Medical College, Manipal Academy of Higher Education, Department of Urology, Manipal, India*

Received 30 January 2019; received in revised form 28 May 2019; accepted 29 November 2019
Available online 31 December 2019

KEYWORDS
Urolithiasis;
Stone management;
Staghorn;
Percutaneous nephrolithotomy;
Residual fragments;
Staghorn stones

Abstract Technological advances in minimally invasive treatment of stone disease and its integration with concomitant clinical practice are amongst the most important achievements in urology. Despite the wealth of information accumulated over the years and the richness of existing literature, the knowledge about the definition, treatment and outcomes of residual stone fragments after percutaneous nephrolithotomy (PNL) is still insufficient. Due to the high stone load a lot of patients with staghorn stones have residual fragments (RFs) after treatment with PNL, which depends on the size of tract, definition of stone free rate (SFR), timing of evaluation and the imaging used. No consensus exists on the imaging modality or their timing in the evaluation of possible RFs. The treatment of residual stones is apparently different depending on the facilities of the department and the preference of the surgeon, which includes active surveillance, shock wave lithotripsy (SWL), retrograde intrarenal surgery (RIRS) or a second look PNL.

* Corresponding author.
E-mail address: osermis@gmail.com (O. Ermis).
Peer review under responsibility of Second Military Medical University.

https://doi.org/10.1016/j.ajur.2019.12.013

1. Introduction

Urolithiasis is a significant source of morbidity worldwide, constituting a common urological disease that affects between 10% and 15% of the population [1]. Although all urinary stones are in general more common in males than females, the incidence of staghorn stones is higher in females [2]. According to previous studies, the overall incidence of staghorn stones is between 10% and 20%, but this seems to have dropped.

Urinary stones are classified according to the European Association of Urology (EAU) guidelines in terms of their size, location, X-ray characteristics, etiology, composition and risk of recurrent stone formation [1—3]. Whilst specific definition remains controversial, staghorn stones are large branching stones that fill part, or all of the renal pelvis and calyces and they can be complete or partial depending on the level of occupancy of the collecting system. In the EAU guidelines, the definition of "complex renal stone" rather than the term "staghorn stone" is given [3].

Staghorn stones are generally composed of struvite (magnesium/ammonium/phosphate) and/or calcium carbonate apatite. Because these stones are often accompanied by urinary tract infections, caused by urease-producing bacteria (Proteus, Klebsiella, Pseudomonas, and Staphylococcus bacteria), evaluation and treatment should be aggressive. In addition, Koga et al. [4] showed that 36% of patients developed significant renal impairment within 10 years following conservative treatment for staghorn stones.

Residual stones are a risk factor for stone reformation, stone regrowth, urinary tract infection (UTI) and ureteric obstruction [5,6]. In the EAU guidelines, the likelihood of clinically significant recurrence of stone disease in patients with residual fragments (RFs) is more likely with infection stones [7]. As a result, residual stones, especially those related to a metabolic disease or infections may act as a nidus for growth, exacerbate acute colic and cause significant urinary obstruction or cause persistent UTIs. However, more than half of the patients with a RF in noncontrast computed tomography (NCCT) images may not experience a stone-related event [3].

The American Association of Urology (AUA) guidelines recommend percutaneous nephrolithotomy (PNL) as a primary treatment option for these stones [8]. Open treatment for staghorn stones is now outdated by more minimally invasive PNL. Chen et al. [9] compared PNL and open surgery in the treatment of staghorn stones and found no significant difference in the final stone free rate (SFR). However, the operative times and hospital stay were significantly shorter in PNL. In addition, the overall complication rate was significantly lower in the PNL group. They concluded that in the treatment of staghorn stones, PNL was shown as a safe and feasible alternative without any significant difference in the final SFR compared to open surgery, and without any increase in complication rates [9].

Here we present a mini-review focusing of definition, treatment and outcome of RF following treatment with PNL for staghorn stones.

2. Definition of RF and SFR in the literature

The definition of RF and SFR is still a controversial issue. At times when open stone surgery was popular, RF of any size was defined as procedural failure. With the introduction of SWL, RFs larger than 5 mm are generally accepted as failure of SWL. The definition of RF, which is currently subject to complex and arbitrary criteria, has been complicated by the introduction of clinically insignificant RF (CIRF) into the literature [10].

