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Does relative renal function improve after intervention for chronic ureteric obstruction?

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Introduction Unilateral renal function often deteriorates with chronic ureteric obstruction. Our objectives were to determine the change in relative renal function (RRF) by MAG3 renography after intervention for ureteric obstruction, and to identify clinical/epidemiological factors which influence long-term outcomes.

Material and methods We identified 228 patients from 2006 to 2017 who underwent MAG3 renography before and after intervention for unilateral ureteric obstruction. Patients were grouped into categories preoperatively- with normal RRF (43–57%) through mild (29–42%), moderate (15–28%) and severe (<15%) impairment of RRF. Patient demographics, types of obstructive uropathy and intervention employed were analysed. Each group was assessed for the absolute change in RRF and change in RRF category postoperatively.

Results The mean patient age was 50.4 years (SD 16.7), and 62.3% were female. Overall, the mean pre- and post-intervention RRF of the obstructed kidney did not differ significantly (32.30% vs. 32.20%, P = 0.835). Most patients remained in their preoperative RRF group: 85.9% of normal, 67.4% of mild, 64.4% of moderate and 73.3% of patients with severe RRF impairment did not change category. Patients with mildly impaired preoperative RRF showed a significant worsening postoperatively (36.37% vs. 34.58%, P = 0.024). The other three groups showed no significant change in RRF following intervention.

Multivariate logistic regression analysis showed no statistically significant association between type of intervention, age, gender or diagnosis and improvement in postoperative RRF category.

Conclusions Our results show that RRF does not improve significantly after intervention for ureteric obstruction. The aim should therefore be to maintain existing renal function and relieve symptoms.

Key Words: renal function ‹› obstruction ‹› MAG3 ‹› relative ‹› improvement

INTRODUCTION

Unilateral renal function often deteriorates with chronic obstructive uropathies. Common aetiologies of unilateral obstruction include ureteric stones, ureteropelvic junction (UPJ) obstruction, ureteric strictures and extrinsic ureteric compression (such as ureteric obstruction in malignancy).

Early animal studies have shown that unilateral ureteric obstruction can cause morphological damage or loss of kidney function [1–6]. These effects are amplified and often irreversible in chronic obstructive uropathies as compared to acute pathologies [6]. A porcine study by Kelleher et al. demonstrated increased scarring, persistently raised upper urinary tract pressures and poorer vascular filling in chroni-

cally obstructed kidneys compared to acutely obstructed kidneys [2].

Several reports in the literature studying the recoverability of unilateral renal function in the affected kidney after relief of obstruction have produced varying results [7–13]. For example, a recent study by Wu et al. found no significant post-operative improvement in relative renal function [13]. This is in contrast to studies analysing paediatric patients, whose renal function had a greater chance of improving postoperatively [7, 9]. The recoverability or stabilisation of existing renal function is dependent on several demographic and clinical factors, but the extent and significance of their effects are subjects of debate [11]. A greater understanding of how patient demographics, pathology and types of intervention affect patient outcomes would be very beneficial to both clinicians and patients.

Technetium-99m mercapto acetyl triglycine (MAG3) renography effectively measures relative renal function (RRF) (Figure 1). Some studies studying paediatric urology patients using this renographic technique have shown that RRF does improve after intervention [9, 14, 15]. Conversely, other reports argue that the timing of diagnosis (prenatal vs. postnatal) and intervention may affect the degree of improvement in RRF postoperatively [16, 17]. Studies examining adult populations have found that RRF does not improve postoperatively, with differing conclusions with regard to the effect of pre-operative RRF on postoperative outcomes [18, 10, 13].

As with any surgical intervention, renal surgery carries significant risks. Therefore, it is important for both clinicians and patients to understand what the desired outcomes of interventions are – quantitative improvement of RRF vs. relief of symptoms and stabilisation of existing renal function. Hence, our objectives are to determine the change in RRF after intervention for obstructive uropathies, as well as to identify clinical/epidemiological factors which influence long-term outcomes.

MATERIAL AND METHODS

We conducted a single-institution retrospective review of patients with unilateral ureteric obstruction, comparing MAG3 results before and after intervention over an 11-year period.

