Author's Accepted Manuscript

The Risk of Chronic Kidney Disease Associated With Urolithiasis and its Urological Treatments: a Review

Giovanni Gambaro , Emanuele Croppi , David Bushinsky , Philippe Jaeger , Adamasco Cupisti , Andrea Ticinesi , Sandro Mazzaferro , Alessandro D'Addessi , Pietro Manuel Ferraro

Please cite this article as: Gambaro G, Croppi E, Bushinsky D, Jaeger P, Cupisti A, Ticinesi A, Mazzaferro S, D'Addessi A, Ferraro PM, The Risk of Chronic Kidney Disease Associated With Urolithiasis and its Urological Treatments: a Review, *The Journal of Urology*® (2017), doi: 10.1016/j.juro.2016.12.135.

DISCLAIMER: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our subscribers we are providing this early version of the article. The paper will be copy edited and typeset, and proof will be reviewed before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to The Journal pertain.

Embargo Policy

All article content is under embargo until uncorrected proof of the article becomes available online.

We will provide journalists and editors with full-text copies of the articles in question prior to the embargo date so that stories can be adequately researched and written. The standard embargo time is 12:01 AM ET on that date. Questions regarding embargo should be directed to jumedia@elsevier.com.

The Risk of Chronic Kidney Disease Associated With Urolithiasis and its Urological Treatments: a Review

Giovanni Gambaro[1], Emanuele Croppi[1], David Bushinsky[2], Philippe Jaeger[3], Adamasco Cupisti[4], Andrea Ticinesi[5], Sandro Mazzaferro[6], Alessandro D'Addessi[7], Pietro Manuel Ferraro*[1]

[1] Division of Nephrology, Fondazione Policlinico Universitario A. Gemelli, Catholic University of the Sacred Heart, Rome, Italy

[2] Nephrology Division, Dept. of Medicine and of Pharmacology and Physiology, University of Rochester School of Medicine, Rochester, New York, USA

[3] UCL Centre for Nephrology, Royal Free Campus and Hospital, University College London, London, UK

[4] Dept. of Clinical and Experimental Medicine, University of Pisa; Nephrology, Transplantation and Dialysis Unit, AOUP Pisa, Italy

[5] Department of Clinical and Experimental Medicine, University of Parma; Geriatric-Medicine Rehabilitation Department, Azienda Ospedaliero-Universitario di Parma, Parma, Italy

[6] Dept. of Cardiovascular Respiratory Nephrologic Anesthetic and Geriatric Sciences, Sapienza University of Rome, Rome, Italy

[7] Division of Urology, Fondazione Policlinico Universitario A. Gemelli, Catholic University of the Sacred Heart, Rome, Italy

Correspondence to: Prof. G. Gambaro, Division of Nephrology, Fondazione Policlinico Universitario A. Gemelli, Catholic University of the Sacred Heart, Largo F. Vito, 1; 00168 Rome, Italy; Fax : +39.06 35034434 Phone: +39.0635034434; e-mail: giovanni.gambaro@unicatt.it

*Requests for the Supplementary Tables should be emailed to pietromanuel.ferraro@unicatt.it.

Word count: 189 words (abstract), 3995 words (manuscript)
Running head: Urolithiasis and chronic kidney disease

Abstract

Purpose. Urolithiasis can impair kidney function. This literature review focuses on the risk of kidney impairment in stone formers, the specific conditions associated with this risk and the impact of urological surgery.

Materials and Methods. The PubMed and Embase databases were searched for publications on urolithiasis, its treatment, and the risk of chronic kidney disease (CKD), end-stage renal disease (ESRD) and nephrectomy in stone formers.

Results. In general, renal stone formers carry twice the risk of CKD or ESRD, and for female and overweight stone formers the risk is even higher. Patients with frequent urinary tract infections, struvite stones, urinary malformations and diversions, malabsorptive bowel conditions, and some monogenic disorders are at high risk of CKD/ESRD. Shock wave lithotripsy or minimally-invasive urological interventions for stones do not adversely affect renal function. Declines in renal function generally occur in patients with pre-existing CKD or with a large stone burden requiring repeated and/or complex surgery.

Conclusions. Although the effect size is modest, urolithiasis may cause CKD thus it is mandatory to assess patients with renal stones for their risk of developing CKD/ESRD. We suggest that all guidelines dealing with renal stone disease should include assessing this risk.