The definition of CIRF has emerged during the treatment of RF after PNL [11,12]. Generally asymptomatic, non-obstructive and non-infectious stones were accepted as CIRF. Besides, absence of having any size stone or CIRF on urinary system ultrasonography (USS) or computerized tomography (CT) scan was described as stone free status [11]. Stones smaller than 4 mm could grow over and cause RF related morbidity in the future [6,13]. However, Osman et al. [14] in their assessment with NCCT reported that stone sizes of 3 mm and below were acceptable for CIRF.

In a study by Opondo et al. [15] related to the standardization of PNL results, this deficiency has been objectively demonstrated. Eighty-three randomized-controlled trials related to PNL were examined and it was seen that 53 of these 83 articles had mentioned SFR. Twenty-nine of these 53 studies (54.7%) did not have a clear definition of SFR. In eight of these studies, the definition of SFR after the PNL was "no stones". The cutoff value used for the definition of SFR across 10 studies varied from 2 mm to 4 mm [15].

The timing of evaluation for RF varied across studies, and RFs were evaluated intraoperatively, postoperatively or both. Postoperative stone evaluation was more common than intraoperative evaluation, but the follow-up timing was highly variable. This varied from postoperative day 1, day 3, 4—6 weeks and 3 months, which were all used for different studies [11—13,16—19]. The method of evaluation was also variable; while most of studies evaluated RF status intraoperatively by fluoroscopy and postoperatively by using USS, some of them followed patients by using NCCT [11—13,16—19]. The RF determination during the operation with direct visualisation of collecting system by nephroscope was also used [12,13,16—19]. Some authors also tried to attempt to predict the SFR of staghorn stones and developed nomograms, such kind of nomograms have not been universally accepted [18].

In a study of pediatric patients, El-Assmy et al. [20] reported that a third of CIRFs developed clinically significant events. They stated that CIRFs are more likely to develop clinical significance in children compared to adults.

3. Treatment of RFs in staghorn stone

There is limited information in the literature regarding the surgical treatment of residual stones after PNL. Theoretically second look nephroscopy, flexible ureteroscopy (fURS) and SWL can all be used. According to our literature review,

there was only one article that focused on the treatment of RFs after PNL for staghorn stones. In the treatment of residual stones after PNL, most studies did not mention the initial stone as a staghorn stone [21].

The retrospective study by Chen et al. [21] was conducted to investigate the treatment of residual stones post single-tract PNL, with fURS and holium laser lithotripsy. In this study, a total of 337 patients who underwent PNL between January 2014 and June 2016 were reviewed retrospectively. Those who didn't have complex stones were excluded from the study. Their definition of a complex stone was defined as stone with a large stone volume, occupying multiple calyces or with peripheral satellites and these complex stones were divided into three sections as full staghorn calculi, partial staghorn calculi and multiple calculi. On the third day after PNL, RFs were examined with kidney-ureter-bladder X-ray (KUB-XR) and those with RFs below 2 mm were excluded. In total, 27 patients were examined. They defined SFR as the first postoperative month without any stone seen on urinary USS or CT, and retrograde intrarenal surgery (RIRS) was performed providing stone-free status in 24 (88.9%) of patients. In one patient, fever was observed after the operation (>38.5 °C) and no blood transfusion was required in any patient. Complications, as defined by Clavien classification, were: Grade 0 (23, 85.2%), Grade 1 (3, 11.1%) and Grade 2 (1, 3.7%). This study has several limitations: Firstly, it is a retrospective paper without a

Table 1 Different authors presenting definitions of RF and SFR, imaging modality used and SFR outcome (%).

