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Title: Heminephrectomy in adults: a systematic review with cumulative analysis
Short title: Heminephrectomy in adults: an evidence-based evaluation

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Abstract

Introduction: Duplex collecting system of the kidney is a relatively common abnormality, with the majority of symptomatic cases discovered in childhood. Treatment is commonly a heminephrectomy of the affected moiety. We aimed to conduct a systematic review of the literature to provide the best available evidence for heminephrectomy for duplex kidneys in the adult population.

Materials and Methods: A literature search was conducted in September 2017 with no limitations being placed on language, region, date or publication type. The data was represented numerically and cumulatively analysed.

Results: Seven retrospective studies with 61 patients were included. 56/66 operations performed were laparoscopically, 5/66 were robot-assisted and 5/66 were open procedures. Complete resolution of symptoms was reported in 53/55 (96.4%) of patients in five studies providing outcome data. Of the six studies reporting complications, there were a total of 9 complications (9/62, 14.5%), however 5 of these were found to be in one study alone.

Conclusions: This review emphasises the sparsity of evidence for heminephrectomy in adults. Nonetheless, it has been shown that this operation may be effective in alleviating patients’ symptoms in addition to being safe in experienced hands.

Keywords:
Duplex, moiety, heminephrectomy, laparoscopy, laparoscopic heminephrectomy
Introduction

Duplex collecting system of the kidney is a relatively common congenital abnormality with a reported prevalence of 1 in 125 births\(^1\). They are bilateral in 20% of cases and are almost twice as common in females than males\(^2,3\). Although this anomaly may be asymptomatic, it is commonly associated with recurrent urinary tract infections (UTIs), flank pain, haematuria, urinary incontinence and obstruction. There are various theories for the underlying pathophysiology of symptoms, including cyst formation of the non-functioning moiety causing pressure symptoms presenting as flank pain, or urinary stasis making urinary tract infections more likely\(^4\). If associated with obstruction, this may cause atrophy and reduced function of the affected pole of the kidney and may exponentiate symptoms further\(^1,5\).

Duplex kidneys are usually diagnosed antenatally or in childhood and treated shortly after. However, diagnosis may also be delayed until adulthood\(^6\). Adult patients with duplex kidneys may present with the symptoms described above, or it may remain asymptomatic and be found incidentally on imaging for other reasons\(^6,7\).

In symptomatic patients with poorly functioning moieties with preserved function of the other moiety, the standard treatment modality is surgery in the form of a heminephrectomy with corresponding moiety ureterectomy if necessary. Traditionally these were open operations\(^8\), however as experience with minimally invasive approaches has improved, many are now performed laparoscopically\(^8-11\), or robotically\(^12\). Post-operatively, most patients recover well and length of stay in hospital is modest. Rarely, patients develop post-operative urinoma, or a decline in function of the remaining moiety which may necessitate further intervention\(^13\).

Despite the ever-growing use of minimally invasive techniques, reports of heminephrectomies in adults are still lacking. The vast majority of published literature is in the paediatric population. To this end we aimed to conduct a systematic review of the literature to establish the efficacy and safety of heminephrectomy for duplex kidneys in the adult population.
Methods

Search strategy and study selection

This systematic review was conducted according to the Preferred Reporting Guidelines for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

A literature search of PubMed and Ovid (MEDLINE) was performed in September 2017 with no limitations being placed on language, region or publication type. Reference lists from articles of interest were also examined for inclusion.

The following search terms were utilized: Adult, Heminephrectomy, Partial nephrectomy, Urogenital abnormalities, Duplex, Ectopic, Ureterocele, Vesico-ureteric reflux, and Reflux.

Medical Subject Heading (MeSH) phrases included: ("Nephrectomy"[Mesh]) AND "Adult"[Mesh] AND "Urogenital Abnormalities"[Mesh]; ("Vesico-Ureteral Reflux"[Mesh]) AND "Adult"[Mesh] AND "Nephrectomy"[Mesh]; ("Nephrectomy"[Mesh]) AND "Adult"[Mesh]) AND "Ureterocele"[Mesh].

Two authors used pre-defined inclusion criteria to independently select articles for potential inclusion. Where there was a lack of consensus, the authors discussed the full text until an agreement was reached with respect to our pre-existing inclusion criteria.