Index words: chronic kidney disease; lithotripsy; nephrectomy; review; uretheroscopy; urolithiasis

Introduction

Urolithiasis is a common condition, with a prevalence of about 9% in the general population.[1,2] Although it is generally considered an unpleasant, but relatively benign condition, urolithiasis can impair kidney function as a consequence of: the renal stone *per se* (obstruction, infection), parenchymal damage induced by the primary condition leading to stone formation (some monogenic disorders, nephrocalcinosis, secondary hyperoxaluria, etc.), or urological treatments for the condition.[3] The present literature review was conducted to ascertain the entity of the risk of kidney impairment in stone formers, whether specific conditions are associated with this risk (e.g. demographics, type of stone, etc.), and the role of urological surgery. We specifically looked for evidence addressing the following questions: i) is there a risk of chronic kidney disease (CKD) and end-stage renal disease (ESRD) associated with nephrolithiasis? ii) which stone patients are at high risk of CKD/ESRD? iii) do urological treatments for stones cause irreversible kidney damage, thereby increasing the risk of CKD/ESRD? iv) which factors are associated with a higher risk of CKD/ESRD after urological treatments for stones? v) what is the risk of nephrectomy in urolithiasis?

Methods

Search strategy

The terms used to search specialized registries (PubMed, Embase) for the purpose of this analysis are listed in the Appendix. The search covered the period from January 1965 up until July 2016; the searches were limited to the English language. A few articles were also retrieved from the reference lists of review articles and relevant studies. We considered randomized controlled trials as well as observational studies.

Data extraction and analysis

All identified publications were scrutinized for relevance to the study before inclusion, based initially on title and abstract, and then by reading the full texts. For all selected articles, data were extracted by one reviewer and checked by a second reviewer using a data extraction form that included patient characteristics, methodological quality, study characteristics, details of interventions, and outcome measures. The GRADE system was used to ascertain the validity of the eligible studies and the strength of the evidence. The outcome measures considered were ESRD or CKD stages,[4] or predetermined levels of glomerular filtration rate (GFR), or serum creatinine.

Results

Risk of CKD/ESRD associated with nephrolithiasis

The literature available on this topic amounted to 399 papers, and 17 of them were considered in the present review. Among the 17 studies, only 5 cohort studies assessed the risk of incident CKD/ESRD in patients with urolithiasis, and 2 cross-sectional studies estimated the probability of CKD associated with a history of renal stones.

In a prospective open cohort study using data from a primary care population of 1.5 million, two scores were developed to estimate the individual 5-year risk of moderate-severe CKD and ESRD. Using both scores, a history of renal stones was associated with a risk of developing CKD in women.[5] The risk of developing a GFR <45 mL/min was 27% higher in female stone formers than in women with no history of stones.

In a registry cohort study, one or more episodes of stones were associated with a higher risk of ESRD (adjusted hazard ratio [HR] 2.16, 95% confidence interval [CI] 1.79, 2.62), new-onset CKD stage 3b-5 (HR 1.74, 95% CI 1.61, 1.88), and doubling serum creatinine levels (HR 1.94, 95% CI 1.56, 2.43). The excess risk of adverse outcomes associated with one or more episodes of stones was greater in women than in men, and in people <50 years of age. However, the absolute rates of adverse renal outcomes associated with stones were modest: the unadjusted rate of ESRD was 2.48 per million person-days for people with a history of stones versus 0.52 per million person-days for the remainder of the population.[6]

A registry study on residents of Olmsted County, Minnesota, confirmed that stone formers were at higher risk of ESRD after adjusting for diabetes, hypertension, dyslipidemia, gout, and CKD (HR 2.09, 95% CI 1.45, 3.01). Compared with controls, stone formers who developed ESRD were more likely to have a history of hydronephrosis (44% versus 4%), recurrent urinary tract infections (26% versus 4%), acquired single kidney (15% versus 3%), neurogenic bladder (12% versus 1%), and ileal conduit (9% versus 0%), but not diabetes or hypertension.[7] The risk of ESRD attributable to urolithiasis - i.e. new cases of ESRD secondary to urolithiasis and its complications or associated conditions - was estimated to be only 5.1% of all ESRD cases.

The Alberta and Olmsted County studies presented very similar estimates of the risk of ESRD in stone formers among the general population, identifying an approximately two-fold risk in the former vis-à-vis the latter.

4

In a population-based retrospective study of 11,570 participants with incident urolithiasis and 127,464 without urolithiasis in The Health Improvement Network, the HR for developing CKD among the former compared with the latter was 1.82 (95% CI 1.67, 1.98).[8]

Among 10,678 participants in the Atherosclerosis Risk in Communities study, the adjusted risk of incident CKD was only 10% higher for those with a history of kidney stones and not statistically significant; however, the risk was significantly higher among those with plasma uric acid levels ≤6 mg/dL (HR, 1.34; 95% CI 1.05, 1.72).[9] The use of diagnostic codes to define CKD could partially explain the overall null findings of this study.

