Review Article
The long-term renal effects of short periods of unilateral ureteral obstruction

Fayez T Hammad

Department of Surgery, College of Medicine & Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

Received October 3, 2021; Accepted January 30, 2022; Epub April 15, 2022; Published April 30, 2022

Abstract: The response of the kidney and its recovery following unilateral ureteral obstruction (UUO) depend on several factors including the duration of obstruction, the species involved and the age of the individual. In neonates, there is compelling evidence to indicate that even short periods of reversible UUO might lead to long-term renal impairment. In adults, the glomerular filtration rate returns to baseline values soon after the release of short periods of UUO. Despite this return to normal, experimental data have demonstrated that short periods of reversible UUO could lead to long-term renal functional alterations including tubular atrophy, interstitial fibrosis and urinary albumin leakage in addition to alterations in pro-inflammatory and pro-fibrotic cytokines. The concentrating ability of the kidney and its response to stimuli such as renal nerve stimulation and physiological doses of angiotensin-II were also shown to be affected at least in the intermediate-term following UUO reversal. In humans, epidemiological studies have also demonstrated a clear association between long-term renal impairment and ureteral obstruction. However, in clinical studies, it is usually difficult to precisely determine the degree and the time of onset of ureteral obstruction and more studies are required in this field.

In conclusion, the available experimental and clinical data indicate that even short periods of UUO can cause long-term renal dysfunction. These findings might have clinical implications related to the early intervention following acute onset of UUO and to the need for long-term monitoring of renal functions particularly in patients with underlying chronic renal disease.

Keywords: Unilateral ureteral obstruction, short duration, long-term, renal functions

Introduction

Obstructive uropathy refers to any structural or functional changes in the urinary tract that impede the normal flow of urine. It can be divided into upper and lower urinary tract obstruction depending on the site of obstruction whether it is above or below the ureterovesical junction. By definition, upper urinary tract obstruction is usually unilateral and lower urinary tract obstruction is bilateral. Unilateral ureteral obstruction (UUO) is a relatively common form of upper urinary tract obstruction and is usually caused by ureteral calculi, trauma, strictures and tumors.

Unilateral ureteral obstruction leads to several alterations in renal functions. Most of the data related to these changes were based on experimental animal studies using clearance and micropuncture techniques because, in humans, it is usually impossible to determine the exact time of the onset of obstruction. Moreover, oftentimes, it is difficult to perform serial comprehensive detailed renal functional measurements.

In neonates, there is compelling evidence to indicate that short periods of reversible UUO result in long-term renal impairment [1-3]. In adult subjects, the presence of long-term renal damage following release of short periods of UUO is less clear. In this review, the recovery and long-term effects of short periods of UUO on the renal functions in the adult are discussed. The first part of this review deals with the available data from experimental animals whereas the clinical data related to the topic is discussed in the second part.

Experimental data

Ureteral obstruction results in a rise in ureteral pressure which leads to alterations in glomeru-
lar and tubular renal functions. The degree of these alterations depends on various factors such as the duration of obstruction, whether it is partial or complete [4-6] and whether it is unilateral or bilateral [7-11]. In this section, the immediate and long-term hemodynamic and tubular renal functional alterations that occur following acute UUO, although interrelated, will be discussed separately.

**Glomerular alterations**

*Hemodynamic and glomerular changes following acute UUO*

Immediately following the onset of UUO, there is an initial increase in ureteral pressure leading to a rise in intra-tubular pressure [12-14] and subsequent alterations in the renal blood flow (RBF). In the rat, following the onset of UUO, RBF passes through three phases [15]. During the first phase or the hyperemic phase, there is a transient rise in RBF which was shown to be mediated by several agents including vasodilatory prostaglandins [16]. In the second phase, which occurs two to five hours after the onset of UUO, RBF starts to drop. This may be due to the rise in the renal interstitial pressure as a direct effect of the increase in ureteral pressure which continues to rise [17]. In the third phase, which starts from 5 hours onward, RBF decreases progressively and by 24 hours it reaches 30-50% of the pre-obstruction value.