Medical record numbers for all patients who underwent MAG3 renograms at the Nuclear Medicine Department at University College Hospital from 1 December 2006 to 31 December 2017 were collected and were then cross-referenced to those on the patient list of the Endourology & Stone Unit at Uni-

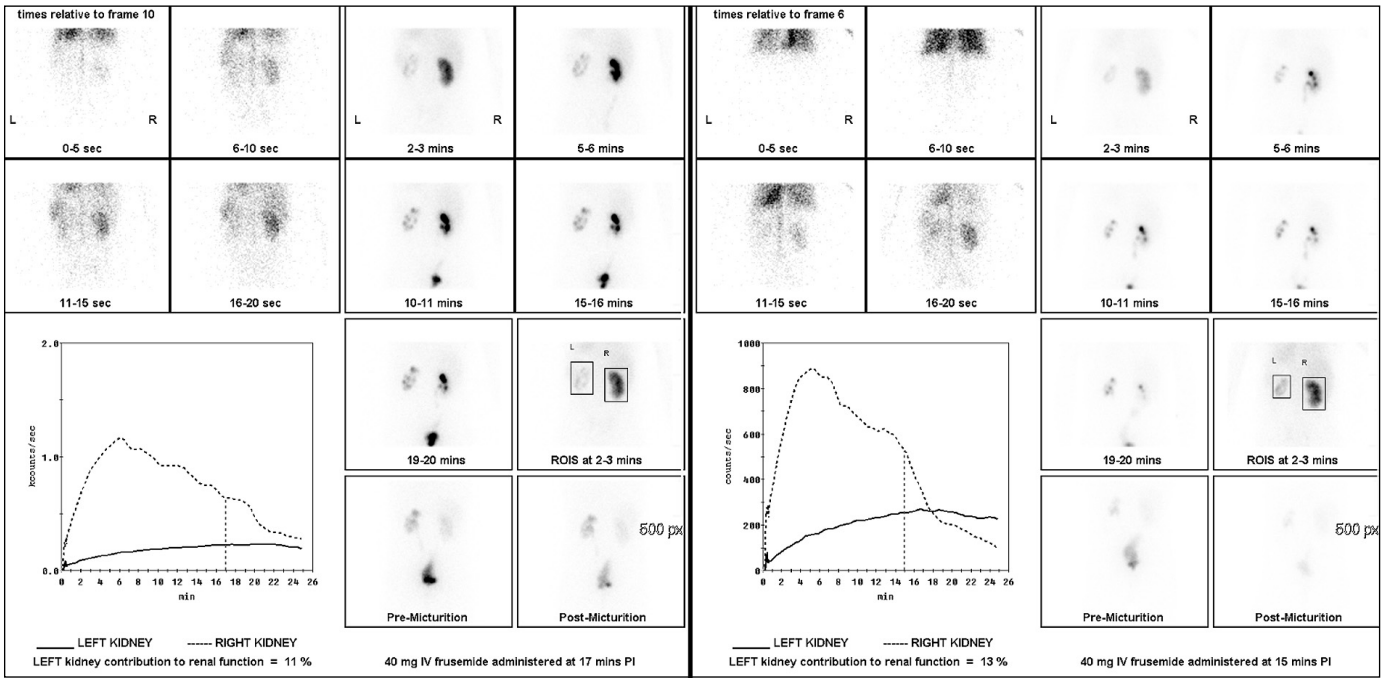

Figure 1. *MAG3 renograms in a patient with a background of ketamine bladder with cystectomy and ileocolic neobladder. The image on the left is the initial MAG3 renogram which showed a scarred left kidney with reduced function and 'sluggish' drainage pattern with a normal functioning and draining right kidney. The image on the right is a repeat renogram at 26 months demonstrating ongoing poor function of the left kidney with no significant change in its relative renal function despite interim relief of obstruction by ureteric reimplantation.*

versity College Hospital. A total of 659 patients were identified. Patients who only received one MAG3 renogram throughout their clinical course were excluded. Patients who had a solitary kidney at the time of MAG renogram were also excluded. Patients who did not undergo any intervention were excluded. All renograms were reviewed visually and reported as showing signs of obstruction by consultants in radiology and nuclear medicine based at University College Hospital Institute of Nuclear Medicine. All patients were obstructed preoperatively. Chronic ureteric obstruction was defined as obstruction of 6 weeks or more.