References	Definition of RF	Definition of SFR	Imaging modality	SFR
Al-Kohlany et al. [7]	CIRF: nonsymptomatic, nonobstructing and noninfected fragments of less than 4 mm in diameter	Completely clearances of stones were considered stone free	KUB and USS (at discharge home and during follow-up)	49%
Zeng et al. [19]	—	The absence of any diameter RF	KUB or CT (at discharge and after auxiliary procedures if necessary)	Initial SFR: 66.4% Final SFR: 86.1% (after auxillary procedures)
Liatsikos et al. [24]	—	The absence of any diameter RF	Non-contrast CT ornephrostography (postoperative)	87%
Netto et al. [25]	—	The absence of any diameter RF after all treatment modalities done	Non-contrast CT or KUB (afterinitial PCNL and allauxiliary procedure)	82.3%
Desai et al. [26]	—	The absence of any diameter RF in the postoperation 30th day and following examinations	—	56.9%
Armitage et al. [27]	—	The absence of any diameter RF	KUB, USG or CT (postoperative day 1)	47%
Soucy et al. [28]	—	The absence of significant residual stone	Initial SFR: KUB, CT orantegrade Initial SFR: KUB, CT or antegrade nephrostography at discharge Final SFR: KUB or USS (3 or 6 months)	Initial SFR: 77.8% Final SFR: 90.5% (after auxillary procedures)
Qi et al. [17]	—	The absence of any diameter RF	Initial SFR: KUB and USS (3 days) Final SFR: KUB and USS (3 months)	Initial SFR: 61.6% Final SFR: 79.0%
Atmoko et al. [23]	—	The absence of any diameter RF	KUB, CT orantegradpyelografi (1 or 2 day after operation)	62.6%

—, no description of RFs.
CT, computerized tomography; KUB, kidney-ureter-bladder; RF, residual fragment; SFR, stone free rate; USG, ultrasonography; CIRF, clinically insignificant RF; PCNL, percutaneous nephrolithotomy.

comparison group; secondly, it's a small case series and finally, the study is from a single center.

4. Outcomes of RFs in staghorn stones

The studies focusing on RFs in staghorn stones are lacking. In this section, we aimed not to treat the RFs, but to tell the readers how the RFs are defined after the treatment of large stones, which imaging methods are preferred and the time to do it.

The Clinical Research Office of the Endourological Society (CROES) global percutaneous nephrolithotomy (PCNL) study, which is the most comprehensive prospective clinical research examining the complications and outcomes of PNL-treated kidney stones showed that approximately 25% of patients in PNL had RF, but only 15% of these patients had further intervention [22]. Ganpule et al. [23] reported the follow-up outcomes of 2 469 patients who underwent PNL in their retrospective study and any stone after the initial procedure was considered as a RF. RF was detected in 7.6% (185) of all patients. They determined RF size, history of intervention, renal failure, metabolic hyperactivity as a predictor for persistence of RF. These two studies with large patient inclusion numbers also showed that the issue of RFs remaining after treatment of kidney stones is important.

In the current EAU guidelines, there is a lack of both the definition and treatment of RF. The guidelines suggest imaging of RF after SWL, URS and PNL, and that it is more appropriate to perform this imaging at an interval, but not in the initial postoperative period. In most of these studies, it was seen that the first imaging was performed on postoperative day 1 or a week later, which caused overtreatment. CT has been reported to have high sensitivity compared to other methods, but radiation exposure is also high. Since there is not enough evidence, the imaging method depends on the surgeon's choice. EAU guidelines suggest that for fragments >5 mm, the need for treatment was higher and that fragments >2 mm was more prone to growth. Similarly, RFs of the infection stones were more likely to grow but the guidelines do not suggest which treatment modality should be applied based on the size, composition and location of these stones [3].

When the literature is examined for SFR of staghorn stones after treatment with PNL, a rate of 47%—86% is obtained (Table 1). It depends on the treatment modality, definition of SFR, timing of evaluation and imaging used. Although Al-Kohlany et al. [7] did not give a clear definition of stone free, they defined CIRF as asymptomatic, nonobstructive, noninfectious stones <4 mm. Other studies have defined stone-free status as no stone of any size by various imaging methods or during endoscopy [7,17,19,24—29]. In some other studies it was defined as the absence of RFs initially or after adjuvant treatment [25,28]. The imaging modality varied between KUB X-ray, CT and USS or a combination of these although the timing of imaging varied in studies (Fig. 1). The timing of imaging to determine SFR is also important. It is understood from the reviewed articles that SFR rates in the initial postoperative period are lower and the fragments clear later on. It is also helped by the subsequent auxiliary procedures. Furthermore, an imaging method with high sensitivity and specificity for stones such as NCCT leads to lower SFR rates [7,17,19,24—29].