Eligibility criteria

The objectives of this review were to assess the efficacy and safety of heminephrectomy in adults for duplex kidney. In studies which included both adults and children, we included only those for which separate data was provided on adult and paediatric patients in order to extract data on adults alone.

Data extraction and analysis

The following variables were extracted from each included study: time period of the study, country where study was undertaken, number of adult patients included (data from children, if also included in the study, were excluded from analysis), patient sex, involvement of upper or lower moiety of duplication system, patient symptoms and presentation, surgical management undertaken, symptom free rate at follow up, and complications.

The data from each included study were tabulated using Microsoft Excel and results represented numerically. A cumulative analysis was done to give a numerical representation of the end results.
**Results**

The study selection process is described in Figure 1. Following the literature search, 953 studies were found. Eight-hundred and eighty of these were excluded for not meeting inclusion criteria based upon the title. A further 52 were excluded following review of the abstract leaving 21 papers for full-text assessment. A further 5 studies were excluded as they were duplicate publications. Ten further studies were excluded for the following reasons: 8 studies included paediatric patients as well as adults, with no differentiation of results and outcomes\(^{15-22}\); one study was excluded as it was a clinical review of the topic with no data presented\(^{23}\); and lastly, one publication was excluded as it investigated the utility of heminephrectomy for horseshoe kidney rather than duplex kidney\(^{24}\). One study was found through the searching of reference lists of included articles.

**Characteristics of included studies**

In total, only 7 studies in the published literature were found describing heminephrectomy in an adult population for duplex kidneys\(^{25-31}\). The basic demographics of each study, as well as reported outcomes and complications are outlined in Table 1.

Four of the studies included were based in the USA, with the remaining three being from Turkey, Iran and China respectively.

All of the included studies were retrospective observational studies on patients undergoing heminephrectomy for a duplex kidney. Two studies included both children and adults but differentiated outcomes between these two groups and therefore the data on children was excluded\(^{28,30}\).

One study was of open heminephrectomies, four of the studies performed laparoscopic surgery, and two studies were of robot-assisted laparoscopic surgery. Four of these six studies employing minimally invasive techniques assessed the utility of transperitoneal surgery\(^{25-28}\), one of retroperitoneal\(^{31}\), and one study utilized both approaches depending on surgeon preference\(^{29}\). All patients (66/66, 100%) were deemed pre-operatively to have an affected upper pole moiety as the underlying cause for presentation.

Two studies did not provide basic demographics of study participants\(^{25,27}\). A further two studies did not provide any useable outcome data\(^{25,29}\). Five of the seven included studies provided data of symptom resolution following surgery\(^{26,27,28,30,31}\) and six provided data on post-operative complications\(^{25-29,31}\).

**Cumulative analysis results**

In total 66 patients were included in this review, with information on the sex of the included patients being provided in only 61 patients (24 males, 37 females)\(^{25,26,28-31}\). The age of included participants ranged from 17 – 56 years in the five studies providing basic demographics for their included patients\(^{26,28-31}\).

**Indications for surgery**
The primary indications for surgery were: flank pain (26/60, 43.3%), recurrent UTIs (14/60, 23.3%), abdominal pain and recurrent UTIs (8/60, 13.3%), abdominal pain (2/60, 3.3%), urine leakage (2/60, 3.3%), difficulty voiding (1/60, 1.7%), flank pain and haematuria (1/60, 1.7%), flank pain with frequency and urge incontinence (1/60, 1.7%), gross haematuria (1/60, 1.7%), hesitancy with nocturia and postvoid dribbling (1/60, 1.7%), flank pain and vaginal discharge (1/60, 1.7%), flank pain and UTI (1/60, 1.7%), and UTI (1/60, 1.7%).

Efficacy of Surgery

Complete resolution of symptoms was reported in 53/55 (96.4%) of patients. Patients were followed up over varying time scales, with a range 0-72 months.

Safety of surgery

Of the studies that reported complication, there was a total of 9 complications (9/62, 14.5%). Individual complications are depicted in table 2.

