



# Follow-up of urolithiasis patients after treatment: an algorithm from the EAU Urolithiasis Panel

Riccardo Lombardo<sup>1</sup> · Lazaros Tzelves<sup>2</sup> · Robert Geraghty<sup>3,4</sup> · Niall F. Davis<sup>5</sup> · Andreas Neisius<sup>6</sup> · Ales Petřík<sup>7,8</sup> · Giovanni Gambaro<sup>9</sup> · Christian Türk<sup>10,11</sup> · Bhaskar Somani<sup>12</sup> · Kay Thomas<sup>13</sup> · Andreas Skolarikos<sup>2</sup>

Received: 11 December 2023 / Accepted: 8 February 2024  
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2024

## Abstract

**Objective** To develop a follow-up algorithm for urinary stone patients after definitive treatment.

**Materials and methods** The panel performed a systematic review on follow-up of urinary stone patients after treatment (PROSPERO: CRD42020205739). Given the lack of comparative studies we critically evaluated the literature and reached a consensus on the follow-up scheme.

**Results** A total of 76 studies were included in the analysis, including 17 RCTs. In the stone-free general population group, 71–100% of patients are stone-free at 12 months while 29–94% remain stone-free at 36 months. We propose counselling these patients on imaging versus discharge after the first year. The stone-free rate in high-risk patients not receiving targeted medical therapy is < 40% at 36 months, a fact that supports imaging, metabolic, and treatment monitoring follow-up once a year. Patients with residual fragments ≤ 4 mm have a spontaneous expulsion rate of 18–47% and a growth rate of 10–41% at 12 months, supporting annual imaging follow-up. Patients with residual fragments > 4 mm should be considered for surgical re-intervention based on the low spontaneous expulsion rate (13% at 1 year) and high risk of recurrence. Plain film KUB and/or kidney ultrasonography based on clinicians' preference and stone characteristics is the preferred imaging follow-up. Computed tomography should be considered if patient is symptomatic or intervention is planned.

**Conclusions** Based on evidence from the systematic review we propose, for the first time, a follow-up algorithm for patients after surgical stone treatment balancing the risks of stone recurrence against the burden of radiation from imaging studies.

**Keywords** Algorithm · Follow-up · Imaging · Metabolic · Urinary stone treatment

✉ Andreas Skolarikos  
andskol@yahoo.com

<sup>1</sup> Sant'Andrea Hospital, Sapienza University, Rome, Italy

<sup>2</sup> National and Kapodistrian University of Athens, Chairman of the EAU Urolithiasis Guidelines, Department of Urology, Sismanogleio Hospital, Athens, Greece

<sup>3</sup> Department of Urology, Freeman Hospital, Newcastle-Upon-Tyne, UK

<sup>4</sup> Institute of Genetic Medicine, Newcastle University, Newcastle-Upon-Tyne, UK

<sup>5</sup> Department of Urology, Connolly Hospital, Blanchardstown, Dublin 15, Ireland

<sup>6</sup> Department of Urology, Hospital of the Brothers of Mercy Trier, Medical Campus University Mainz, Trier, Germany

<sup>7</sup> Department of Urology, Region Hospital, Ceske Budejovice, Czech Republic

<sup>8</sup> Department of Urology, First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic

<sup>9</sup> Division of Nephrology and Dialysis, Department of Medicine, University of Verona, Verona, Italy

<sup>10</sup> Department of Urology, Hospital of the Sisters of Charity, Vienna, Austria

<sup>11</sup> Urologische Praxis, Vienna, Austria

<sup>12</sup> Department of Urology, University Hospital Southampton NHS Foundation Trust, Southampton, UK

<sup>13</sup> Department of Urology, Guy's and St Thomas' Hospital, London, UK

## Introduction

The incidence of urolithiasis is increasing. Several factors such as ethnicity, diet, geographic region, and genetics impact the incidence of stone disease. Globally, the prevalence of stone disease ranges from 1 to 20% [1–3]. Moreover, incidence rates have recently increased as much as 37% in some countries [1]. Management of stone disease includes extracorporeal, endoscopic, percutaneous, open techniques, surveillance, and medical therapy.

Approximately 50% of stone patients develop only 1 recurrence during their lifetime; however, 10% of stone patients will develop highly recurrent stone disease [4]. Furthermore, the 5-year recurrence rate among first-time stone formers is 26% [1, 5]. Therefore, accurate and appropriate follow-up of stone patients may lead to improved diagnosis of recurrent disease, prevention of symptomatic stone episodes, and decreased exposure to unnecessary radiation. Hitherto, the follow-up of stone disease in urology varies between clinicians and departments [6, 7].

The EAU Urolithiasis Guidelines panel performed a systematic review to summarize existing literature regarding follow-up in urolithiasis patients after treatment. We then aimed to provide a consensus statement on methods, duration, and frequency of urolithiasis follow-up.

## Materials and methods

This systematic review undertaken under the auspices of the EAU was conducted according to the Preferred Reporting Items for Systematic Reviews (PRISMA) statement and was guided by the EAU Guidelines Office Methods Committee [8, 9].

### Literature search

A literature search was performed using Medline/PubMed, EMBASE, and Cochrane Library, while registered randomized controlled trial protocols were screened from clinicaltrials.gov from 1970 to 31/09/2020. The reference lists of all manuscripts reviewed as full text were also screened for eligible studies. Two independent authors (LT, RL) screened the databases, and disagreements were resolved upon consensus with a senior author (AS). PRISMA flowchart is available in Supplementary Fig. S1 and detailed search algorithm in Supplementary Appendix A.

## Study eligibility criteria-PICO

The initial protocol as registered and approved by PROSPERO Database (ID: CRD42020205739), referred to the comparison of urolithiasis patients (both genders, age  $\geq 18$  years old, primary/recurrent stone formers, renal/ureteric stones, any stone size or composition, stone-free patients or those with residuals, any type of intervention (i.e., simple observation-spontaneous expulsion, medical or surgical management) who were followed up with imaging (CT scan, X-ray, ultrasound, intravenous pyelography-IVU or combination of these methods) or/and metabolic urine screening (24-h urine tests) compared to patients who were not followed. The primary outcome included the incidence of symptomatic urolithiasis episodes or asymptomatic stone growth as defined by trialists.

Due to the total lack of comparative studies (either randomized or observational) in urolithiasis patients regarding follow-up versus no follow-up, we considered studies that included data about new stone growth in initially stone-free patients (as defined by study authors), stone growth in patients with residual stone fragments (as defined by study authors), intervention, and spontaneous passage rates with a follow-up after main treatment of  $> 3$  months. Observational and randomized studies with more than 10 patients in each group, either prospective or retrospective, and both single-arm and comparative studies were eligible. We excluded study protocols, abstracts, review articles, case reports, studies with  $< 10$  patients, as well as those including patients with neurological conditions, urinary diversions, or anatomical abnormalities.