These changes in intra-tubular pressure and RBF lead to progressive deterioration in the GFR immediately following the onset of UUO. In rats, for example, the GFR falls to 2% of the control value by 48 hours after the onset of UUO and remains at this level thereafter if the obstruction is not relieved. The reduction in GFR is caused by the fall in RBF, the alterations in the hydraulic pressure gradient and the reduction in the ultrafiltration coefficient [18-20].

*Recovery of glomerular function following reversal of ureteral obstruction*

Following the release of UUO, the rate and extent of recovery of glomerular functions depend on several factors such as the species involved and the duration of obstruction [21-26]. In rats, it has been shown that a permanent degree of damage occurs beyond 72 hours of obstruction [26] whereas shorter periods of obstruction result in complete recovery of GFR within few days to weeks after reversal [21, 23, 27]. For instance, following reversal of a 24-hour UUO, Bander et al demonstrated that the GFR of the post-obstructed kidney (POK) had improved gradually following UUO reversal, returned to values similar to the non-obstructed kidney (NOK) within two weeks and continued to be comparable to the NOK up to 60 days post-reversal [21].

In the rat also, 72-hour reversible UUO, led to a reduction in GFR, which recovered by 28 days following reversal [28]. In addition, Hammad et al studied renal functions serially up to 18 months following 72-hour reversible UUO in the rat [29]. They demonstrated that the GFR of the POK was similar to the contralateral NOK when measured one, four and eighteen months following the UUO reversal. This was the longest follow-up of the GFR following reversal of relatively short periods of UUO in experimental animals and it is unknown if the GFR would continue to be normal after longer periods of follow-up.

Despite this apparent recovery in the total GFR following relatively short periods of UUO, there is evidence to suggest that some nephrons might still be non-filtering. In a 60-day follow-up study following 24-hour reversible UUO, it was demonstrated that only 85% of the nephrons in the POK were filtering at 60 days post-UUO reversal i.e. almost 45 days following the recovery of total GFR [21]. This has indicated that the complete ‘recovery’ of the GFR was achieved at the expense of an increase in single nephron GFR or ‘hyperfiltration’ in some nephrons. The filtering status of the nephrons has not been studied beyond 60 days post-UUO reversal.

*Histological features of the glomeruli after UUO and recovery after release:* Following UUO, glomerular structural changes tend to develop more slowly compared to tubular changes and, in most instances, there is a tendency for glomerular histological preservation [30]. This is probably due to the presence of some degree of filtration even with complete obstruction and this, in turn, results in maintaining the integrity...
Short periods of unilateral ureteral obstruction and long-term renal functions

of the glomerulus [30]. It usually takes few weeks of obstruction for significant glomerular changes to be seen histologically. For instance, in rats, UUO led to the congestion of the glomerular capillaries and fusion of the foot processes at some sites within the first few days following UUO but this disappeared shortly afterwards [31]. In addition, starting from the first day following obstruction, a small amount of eosinophilic coagulum consistent with granules and fibrillar material, was seen in the Bowman’s capsule. With longer periods of obstruction, however, significant changes ultimately occur. In a canine model, four weeks of UUO led to a reduction in the number and diameter of the glomeruli [32]. Blocked nephrons eventually atrophy due to disuse and reduced blood flow in addition to the presence of inflammatory changes [30, 31, 33, 34].

Following short periods of UUO, the recovery of the minor histological glomerular changes is relatively rapid. So, in rats, glomeruli looked normal on both light and electron microscopy shortly following reversal of 2-day UUO [31]. This recovery of glomeruli was maintained when the kidney was examined few weeks [28, 35] or even up to 18 months following reversal of short period of UUO (Table 1) [29].

Table 1. Important experimental (Table 1A) and clinical (Table 1B) studies which directly addressed the effect of short periods of reversible unilateral ureteral obstruction on the renal functions in the long-term.

