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Retrospective Cohort Study

Long term outcomes of Cohen's cross trigonal reimplantation for primary vesicoureteral reflux in poorly functioning kidney

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Abstract

BACKGROUND

Open ureteric reimplantation by cross trigonal technique described by Cohen is considered a common surgical option for correction of vesicoureteral reflux (VUR). There is a lack of evidence in literature though for what happens to such kidneys, in the long run, particularly those which are poorly functioning.

AIM

To assess the long-term outcomes of ureteric reimplantation in poorly functioning kidneys in children with unilateral primary VUR.

METHODS

Children with unilateral primary VUR and a relative renal function of less than 35% who underwent open or laparoscopic ureteric reimplantation between January 2005 and January 2017 were included in the study. Patients who had a follow up of less than five years were excluded. Preoperative evaluation consisted of a voiding cystourethrogram and Dimercaptosuccinic acid (DMSA) scan. In the follow-up period, patients underwent a diuretic scan at 6 weeks and 6 months. Follow up ultrasound was done for change in

grade of hydronephrosis and retrovesical ureteric diameter. Subsequent follow up was done at 6 monthly intervals with evaluation for proteinuria and hypertension and any recurrent urinary tract infection (UTI). For assessment of cortical function, DMSA was repeated annually for 5 years after surgery. A paired-samples *t*-test was used to test the mean difference of DMSA between pre-post observations.

RESULTS

During this period, 36 children underwent ureteric reimplantation for unilateral primary VUR. After excluding those with insufficient follow-up, 31 were included in the analysis. Most of the patients were males (n = 26/31, 83.8%). Patient's age (mean ± SD, range) was 5.21 ± 3.71, 1-18 years. The grades of VUR were grade II (1 patient), grade III (8 patients), grade IV (10 patients), and grade V (12 patients). The pre and postoperative DMSA was 24.064 ± 12.02 and 24.06 ± 10.93, which was almost the same (statistically equal, paired-samples *t*-test: P = 0.873). The median (range) follow-up duration was 82 (60-120) mo. One patient had persistent reflux after surgery (preoperative: grade IV, postoperative: grade III), and the very same patient developed recurrent UTI. The difference in the preoperative and postoperative DRF was less than 10% in 29 patients. In one patient, the DRF decreased by 17% (22% to 05%) while in another patient, the DRF increased by 12% (25% to 37%) after surgery. None of the patients had an increase in scarring after surgery. 15% of patients were hypertensive before surgery and all of them continued to be hypertensive after surgery while none developed hypertension after surgery. None of the patients had significant proteinuria (> 150 mg/d) during the follow-up period.

CONCLUSION

Children with unilateral primary VUR and poorly functioning kidney maintain the renal function over the long term in most cases. Hypertension and proteinuria do not progress over time in these patients.

INTRODUCTION

Vesicoureteral reflux (VUR) is defined as the retrograde flow of urine from the bladder to the upper urinary tracts[1]. Its clinical challenges arise from the fact that it is usually asymptomatic and even in asymptomatic cases it is responsible for pyelonephritic scarring and can be associated with congenital renal dysmorphism. In most cases, VUR resolve spontaneously; 20% to 30% will have further infections, and few of them will experience long-term sequelae like renal scarring[2]. Extensive renal scarring decreases renal function and can result in renal insufficiency, hypertension, or end-stage renal disease[3]. A dilemma exists whether to opt for nephrectomy or ureteric reimplantation for the poorly functional kidney. Open ureteric reimplantation by cross trigonal technique described by Cohen is amongst the most common options for surgical correction of VUR, but there is a dearth of evidence in the literature for what happens to such kidneys, in the long run, particularly those which are poorly functioning. We at our institute conducted a retrospective study to assess the long-term outcomes of unilateral ureteric reimplantation in poorly functioning kidneys in children with unilateral primary VUR. The primary objective of our study was to determine if a kidney with significant unilateral reflux nephropathy maintains relative renal function after ureteric reimplantation on long term follow up (5 years or more).

MATERIALS AND METHODS

We retrospectively reviewed data of 168 patients who underwent ureteric reimplantation from 2003-2019. Children with unilateral primary VUR and a relative renal function of less than 35% who underwent open or laparoscopic ureteric reimplantation between January 2005 and December 2017 were included in the study. Patients who had a follow up of less than five years, patients older than 18 years, having a neurogenic bladder, posterior urethral valves, bladder exstrophy and bilateral VUR were excluded. Data was collected by two independent researchers to minimize bias. Preoperative evaluation consisted of a voiding cystourethrogram and

Dimercaptosuccinic acid (DMSA) scan, EC scan, and S. Creatinine. In the follow-up period, patients underwent an EC scan at 6 wk and 6 mo. Ultrasounds for hydronephrosis and retrovesical ureteral diameter were done at 6 mo interval. Subsequent follow up was done at 6-monthly intervals with evaluation for proteinuria and hypertension. For assessment of cortical function, DMSA was repeated 1 year after surgery and annually thereafter. A paired-samples *t*-test was used to test the mean difference between pre-post observations. Only the patients with complete data records and regular follow up were included in the study.