### Data collection

Two authors (LT, RL) independently extracted data from eligible studies, using a pre-defined Microsoft Excel sheet. Study characteristics (author, country/center, period, retrospective/prospective design, inclusion and exclusion criteria, comparative/single-arm design, observational/RCT design), patient baseline characteristics (type of treatment used, preoperative imaging for diagnosis, method used to define stone-free rate, method and interval of imaging follow-up, method of metabolic follow-up, proportion of patients lost during follow-up, proportion of high-risk stone formers, number of patients, male proportion, stone max size, stone burden, stone composition, body mass index, number and location of stones) and follow-up duration. Moreover, we extracted data regarding defined outcomes (recurrence—new

stone growth proportion, stone formation rate, stone size increase, pain-colic episodes, visible haematuria rate, intervention rate, infection rate, number of hospital admissions and emergency room visits, renal failure, and renal scarring rate, changes in quality-of-life measures, long-term complication rate, cost per patient follow-up and stone-free rate). We extracted data only from studies reporting outcomes separately for stone-free patients and those with residual stone fragments. Data extraction was performed according to several follow-up time intervals categorizing studies according to mean/median reported follow-up duration (6 months, 6–12 months, 12–24 months, 24–36 months, 36–48 months, 48–60 months, 5–10 years, > 10 years).

Based on the literature search four different categories were identified and selected to propose different follow-up schedules:

- Stone-free patients (study defined) in the general population. Due to the lack of separate data on stone-free low-risk and stone-free high-risk patients we present data for stone-free patients as one group: the general population.
- High-risk stone-free patients are defined as stone-free patients with a known biochemical abnormality (=hypercalciuria, hypocitraturia, hyperuricosuria, renal tubular acidosis (RTA) or high-risk stone type such as struvite) (as were the only categories clearly defined as high-risk in the revised studies)
- Residual stone fragments  $\leq 4$  mm
- Residual stone fragments  $> 4$  mm.

### Risk of bias assessment

The risk of bias of each included study was assessed by two review authors working independently using the Cochrane Collaboration Risk of Bias Tool for Randomized Controlled Trials [10] and Newcastle–Ottawa scale for observational studies [11]. For case-series/non-comparative observational studies, we evaluated whether an a priori protocol existed, whether the total population was included, whether there was a report of all prespecified outcomes in all patients, and finally whether appropriate measurement of benefits and harms was performed by the authors [8]. The overall risk of bias was considered low if all answers were ‘yes’ and high if at least one of these answers was ‘no’ [12] (Supplementary Table S4, Supplementary Figs. S2–S7).

### Consensus statement

The consensus on the appropriate follow-up flowchart after stone treatment was developed in three different phases. In Phase I, two associates (RL and LT) divided the available

evidence derived from the systematic review into four different groups creating tables including data on stone-free rates, growth rates, and spontaneous expulsion rates at different time points. In Phase II, analyses based on data [12] from Phase I were used to generate possible follow-up algorithms. In Phase III, the algorithms from Phase II were independently reviewed by a steering committee consisting of the other Urolithiasis Panel members based on a benefit/harm principle and the analyses performed using the Phase I data [12]. Each question was posed on 3 separate occasions to ensure consensus. If there was no consensus on a particular question or part of the algorithm, then this was altered and reintroduced on the next cycle. A consensus was defined as  $\geq 80\%$  agreement on questions and algorithms. Questions created and discussed by the panel members are listed in Supplementary Table S5.

## Results

Overall, 3075 references were screened, and 2930 were excluded based on title and abstract. 145 full texts were screened after reading the full text, and 76 studies [13–88] were included for analysis, from which 17 were randomized controlled trials (RCTs) [15, 19, 20, 26, 33–41, 46, 66, 67, 78]. The total number of patients included in eligible studies regarding follow-up was 11,989, while in studies negotiating radiation [80, 82, 83, 86] exposure during follow-up a total of 503,085 stone patients were analyzed. Stone-free rate, stone growth, and rate of spontaneous expulsion were assessed at different time points.

### Quantitative analysis

#### Stone free: general population

Overall, 27 studies evaluated follow-up after stone treatment in the general population including stone-free patients (Supplementary Table S1). More specifically, 12 studies evaluated patients after ESWL, 7 studies after PCNL, 1 study after URS, 2 studies after open stone surgery, and 5 studies after medical treatment.

Among these, 5 studies presented a median follow-up of 6–12 months and reported a stone-free rate between 71 and 100%. However, 4 of the 5 studies reported follow-up after ESWL treatment. Ten studies presented a median follow-up of 12–24 months. Stone-free rate was 65–95% after ESWL, 77–100% after PCNL and 60–100% after medical treatment/dietary modifications. Seven studies reported a median follow-up of 24–36 months with a stone-free rate of 29–94%. More specifically SFR was 60–94% in the ESWL group and 29–91% after PCNL. Four studies reported a median follow-up of 36–48 months with a stone-free rate of 50–90%.

More specifically SFR was 50–90% after ESWL and 75% after PCNL. Two studies presented a median follow-up of 48–60 months and presented a SFR of 73–88%. Finally, seven studies presented a median follow-up > 5 years with a SFR of 62–87%. More specifically SFR ranged from 72 to 80% after ESWL, 62% after PCNL, 87% after URS, 70–83% after open stone surgery, and 73% after medical treatment.

### Stone free: high-risk patients

High-risk stone patients were defined as patients with a known biochemical abnormality (i.e., hypercalciuria, hypocitraturia, hyperuricosuria, RTA) or high-risk stone type such as struvite. These categories were clearly defined in the selected studies as high-risk for recurrence. In this group of patients, we analyzed data according to whether patients received targeted medical treatment or not.

In high-risk patients not under medical treatment, there were no studies available with a median follow-up of < 12 months. Therefore, no data on SFR at this time point was recorded. At 12–24 months, SFR was 50%, at 24–36 months (only one study) it was equal to 39%, while at 36–48 months it was nearly 27%.

In high-risk patients under medical treatment, there were no studies available with a median follow-up of < 12 months. Therefore, no data on SFR at this time point was recorded. At 12–24 months SFR was 81%, at 24–36 months it was equal to 70% (only one study), at 36–48 months it ranged between 31 and 71%, while at a median follow-up > 48 months it was equal to 88–100% (Supplementary Table S1).