Table 1A: experimental

<table>
<thead>
<tr>
<th>UUO Duration</th>
<th>Follow-up</th>
<th>Species</th>
<th>Main Findings</th>
</tr>
</thead>
</table>
| Bander et al [21] | 24 hours | 60 days | Rat | 1. GFR continued to be normal during follow-up  
2. At 60 days, only 85% of the nephrons were filtering  
3. Persistently low urine osmolality and net acid excretion |
| Ito et al [28] | 72 hours | 28 days | Rat | 1. GFR was normal by 28 days  
2. Persistent dilation of the collecting ducts and distal tubules in addition to the tubular atrophy  
3. Persistent and increased Interstitial fibrosis  
4. Persistent rise in TGFβ-1 up to 28 days |
| Hammad et al [29] | 72 hours | 18 months | Rat | 1. GFR continued to be normal during follow-up  
2. Albuminuria at 18 months post-UUO  
3. Persistent tubular dilatation and atrophy, mononuclear cell infiltration and interstitial fibrosis  
4. Persistently raised gene expression of procollagen-type-1, TGFβ-1, PAI-1, MCP-1 and p53 |

Table 1B: clinical

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Etiology</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucarelli et al [109]</td>
<td>Median 60.8 months</td>
<td>Trauma</td>
</tr>
</tbody>
</table>

UUO: unilateral ureteral obstruction; TGF-1: transforming growth factor-1; PAI-1: plasminogen activator inhibitor-1; MCP-1, monocyte chemoattractant protein-1.

Renal tubular alterations

Alterations in tubular functions following acute unilateral ureteral obstruction

Alterations in tubular functions are very common following UUO and even short periods of obstruction could result in marked and prolonged alterations in tubular functions [21, 35-37]. For instance, the fractional excretion of sodium (FE\textsubscript{Na}) increases immediately following the release of 24-hour UUO in the rat [21, 35, 38]. This is probably due to the reduced absorption ability of the thick ascending loop of Henle causing a fall in medullary tonicity which results in an impairment in the concentrating ability of the POK [39, 40].

The reduced concentrating ability affects also the urine osmolality. So, in rats, the urine osmolality of the POK following 18 hours of UUO, was found to be 400 mOsm/kg compared to more than 1800 mOsm/kg in the contralateral NOK [40]. Similar findings were reported by other researchers [21]. The reabsorption of other electrolytes such as phosphate [41] and the excretion of potassium [21, 42] and hydrogen [21, 43] as well as the net acid excretion [21] were also altered by UUO.
Recovery of tubular functions following reversal of ureteral obstruction

Following the release of short periods of UUO, tubular functions show evidence of some ‘recovery’ if the obstruction is not very prolonged. Although the effect of UUO on tubular functions in the immediate period following reversal has been extensively studied, the long-term effect is far less investigated (Table 1) [21, 29, 36]. In one of the early studies in a 24-hour reversible UUO in the rat, it was shown that the $\text{FE}_{\text{Na}}$ and fractional excretion of potassium of the POK had returned to normal within the first two weeks following UUO reversal and continued to be comparable to the contralateral NOK up to sixty days post-reversal [21]. These findings were consistent with other reports when the renal functions were measured one month post-reversal in a similar model [36] or even at 18 months following 72-hour reversible UUO in the rat [29]. Similar to the $\text{FE}_{\text{Na}}$ and fractional excretion of potassium, urine pH and bicarbonate excretion had also returned to normal 14 days following 24-hour reversible UUO [21]. Nevertheless, the urine osmolality was persistently low at all times up to sixty days post release. The net excretion of acid was also consistently low and this was attributed to a decrease in the absolute excretion of ammonium. These abnormalities were thought to indicate a persistent functional defect in the distal tubular or collecting duct function and/or a loss in the functional juxtaglomerular nephrons. It is unknown if these abnormalities would persist in the long-term or if they return to normal at some stage. Further studies are required to address these points in experimental models.