RESULTS

During this period, 36 children underwent ureteric reimplantation for unilateral primary VUR. After excluding those with insufficient follow-up (*i.e.* follow up less than 5 years), 31 were included in the analysis. Most of the patients were males (n = 26/31, 83.8%). Patient's age (mean ± SD, range) was 5.21 ± 3.71, 1-18 years. The grades of VUR were grade- II (1 patient), grade- III (8 patients), grade- IV (10 patients), and grade- V (12 patients)[4]. The renal function estimated by pre and postoperative DMSA scan was 24.06 ± 12.02 and 24.06 ± 10.93, which was almost the same (statistically equal, paired-samples *t*-test: P = 0.873). The median (range) follow-up duration was 82 (60-120) months. One patient had persistent reflux after surgery (preoperative: Grade IV, postoperative: grade III). One patient had recurrent UTI. The difference in the preoperative and postoperative DRF was less than 10% in 26 patients. In one patient, the DRF decreased by 17% (22% to 05%) while in another patient, the DRF increased by 12% (25% to 37%) after surgery. There was no significant change in Serum creatinine in almost all patients, as mean serum creatinine preoperatively and postoperatively was 0.866 ± 0.68 and 0.811 ± 0.54 respectively (statistically equal, paired – sample *t*-test: P = 0.583). None of the patients had any increase in scarring after surgery or any development of new scars. A total of 15% of patients were hypertensive before surgery and all of them continued to be hypertensive after surgery, while no new patients developed hypertension. None of the patients showed significant proteinuria (> 150

mg/d) during the follow-up period. No patients presented an increase in hydronephrosis or retrovesical ureteric diameter after surgery.

DISCUSSION

Primary VUR is still a significant health problem for many children and young adolescents, as these patients are at high risk of developing reflux nephropathy[5]. The association of nephropathy with UTI and VUR is well established[6]. Reflux nephropathy is irreversible and may lead to renal insufficiency, renin-mediated hypertension, chronic renal failure, decreased somatic growth and morbidity during pregnancy. To avoid renal scarring these patients must be tested appropriately and promptly treated with antibiotics. In the present study, we found that the majority of children who have primary VUR and a poorly functioning kidney, maintain their renal function for a long time. In addition, hypertension and proteinuria in these patients usually do not progress with time.

Earlier studies used IVP for follow up after ureteric reimplantation to look for new scar formation and most of them reported a substantial rate of new scar formation (5% to 31%) and scar progression (12%to 20%)[7-10]. But soon the accuracy of IVP to assess reflux related renal scars was questioned and renal scintigraphy became a well-established method to quantitatively measure renal damage in kidneys with reflux and accuracy of this modality is well established now. A study performed by Choi *et al*[11] was the first of its kind which used dimercaptosuccinic acid renal scintigraphy instead of IVP. This study reported 0% new scar formation and 2.6% progression of renal scarring. Our study results are similar to study by Choi *et al*[11] and we also report 0% new scar formation and 0% progression of renal scarring.

The observation of our study is not in accordance with studies conducted by Atwell *et al*[12], Scott *et al*[13], and Carson *et al*[14] who reported accelerated renal growth after surgical correction of VUR. Conversely, large series reported by Rushton *et al*[15] and Olbing *et al*[16] concluded that there was no significant difference in renal size after

surgical correction in children with primary VUR which is like the observations of our study.

Renal functional impairment is one of the most devastating complications associated with VUR and is rare fortunately. The outcome of relative and overall renal function after ureteric reimplantation in children with unilateral primary VUR with significantly diminished relative renal function was assessed. A study by Schiepers *et al*[17]. Found that DMSA uptake did not change significantly during the 5 years interval in 89% of children after surgical correction of VUR, although this study had only 13 children with diminished RRF. A previous study by Nepple *et al*[18] in 2005, which included 32 children showed that relative renal function is maintained in such patients, although the mean follow-up period in their study was 3.7 years (0.3 to 12.9 years). In our series we observed 31 children who had strictly minimum 5 year follow up with mean follow up of 82 mo (60-120 mo) and most of our patients maintained their RRF in the long term. In this study we identified only one patient who had significantly decreased renal function and one patient also had significantly improved renal function.

Serum creatinine was measured preoperatively and was measured on follow up along with DMSA scan. Preoperative and post-operative serum creatinine show insignificant difference.