### Residual stone fragments $\leq$ 4 mm

After a median follow-up of 6 months, the rate of residual regrowth was 55% and the spontaneous expulsion rate was 7–93% (Supplementary Tables S2–S3). After a median follow-up of 6–12 months, the rate of residual regrowth was 10–41% and the spontaneous expulsion rate was 18–47%. After a median follow-up of 12–24 months, the rate of residual regrowth was 18–60% and the spontaneous expulsion rate was 14–40%. Studies with more than 36 months of median follow-up were few; however, the rate of residual regrowth was between 32 and 79% and the spontaneous expulsion rate was 23–79%.

Overall, eight studies evaluated ‘high-risk’ stone patients with residual fragments, without a uniform definition of residual stone fragments. After a median follow-up of up to 12 months, stone regrowth ranged between 0 and 5% for patients under medical treatment and between 0 and 63% for patients not under targeted drug therapy. At 12–24 months, one study recorded a stone regrowth of 27%. At a follow-up between 24 and 120 months, stone regrowth ranged between 0 and 78%.

### Residual fragments > 4 mm

After a median follow-up of 6 months, the spontaneous expulsion rate was 31%, while after a median follow-up of 6–12 months, the rate of residual regrowth reached 35% and the spontaneous expulsion rate was 13% (Supplementary Tables S2–S3). Few studies reported longer follow-ups; however, the rate of residual regrowth reached 88% with a low spontaneous expulsion rate of 9–18%.

## Consensus statement

### General questions

**Is it necessary to adapt follow-up according to the type of stone intervention performed?** After analyzing the available evidence, no studies adapted follow-up according to the type of stone intervention performed. The participants agreed that based on the current evidence, the treatment modality does not change the follow-up recommendations (agreement = 100%).

**How often should stone patients undergo follow-up?** In all retrieved studies, patients were followed every 3–24 months based on the clinicians' preference. The Panel agreed that following patients every 3 months may result in an untenable workload with a little added benefit when compared to the every 6 months regimen (agreement > 80%). Moreover, radiation exposure may increase with a 3-month regimen (agreement > 80%). All panel members agreed to follow up with all patients at 6 months and 12 months no matter the group they belong to, based on their common clinical practice (agreement > 80%). The decision on a 6-monthly or annual follow-up is dependent on stone-free status and the patient's risk category (agreement 100%).

**Which imaging modalities should be performed for follow-up of stone patients?** Ideally, all patients should undergo a non-contrast CT for follow-up; however, the radiation dose outweighs the benefits of investigation (agreement 100%). The first proposal was to decide on the type of imaging based on the analyzed data, however, the Panel disagreed (agreement < 80%). The second proposal was to perform non-contrast CT at 6 months in all patients, however, the panel disagreed on this (agreement < 50%). The third proposal was not to use CT at any specific time point (agreement > 80%). All Panel members agreed that clinicians should decide on whether to perform plain film KUB and/or ultrasound (U/S) (KUS) based on local circumstances, and patient and stone characteristics (agreement > 80%). All Panel members agreed that patients should undergo non-contrast CT when a symptomatic episode occurs and/or before surgical intervention (agreement = 100%).

**In high-risk patients is metabolic follow-up and treatment monitoring necessary?** In patients with a known biochemical abnormality, metabolic follow-up is more beneficial than not performing the work-up (agreement > 80%). Monitoring of medical treatment is more beneficial than the absence of monitoring (agreement > 80%).

**When is re-intervention needed for kidney stones?** The Panel members agreed that patients with residual stone fragments > 4 mm should be offered elective re-intervention (agreement > 80%).

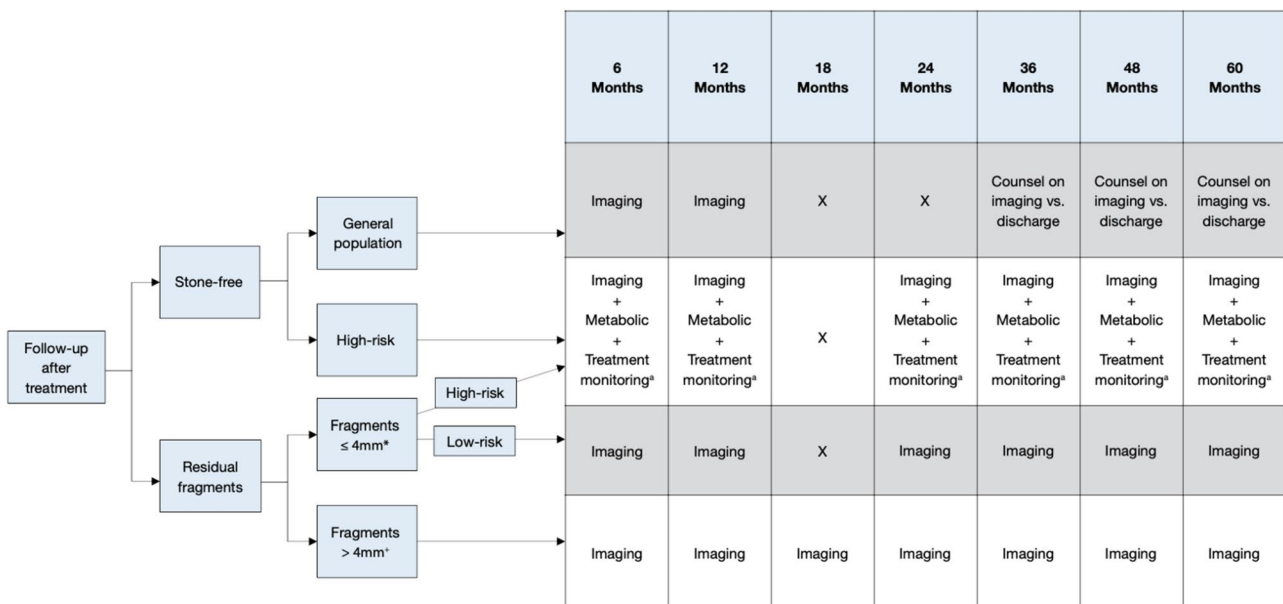
**What is a safe stone-free rate to discharge patients?** An 80% stone-free rate safety margin was the consensus threshold for discharge from follow-up (agreement > 80%). This was based on the findings of the meta-analysis performed in the data extracted from a Panel systematic review [12].

**In selected patients with residual fragments ≤ 4 mm re-intervention may be performed?** The Panel members agreed that selected patients may need re-intervention even if residual stone fragments are ≤ 4 mm depending on patient and stone characteristics (agreement > 80%).