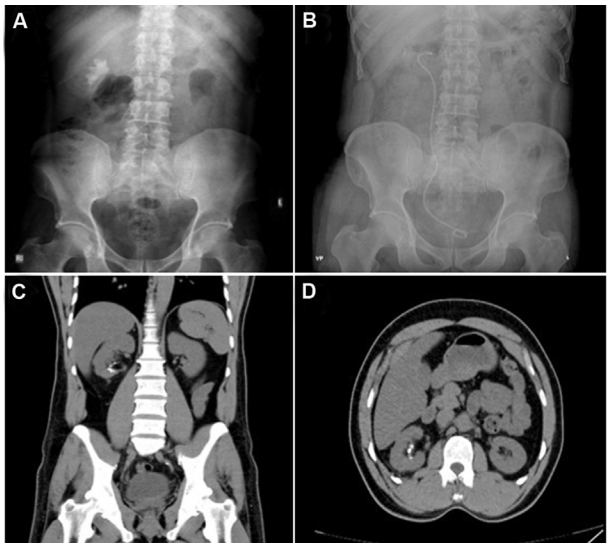

Figure 1 Illustrating stone size and location pre- and postoperative illustrating differences in SFR outcome based on imaging modality used. (A) KUB X-ray preoperative; (B) KUB X-ray postoperative; (C and D) CT postoperative. SFR, stone free rate; KUB, kidney-ureter-bladder; CT, computerized tomography.

To standardize the definition of SFR, previously Somani et al. [30] had proposed a simple classification based on the type and timing of imaging used postoperatively. Clearly with more CT scans being used for diagnosis [31], it is time that the EAU and AUA guidelines highlight this and come to a consensus on how best to define SFR, CIRF and RF especially in the context of complex especially staghorn type kidney stones [3,8].

5. Discussion

Stone disease is a recurrent disease and although the initial treatment can be curative, recurrence leads to further stone formation. Therefore, ideally there should be no RF. A RF of any size will be the nidus for future stones. Today, open surgery is almost completely abandoned. However, all invasive or non-invasive stone treatment modalities result in an increase in RFs. This inevitably brought about clinically important and insignificant RFs in play. In any case, some small stones that may affect stone formation in the long term have been considered clinically insignificant. There is no consensus regarding this and in general, stones <4 mm or less are considered CIRF.

The methods used in defining RF do not show standardization in the studies. Given the variation, it is difficult to establish a standard protocol for different clinics in different countries. This is because the approaches of third parties, such as equipment, patient volumes and insurance companies, can affect these issues. In general, RF evaluation with fluoroscopy and endoscopic examination during

procedures, and subsequent control with USS and KUB are widely used. Of course, the gold standard to determine RF is with NCCT.

Currently there is no specific protocol for the follow-up and intervention of RFs, and the follow-up modality or interval. The advent of minimally invasive PNL and the percentage of RF is increasing. There seems to be insufficient literature on the treatment of RFs that remain after the treatment of staghorn stones. Similarly, although the overall number of reported studies on PNL is increasing, more studies need to be done to address the cost and quality of life of these patients [32—34].

6. Conclusion

Limited data in staghorn stones show RF range from 47% to 87%. Conversely there is confusion about the overall SFR, and this may vary between 79.0% and 90.5% depending on the definition and possible adjuvant treatments carried out. The latter is usually left to the discretion of the surgeon and patient preference, and may include active surveillance, SWL, URS or second look PNL. No consensus exists on the imaging modality or their timing in the evaluation of possible RFs.

Author contributions

Study design: Osman Ermis, Selcuk Guven, Jean de la Rosette.
Data acquisition: Osman Ermis, Selcuk Guven, Bhaskar Somani, Thomas Reeves.
Data analysis: Osman Ermis, Selcuk Guven, Jean de la Rosette, Thomas Reeves.
Drafting of manuscript: Osman Ermis, Bhaskar Somani, Selcuk Guven, Jean de la Rosette.
Critical revision of the manuscript: Selcuk Guven, Pilar Laguna Pes, Arun Chawla, Padmaraj Hegde, Jean de la Rosette.