Ureteral reflux resolution rate was 96.4% which is similar to the success rate of 92%-99% reported by others. In a study by Nepple *et al*[18] reflux persisted in 4 of 32 children, which was treated with the Glenn-Anderson ureteral advancement procedure. Reflux persisted in 2 of 51 in the study by Grossklaus *et al*[19]. In the present study reflux persisted in 1of 31 children (preoperative: grade IV, postoperative: grade III) which was treated by endoscopic method, and we continue to use this modality in patients with recurrence with a lower grade of reflux and surgical treatment is reserved for those with a higher or similar grade of reflux with UTI.

Hypertension is a known complication of reflux for many years and was present in 15% of the patients, while no patient developed newly detected hypertension after

surgery. Wallace *et al*[20] conducted a study 12 years after correcting reflux, found hypertension in 12.8% of the patients (18.5% among children with bilateral scarring and 11.3% among those with unilateral scars). On the contrary, Belloli *et al*[21] detected hypertension in only 4.4% of patients who had corrective surgery. In our study we followed up patients with a mean period of 82 mo (60-120 mo) and none of the patients developed new-onset hypertension or proteinuria.

A similar study was conducted by Mor *et al*[22] showed that even patients who were treated successfully by ureteric reimplantation during childhood are prone to recurrent UTI, progressive renal scarring, hypertension, and complications during pregnancy. In that study only 31% (100) of the potential original study group of 322 patients could be fully evaluated. It was assumed that patients who had an uneventful did not enrolled themselves for the study and therefore showed the above results. This was the drawback of the study which reflected negatively biased results.

There are limitations to this retrospective study. The finding of no change in relative renal function may be the result of low statistical power from a small sample size. Although the follow-up period was good enough to determine that these patients maintain overall relative renal function. Since most of the patients in our study were males, we did not compare the outcomes between males and females. Future studies can take this limitation into account. Further, we did not explore the effect of bilateral VUR on renal function and thus, similar renal dynamics may not be observed with bilateral reflux nephropathy.

CONCLUSION

Even poorly functional kidneys maintain their function in the long term and there is need to establish a protocol for the long-term follow-up of patients who have had ureteric reimplantation during childhood. Management with ureteric reimplantation rather than nephrectomy may be warranted even in children with significantly reduced RRF based on the continued stability of relative renal function of the affected kidney. Hypertension and proteinuria do not progress over time in these patients.

ARTICLE HIGHLIGHTS

Research background

Vesicoureteral reflux (VUR) is when urine flows backwards from the bladder to the upper urinary tracts. It often has no symptoms but can cause kidney damage and scarring, leading to renal insufficiency, hypertension, or end-stage renal disease. Surgical options like ureteric reimplantation may be considered for poorly functioning kidneys, but there is limited evidence on long-term outcomes.

Research motivation

The motivation behind the research was to address the lack of evidence in the literature regarding the long-term outcomes of open ureteric reimplantation for poorly functioning kidneys with VUR. This research was conducted to provide better insights and guidance on the optimal management of VUR with poorly functioning kidneys.

Research objectives

The aim of the study was to determine if poorly functioning kidneys with VUR maintain relative renal function after the surgery on long-term follow-up of 5 years or more.

Research methods

The study involved a retrospective review of medical data for 168 patients who underwent ureteric reimplantation between 2003-2019. The research focused on children with unilateral primary VUR and a relative renal function of less than 35% who underwent open or laparoscopic ureteric reimplantation between January 2005 and December 2017. Data was collected by two independent researchers, and patients were excluded based on specific criteria. Preoperative evaluation included a voiding cystourethrogram and Dimercaptosuccinic acid (DMSA) scan, EC scan, and S. Creatinine. Follow-up was done at 6-month intervals, and data was collected through

various tests to assess the patient's cortical function. A paired-samples t-test was used to compare pre- and post-surgery observations. Only patients with complete data records and regular follow-up were included in the study.

Research results

The study included 31 children who underwent ureteric reimplantation for unilateral primary VUR. The patients were predominantly male, and their mean age was 5.21 ± 3.71 years. The pre- and postoperative renal function, as measured by DMSA scan, remained statistically equal in most patients, and there was no significant change in serum creatinine. Only one patient had persistent reflux after surgery, and one had a recurrent UTI. None of the patients showed an increase in scarring, proteinuria, or hydronephrosis after surgery, and there were no new cases of hypertension.

Research conclusions

The study found that even poorly functioning kidneys maintain their function in the long term after undergoing ureteric reimplantation, suggesting that this procedure may be a better option than nephrectomy. The results also indicate the need to establish a protocol for long-term follow-up of patients who have undergone this procedure, as hypertension and proteinuria do not progress over time in these patients.

Research perspectives

The study findings suggest the need for further research on the long-term outcomes of ureteric reimplantation in poorly functioning kidneys in children with VUR. Future studies could investigate the factors that influence the success of ureteric reimplantation, such as age of the patient, severity of VUR, and degree of renal scarring. Additionally, studies could explore alternative treatments for VUR and their long-term outcomes, such as endoscopic injection of bulking agents or laparoscopic ureteric reimplantation.

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