Methodological quality assessment

We identified no randomized controlled trials with each of the five included studies being a retrospective observational study of a case series with no control group. The included patients and the reporting of outcomes were heterogeneous. The quality of the evidence available is therefore limited by high risk of bias.
Discussion

Duplication of the urinary collection system is a relatively common anomaly\(^1\). Although many cases are diagnosed and treated in childhood, a number of patients may make it to adulthood before presentation\(^26\). There have been a number of published case series of paediatric patients undergoing heminephrectomy\(^{32-36}\) with only a small numbers of case series in the adult population with a limited cohort of included patients\(^{25-31}\).

The most common presentation was flank pain. Although patient symptoms and the indication for surgery appeared to vary widely between studies, this may have been compounded by the variable reporting terms used. Of the 8 patients with recurrent UTI may well have also been suffering from flank pain, and the two patients with difficulty voiding may have also had urine leakage present. The lack of guidelines for the standardization of terminology akin to those available for urological imaging\(^ {37}\) and lower urinary tract function\(^ {38}\) may have exacerbated this apparent variability in indications for surgery.

We identified that the success of surgery was reported differently between studies, although success was reported in 96.4% of cases in total. All the studies agreed that the operation had resolved the patients presenting complaint. Previous studies in the paediatric population have reported similar outcomes\(^ {39,40}\). This emphasizes that the operation regardless of technique is successful and results in good patient treatment in symptom resolution, mirroring that of the paediatric population.

Complication rates again varied between included studies in both rate and severity of complications. Li et al reported a 6.3% complication rate (2/32 patients), both of which were deemed minor (Clavien-Dindo Grade 1) (one wound infection, one post-operative subcutaneous emphysema)\(^ {31}\). However, of the ten patients operated on in Donmez’ series, five had post-operative complications (50%)\(^ {29}\). These included urine leak requiring stent insertion, and prolonged drainage requiring selective angio-embolization of an aberrant renal vessel. Donmez et al’s study represented the majority of complications and were deemed major (Clavien-Dindo Grade 3a-3b), which could reflect the learning curve of their practice. The complications in the remaining studies were deemed minor, therefore when excluding Donmez et al’s series, which has skewed the overall results, the complication rate dropped from about 14.5% to 6.5%. This ratifies that in experienced hands heminephrectomy in adults can be seen to be relatively safe.

Conversely, in published paediatric series, complication rates are reported to be relatively low in number, such as in Mushtaq et al’s series of 54 patients (4/54 complications, 7.5%) and a series of 48 patients by Leclair et al (1/48 complications, 2.1%)\(^ {34,40}\). It may be that complications are less common in the paediatric population due to heminephrectomies for duplex kidneys being a more commonly performed operation, and therefore performed by surgeons with more experience in the techniques utilised. This may also be explained by surgery in the adult, due to a longer untreated period, being somewhat more complicated.

Of the 66 operations analysed in this review, all were upper-pole nephrectomies for duplication of the upper pole moiety. Therefore, there were no data available on removal of a lower pole moiety for duplication. This is significant as lower pole heminephrectomy is generally considered more complicated surgery than upper pole nephrectomy, as the lower
pole nests in to the upper pole, which may make it more difficult to separate. Sakellaris et al reported a post-operative complication rate of 23% in their case series of 31 lower pole heminephrectomies in children. This might reflect a reporting bias, where centres do not report their lower pole heminephrectomy series due to increased complication rates.

The main limitation of this review is that all of the five included studies were retrospective analyses of case series with no control groups or randomization taking place. Furthermore, the included studies were heterogeneous in the way in which they reported outcomes. It is the opinion of the authors of this review that the quality of the evidence for each study was of low quality. Given the relative rarity of adult patients undergoing operation for duplex kidneys, as most of these operations are done in childhood, the likelihood of a randomised study being conducted is low. In situations such as these, it is useful to perform systematic review of case series to provide the evidence for established best practice. Therefore, this systematic review reflects the reported literature and adds to a better understanding of the uses and outcomes of heminephrectomy in adults.
**Conclusion**

This review emphasises the need for more centres to report their results of heminephrectomy in an adult population. Large national or international databases may be a source of evidence to add to that which has already been published. This would better establish both the efficacy and safety of this procedure. Nonetheless, this review has shown that this operation may be effective in alleviating patients symptoms in addition to being safe in experienced hands.
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