Conflicts of interest

The authors declare no conflict of interest.

References

[1] Desai M, Sun Y, Buchholz N, Fuller A, Matsuda T, Matlaga B, et al. Treatment selection for urolithiasis: percutaneous nephrolithomy, ureteroscopy, shock wave lithotripsy, and active monitoring. World J Urol 2017;35:1395—9.

[2] Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. Renal stone epidemiology: a 25-year study in Rochester, Minnesota. Kidney Int 1979;16:624—31.

[3] Türk C, Neisius A, Petrik A, Seitz C, Skolarikos A, Thomas K. EAU guideline on urolithiasis. [Accessed 3 January 2019]. https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Urolithiasis-2018-large-text.pdf.

[4] Koga S, Arakaki Y, Matsuoka M, Ohyama C. Staghorn calculi-long-term results of management. Br J Urol 1991;68:122—4.

[5] Khaitan A, Gupta NP, Hemal AK, Dogra PN, Seth A, Aron M. Post-ESWL, clinically insignificant residual stones: reality or myth? Urology 2002;59:20—4.

[6] Osman MM, Alfano Y, Kamp S, Haecker A, Alken P, Michel MS, et al. 5-year-follow-up of patients with clinically insignificant residual fragments after extracorporeal shockwave lithotripsy. Eur Urol 2005;47:860—4.

[7] Al-Kohlany KM, Shokeir AA, Mosbah A, Mohsen T, Shoma AM, Eraky I, et al. Treatment of complete staghorn stones: a prospective randomized comparison of open surgery versus percutaneous nephrolithotomy. J Urol 2005;173:469—73.

[8] Preminger GM, Assimos DG, Lingeman JE, Nakada SY, Pearle MS, Wolf Jr JS, et al. Chapter 1: AUA guideline on management of staghorn calculi: diagnosis and treatment recommendations. J Urol 2005;173:1991—2000.

[9] Chen Y, Feng J, Duan H, Yue Y, Zhang C, Deng T, et al. Percutaneous nephrolithotomy versus open surgery for surgical treatment of patients with staghorn stones: a systematic review and meta-analysis. PLoS One 2019;14:e0206810. https://doi.org/10.1371/journal.pone.0206810.

[10] Smith AD, Badlani G, Preminger G, Badlani G, Kavoussi L. Smith's textbook of endourology, 3rd ed.. Wiley-Blackwell. Chapter 58 Management of residual stone fragments, Page 662, [Introduction and definitions Part I].

[11] Altunrende F, Tefekli A, Stein RJ, Autorino R, Yuruk E, Laydner H, et al. Clinically insignificant residual fragments after percutaneous nephrolithotomy: medium-term follow-up. J Endourol 2011;25:941—5.

[12] Olvera-Posada D, Ali SN, Dion M, Alenezi H, Denstedt JD, Razvi H. Natural history of residual fragments after percutaneous nephrolithotomy: evaluation of factors related to clinical events and intervention. Urology 2016;97:46—50.

[13] Scoffone CM, Cracco CM, Cossu M, Grande S, Poggio M, Scarpa RM. Endoscopic combined intrarenal surgery in Galdakao-modified supine Valdivia position: a new standard for percutaneous nephrolithotomy? Eur Urol 2008;54:1393—403.

[14] Osman Y, Harraz AM, El-Nahas AR, Awad B, El-Tabey N, Shebel H, et al. Clinically in significant residual fragments: an acceptable term in the computed tomography era? Urology 2013;81:723—6.

[15] Opondo D, Gravas S, Joyce A, Pearle M, Matsuda T, Sun YH, et al. Standardization of patient outcomes reporting in percutaneous nephrolithotomy. J Endourol 2014;28:767—74.

[16] Hamamoto S, Yasui T, Okada A, Taguchi K, Kawai N, Ando R, et al. Endoscopic combined intrarenal surgery for large calculi: simultaneous use of flexible ureteroscopy and mini-percutaneous nephrolithotomy overcomes the disadvantageous of percutaneous nephrolithotomy monotherapy. J Endourol 2014;28:28—33.