**Specific consensus for different groups of patients (Fig. 1)**

**Consensus statement on stone-free patients** The Panel proposes to follow up patients with imaging at 6 and 12 months. Thereafter, clinicians may consider imaging at 36, 48, and 60 months or discharge patients at any time point. Patient counselling on imaging versus discharge is mandatory. The decision to discharge patients at 36 months is based on a SFR safety margin of 80% derived from a pooled analysis performed in another systematic review/meta-analysis performed by the panel [12]. In addition, there is a 90% SFR safety margin to discharge patients after 60 months.

**Consensus statement on stone-free high-risk patients** Based on the analyzed data, Panel strongly recommends starting prophylactic medication in high-risk patients considering the low SFRs reported in patients not taking prophylaxis. In patients taking prophylaxis, close follow-up is required including imaging, metabolic evaluation, and treatment monitoring (i.e., side effects and compliance to treatment). More specifically patients should be followed every 6 months for the first 2 years and then annually.



**Stone free = No stone fragments on post-operative imaging (i.e., no stone fragments on CT/KUB/US)**

**High-Risk = Known biochemical abnormality (e.g., hypercalciuria, hypocitraturia, hyperuricosuria, or RTA high-risk stone type such as struvite)**

Imaging consists of plain film KUB and/or kidney ultrasonography (KUS) based on clinicians' preference and stone characteristics. Consider CT if patient is symptomatic or if intervention is planned.

<sup>a</sup> Treatment monitoring for side effects, intolerance, and compliance

<sup>\*</sup> Panel recommends reintervention; however, close follow up may be considered for some patients at high risk for re-intervention based on clinicians' preference.

\* Clinicians may choose the imaging-only pathway in patients with fragments ≤ 2 mm

**Fig. 1** Follow-up algorithm for patients after stone treatment

**Consensus on residual stone fragments  $\leq 4$  mm** Based on the analyzed data, the Panel proposed a 6-month follow-up initially and an annual follow-up examination thereafter, for patients with residual fragments  $\leq 4$  mm and a low risk of stone recurrence. High-risk stone patients with residual fragments  $\leq 4$  mm should be followed with the same follow-up schedule as high-risk stone-free patients. More specifically patients are followed with imaging, metabolic evaluation, and treatment monitoring every 6 months for the first 2 years and then annually.

**Consensus on residual stone fragments  $> 4$  mm** Based on the low rates of spontaneous expulsion and the high risk of stone regrowth the Panel recommends scheduled re-intervention. However, if re-intervention is contraindicated, clinicians should follow up with patients every 6 months for the first 2 years followed by annual follow-up with imaging.

## Discussion

The present study represents the first algorithm developed for follow-up patients after stone disease treatment. Given the current lack of high-level evidence on the subject, the EAU Urolithiasis Guidelines Panel developed a consensus statement based on evidence from the systematic review to propose a follow-up chart for patients after kidney stone treatment. The final algorithm is the result of a data-based consensus and on a benefit-to-harm principle. Especially in patients at high risk of recurrence, there is the need to establish an adequate follow-up to avoid complications related to stone disease, such as urosepsis or kidney failure. Management of stone disease should follow the example of oncology where an adapted follow-up is based on the risk of recurrence.

The main issues for follow-up of stone patients are increased workload, patient compliance, and risks related to radiation exposure. A close follow-up of all stone patients places a significant burden on radiology departments and in some countries healthcare systems may not be able to accommodate a high number of radiological exams. As a result of the increase in workload, the interpretation accuracy may diminish and the psychological stress of radiologists may increase [89]. Conversely, patients may seek private practice to perform exams that may not be available in some national health care systems. Moreover, patients may not be compliant with close follow-up protocols [90]. Finally, the proposed algorithm may improve radiation exposure of patients during follow-up, considering that KUB (typical effective dose = 0.02 mSv) and/or KUS (typical effective dose = 0 mSv) are proposed instead of CT scan (typical effective dose = 8 mSv) [91].

The benefits of a well-balanced follow-up include prevention of symptomatic episodes, prevention of kidney function deterioration (especially in high-risk patients), and prevention of septic episodes [92]. Our algorithm carefully considers these potential clinical scenarios and adapts the follow-up frequency to the risk of stone recurrence.

In high-risk stone formers, data are very heterogeneous, and it is very difficult to draw definitive conclusions regarding this group of patients. Most of the studies included in our analysis are old and very few of them include large cohorts. Considering the high risk of recurrence and symptomatic episodes, the panel recommends a close follow-up in these patients with an adequate metabolic treatment to avoid complications. Although some clinicians may argue that such a close follow-up including metabolic evaluation may not be feasible in every country, we believe that these patients need to be followed continuously due to their risk of recurrence as high as 25% even 10 years after surgery [93]. Moreover, if high-risk patients are not followed closely, they may experience a health-related quality of life deterioration, which may be improved by the implementation of our algorithm [94].

The present review highlights the lack of strong evidence in the literature regarding follow-up of stone patients after treatment. Panel members strongly believe that the implementation of the proposed algorithm may improve patient care and disease management. Notably, the Panel made the important decision to exclude the routine use of non-contrast CT during follow-up. After extensive discussion, the Panel agreed that the harms in terms of high radiation exposure outweigh the diagnostic advantages when compared to plain film KUB and/or KUS. The Panel agreed that the decision on whether to use plain film KUB and/or KUS depends on urologist preference, patient and stone characteristics, and stone location. However, all Panel members agreed that a CT scan should be performed in cases of symptomatic stone episodes or before surgical intervention, as per existing guidance. In view of ultra-low dose CT scans availability, high-risk patients could benefit from more detailed imaging during follow-up using this technology; however, this should be carefully balanced between risks and benefits, as well as availability and accompanying costs. Furthermore, most studies defined SFR based on X-ray, ultrasound or even IVU; however, these studies are not as accurate as CT scan and SFRs might be even lower than the reported one, further highlighting the need for well-designed follow-up studies in urolithiasis patients. The timepoint to define SFR after surgical treatment is also not universal and ranges between 1 and 3 months in most settings; further consensus is needed to determine when the final SFR should be assessed, especially after implementation of more efficient laser types in producing finer stone particles, which can be expelled sooner.