Albumin leak following relief of UUO: Albuminuria is the earliest marker of glomerular disease as it usually occurs before the impairment in the GFR [44, 45]. Several studies have demonstrated that long periods of UUO result in albuminuria [46-50]. Interestingly, even short periods of reversible UUO were also shown to cause significant albuminuria in the long-term [29]. For instance, in a 72-hour reversible UUO model in the rat, both 24-hour urine albumin and albumin creatinine ratio in the first day post-reversal were significantly higher than the pre-UUO value [29]. Both parameters returned to pre-UUO values when measured one-month post-reversal but increased again at four- and 18-months post-reversal. These changes were associated with histologically normal glomeruli but abnormal tubules at all times post-reversal. According to the authors, this albuminuria could have been due to ultrastructural changes in the glomeruli which were not detected by light microscopy especially if one adopts the traditional view that albuminuria is the result of damage to an essentially impermeable glomerular membrane [51-53]. Alternatively, it could have been caused by the UUO-associated proximal tubular damage and associated impairment in the retrieval and handling of the absorbed albumin molecules [51, 54, 55].

The response of the post-obstructed kidney to various stimuli

Despite the recovery of the GFR following reversal of short periods of UUO (vide supra) [21, 23, 28], the response of the kidney to some stimuli remains alerted. For instance, in a rat model of reversible 24-hour UUO, the GFR returned to basal values when measured 14 days post-reversal. Nevertheless, captopril failed to cause any increase in the GFR and $\text{FE}_{\text{Na}}$ in the POK compared to the expected increase observed in the NOK [23]. Moreover, physiological doses of angiotensin-II led to unexpected increase in both the GFR and $\text{FE}_{\text{Na}}$ in the POK whereas they resulted in significant reductions in these parameters in the NOK. These abnormal responses disappeared spontaneously when assessed at two months following UUO reversal.

There is also evidence to suggest that UUO might also impair the neural responses of the POK. So, in a 24-hour reversible UUO model in the rat, renal nerve stimulation led to an increase in the GFR by 22% in the POK whereas it did not alter the GFR in the NOK kidney [56].

Collectively, these data suggest an abnormal response of the POK to certain physiological, pharmacological and neural stimuli. Although some of these responses return to normal by time it is unknown if this recovery occurs in all abnormalities. Furthermore, the response of the POK to other stimuli has not been studied and further research is required to address this point.
Short periods of unilateral ureteral obstruction and long-term renal functions

Histological features of the renal tubules and interstitium after UUO and recovery after release: Ureteral obstruction leads to significant histopathological changes in the renal tubules and interstitium [30, 31, 34, 57-62]. It results in early dilatation of the tubules predominantly the collecting ducts and distal tubules with subsequent flattening and atrophy of the cells of the proximal tubules and subsequent release of a number of autocrine factors and cytokines [63-70] (vide infra). This in turn, leads to the infiltration of the renal interstitium with inflammatory cells. All these factors accelerate the development of interstitial fibrosis by increasing the production of extracellular matrix, cell infiltration, apoptosis, and accumulation of activated myofibroblasts [28]. These changes result in further tubular dilatation, tubular basement membrane thickening, cell flattening, and cytoplasmic hyalinization [60-62] with ultimate tubular loss.

With release of short periods of UUO, renal tubules show evidence of some initial recovery. So, in a rat model of 2-day reversible UUO, Shimamura and colleagues demonstrated that the collecting ducts dilation had started to decrease on the first day after release. However, this recovery was incomplete and on the third day, the lining of tubular epithelial cells, which were flat on the second day post-reversal, became swollen and projected into the lumen. From the fourth to seventh day, there were persistent focal areas of collecting ducts dilation [31].

In a longer follow-up after reversal of 3-day UUO in the rat, Ito et al demonstrated a persistent dilation of the collecting ducts and distal tubules in addition to the tubular atrophy, which gradually increased throughout the 28 days period of follow-up despite the preservation of glomeruli [28]. In the immediate post-release period, these tubular changes were associated with an increase in the number of macrophages, which decreased by 14 days but surprisingly, increased again at 28 days. Interstitial fibrosis was not immediately seen after release but started to appear on day 7 and this has increased by 28 days post-reversal.