Among participants in the National Health and Nutrition Examination Survey (NHANES) III with a history of kidney stones and a BMI ≥27 kg/m^2, the probability of having a GFR <60 mL/min compared to a GFR >90 mL/min was 87% higher than in overweight people who were not stone formers.[10]

In the NHANES 2007-2010 database, a history of kidney stones was associated with CKD, i.e. GFR <60 mL/min (odds ratio [OR] 1.76, 95% CI 1.13, 2.76) in women, but not in men, and with dialysis (OR 3.26, 95% CI 1.48, 7.16).[11] A community-based study in Shanghai, China, found nephrolithiasis more prevalent in CKD patients than in non-CKD subjects.(Suppl. Table 1, Ref. #13).

A number of generally poor-quality, often case-control and single-center studies, also support the role of renal stones as a risk factor for CKD. In a case-control study on Egyptian hemodialysis patients, a history of renal stones emerged as an independent risk factor for ESRD.(Suppl. Table 1, Ref. #14) In another case-control study on newly-diagnosed CKD patients, the odds of CKD (based on kidney-related ICD-9 discharge diagnoses) among those without hypertension was three times higher (95% CI 1.3, 6.8) for patients with versus without kidney stones, after adjusting for all co-variables.[12]

The risk factors for CKD/ESRD in stone formers from studies on the general population are listed in Table 1.

None of these studies distinguished the risk of CKD by phenotype of the underlying disorder causing the stone. However renal stones have a different risk of inducing CKD depending on their etiology and composition. This was demonstrated by Worcester et al[13], who analyzed creatinine clearance in over 1,800 patients with urolithiasis. The lowest creatinine clearance values (though still not severe enough to be classified as CKD 3 or more) were seen in cystinuria, in uric acid and struvite stones, and in overt renal tubular acidosis and intestinal-related nephrolithiasis. In a study on 40 cystinuric patients, only 30% had functionally unaffected kidneys with normal GFR and bilaterally normal renography.(Suppl. Table 1, Ref. #21) In a larger cohort of 95 cystinuric patients,

Assimos et al[14] found higher serum creatinine levels and a higher prevalence of nephrectomy than in calcium oxalate stone formers. The high prevalence of CKD in cystinuria was confirmed in a recently-published French study on 442 cystinuric patients[15]: 26.7% had CKD (though only 5 patients had ESRD), and only 22.5% had eGFR >90 mL/min. In these studies on cystinuric stone formers, a history of staghorn stones and of multiple open surgical procedures for stone removal constituted a relevant risk factor for CKD and nephrectomy.

In a cross-sectional study on over 1900 patients in which stones were analyzed by infrared spectroscopy, patients with struvite and uric acid stones had a lower GFR than those with calcium oxalate and phosphate stones.[16]

Among patients treated with bariatric surgery techniques, Standard Roux-en-Y gastric bypass and malabsorptive procedures are both associated with an increased risk of stones, but only the latter raise the risk of CKD as well (adjusted HR 1.96).[17]

In patients with primary hyperparathyroidism renal stones were not associated with CKD stage 3.(Suppl. Table 1, Ref. #6)

Urological treatments and CKD

Our database search on this topic retrieved 274 papers, and 25 were considered in this review. Shock-wave lithotripsy (SWL) and percutaneous nephrolithotomy (PCNL) have been shown to damage the renal parenchyma. The amount of tissue irreversibly injured during a single procedure is generally very small[18], so there is generally an unmeasurable decline in the function of an otherwise normal kidney. However, leaving a stone untreated can risk damaging the whole kidney. There are numerous caveats to take into account when analyzing the available literature on this topic. Baseline renal function is crucially important when investigating renal dysfunction occurring after a treatment because the contribution of the small parenchymal loss is dependent on its relative contribution to overall renal function. A variety of available urological treatments may have been used, alone or in different combinations, in the same patient, and some patients must be treated repeatedly for the same stone or for recurrent stones. Unfortunately, only a few articles enable us to disentangle these complexities. Any hypertension developing after SWL described in the past[19] is another aspect to consider because it may well be a sign of renal damage.

As a general observation, the available evidence on the impact on the GFR of different urological techniques for removing stones is of very poor quality, deriving essentially from a number of small observational, single-center, retrospective studies. Many of them are flawed for the following reasons:

1. renal function was only assessed in the very short term (<3 months);

2. cases with obstructive uropathy and/or complex/staghorn stones were included in the sample. In these conditions, it may be difficult to quantify the net impact of factors potentially impacting renal functions in opposite directions, e.g. the damage caused by the surgical procedureor by the prior obstructive/inflammatory damage, and any improvement in renal function after the obstruction was removed;

3. the methods used to assess renal function were inadequate (i.e. estimated GFR in patients with two kidneys); for the specific question addressed here, the most informative studies are those concerning patients with single kidneys, or that assess renal function separately in each kidney by means of nuclear scanning).

