Literature Review: Prevalence of chronic kidney disease in patients with kidney stones: is there an association?

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Introduction

- Urolithiasis is a benign but troublesome condition that has a lifetime incidence of 5% to 12%.
- Associated with impaired renal function, the development of chronic kidney disease (CKD) and subsequent end-stage renal disease (ESRD) (Worcester *et al.* 2006) (Gambaro *et al.* 2016).
- Association appears to be independent of CKD risk factors that are common in stone formers like hypertension.
- Underlying pathophysiology is not understood, but predisposing factors are objectively present.
- Kidney stones are potentially preventable, so accurately assessing the long-term consequences of urolithiasis on renal function and the risk of kidney impairment in stone formers can help inform health interventions to prevent the development of adverse renal outcomes in at-risk patients.

Methods

1. Ovid Medline search was performed to locate suitable articles (2000 to 2020).
2. Articles were locate using certain search terms like 'renal function' and 'nephrolithiasis'.
3. Selected publications were chosen based on title and abstract, and were then fully analysed.
4. Cohort studies and case control studies were considered in this review.

Results

Risk of impaired renal function/CKD following urolithiasis

Associated with various pathways of damage.

1. One example by Klahr et. al showed that **obstruction by stone -> decreased renal perfusion to normalise intratubular pressure -> ischaemia -> glomerulosclerosis, interstitial fibrosis & tubular atrophy in affected kidney-> loss of functional nephrons -> decreased eGFR and CKD.**
2. A study by Bander SJ *et al.* looked at the effect of **complete unilateral obstruction** in a rat model for 24 hours, the outcome of which was the **"loss of function of 15% of nephrons in the implicated kidney"**.
3. Sigurjonsdottir VK *et al.* showed a **significant difference in the mean eGFR between recurrent stone formers and controls** (9.3% vs. 1.3% (p<0.001) respectively), even after adjustment for co-morbid conditions and body size.
4. Alexander *et al. and Haley et al.* showed that **following stone resolution in first time stone formers, patients may still suffer persistent decline in renal function** due to sustained proteinuria and higher cystatin c levels.

Effect of different stone factors on the development of CKD in stone formers

- **Significant heterogeneity** exists CKD risk associated with different stone types.
- **Struvite stones** contribute the most to development of ESRD (42%).
- Calcium stones caused 28% of cases and uric acid stones 18%. The remainder were due to rare causes like cystinuria.
- Figure 1 shows that cystinuric stones were associated with the lowest pre-treatment creatinine clearance out of all the stone types. In high risk groups like these, it is therefore important to employ early interventions to prevent the rapid rate of renal function decline.
- **Calcium-containing stones** (e.g. calcium oxalate) were associated with better renal outcomes than non-calcium-containing stones (e.g. uric acid and struvite). **Analysis of stone composition** is therefore essential in allowing the change in kidney function in stone formers to be better predicted (Chou *et al.* 2011; Nassir *et al.* 2018)

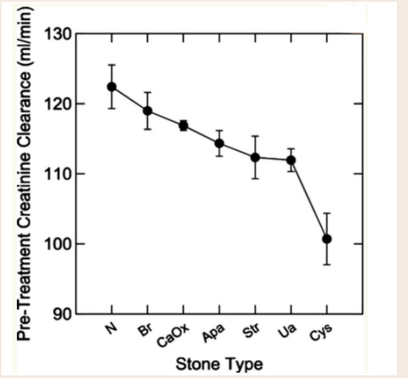


Figure 1. Pre-treatment urinary creatinine clearance in control patients and in patients with varying stone types. "Normal (N), Brushite (Br), Calcium oxalate (CaOx), Apatite (Apa), Struvite (Str), Uric acid (Ua), and Cystine (Cys)" (Worcester *et al.* 2006).

Risk of CKD following urological treatments

- When the **stone burden is large**, and **multiple complex interventions** are required, the risk of renal deterioration can potentially increase.
- Much of the evidence shows that, other than nephrectomy, there is n**o association between stone removal surgery and progressive CKD** (Carvalho *et al.* 2013)
- Reeves *et al.* showed that in patients with **ureteral or renal stones who underwent ureteroscop**y and laser stone (URSL) treatment, the renal function either **remained stable or improved** (63 to 68, p<0.002).
- Damage observed in stone formers was more likely related to the main condition requiring complex and/or repeated surgeries, and less due to the stone-removing technique itself.

Conclusions & Recommendations

- An abundant amount of literature exists on the link between urolithiasis and CKD but there is room for improvement.
- Research into factors that distinguish different stone formers from one another is needed to predict the risk of future renal damage more accurately.
- Incorporating a risk assessment following first stone events might enhance management.
- Early interventions are crucial in avoiding kidney damage, nephrectomies and ESRD in recurrent stone formers.
- Most studies found were retrospective in nature, small in sample size and had short follow-up periods, thus limiting reliability of results found.
- Extensive studies are therefore needed to better characterise CKD associated with urolithiasis, to ultimately address the risk of adverse renal outcomes in high-risk stone formers.

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