Due to existing heterogeneity between eligible studies in our analysis, we chose to define high-risk patients as those

with biochemical abnormalities where the risk of recurrence is high, especially if left without appropriate treatment. As discussed, that was the only clear definition of high-risk stone formers in the studies included based on our protocol. However, we recognize that there are other patient categories listed as high-risk in literature and EAU Urolithiasis Guidelines [6]. In contrast, many first-time stone formers may experience only a single episode. Vaughan et al. created a revised model for calculating Recurrence of Kidney Stones (ROKS) in patients who are first-time symptomatic kidney stone formers, using 27 clinical, imaging, and intervention-related predictors [95]. Based on a sample of 3,364 stone disease patients, experiencing 4,951 episodes, they found that patients who are younger males have higher body mass index, a family history of urolithiasis, asymptomatic kidney stones before the first stone episode, those with brushite/struvite/urate stones, stones in the pelvis or lower calyx, as well as those with larger number and size of stones, have a greater risk of subsequent recurrence [95]. Pregnancy was also identified as an independent risk factor [95]. All those factors should be considered when advising an appropriate follow-up plan in a patient who experienced a first, symptomatic stone episode, in conjunction with existing Guidelines and patient preference.

The proposed algorithm represents a guide for clinicians to ensure an adequate follow-up after stone treatment. In the past, the concept of patient-centered medicine has been widely adopted in all medical areas and is also essential in stone disease [94, 96, 97]. The follow-up strategy versus re-intervention should always be discussed with the patient, considering the pros and cons of both strategies. In patients with stone fragments  $\leq 4$  mm, re-intervention may be offered after discussion with the patient. Some studies suggest that fragments between 2 and 4 mm have a higher risk of stone-related events when compared to smaller fragments [13]. Although there is lack of strong data to support this finding, future studies may lead to redefining the 4 mm cut-off for residual fragments, especially with the current implementation of high-power holmium and thulium fiber lasers, which improve dusting technique. Conversely, in selected cases, patients with stone fragments  $> 4$  mm may be followed instead of treated. Overall, clinicians should take into consideration stone characteristics, age, comorbidities, and patient social context to guide the shared decision-making process. Our algorithm, if successfully implemented, may diminish both the related healthcare costs and radiation burden arising from repeated imaging examinations, since low-risk patients can be discharged. The implementation of the algorithm will probably demonstrate important improvements in the management of stone patients as there is a knowledge gap regarding follow-up algorithms for benign compared to malignant diseases.

Our study has several limitations, mainly related to the scarcity and poor quality of available evidence. We used a

wide range of dates; therefore, our results may be biased by the recent technological advances which alter clinical outcomes. Another possible limitation lies in the lack of data regarding patients with residual fragments 2–4 mm versus less than 2 mm, therefore our recommendations apply to patients with residual fragments  $\leq 4$  mm considered as one broad category. Considering the existing literature, we had to establish a cut-off of 4 mm; however, we are aware that some studies use 5 mm as a cut-off. Moreover, great heterogeneity was demonstrated in eligible studies regarding the imaging modalities which were used by authors, as well as definitions of stone-free rate, regrowth, and disease progression. Data on high-risk patients are very heterogeneous and some studies were published many years ago, which may limit the interpretation of their findings. Due to the low quality of evidence, the Panel proposed a closer follow-up for this group. Moreover, we could not analyze patients with the classic definition of high-risk patients due to the lack of follow-up data; however, our study highlights the need for further research regarding this group. Studies included presented mainly aggregated follow-up data as means or medians, while very few studies presented consecutive data for each specific time point. Finally, regarding the consensus methodology, the Panel consisted of EAU Urolithiasis Guideline Panel members and associate members, covering the field of Urology and Nephrology across a number of different countries with differing resources at their disposal. There was no patient representative or radiologist involved in this process, which could be considered a methodological flaw. The Delphi methodology [98] was not followed as this consensus was based on specific data [12], rather than an a priori consensus of expert opinion.

Notwithstanding all these limitations, The Panel performed a consensus statement based on several discussions and the follow-up diagram is the result of an expert consensus statement. These consensus statements represent provisional proposals for the follow-up of patients after stone treatment. We reinforce the point that these guidelines are based on expert opinion, albeit following an extensive literature review, and therefore individual clinicians may decide not to adopt, or partially adopt, these guidelines along with their clinical judgment. It is clear, that evidence derived from well-designed, future trials is needed to delineate a safe and effective follow-up pathway for stone patients following surgical treatment.

## Conclusions

The EAU Urolithiasis Guidelines panel consensus has produced for the first time a structured follow-up for stone patients after urolithiasis treatment. The proposed algorithm stratifies the management of patients after stone

disease treatment based on stone burden and risk category. The implementation of the former algorithm will certainly improve the radiological burden, radiation exposure, and health economics of stone patients.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00345-024-04872-y>.

**Author contributions** LR: Protocol/project development, data collection or management, data analysis, manuscript writing/editing. TL: protocol/project development, data collection or management, data analysis, manuscript writing/editing. GG: protocol/project development, data analysis, manuscript writing/editing. DNF: protocol/project development, manuscript writing/editing. NA: Protocol/project development, Manuscript writing/editing. PA: protocol/project development, manuscript writing/editing. GG: protocol/project development, manuscript writing/editing. TC: protocol/project development, manuscript writing/editing. SB: protocol/project development, manuscript writing/editing. TK: protocol/project development, manuscript writing/editing. SA: protocol/project development, manuscript writing/editing.

**Funding** No funds, grants, or other support was received.

**Data availability** Data can be provided from authors upon reasonable request.

## Declarations

**Conflict of interest** Authors represent the European Association of Urology Guideline Panel on Urolithiasis.

**Ethical approval** No ethical approval was needed since this study is based on a consensus using data from systematic literature review.