It is also important for studies on the risk of CKD following SWL to report the specific treatment given, i.e. the number of shocks delivered per session, and the number of sessions, which are bound to have changed over the course of almost 30 years (the first study retrieved dated from 1988). When we considered only the SWL studies published since 1995 and concerning adult patients with single kidneys, or whose renal function was assessed with a split nuclear scan, we retrieved three reports dealing with a total of 309 kidneys.[20–22] No effect of SWL on GFR or blood pressure was observed after a follow-up of at least 12 months. Two retrospective studies on a total of 439 patients whose bilateral renal stones were treated simultaneously with SWL, found no variation in serum creatinine levels over a 12-month follow-up.[23,24] In a small prospective study, only 1 of 25 patients developed hypertension more than 8 months after SWL.(Suppl. Table 2, Ref. #37) In four studies on 231 children, renal scans performed after a follow-up of more than 3 months revealed deterioration in renal function in only one kidney.[25–28] Very few studies have examined the risk of hypertension developing after SWL in children, and appear to rule out this possibility.[25,29]

As for ureteroscopic lithotripsy (URSL), one study on single-kidney patients compared URSL with SWL and found no differences in terms of subsequent renal function.[30] Multiple URSL procedures did not alter the long-term GFR in stone-forming patients with CKD stages 2-3(Suppl. Table 2, Ref. #59); and the GFR did not change after URSL in 9 patients whose renal function was examined by renal scan.(Suppl. Table 2, Ref. #58)

In a retrospective study, the risk of CKD (serum creatinine higher than 1.4 mg/dL in males, or 1.2 mg/dL in females) developing in 87 stone formers treated by percutaneous nephrolithotomy (PCNL) was much the same after a 19-year follow-up as in historical, unmatched cohorts of patients with stones not treated surgically, or treated with SWL, giving the impression that PCNL is at least as safe as other procedures.[31] In two studies on a total of 243 patients, PCNL caused some deterioration in renal function in 9-15% of cases.[32,33] This was probably related to multiple

punctures and a previously impaired renal function. Similar data emerged from a retrospective study on children.(Suppl. Table 2, Ref. #31)

In a cross-sectional study of 171 patients with severe idiopathic calcium nephrolithiasis, those with a GFR <80 mL/min experienced more extensive stone surgery and complications than those whose GFR was >80.(Suppl. Table 2, Ref. #24) Similar findings recently emerged from the CROES PCNL study of a registry cohort of more than 5,600 patients who underwent PCNL. Patients with CKD stages 4-5 were those with a history of PCNL, URSL or nephrostomy; and they had positive urine cultures consistent with their higher prevalence of staghorn stones.[34] The risk of CKD was also associated with the number of stone removal procedures performed, and with a lower stone-free rate in single-kidney patients.[35]

A retrospective study on SWL-treated stone formers identified a 20% increase in the risk of CKD stage 3 for every 1 mm increase in the stone burden up to 20 mm. Oddly enough, this association was not seen for greater stone burdens.(Suppl. Table 2, Ref. #23)

In patients with bilateral obstructive urolithiasis treated with flexible URS or PCNL, the risk of CKD stage 5 at 1 year of follow-up was predicted independently by a combination of reduced cortical thickness, proteinuria, positive urine culture, and lower preoperative GFR.(Suppl. Table 2, Ref. #47) Apart from urinary infection, the other conditions are signs of a CKD existing prior to the treatment, and are conditions typically considered when estimating the risk of CKD progression.

In a recent retrospective study on 2,238 urolithiasis patients with at least one SWL or URS procedure, neither SWL nor ureteroscopy was associated with incident CKD.[8]

In conclusion, the number and complexity of urological treatments, staghorn stones, stone burden, and prior advanced CKD appear to be the most relevant risk factors for severe, chronic renal damage after urological treatments for stones.

Risk of nephrectomy in urolithiasis

We retrieved 2,118 papers from the databases queried on the risk of nephrectomy in patients with urolithiasis and 13 of them were considered in this review. In renal stone patients, nephrectomy may be due to complications of kidney stones or of urological treatments. Some studies do not distinguish between these two situations. No one is certain how often nephrectomy is performed in patients with renal stones, nor the reasons for it.