In a rat model of 3-day reversible UUO, the kidney was examined up to 18 months following release of the obstruction [29]. Significant tubular dilation and atrophy were observed even at one-month post-release. The extent of these tubular changes improved at four months, but surprisingly, they deteriorated again when assessed at 18 months despite the normal glomerular histology (Figure 1). The extent of mononuclear cell infiltration in the POK, which was significantly more severe than the NOK at one-month post-release, had gradually improved until 18 months, albeit it was still significantly more severe compared to the NOK. Similar trend was observed with interstitial fibrosis, the extent of which was significant at one month. This was followed by some improvement although it was still more severe than the NOK at 18 months. This was associated with a persistently raised gene expression of procollagen-type-1. These data indicate the presence of ongoing tubulointerstitial abnormalities despite the fact that some of these abnormalities might show transient

Figure 1. The scoring of various histological features in the post-obstructed kidney (POK) one (G-1), four (G-2) and eighteen (G-3) months following the release of 3-day unilateral ureteral obstruction in the rat; *Statistical significance between groups (Reproduced with permission from reference #29).
improvement few weeks following the release of obstruction.

The predominance of tubular changes in the UUO in contrast to the interstitial changes observed in other models of chronic kidney disease is probably due to the differences in the mechanism of injury in these models. In UUO, several factors contribute to the tubular atrophy and dilatation. Firstly, the rise in tubular pressure causes mechanical stretching and flattening of the tubules [71] and leads to cell injury and apoptosis probably due to caspase-dependent mechanism associated with the oxidative stress injury [72, 73]. Secondly, the initial vasoconstriction generates a hypoxic environment leading to tubular cell death [74]. Thirdly, the interstitial fibrosis and accumulation of the extracellular matrix can further deprive the tubules from adequate blood supply. Lastly, the proteinuria and albuminuria might also lead to tubular toxicity and damage due to the increased lysosomal activity in tubular cells [75]. The last three factors which potentially lead to tubular atrophy, are present in almost all types of chronic kidney disease. However, the backpressure and tubular stretching is peculiar to this model indicating that different mechanisms of kidney injury might lead to different long-term outcomes as previously suggested by some authors [76].

Despite the presence of tubular changes, none of the experimental studies had shown a deterioration of the GFR in the long-term after return to normal following release of short periods of UUO in adult animals. This could be due to the lack of very long-term follow-up in experimental models (maximum follow-up of 18 months in a rat model [29]). There are several reasons to suggest a possible long-term deterioration in the GFR. In several other renal conditions, the presence of interstitial fibrosis has been shown to be associated with GFR deterioration in the long-term [77, 78]. Interstitial fibrosis causes tubular atrophy, tubular ischemia, and ultimately obliteration of the postglomerular peritubular capillaries which would affect glomerular filtration [77, 79-81]. Moreover, the deterioration in renal tubular histological features observed following short periods of UUO in addition to the alterations in the pro-inflammatory, pro-fibrotic and pro-apoptotic mediators might also contribute to the possible deterioration of the GFR in the long-term.

The role of pro-inflammatory cytokines and chemokines in the tubule interstitial fibrosis following UUO reversal

Urteral obstruction results in the release and activation of several cytokines and chemokines [16, 18, 28, 29, 35, 38, 64, 67-69]. For instance, reactive oxygen species [82, 83], tumor necrosis factor alpha (TNF-α) [35, 82, 84] and the apoptotic p53 gene [35, 38, 85] were shown to be involved in the cell injury, apoptosis and proliferation of tubular cells following UUO. Factors such as the monocyte chemotactic protein-1 (MCP-1) [86], interleukin 1 beta (IL-1β) [87] and platelet activator inhibitor [66] have also been associated with the UUO-related interstitial inflammation. Renin-angiotensin system [38, 88-91] and transforming growth factor beta-1 (TGFβ-1) [35, 65, 92, 93] are among the factors which were linked to the fibroblast proliferation.

These agents and cytokines also play an important role in the recovery following UUO reversal. In a 3-day reversible UUO in the rat, it was demonstrated that the tissue level of TGFβ-1 in the POK was significantly higher than the basal value and continued to rise up to 28 days post-reversal even when the GFR and FE\textsubscript{Na} had returned to basal values [28]. This was associated with an increase in the interstitial fibrosis and tubular apoptosis. In addition, Western blot and immunohistochemistry confirmed the increased expression of both iNOS and eNOS in the POK suggesting an increase in the synthesis of NO which indicated an attempt by the kidney to oppose the action of TGFβ-1 in the recovery period.