Outcomes then harvested from patient data were as follows: (1) the time intervals between the initial MAG3 renogram, any surgical intervention and follow-up MAG3 renography; (2) the degree of improvement/decline in RRF after intervention (other than nephrectomy) up to November 2018. We also collected data on patient demographics, aetiology of obstruction and type of intervention performed.

Taylor et al. have determined that a minimum 7% change in RRF is required to validate clinical significance because of the inherent variability of renal scintigraphy [19]. Allowing for inherent variability of scintigraphic renography, a normal renal unit would therefore contribute a minimum RRF if 43% and a maximum of 57%. We therefore stratified patients approximately into quartiles according to the severity of loss of renal function as normal (43–57%), mild loss of function (42–29%), moderate loss of function (28–15%) and severe (<15%) impairment of RRF.

Since patients with a low preoperative RRF would have a greater numerical potential for improvement in RRF postoperatively compared to patients with higher preoperative relative function, change in RRF was modelled using the following equation:

Log transformation: Log-transformed RRF = ln (57) − ln (57 − RRF)

This is to account for renal function potentially improving towards an asymptote of 57% post-intervention. Preoperative and postoperative RRF were compared, and the type of procedure performed noted. Procedures included pyeloplasty, ureteric stent placement, stone removal surgery and others listed in Table 1.

Continuous variables were analysed using student's t-tests, using paired t-tests for comparisons of variables in the same patient, and unpaired t-tests for comparisons between patients. Pearson's correlation was used to assess correlation where variables followed a normal distribution, and Spearman's rank where variables did not. Linear regression analyses and Spearman's rank correlation of log-transformed RRF were used to analyse pre-operative and post-operative RRF. One-way ANOVA analyses were carried out when comparing change in log-transformed RRF between different types of pathologies and interventions. Multiple linear regression analyses were used to study the relationship between continuous variables and the improvement in postoperative RRF category, while ordinal logistic regression was used to study the effect of categorical variables. P values were two-tailed for t-tests and Pearson's correlation, and one-tailed for other tests, and a value of <0.05 was considered to represent statistical significance.

Table 1. *Patient demographics, type of obstructive uropathy and intervention received*

	N	Marginal percentage
Gender		
Female	142	62.3%
Male	86	37.7%
Age		
Less than 50	112	49.1%
50 and above	116	50.9%
Pathology		
Stone disease	54	23.7%
Iatrogenic	31	13.6%
Oncological obstruction/effects	31	13.6%
UPJ obstruction	26	11.4%
Non-iatrogenic ureteric stricture	24	10.5%
Endometriosis	16	7.0%
Other congenital abnormalities	16	7.0%
Spina bifida/neurogenic bladder	15	6.6%
Other extrinsic compression	7	3.1%
Other e.g. hydronephrosis of pregnancy	6	2.6%
Metabolic/chronic inflammatory disease	2	0.9%
Type of intervention		
Ureteric stent placement	86	37.7%
Stone removal surgery	49	21.5%
Reconstructive surgery	27	11.8%
Endopyelotomy	18	7.9%
Ureteric reimplantation	8	3.5%
Pyeloplasty	7	3.1%
Chemotherapy/bladder tumour resection	6	2.6%
SWL	6	2.6%
Nephrostomy	6	2.6%
Ureterotomy	4	1.8%
Endometrial ablation/surgery	3	1.3%
Ureteric/urethral dilatation	3	1.3%
Conservative interventions	2	0.9%
TURP	2	0.9%
Incontinence surgery	1	0.4%

SWL – shock wave lithotripsy; TURP – transurethral resection of the prostate; UPJ – ureteropelvic junction

RESULTS

A total of 228 patients met the inclusion criteria, as shown in Figure 2. Their mean age (SD) was 50.4 years (16.7), 62.3% (142/228) were female and 50.9% (116/228) were above 50 years old. Age of patients ranged from 18 to 84 years old. Mean overall

follow-up interval was 25.7 months (median = 25.1). Types of obstructive uropathy and intervention performed are detailed in Table 1.