Among 3,266 prevalent patients attending a large outpatient stone clinic, 3.5% had lost a kidney, and the prevalence of kidney loss did not vary over three decades (1970-2003).[36] During the years 2002-2007, nephrectomy was performed in less than 1% of 3,170 children hospitalized for renal

stones in the US.[37] A study on the trend of treatments for upper urinary tract calculi in the US found no significant change in the need for nephrectomy during the period from 1999 to 2009.[38]

The reasons for kidney loss in renal stone patients are: obstruction, stone burden, and infection.[36] In a Chinese study conducted between 2001 and 2010, the risk factors for kidney loss and nephrectomy in patients with upper urinary tract stones were: calculus >10 mm, loss to follow-up, and poor living standards.[39]

Only a few studies have investigated the risk of nephrectomy in specific nephrolithiasis phenotypes. Struvite and calcium phosphate stones are more prevalent among single-kidney stone formers[36] and, as already mentioned, cystinuric patients are at higher risk of nephrectomy than calcium oxalate stone formers (14.1% versus 2.9%).[14] According to the findings of a case population of 48 cystinuric stone patients, however, the risk of nephrectomy has decreased since 1990 apparently due to the use of minimally-invasive urological procedures.[40]

A few single-institution studies have reported on the risk of nephrectomy as a complication of PCNL. In the two largest series, involving 1,039 and 568 kidneys undergoing PCNL, only one patient in each series (0.1% and 0.2% of the sample, respectively) required urgent nephrectomy for severe bleeding.[41,42] Other, smaller studies found prevalences of up to 1%.[43,44] In a Japanese study on 2,129 patients with ureteral stones who underwent URSL between 1985 and 2006, there were only 2 cases of nephrectomy being performed for ureteral perforation.[45]

Taken together, these studies demonstrate that currently-used urological treatments of renal and ureteral stones are safe. Although the risk of nephrectomy is low globally and may be decreasing, apparently due to modern urological approaches to stone removal, some types of stone (cystine and struvite stones) still carry a risk of nephrectomy. A careful patient follow-up is crucial to the prevention of such a severe complication.

Discussion

Renal stone formers have approximately a two-fold higher risk of impaired renal function or need for renal replacement therapy than the general population. Female and overweight stone formers are at greater risk, together with those who frequently have UTI or struvite stones. Patients with urinary malformations and diversions, malabsorptive bowel syndromes, or monogenic disorders that cause stones are at particularly high risk of CKD/ESRD. For the rarer forms of kidney stones, an estimate of the risk of CKD/ESRD is proposed in Table 2 on the grounds of personal experience, case reports, previously-cited studies and very small observational studies.[18] While it is difficult to separate the relative contribution of mechanical and metabolic factors affecting renal function, it

can be hypothesized that some conditions such as cystinuria, renal tubular acidosis and intestinal-related nephrolithiasis carry a higher risk of kidney damage.

Although there are no studies of sufficiently good quality available on the effects of non-invasive or minimally-invasive urological treatment for stones on renal function, it would seem that whenever clinically relevant renal damage is observed, this is due mainly to primary conditions demanding repeated and/or complex surgeries.

Early access to the best urological treatments seems to be indispensable in order to avoid severe renal damage, nephrectomy and ESRD.

Conclusions

Although the effect size is modest, urolithiasis should be seen as a condition that may lead to CKD, so it is mandatory to assess renal stone formers in terms of their global risk of developing CKD/ESRD. We recommend that all guidelines dealing with renal stone disease include an assessment of this risk.

Appendix

Search strategy for the section "Risk of CKD/ESRD associated with nephrolithiasis"

PubMed:

(urolithiasis[mesh] OR urolithiasis[tiab] OR nephrolithiasis[tiab] OR ((renal[tiab] OR kidney[tiab]) AND (stone*[tiab] OR calculi[tiab] OR calculus[tiab])))

AND

(renal insufficiency, chronic[mesh] OR chronic kidney disease[tiab] OR chronic renal insufficiency[tiab])

AND

risk[tiab]

AND

english[la]

AND

"1965/01"[pdat] : "2016/07"[pdat]

Embase:

('urolithiasis'/exp OR urolithiasis:ab,ti OR nephrolithiasis:ab,ti OR ((renal:ab,ti OR kidney:ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti)))

AND

('chronic kidney disease'/exp OR 'chronic kidney disease':ab,ti OR 'chronic renal insufficiency':ab,ti)

AND

risk:ab,ti

AND

english:la

AND

[1965-2016]/py

Search strategy for the section "Urological treatments and CKD"

PubMed:

(renal insufficiency, chronic[mesh] OR chronic kidney disease[tiab] OR chronic renal insufficiency[tiab] OR kidney damage[tiab] OR renal damage[tiab])

AND

11

(lithotripsy[mesh] OR lithotripsy[tiab] OR eswl[tiab] OR ureteroscopy[tiab])

AND

english[la]

AND

"1965/01"[pdat] : "2016/07"[pdat]

Embase:

('chronic kidney disease'/exp OR 'chronic kidney disease':ab,ti OR 'chronic renal insufficiency':ab,ti