## References

- Hesse A, Brändle E, Wilbert D, Köhrmann KU, Alken P (2003) Study on the prevalence and incidence of urolithiasis in Germany comparing the years 1979 vs. 2000. *Eur Urol* 44(6):709–713
- Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC (2003) Time trends in reported prevalence of kidney stones in the United States: 1976–1994. *Kidney Int* 63(5):1817–1823
- Okuyama M (2011) Epidemiology of urolithiasis. *Clin Calcium* 21(10):1442–1447
- Strohmaier WL (2000) Course of calcium stone disease without treatment. What can we expect? *Eur Urol* 37(3):339–344
- Ferraro PM, Curhan GC, D'Addessi A, Gambaro G (2017) Risk of recurrence of idiopathic calcium kidney stones: analysis of data from the literature. *J Nephrol* 30(2):227–233
- Türk CNA, Petřík A, Seitz C, Skolarikos A, Somani B et al (2021) EAU guidelines on urolithiasis. EAU Guidelines Office, Arnhem, The Netherlands. Accessed on October 2021
- Tzelvels L, Türk C, Skolarikos A (2021) European association of urology urolithiasis guidelines: Where are we going? *Eur Urol Focus* 7(1):34–38
- Knoll T, Omar MI, MacLennan S, Hernández V, Canfield S, Yuan Y et al (2018) Key steps in conducting systematic reviews for underpinning clinical practice guidelines: methodology of the European association of urology. *Eur Urol* 73(2):290–300
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71
- J. H. Cochrane Risk of Bias Tool—Appendix F. 2011;1–2
- Wells GASB, O'Connell D, Peterson J, Welch V (2011) The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. Oxford 2011:1
- Tzelvels L, Geraghty R, Lombardo R, Davis NF, Petřík A, Neisius A et al (2022) Duration of follow-up and timing of discharge from imaging follow-up, in adult patients with urolithiasis after surgical or medical intervention: a systematic review and meta-analysis from the European association of urology guideline panel on urolithiasis. *Eur Urol Focus* 9:188–198
- Raman JD, Bagrodia A, Gupta A, Bensalah K, Cadeddu JA, Lotan Y et al (2009) Natural history of residual fragments following percutaneous nephrostolithotomy. *J Urol* 181(3):1163–1168
- Newman DMSJ, Lingeman JE (1988) Two-year follow-up of patients treated with extracorporeal shock wave lithotripsy. *J Endourol* 2(2):163–171
- Soygür T, Akbay A, Küpeli S (2002) Effect of potassium citrate therapy on stone recurrence and residual fragments after shock-wave lithotripsy in lower caliceal calcium oxalate urolithiasis: a randomized controlled trial. *J Endourol* 16(3):149–152
- Carr LK, John DAH, Jewett MA, Ibanez D, Ryan M, Bombardier C (1996) New stone formation: a comparison of extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy. *J Urol* 155(5):1565–1567
- Mays N, Petruckevitch A, Burney PG (1992) Results of one and two year follow-up in a clinical comparison of extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy in the treatment of renal calculi. *Scand J Urol Nephrol* 26(1):43–49
- Zanetti G, Seveso M, Montanari E, Guarneri A, Del Nero A, Nespoli R et al (1997) Renal stone fragments following shock wave lithotripsy. *J Urol* 158(2):352–355
- Di Silverio F, Ricciuti GP, D'Angelo AR, Fraioli A, Simeoni G (2000) Stone recurrence after lithotripsy in patients with recurrent idiopathic calcium urolithiasis: efficacy of treatment with fluggi water. *Eur Urol* 37(2):145–148
- Sarica K, Erturhan S, Altay B (2007) Effect of verapamil on urinary stone-forming risk factors. *Urol Res* 35(1):23–27
- Beck EM, Riehle RA Jr (1991) The fate of residual fragments after extracorporeal shock wave lithotripsy monotherapy of infection stones. *J Urol* 145(1):6–9 (**Discussion-10**)
- Fuchs AMWB, Fuchs GJ (1991) Staghorn stone treatment with extracorporeal shock wave lithotripsy monotherapy: long-term results. *J Endourol* 5(1):45–48
- Fine JK, Pak CY, Preminger GM (1995) Effect of medical management and residual fragments on recurrent stone formation following shock wave lithotripsy. *J Urol* 153(1):27–32 (**Discussion-3**)
- Yu CC, Lee YH, Huang JK, Chen MT, Chen KK, Lin AT et al (1993) Long-term stone regrowth and recurrence rates after extracorporeal shock wave lithotripsy. *Br J Urol* 72(5 Pt 2):688–691
- El-Assmy A, El-Nahas AR, Madbouly K, Abdel-Khalek M, Abo-Elghar ME, Sheir KZ (2006) Extracorporeal shock-wave lithotripsy monotherapy of partial staghorn calculi. Prognostic factors and long-term results. *Scand J Urol Nephrol* 40(4):320–325
- Yuruk E, Binbay M, Sari E, Akman T, Altinyay E, Baykal M et al (2010) A prospective, randomized trial of management for asymptomatic lower pole calculi. *J Urol* 183(4):1424–1428
- DE Patterson SJ, Leroy AJ (1987) Long-term follow-up of patients treated by percutaneous ultrasonic lithotripsy for struvite staghorn calculi. *J Endourol* 1(3):177–180
- Kang DE, Maloney MM, Haleblan GE, Springhart WP, Honeycutt EF, Eisenstein EL et al (2007) Effect of medical management