Overall, the mean pre- and postoperative RRF [SD] did not differ significantly (32.30 [13.5]% vs. 32.20 [14.1]%, P = 0.835). Patients with mildly impaired preoperative RRF showed a statistically significant worsening postoperatively (36.37 [3.77]% vs. 34.58 [8.21]%, P = 0.024) (Table 2), although the small magnitude this represents may not be clinically relevant. The other three groups (normal RRF [46.6 vs. 46.2%, P = 0.53], moderate impairment [21.71 vs. 23.29%, P = 0.27], severe impairment [8.45 vs. 11.06%, P = 0.09]) showed no significant change in RRF postoperatively, as shown in Figure 3.

Consistent with this, most patients remained in their preoperative RRF group: 85.9% of normal, 67.4% of mild, 64.4% of moderate and 73.3% of patients with severe RRF loss remained in those respective categories. Indeed, overall, 96.9% of patients either remained in their preoperative group, or improved/deteriorated by just one category, representing a large majority of patients who did not undergo a clinically significant change postoperatively (Table 3).

Simple linear regression was carried out to investigate the relationship between log-transformed pre- and postoperative RRF (Figure 4). These data were significantly positively correlated (R2 = 0.6737, P <0.001) and this was confirmed with a Spearman's rank correlation co-efficient (rS) of 0.874 (P <0.001), indicating a strong positive correlation between log-transformed pre- and postoperative RRF.

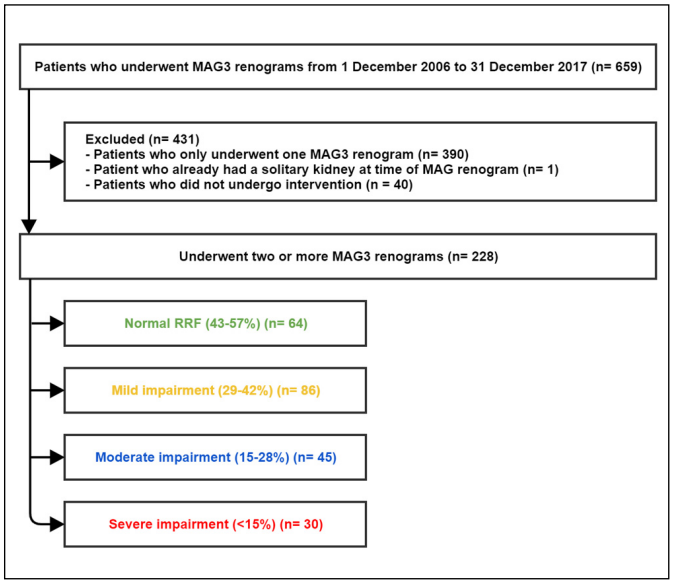

Figure 2. *Flow chart detailing inclusion and exclusion of patients.*

RRF – relative renal function

Table 2. *Relative renal function RRF before and after intervention, stratified by preoperative RRF*

Preoperative RRF category	N	Mean preoperative RRF (%)	Mean postoperative RRF (%)	P value of difference (2-tailed)
Normal RRF (43–57%)	64	46.6	46.2	0.53
Mild impairment (29–42%)	86	36.4	34.6	0.03
Moderate impairment (15–28%)	45	21.7	23.3	0.27
Severe impairment (<15%)	30	8.45	11.06	0.09

RRF – relative renal function

Table 3. *Degree of improvement in RRF category post-intervention*

Degree of improvement	N	Percentage	
Improved by two categories	2	0.9%	
Improved by one category	28	12.3%	
Remained in original category	167	73.2%	96.9%
Deteriorated by one category	26	11.4%	
Deteriorated by two categories	5	2.2%	