OR 'kidney damage':ab,ti OR 'renal damage':ab,ti)

AND

('lithotripsy'/exp OR lithotripsy:ab,ti OR eswl:ab,ti OR ureteroscopy:ab,ti)

AND

english:la

AND

[1965-2016]/py

Search strategy for the section "Risk of nephrectomy in urolithiasis"

PubMed:

(urolithiasis[mesh] OR urolithiasis[tiab] OR nephrolithiasis[tiab] OR ((renal[tiab] OR kidney[tiab])

AND (stone*[tiab] OR calculi[tiab] OR calculus[tiab])))

AND

(nephrectomy[mesh] OR nephrectomy[tiab] OR single kidney[tiab])

AND

english[la]

AND

"1965/01"[pdat] : "2016/07"[pdat]

Embase:

('urolithiasis'/exp OR urolithiasis:ab,ti OR nephrolithiasis:ab,ti OR ((renal:ab,ti OR kidney:ab,ti)

AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti)))

AND

('nephrectomy'/exp OR nephrectomy:ab,ti OR 'single kidney':ab,ti)

AND

english:la

AND

[1965-2016]/py

AND

[1965-2016]/py

References

1. Scales CD Jr, Smith AC, Hanley JM, Saigal CS et al: Prevalence of kidney stones in the United States. *Eur Urol*. 2012;62:160–165. doi:10.1016/j.eururo.2012.03.052.

2. Croppi E, Ferraro PM, Taddei L, Gambaro G et al: Prevalence of renal stones in an Italian urban population: a general practice-based study. *Urol Res*. 2012;40(5):517-522. doi:10.1007/s00240-012-0477-z.

3. Gambaro G, Croppi E, Coe F et al: Metabolic diagnosis and medical prevention of calcium nephrolithiasis and its systemic manifestations: a consensus statement. *J Nephrol*. 2016; **29:** 715. doi:10.1007/s40620-016-0329-y.

4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):4-4. doi:10.1038/kisup.2012.76.

5. Hippisley-Cox J and Coupland C. Predicting the risk of chronic Kidney Disease in men and women in England and Wales: prospective derivation and external validation of the QKidney Scores. *BMC Fam Pract*. 2010;11:49. doi:10.1186/1471-2296-11-49.

6. Alexander RT, Hemmelgarn BR, Wiebe N et al: Kidney stones and kidney function loss: a cohort study. *BMJ*. 2012;345:e5287.

7. El-Zoghby ZM, Lieske JC, Foley RN et al: Urolithiasis and the risk of ESRD. *Clin J Am Soc Nephrol*. 2012;7(9):1409–15. doi:10.2215/CJN.03210312.

8. Denburg MR, Jemielita TO, Tasian GE et al: Assessing the risk of incident hypertension and chronic kidney disease after exposure to shock wave lithotripsy and ureteroscopy. *Kidney Int*. 2016;89(1):185-192. doi:10.1038/ki.2015.321.

9. Kummer AE, Grams M, Lutsey P et al: Nephrolithiasis as a Risk Factor for CKD: The Atherosclerosis Risk in Communities Study. *Clin J Am Soc Nephrol*. 2015;10(11):2023-2029. doi:10.2215/CJN.10111014.

10. Gillen DL, Worcester EM and Coe FL: Decreased renal function among adults with a history of nephrolithiasis: a study of NHANES III. *Kidney Int*. 2005;67(2):685-690. doi:10.1111/j.1523-1755.2005.67128.x.

11. Shoag J, Halpern J, Goldfarb DS, Eisner BH. Risk of Chronic and End Stage Kidney Disease in Patients with Nephrolithiasis. *J Urol*. 2014;192(5):1440-1445. doi:10.1016/j.juro.2014.05.117.

12. Vupputuri S, Soucie JM, McClellan W, Sandler DP. History of kidney stones as a possible risk factor for chronic kidney disease. *Ann Epidemiol*. 2004;14(3):222-228. doi:10.1016/S1047-2797(03)00126-1.

13. Worcester EM, Parks JH, Evan AP, Coe FL. Renal function in patients with nephrolithiasis. *J Urol*. 2006;176(2):600-603; discussion 603. doi:10.1016/j.juro.2006.03.095.

14. Assimos DG, Leslie SW, Ng C, Streem SB, Hart LJ. The impact of cystinuria on renal function. *J Urol*. 2002;168(1):27-30.

15. Prot-Bertoye C, Lebbah S, Daudon M et al: CKD and Its Risk Factors among Patients with Cystinuria. *Clin J Am Soc Nephrol*. 2015;10(5):842-851. doi:10.2215/CJN.06680714.