- on recurrent stone formation following percutaneous nephrolithotomy. *J Urol* 177(5):1785–1788 (**Discussion 8–9**)
29. El-Nahas AR, Eraky I, Shokeir AA, Shoma AM, El-Assmy AM, El-Tabey NA et al (2011) Long-term results of percutaneous nephrolithotomy for treatment of staghorn stones. *BJU Int* 108(5):750–754
  30. Nakamoto T, Sagami K, Yamasaki A, Ueda M, Fujiwara S, Igawa M et al (1993) Long-term results of endourologic treatment of urinary calculi: investigation of risk factors for recurrence or regrowth. *J Endourol* 7(4):297–301
  31. Huei Lee Y, Chu Huang W, Chang LS, Tsun Chen M, Yang YF, Huang JK (1994) The long-term stone recurrence rate and renal function change in unilateral nephrectomy urolithiasis patients. *J Urol* 152(5, Part 1):1386–1388
  32. Sleight MW, Wickham JE (1977) Long-term follow-up 100 cases of renal calculi. *Br J Urol* 49(7):601–604
  33. Mortensen JT, Schultz A, Ostergaard AH (1986) Thiazides in the prophylactic treatment of recurrent idiopathic kidney stones. *Int Urol Nephrol* 18(3):265–269
  34. Brocks P, Dahl C, Wolf H, Transbøl I (1981) Do thiazides prevent recurrent idiopathic renal calcium stones? *Lancet* 2(8238):124–125
  35. Griffith DP, Gleeson MJ, Lee H, Longuet R, Deman E, Earle N (1991) Randomized, double-blind trial of Lithostat (acetohydroxamic acid) in the palliative treatment of infection-induced urinary calculi. *Eur Urol* 20(3):243–247
  36. Ohkawa M, Tokunaga S, Nakashima T, Orito M, Hisazumi H (1992) Thiazide treatment for calcium urolithiasis in patients with idiopathic hypercalciuria. *Br J Urol* 69(6):571–576
  37. Ettinger B (1976) Recurrent nephrolithiasis: natural history and effect of phosphate therapy. A double-blind controlled study. *Am J Med* 61(2):200–206
  38. Hiatt RA, Ettinger B, Caan B, Quesenberry CP Jr, Duncan D, Citron JT (1996) Randomized controlled trial of a low animal protein, high fiber diet in the prevention of recurrent calcium oxalate kidney stones. *Am J Epidemiol* 144(1):25–33
  39. Hofbauer J, Höbarth K, Szabo N, Marberger M (1994) Alkali citrate prophylaxis in idiopathic recurrent calcium oxalate urolithiasis—a prospective randomized study. *Br J Urol* 73(4):362–365
  40. Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A (1996) Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. *J Urol* 155(3):839–843
  41. Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U et al (2002) Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. *N Engl J Med* 346(2):77–84
  42. D'Costa MR, Haley WE, Mara KC, Enders FT, Vrtiska TJ, Pais VM et al (2019) Symptomatic and radiographic manifestations of kidney stone recurrence and their prediction by risk factors: a prospective cohort study. *J Am Soc Nephrol* 30(7):1251–1260
  43. Whalley NA, Meyers AM, Martins M, Margolius LP (1996) Long-term effects of potassium citrate therapy on the formation of new stones in groups of recurrent stone formers with hypocitraturia. *Br J Urol* 78(1):10–14
  44. Jarrar K, Amasheh RA, Graef V, Weidner W (1996) Relationship between 1,25-dihydroxyvitamin-D, calcium and uric acid in urinary stone formers. *Urol Int* 56(1):16–20
  45. Trinchieri A, Boccafoschi C, Chisena S, De Angelis M, Seveso M (1999) Study of the diuretic efficacy and tolerability of therapy with Rocchetta mineral water in patients with recurrent calcium kidney stones. *Arch Ital Urol Androl* 71(2):121–124
  46. Cicerello E, Merlo F, Gambaro G, Maccatrozzo L, Fandella A, Baggio B et al (1994) Effect of alkaline citrate therapy on clearance of residual renal stone fragments after extracorporeal shock wave lithotripsy in sterile calcium and infection nephrolithiasis patients. *J Urol* 151(1):5–9
  47. Khaitan A, Gupta NP, Hemal AK, Dogra PN, Seth A, Aron M (2002) Post-ESWL, clinically insignificant residual stones: reality or myth? *Urology* 59(1):20–24
  48. Shigetani M, Kasaoka Y, Yasumoto H, Inoue K, Usui T, Hayashi M et al (1999) Fate of residual fragments after successful extracorporeal shock wave lithotripsy. *Int J Urol* 6(4):169–172
  49. Strem SB (1997) Contemporary clinical practice of shock wave lithotripsy: a reevaluation of contraindications. *J Urol* 157(4):1197–1203
  50. Chen RN, Strem SB (1996) Extracorporeal shock wave lithotripsy for lower pole calculi: long-term radiographic and clinical outcome. *J Urol* 156(5):1572–1575
  51. El-Nahas AR, El-Assmy AM, Madbouly K, Sheir KZ (2006) Predictors of clinical significance of residual fragments after extracorporeal shockwave lithotripsy for renal stones. *J Endourol* 20(11):870–874
  52. Buchholz NP, Meier-Padel S, Rutishauser G (1997) Minor residual fragments after extracorporeal shockwave lithotripsy: Spontaneous clearance or risk factor for recurrent stone formation? *J Endourol* 11(4):227–232
  53. Michaels EK, Fowler JE Jr (1991) Extracorporeal shock wave lithotripsy for struvite renal calculi: prospective study with extended follow-up. *J Urol* 146(3):728–732
  54. Candau C, Saussine C, Lang H, Roy C, Faure F, Jacqmin D (2000) Natural history of residual renal stone fragments after ESWL. *Eur Urol* 37(1):18–22
  55. Osman MM, Alfano Y, Kamp S, Haecker A, Alken P, Michel MS et al (2005) 5-year-follow-up of patients with clinically insignificant residual fragments after extracorporeal shockwave lithotripsy. *Eur Urol* 47(6):860–864
  56. Osman Y, Harraz AM, El-Nahas AR, Awad B, El-Tabey N, Shebel H et al (2013) Clinically insignificant residual fragments: An acceptable term in the computed tomography era? *Urology* 81(4):723–726
  57. Park J, Hong B, Park T, Park HK (2007) Effectiveness of noncontrast computed tomography in evaluation of residual stones after percutaneous nephrolithotomy. *J Endourol* 21(7):684–687
  58. Emmott AS, Brotherhood HL, Paterson RF, Lange D, Chew BH (2018) Complications, re-intervention rates, and natural history of residual stone fragments after percutaneous nephrolithotomy. *J Endourol* 32(1):28–32
  59. Ganpule A, Desai M (2009) Fate of residual stones after percutaneous nephrolithotomy: a critical analysis. *J Endourol* 23(3):399–403
  60. Altunrende F, Tefekli A, Stein RJ, Autorino R, Yuruk E, Laydner H et al (2011) Clinically insignificant residual fragments after percutaneous nephrolithotomy: medium-term follow-up. *J Endourol* 25(6):941–945
  61. Olvera-Posada D, Ali SN, Dion M, Alenezi H, Denstedt JD, Razvi H (2016) Natural history of residual fragments after percutaneous nephrolithotomy: evaluation of factors related to clinical events and intervention. *Urology* 97:46–50
  62. Rebeck DA, Macejko A, Bhalani V, Ramos P, Nadler RB (2011) The natural history of renal stone fragments following ureteroscopy. *Urology* 77(3):564–568
  63. Kang HW, Lee SK, Kim WT, Kim YJ, Yun SJ, Lee SC et al (2013) Natural history of asymptomatic renal stones and prediction of stone related events. *J Urol* 189(5):1740–1746
  64. Ozgor F, Sahan M, Cubuk A, Ortac M, Ayranci A, Sarilar O (2019) Factors affecting infectious complications following flexible ureteroscopy. *Urolithiasis* 47(5):481–486
  65. Williams JJ, Rodman JS, Peterson CM (1984) A randomized double-blind study of acetohydroxamic acid in struvite nephrolithiasis. *N Engl J Med* 311(12):760–764