RRF – relative renal function

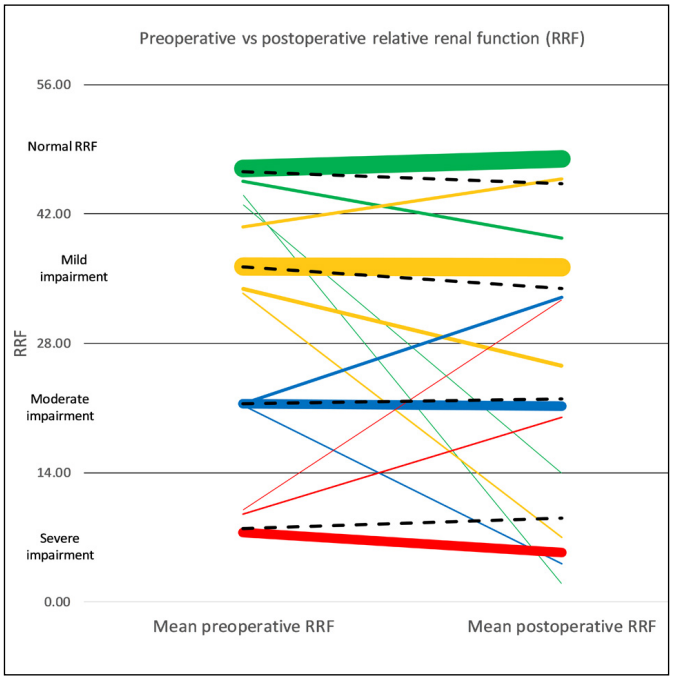

Figure 3. *Mean preoperative vs postoperative RRF stratified into categories; widths of lines are proportional to number of patients. Dotted lines show the overall trend within each category.*

RRF – relative renal function

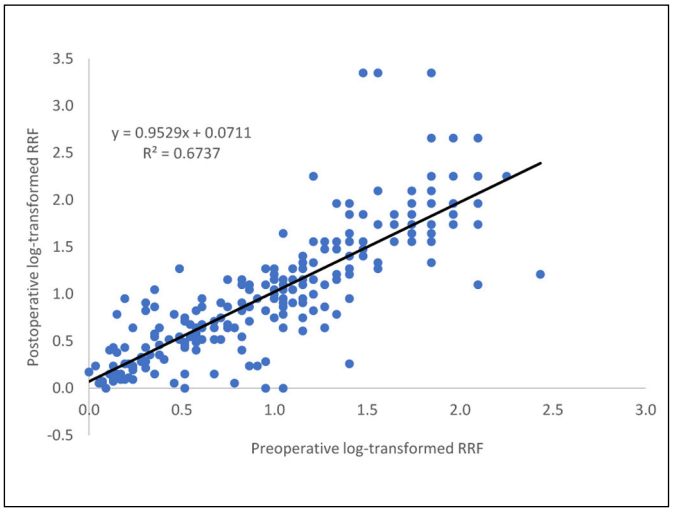

Figure 4. *Preoperative vs. postoperative log-transformed RRF linear regression analysis.*

RRF – relative renal function

Log-transformed RRF [SD] similarly did not differ significantly before and after intervention (0.99 [0.58] vs. 1.01 [0.65], P = 0.32). When patients were stratified by preoperative RRF, (normal RRF, mild impairment, moderate impairment, severe impairment) no group showed significant improvement in log-transformed RRF postoperatively (P = 0.484, 0.286, 0.087 and 0.062).

The age of the patient was not significantly correlated to improvement in log-transformed RRF post-intervention (P = 0.71). There was also no significant difference in improvement in log-transformed RRF post-intervention between male and female patients (P = 0.50). Neither the preoperative interval nor the postoperative follow-up interval was significantly correlated to change in log-transformed RRF (P = 0.83 and 0.21 respectively).

Improvement in log-transformed RRF did not differ significantly between different types of pathologies (F (10, 217) = 0.732, P = 0.694). There was also no significant difference in log-transformed RRF change between all types of interventions studied (F (14, 213) = 0.796, P = 0.673).

Using multivariate ordinal logistic regression analysis, we found no statistically significant association between type of intervention, age, gender or diagnosis and improvement in post-operative RRF category.

Examining the subset of patients who presented with malignant obstruction (n = 33), the mean pre- and postoperative RRF (SD) of cancer patients did not differ significantly (21.48 [11.2]% vs. 19.18 [9.85]%, P = 0.194). The majority of cancer patients (18/33; 54.5%) remained in their original RRF category (Table 4).

Log-transformed RRF [SD] similarly did not differ significantly before and after intervention (0.65 [0.44] vs. 0.53 [0.32], P = 0.11). Multivariate ordinal logistic regression analysis showed no significant association between age, gender or type of intervention and improvement in post-operative RRF category within the subset of patients with cancer of any type.