16. Chou Y-H, Li C-C, Hsu H et al: Renal function in patients with urinary stones of varying compositions. *Kaohsiung J Med Sci*. 2011;27(7):264-267. doi:10.1016/j.kjms.2010.11.008.

17. Lieske JC, Mehta RA, Milliner DS, Rule AD, Bergstralh EJ, Sarr MG. Kidney stones are common after bariatric surgery. *Kidney Int*. 2015;87(4):839-845. doi:10.1038/ki.2014.352.

18. Gambaro G, Favaro S and D'Angelo A: Risk for renal failure in nephrolithiasis. *Am J Kidney Dis*. 2001;37(2):233-243.

19. Janetschek G, Frauscher F, Knapp R, Höfle G, Peschel R, Bartsch G. New onset hypertension after extracorporeal shock wave lithotripsy: age related incidence and prediction by intrarenal resistive index. *J Urol*. 1997;158(2):346-351.

20. el-Assmy A, el-Nahas AR, Hekal IA, Badran M, Youssef RF, Sheir KZ. Long-term effects of extracorporeal shock wave lithotripsy on renal function: our experience with 156 patients with solitary kidney. *J Urol*. 2008;179(6):2229-2232. doi:10.1016/j.juro.2008.01.095.

21. Eassa WA, Sheir KZ, Gad HM, Dawaba ME, El-Kenawy MR, Elkappany HA. Prospective Study of the Long-Term Effects of Shock Wave Lithotripsy on Renal Function and Blood Pressure. *J Urol*. 2008;179(3):964-969. doi:10.1016/j.juro.2007.10.055.

22. Liou LS and Streem SB. Long-term renal functional effects of shock wave lithotripsy, percutaneous nephrolithotomy and combination therapy: a comparative study of patients with solitary kidney. *J Urol*. 2001;166(1):36; discussion 36-37.

23. Perry KT, Smith ND, Weiser AC, User HM, Kundu SD, Nadler RB. The efficacy and safety of synchronous bilateral extracorporeal shock wave lithotripsy. *J Urol*. 2000;164(3 Pt 1):644-647.

24. Pienkny AJ and Streem SB. Simultaneous versus staged bilateral extracorporeal shock wave lithotripsy: long-term effect on renal function. *J Urol*. 1999;162(5):1591-1593.

25. Picramenos D, Deliveliotis C, Alexopoulou K, Makrichoritis C, Kostakopoulos A, Dimopoulos C. Extracorporeal shock wave lithotripsy for renal stones in children. *Urol Int*. 1996;56(2):86-89.

26. Sarica K, Küpei S, Sarica N, Gögüş O, Kiliç S, Saribaş S. Long-term follow-up of renal morphology and function in children after lithotripsy. *Urol Int*. 1995;54(2):95-98.

27. Fayad A, El-Sheikh MG, Abdelmohsen M, Abdelraouf H. Evaluation of renal function in children undergoing extracorporeal shock wave lithotripsy. *J Urol*. 2010;184(3):1111-1114. doi:10.1016/j.juro.2010.05.016.

28. Griffin SJ, Margaryan M, Archambaud F, Sergent-Alaoui A, Lottmann HB. Safety of shock wave lithotripsy for treatment of pediatric urolithiasis: 20-year experience. *J Urol*. 2010;183(6):2332-2336. doi:10.1016/j.juro.2010.02.030.

29. Adanur S, Ziypak T, Yılmaz AH et al: Extracorporeal shockwave lithotripsy under sedoanalgesia for treatment of kidney stones in infants: a single-center experience with 102 cases. *Int Urol Nephrol*. 2014;46(11):2095-2101. doi:10.1007/s11255-014-0788-9.

15

30. Yuruk E, Binbay M, Ozgor F, Sekerel L, Berberoglu Y, Muslumanoglu AY. Comparison of shockwave lithotripsy and flexible ureteroscopy for the treatment of kidney stones in patients with a solitary kidney. *J Endourol*. 2015;29(4):463-467. doi:10.1089/end.2014.0613.

31. Krambeck AE, LeRoy AJ, Patterson DE, Gettman MT. Long-Term Outcomes of Percutaneous Nephrolithotomy Compared to Shock Wave Lithotripsy and Conservative Management. *J Urol*. 2008;179(6):2233-2237. doi:10.1016/j.juro.2008.01.115.

32. Al-Kohlany KM, Shokeir AA, Mosbah A et al: Treatment of complete staghorn stones: a prospective randomized comparison of open surgery versus percutaneous nephrolithotomy. *J Urol*. 2005;173(2):469-473. doi:10.1097/01.ju.0000150519.49495.88.

33. El-Tabey NA, El-Nahas AR, Eraky I et al: Long-term Functional Outcome of Percutaneous Nephrolithotomy in Solitary Kidney. *Urology*. 2014;83(5):1011-1015. doi:10.1016/j.urology.2013.12.025.