In a similar 3-day reversible UUO in the rat, the gene expressions of several cytokines at four months were significantly lower than the values seen at one-month post-reversal [29]. These include TNF-α, TGFβ-1, plasminogen activator inhibitor-1 (PAI-1), MCP-1 and p53 gene. Surprisingly, these factors remained altered or even significantly increased again when measured at 18 months following the UUO reversal i.e., longtime after all renal functions and sodium excretion had returned to normal. As discussed previously, this was associated with deterioration in tubular dilation and atrophy indicating an ongoing inflammatory and fibrotic process long after the release of UUO.
Clinical data which indicates a deterioration in renal functions following short periods of UUO

In clinical practice, UO is caused by several conditions such as urinary stones, ureteric tumors, and ureteric injury. Urolithiasis is a common disease worldwide and the relationship between urolithiasis and long-term renal disease is well established [94-101]. In a Canadian population-based epidemiological study of more than 3 million adults and a median follow-up of 11 years, it was shown that a history of one or more stone episodes was associated with an increased risk of chronic kidney disease [94]. In another population-based cohort study with over 25 years of follow-up from Olmsted County, it was demonstrated that stone formers were at 2.1-fold higher risk of developing end-stage renal disease independent of the baseline renal functions and other cardiovascular risk factors [102]. The mechanism of renal dysfunction in urinary stone disease is multifactorial. In addition to causing ureteric obstruction, renal stones are associated with urinary tract infections and inflammatory changes [103]. Patients with urolithiasis are also more likely to have frequent exposure to nephrotoxic analgesics. Furthermore, urolithiasis share several common factors with chronic kidney disease such as low water intake, high protein diet [104] and urinary tract abnormalities [105]. Therefore, the mere finding of an association between urolithiasis and renal dysfunction might not indicate a strong clinical correlation between ureteric obstruction and chronic kidney disease and this can only be demonstrated by studying patients with ureteric obstruction due to causes other than urolithiasis.

The association between long-term renal impairment and obstructive uropathy regardless of the etiology has been well-established by several epidemiological studies [106-108]. For instance, Kaufman and colleagues demonstrated that urinary obstruction had accounted for 17% of the community-acquired acute kidney injury [106]. Similarly, 10% of the community-acquired acute kidney injury in a Spanish study, were shown to be due to obstructive uropathy [107]. Despite the establishment of the association between renal impairment and urinary obstruction, the majority of these studies did not specifically differentiate between bilateral and unilateral urinary obstruction as the majority of these patients had bilateral obstruction due to bladder outlet obstruction [106-108]. In addition, the exact duration of obstruction and whether it is partial or complete was not precisely defined due to the inherent difficulties in determining these issues in humans.

These concerns were addressed by the study of Lucarelli and colleagues (Table 1) who evaluated the long-term (median 60.8 months) renal functions following iatrogenic renal injury caused by ureteric obstruction [109]. Using multivariable logistic regression, it was shown that the time elapsed before the relief of obstruction was the only significant predictor of the outcome. So, if the obstruction was relieved in less than two weeks, the probability of developing long-term renal damage was significantly less than if the release was delayed for more than two weeks.

The observed discrepancy between humans and experimental animals regarding the duration of UUO which results in long-term renal impairment is due to the fact that different species have different time scale regarding their biological responses to various stimuli. In this regard, it has been estimated that one day of rat’s life might be equivalent to several days of human life in terms of biological changes [63, 110, 111].