[17] Qi S, Li L, Liu R, Qiao B, Zhang Z, Xu Y. Impact of stone branch number on outcomes of percutaneous nephrolithotomy for treatment of staghorn calculi. J Endourol 2014;28:152—7.

[18] Sfoungaristos S, Gofrit ON, Pode D, Landau EH, Duvdevani M. Percutaneous nephrolithotomy for staghorn stones: which nomogram can better predict postoperative outcomes? World J Urol 2016;34:1163—8.

[19] Zeng G, Zhao Z, Wan S, Mai Z, Wu W, Zhong W, et al. Minimally invasive percutaneous nephrolithotomy for simple and complex renal caliceal stones: a comparative analysis of more than 10 000 cases. J Endourol 2013;27:1203—8.

[20] El-Assmy A, El-Nahas AR, Harraz AM, El Demerdash Y, Elsaadany MM, El-Halwagy S, et al. Clinically insignificant residual fragments: is it an appropriate term in children? Urology 2015;86:593—8.

[21] Chen L, Sha ML, Li D, Zhuo J, Jiang CY, Zhu YP, et al. Treatment for residual stones using flexible ureteroscopy and holmium laser lithotripsy after the management of complex calculi with single-tract percutaneous nephrolithotomy. Lasers Med Sci 2017;32:649—54.

[22] de la Rosette J, Assimos D, Desai M, Gutierrez J, Lingeman J, Scarpa R, et al. The clinical research office of the endourological society percutaneous nephrolithotomy global study: indications, complications, and outcomes in 5 803 patients. J Endourol 2011;25:11—7.
[23] Ganpule A, Desai M. Fate of residual stones after percutaneous nephrolithotomy: a critical analysis. J Endourol 2009; 23:399—403.
[24] Liatsikos EN, Kapoor R, Lee B, Jabbour M, Barbalias G, Smith AD. "Angular percutaneous renal access". Multiple tracts through a single incision for staghorn calculous treatment in a single session. Eur Urol 2005;48:832—7.
[25] Netto Jr NR, Ikonomidis J, Ikari O, Claro JA. Comparative study of percutaneous access for staghorn calculi. Urology 2005;65:659—62.
[26] Desai M, De Lisa A, Turna B, Rioja J, Walfridsson H, D'Addessi A, et al. The clinical research office of the endourological society percutaneous nephrolithotomy global study: staghorn versus nonstaghorn stones. J Endourol 2011;25:1263—8.
[27] Armitage JN, Irving SO, Burgess NA, British Association of Urological Surgeons Section of Endourology. Percutaneous nephrolithotomy in the United Kingdom: results of a prospective data registry. Eur Urol 2012;61:1188—93.
[28] Soucy F, Ko R, Duvdevani M, Nott L, Denstedt JD, Razvi H. Percutaneous nephrolithotomy for staghorn calculi: a single center's experience over 15 years. J Endourol 2009;23: 1669—73.
[29] Atmoko W, Birowo P, Rasyid N. Factors affecting stone free rate of primary percutaneous nephrolithotomy on staghorn calculi: a single center experience of 15 years. Version 2. F1000Res 2016;5:2106. eCollection 2016.
[30] Somani BK, Desai M, Traxer O, Lahme S. Stone free rate (SFR): a new proposal for defining levels of SFR. Urolithiasis 2014;42:95.
[31] Rob S, Bryant T, Wilson I, Somani BK. Ultra low dose, low dose and standard dose CT of the kidney, ureters, and bladder: is there a difference? Results from a systematic review of literature. Clin Radiol 2017;72:11—5.
[32] Pietropaolo A, Proietti S, Geraghty R, Skolarikos A, Papatsoris A, Liatsikos E, et al. Trends of 'urolithiasis: interventions, simulation and laser technology' over the last 16 years (2000—2015) as published in the literature (PubMed): a systematic review. World J Urol 2017;35:1651—8.
[33] New F, Somani BK. A complete world literature review of quality of life in patients with kidney stone disease. Curr Urol Rep 2016;17:88.
[34] Wright A, Rukin N, Smith D, de la Rosette J, Somani BK. 'Mini, Ultra, Micro' — Nomenclature and cost of these new minimally invasive percutaneous nephrolithotomy (PCNL) techniques. Ther Adv Urol 2016;8:142—6.