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Review

Definition, treatment and outcome of residual fragments in staghorn stones

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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.

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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 holmium 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 post-operative 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 auxiliary procedures)
Liatsikos et al. [24]	—	The absence of any diameter RF	Non-contrast CT or nephrostography (postoperative)	87%
Netto et al. [25]	—	The absence of any diameter RF after all treatment modalities done	Non-contrast CT or KUB (after initial PCNL and all auxiliary 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 or antegrade nephrostography at discharge Final SFR: KUB or USS (3 or 6 months)	Initial SFR: 77.8% Final SFR: 90.5% (after auxiliary 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 or antegradepyelografi (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, non-obstructive, 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

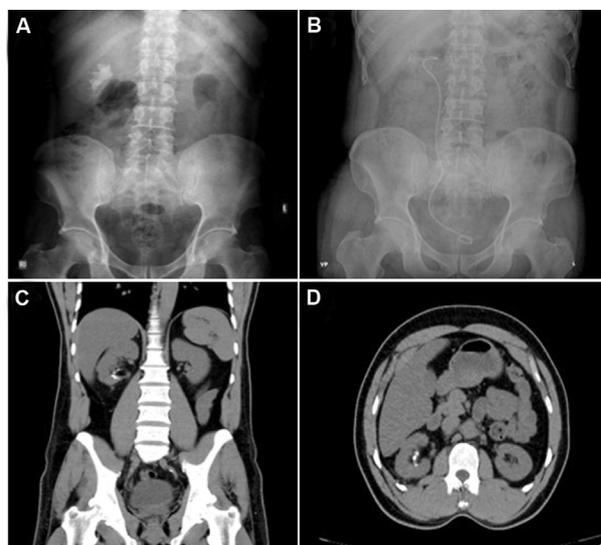


Figure 1 Illustrating stone size and location pre- and post-operative illustrating differences in SFR outcome based on imaging modality used. (A) KUB X-ray preoperative; (B) KUB X-ray postoperative; (C and D) CT postoperative. SFR, stone free rate; KUB, kidney-ureter-bladder; CT, computerized tomography.

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].

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

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Conflicts of interest

The authors declare no conflict of interest.

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