Despite the presence of several clinical studies which have addressed the long-term renal functions in patients with history of urinary stones episodes and in patients with bilateral ureteric obstruction which is usually caused by bladder outlet obstruction, the clinical studies which specifically investigated the effect of short periods of UUO on long-term renal functions are rare and further studies are required to determine the exact duration of UUO which leads to long-term renal consequences. In the patient with unilateral ureteral colic due to an obstructing ureteral stone, there are still no clear clinical guidelines on the best time for surgical intervention to release the ureteral obstruction. So, despite indicating that two weeks of UUO might be the critical time after which there might be a significant increase in the probability of having long-term renal impairment, the study of Lucarelli et al had a median follow-up of only 60.8 months (vide supra)
by extrapolating the data from experimental animals, this duration of follow-up might not be sufficient to show long-term renal alterations. Furthermore, the study did not address the renal histological changes which will be extremely difficult to perform in humans. Moreover, a good percentage of ureteral stone episodes in humans results in partial UUO which obviously has less impact on renal functions compared to complete UO. Certainly, there is a need for further studies which also provide the risk benefit analysis in patients with UO due to ureteric stones to compare between the benefits and risks of early versus delayed surgical intervention which is associated with potential risk of long-term renal impairment. Such studies might be difficult to perform in humans due to difficulty in determining the exact time of onset of UUO and whether it is complete or partial. Other confounding factors such as the status of the baseline renal functions and the presence of other comorbidities and medications which might also affect renal response to UUO, need to be taken into consideration. Until that time when these data are available in humans, these patients must be thoroughly counselled about the known risks and benefits of early surgical intervention which would decrease the risk of long-term effects of UUO on renal functions. Moreover, these patients might also require long-term monitoring of renal functions despite the apparent initial recovery in the clinical parameters. This is particularly important in patients with underlying primary or secondary renal diseases.

**Conclusions**

The available experimental and clinical data, despite their rarity, strongly indicate that short periods of unilateral ureteral obstruction in adults might lead to long-term renal dysfunction. Studies in experimental animals have shown that periods as short as 24-72 hours of unilateral ureteral obstruction, had led to long-term renal dysfunction such as the impairment in the ability to concentrate urine, urinary albumin leakage, tubulointerstitial fibrosis and alterations in pro-inflammatory, pro-fibrotic and pro-apoptotic markers as well as the impairment in the response of the previously obstructed kidney to various stimuli. In humans, two weeks of unilateral ureteral obstruction led to long-term renal impairment. These findings might change our current clinical practice in relation to the best time to intervene in patients with acute onset of unilateral ureteral obstruction such as those with obstructing ureteral calculi. Moreover, these patients might also require long-term monitoring of renal functions despite the apparent initial recovery after the release of obstruction. This is particularly important in patients with underlying primary or secondary renal diseases.

**Disclosure of conflict of interest**

None.

**Abbreviations**

UUO, Unilateral ureteral obstruction; RBF, renal blood flow; GFR, glomerular filtration rate; POK, post-obstructed kidney; NOK, non-obstructed kidney; FE$_{Na}$, fractional excretion of sodium.

**Address correspondence to:** Dr. Fayez T Hammad, Department of Surgery, College of Medicine & Health Sciences, PO Box 17666, Al Ain, United Arab Emirates. Tel: +00971-50-4880021; +00971-3-7137-590; Fax: +00971-3-7672067; E-mail: fayezhammad@hotmail.com; fayezh@uaeu.ac.ae

**References**


[7] Gulmi FA, Matthews GJ, Marion D, von Lutterotti N and Vaughan ED. Volume expansion enhances the recovery of renal function and pro-
Short periods of unilateral ureteral obstruction and long-term renal functions


Short periods of unilateral ureteral obstruction and long-term renal functions


Short periods of unilateral ureteral obstruction and long-term renal functions


[84] Hammad FT and Lubbad L. The effect of epigallocatechin-3-gallate on the renal dysfunc-
Short periods of unilateral ureteral obstruction and long-term renal functions


Short periods of unilateral ureteral obstruction and long-term renal functions

[107] Liaño F and Pascual J. Epidemiology of acute renal failure: a prospective, multicenter, comm-
818.

[108] Organ M and Norman RW. Acute reversible kidney injury secondary to bilateral ureteric ob-

[109] Lucarelli G, Ditonno P, Betocchi C, Grandalia-
no G, Gesualdo L, Selvaggi FP and Battaglia M. De-
layed relief of ureteral obstruction is implicated in the long-term development of renal
189: 960-965.

[110] Andreollo NA, Santos EF, Araujo MR and Lopes
LR. Rat’s age versus human’s age: what is the relationship? Arq Bras Cir Dig 2012; 25: 49-
51.

630.