34. Sairam K, Scoffone CM, Alken P et al: Percutaneous Nephrolithotomy and Chronic Kidney Disease: Results from the CROES PCNL Global Study. *J Urol*. 2012;188(4):1195-1200. doi:10.1016/j.juro.2012.06.027.

35. Bucuras V, Gopalakrishnam G, Wolf JS Jr et al: The Clinical Research Office of the Endourological Society Percutaneous Nephrolithotomy Global Study: Nephrolithotomy in 189 Patients with Solitary Kidneys. *J Endourol*. 2012;26(4):336-341. doi:10.1089/end.2011.0169.

36. Worcester E, Parks JH, Josephson MA, Thisted RA, Coe FL. Causes and consequences of kidney loss in patients with nephrolithiasis. *Kidney Int*. 2003;64(6):2204-2213. doi:10.1046/j.1523-1755.2003.00317.x.

37. Bush NC, Xu L, Brown BJ et al: Hospitalizations for pediatric stone disease in United States, 2002-2007. *J Urol*. 2010;183(3):1151-1156. doi:10.1016/j.juro.2009.11.057.

38. Ghani KR, Sammon JD, Karakiewicz PI et al: Trends in surgery for upper urinary tract calculi in the USA using the Nationwide Inpatient Sample: 1999-2009. *BJU Int*. 2013;112(2):224-230. doi:10.1111/bju.12059.

39. Mao S, Jiang H, Wu Z, Fang Z, Xia G, Ding Q. Urolithiasis: the most risk for nephrectomy in nonrenal tumor patients. *J Endourol Endourol Soc*. 2012;26(10):1356-1360. doi:10.1089/end.2012.0080.

40. Trinchieri A, Montanari E, Zanetti G, Lizzano R. The impact of new technology in the treatment of cystine stones. *Urol Res*. 2007;35(3):129-132. doi:10.1007/s00240-007-0089-1.

41. el-Kenawy MR, el-Kappany HA, el-Diasty TA, Ghoneim MA. Percutaneous nephrolithotripsy for renal stones in over 1000 patients. *Br J Urol*. 1992;69(5):470-475.

42. Keoghane SR, Cetti RJ, Rogers AE, Walmsley BH. Blood transfusion, embolisation and nephrectomy after percutaneous nephrolithotomy (PCNL). *BJU Int*. 2013;111(4):628-632. doi:10.1111/j.1464-410X.2012.11394.x.

43. Ali S, Kumar N and Baloch U: Outcome of percutaneous nephrolithotomy. *J Coll Physicians Surg Pak*. 2014;24(4):261-264. doi:04.2014/JCPSP.261264.

44. Fu Y-M, Chen Q-Y, Zhao Z-S et al: Ultrasound-guided minimally invasive percutaneous nephrolithotomy in flank position for management of complex renal calculi. *Urology*. 2011;77(1):40-44. doi:10.1016/j.urology.2010.04.054.

45. Kurahashi T, Miyake H, Oka N et al: Clinical outcome of ureteroscopic lithotripsy for 2,129 patients with ureteral stones. *Urol Res*. 2007;35(3):149-153. doi:10.1007/s00240-007-0095-3.

Table 1

Risk factors for CKD/ESRD in stone formers from studies on the general population

Female gender

Overweight

Frequent UTI

Struvite stones

Acquired single kidney

Neurogenic bladder

Previous obstructive nephropathy

Ileal conduit

Table 2

Risk of CKD/ESRD in special forms of nephrolithiasis

Special forms of urolithiasis	Risk of CKD/ESRD
Xanthine stones	Possible but low
Dihydroxyadenine stones	Possible but low
Cystine stones	High
Infection stones	High
Indinavir stones	Possible but low
Distal renal tubular acidosis (complete)	High
Distal renal tubular acidosis (incomplete)	Very low
Primary hyperoxaluria	Very high
Secondary hyperoxaluria (bariatric surgery, inflammatory bowel disease, bowel resection, malabsorptive syndromes)	High
Medullary sponge kidney	Possible but low
Other forms of nephrocalcinosis (often associated with genetic hypercalciurias)	High
Stones associated with anatomical abnormalities of the kidney and urinary tract (horseshoe kidney; ureterocele, vesico-ureteral reflux, etc.) and neurological bladder	Intermediate-high

Abbreviations

Chronic kidney disease (CKD), confidence interval (CI), end-stage renal disease (ESRD), glomerular filtration rate (GFR), hazard ratio (HR), National Health and Nutrition Examination Survey (NHANES), percutaneous nephrolithotomy (PCNL), shock-wave lithotripsy (SWL), ureteroscopic lithotripsy (URSL)