66. Barcelo P, Wuhl O, Servitge E, Rousaud A, Pak CY (1993) Randomized double-blind study of potassium citrate in idiopathic hypocitraturic calcium nephrolithiasis. *J Urol* 150(6):1761–1764
67. Sener NC, Bas O, Sener E, Zengin K, Ozturk U, Altunkol A et al (2015) Asymptomatic lower pole small renal stones: Shock wave lithotripsy, flexible ureteroscopy, or observation? A prospective randomized trial. *Urology* 85(1):33–37
68. Kang M, Son H, Jeong H, Cho MC, Cho SY (2016) Clearance rates of residual stone fragments and dusts after endoscopic lithotripsy procedures using a holmium laser: 2-year follow-up results. *World J Urol* 34(11):1591–1597
69. Koh LT, Ng FC, Ng KK (2012) Outcomes of long-term follow-up of patients with conservative management of asymptomatic renal calculi. *BJU Int* 109(4):622–625
70. Burgher A, Beman M, Holtzman JL, Monga M (2004) Progression of nephrolithiasis: long-term outcomes with observation of asymptomatic calculi. *J Endourol* 18(6):534–539
71. Dropkin BM, Moses RA, Sharma D, Pais VM Jr (2015) The natural history of nonobstructing asymptomatic renal stones managed with active surveillance. *J Urol* 193(4):1265–1269
72. Kanno T, Takahashi T, Ito K, Okada T, Higashi Y, Yamada H (2020) The natural history of asymptomatic renal stones  $\leq 5$  mm: comparison with  $\geq 5$  mm. *J Endourol* 34(11):1188–1194
73. Li X, Zhu W, Lam W, Yue Y, Duan H, Zeng G (2019) Outcomes of long-term follow-up of asymptomatic renal stones and prediction of stone-related events. *BJU Int* 123(3):485–492
74. Inci K, Sahin A, Islamoglu E, Eren MT, Bakkaloglu M, Ozen H (2007) Prospective long-term follow-up of patients with asymptomatic lower pole caliceal stones. *J Urol* 177(6):2189–2192
75. Darrad MP, Yallappa S, Metcalfe J, Subramonian K (2018) The natural history of asymptomatic calyceal stones. *BJU Int* 122(2):263–269
76. Moon YT, Kim SC (1993) Fate of clinically insignificant residual fragments after extracorporeal shock wave lithotripsy with EDAP LT-01 lithotripter. *J Endourol* 7(6):453–456
77. Sahin C, Tuncer M, Yazıcı O, Horuz R, Çetinel AC, Eryıldırım B et al (2014) Do the residual fragments after shock wave lithotripsy affect the quality of life? *Urology* 84(3):549–554
78. Keeley FX Jr, Tilling K, Elves A, Menezes P, Wills M, Rao N et al (2001) Preliminary results of a randomized controlled trial of prophylactic shock wave lithotripsy for small asymptomatic renal calyceal stones. *BJU Int* 87(1):1–8
79. Chew BH, Brotherhood HL, Sur RL, Wang AQ, Knudsen BE, Yong C et al (2016) Natural history, complications and re-intervention rates of asymptomatic residual stone fragments after ureteroscopy: a report from the EDGE research consortium. *J Urol* 195(4 Pt 1):982–986
80. Dai JC, Chang HC, Holt SK, Harper JD (2019) National trends in CT utilization and estimated CT-related radiation exposure in the evaluation and follow-up of stone patients. *Urology* 133:50–56
81. El-Abd AS, Suliman MG, Abo Farha MO, Ramadan AR, El-Tatawy HH, El-Gamal OM et al (2014) The development of ureteric strictures after ureteroscopic treatment for ureteric calculi: a long-term study at two academic centres. *Arab J Urol* 12(2):168–172
82. Fahmy NM, Elkoushy MA, Andonian S (2012) Effective radiation exposure in evaluation and follow-up of patients with urolithiasis. *Urology* 79(1):43–47
83. Ferrandino MN, Bagrodia A, Pierre SA, Scales CD Jr, Ramperaud E, Pearle MS et al (2009) Radiation exposure in the acute and short-term management of urolithiasis at 2 academic centers. *J Urol* 181(2):668–672 (**Discussion** 73)
84. Iremashvili V, Li S, Penniston KL, Best SL, Hedican SP, Nakada SY (2019) Role of residual fragments on the risk of repeat surgery after flexible ureteroscopy and laser lithotripsy: single center study. *J Urol* 201(2):358–363
85. Karadag MA, Tefekli A, Altunrende F, Tepeler A, Baykal M, Muslimanoglu AY (2008) Is routine radiological surveillance mandatory after uncomplicated ureteroscopic stone removal? *J Endourol* 22(2):261–266
86. Kaynar M, Tekinarslan E, Keskin S, Buldu İ, Sönmez MG, Karatag T et al (2015) Effective radiation exposure evaluation during a one year follow-up of urolithiasis patients after extracorporeal shock wave lithotripsy. *Cent Eur J Urol* 68(3):348–352
87. Li X, He L, Li J, Duan Z, Gao Z, Liu L (2015) Medium-term follow-up of clinically insignificant residual fragments after minimal invasive percutaneous nephrolithotomy: prognostic features and risk factors. *Int J Clin Exp Med* 8(11):21664–21668
88. Pullar B, Lunter C, Collie J, Shah S, Shah N, Hayek S et al (2017) Do renal stones that fail lithotripsy require treatment? *Urolithiasis* 45(6):597–601
89. Simon AF, Holmes JH, Schwartz ES (2020) Decreasing radiologist burnout through informatics-based solutions. *Clin Imaging* 59(2):167–171
90. Bos D, Kim K, Hoogenes J, Lambe S, Shayegan B, Matsumoto ED (2018) Compliance of the recurrent renal stone former with current best practice guidelines. *Can Urol Assoc J* 12(3):E112–E120
91. McCollough CH, Bushberg JT, Fletcher JG, Eckel LJ (2015) Answers to common questions about the use and safety of CT scans. *Mayo Clin Proc* 90(10):1380–1392
92. Gambaro G, Croppi E, Bushinsky D, Jaeger P, Cupisti A, Ticinesi A et al (2017) The risk of chronic kidney disease associated with urolithiasis and its urological treatments: a review. *J Urol* 198(2):268–273
93. Skolarikos A, Straub M, Knoll T, Sarica K, Seitz C, Petřík A et al (2015) Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines. *Eur Urol* 67(4):750–763
94. Serna J, Talwar R, Ziemba JB (2020) Health-related quality of life in renal stone formers: are we improving? *Curr Opin Urol* 30(2):190–195
95. Vaughan LE, Enders FT, Lieske JC, Pais VM, Rivera ME, Mehta RA et al (2019) Predictors of symptomatic kidney stone recurrence after the first and subsequent episodes. *Mayo Clin Proc* 94(2):202–210
96. Garg T, Polenick CA, Schoenborn N, Jih J, Hajduk A, Wei MY et al (2021) Innovative strategies to facilitate patient-centered research in multiple chronic conditions. *J Clin Med* 10(10):2112
97. Spratt DE, Shore N, Sartor O, Rathkopf D, Olivier K (2021) Treating the patient and not just the cancer: therapeutic burden in prostate cancer. *Prostate Cancer Prostatic Dis* 24(3):647–661
98. Hasson F, Keeney S, McKenna H (2000) Research guidelines for the Delphi survey technique. *J Adv Nurs* 32(4):1008–1015

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.