DISCUSSION

To our knowledge, this study represents the largest retrospective study of RRF change postoperatively in patients with unilateral obstructive uropathies.

A brief summary of our findings are as follows:

1) Intervention does not confer statistically significant improvement in postoperative RRF
2) Patients with mildly impaired preoperative RRF showed a statistically significant worsening postoperatively
3) 96.9% of patients either remained in their preoperative RRF group postoperatively, or improved/deteriorated by one category
4) Log-transformed RRF similarly did not differ significantly before and after intervention

Vannahme et al. compared the outcomes between secondary pyeloplasty and endopyelotomy in 58 patients with failed primary intervention for UPJ obstruction; reported a 96% resolution on MAG3 renography for the former and 74% for the latter procedure. However, no clear criteria for radiological improvement were given [12]. In our study, in line with Taylor et al., we have defined an improvement in RRF to be an increase of >7% due to the inherent variability of renal scintigraphy [19].

A 2008 review of 36 studies by Castagnetti et al., which focussed on pyeloplasty for UPJ in paediatric patients, found that chance of improvement in RRF was greater in patients with moderately rather than severely impaired preoperative function [7]. This finding was reiterated by Harraz et al., who reported that RRF improves after pyeloplasty in children [9]. This contrasts with our findings which show that no groups show significant postoperative improvement in RRF. However, the various studies had different stratifications for preoperative RRF groups and the authors of the review considered a 5% change in RRF to be significant, while we used 7% in our study instead [7,9]. Patient populations studied were also vastly different - the mean age of patients in the review was 5.5 years, compared to 50.4 years in our study.

Ortapamuk et al. similarly reported that mean RRF did not improve after pyeloplasty in their study of 32 adults [10]. However, interestingly, the authors found that RRF showed a significant postop-

erative improvement after stratifying patients into two groups – one with preoperative RRF of ≥30% and the other with <30%. This contrasts with our findings which show no significant postoperative improvements between all groups, except those with mild impairment, which conversely showed a significant deterioration in postoperative RRF.

In Gulur and co-author's study of 23 adults whose UPJ obstruction was managed conservatively, they found that the mean RRF decreased marginally after a mean follow-up period of 47.7 months [8]. In our study, patients who received conservative management showed a slight improvement in their follow-up RRF category, although this was not statistically significant. This however could be due to selection bias, as patients who receive conservative management strategies often have milder pathologies.

Wu et al., who also studied an adult population of 85 patients with multiple aetiologies of obstruction, found no significant postoperative improvement in RRF, even when stratified by preoperative RRF [13]. In contrast to their findings, ours show that patients with mild impairment show a significant worsening in RRF postoperatively. Our study did, however, share the finding that log-transformed preoperative and postoperative RRF values did not correlate linearly [13].

There are several confounding factors which could have affected this present study. Firstly, using MAG3 renography as a measure of RRF assumes that the contralateral kidney has remained unaffected throughout the clinical course. This is an inherent disadvantage of MAG3 scans, hence a composite equation involving estimated glomerular filtration rate (eGFR) or creatinine clearance and MAG3 results could be the focus of future studies. Finally, as this is a retrospective study, unknown factors could have affected the analysis.

CONCLUSIONS

Overall, relative renal function does not change significantly after intervention, except in patients with mildly impaired RRF preoperatively, whose RRF deteriorated post-operatively. There was no association found between types of intervention, diagnosis, age or gender and the recoverability of relative renal function postoperatively. The aim of intervention should therefore be maintaining existing renal function and relieving symptoms, in which regard the pros and cons of nephrostomy versus stent drainage should be discussed. The broad lines in Figure 3 (i.e. proportional to the number of patients in each category) showed that patients with normal relative function have their relative function maintained whereas the majority of patients with moderate and severe loss of RRF continue to decline despite intervention to improve drainage, presumably due to the irreversible insult to their glomerular function that chronic obstruction has caused.

This is important for patient counselling and establishing appropriate expectation following intervention to improve ureteric drainage in patients with established loss of relative function due to obstructive uropathy. This might be an important factor to consider in treatment strategy in general, and particularly in patients with malignant extrinsic obstruction, where quality of life is as important a factor as any hoped-for improvement in renal function.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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