

Pre-transplant treatment of large polycystic kidney

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Abstract

AIM: To evaluate the indications, optimal timing and

outcomes of native nephrectomy and other techniques in pretransplant treatment of autosomal dominant polycystic kidney disease (PKD).

METHODS: A literature review was conducted using the PubMed and Epistemonikos databases. Keywords for pre-transplant surgical management of polycystic kidneys were: Transplant, treatment and PKD. Keywords for pre-treatment embolization of PKD were: Embolization, transplant and polycystic kidney disease. The inclusion criteria were all articles found using this search method. The exclusion criteria were articles found to include bias and not attending pre-transplant treatment options. Fifteen articles were included in our final analysis. Ten articles were found regarding embolization of PKD of which three reviews were selected for final analysis. The reviews were divided into pre transplant and intra transplant treatment for the surgical treatment of PKD. All articles meeting inclusion criteria were thoroughly analyzed by two independent reviewers. A third independent reviewer was consulted if the reviewers did not agree upon the inclusion or exclusion of a specific article. No statistical analysis was performed.

RESULTS: Studies vary regarding the technique used (open or laparoscopic), laterality (single or bilateral) and temporality of nephrectomy with respect to renal transplant (pre-transplant or simultaneous to transplant). Several groups argue in favor of simultaneous nephrectomy and kidney transplant since it avoids the deleterious effects of being anefric. Long-term results and patient satisfaction are acceptable. However, it is associated with increased operative time, transfusion rate, morbidity and length of hospital stay. Based on small sample studies, bilateral nephrectomy prior to transplant has been associated with a higher risk of morbidity and mortality. Studies on laparoscopic approach report it as a feasible and safe alternative to the open surgery approach, highlighting its lower complication rate, transfusions and shorter hospital stay. Arterial embolization of the kidney appears as an effective

and low morbid alternative for the management of large native kidneys. The reduction in renal size allow transplant in a significant number of patients, which makes it an appealing alternative to surgery.

CONCLUSION: There is limited evidence regarding best pretransplant treatment of large PKD but to date embolization seems an appealing alternative to augment space for renal graft allocation.

Key words: Polycystic Kidneys; Kidney transplant; End stage renal disease; Kidney embolization

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Core tip: Pre-transplant management of polycystic kidneys for patients with end-stage renal disease is unclear. A number of studies have advocated in favor of bilateral nephrectomy prior to transplant, others promote simultaneous nephrectomy and kidney transplant. Arterial embolization to reduce native kidney volume appears as an effective and attractive alternative.

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INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is responsible for approximately 10% of all cases of end stage renal disease^[1] and is the leading cause of inherited kidney failure in the United States and Europe^[2-7].

For patients with ADPKD who reach end stage renal disease, the preferred treatment is kidney transplant, which permits an improved survival and lower morbidity rate compared to other forms of renal replacement therapy^[8-13].

The indications for native nephrectomy in patients with ADPKD are: (1) Very large kidneys, causing lack of space for the transplant; (2) chronic and severe abdominal or lumbar pain attributable to the mass; (3) recurrent UTI or urosepsis due to cyst infection, especially in those not responding to medical treatment; (4) hematuria requiring recurrent or persistent blood transfusions; (5) gastrointestinal symptoms (early satiety) secondary to mass compression; and (6) suspicious of malignancy on preoperative diagnostic images.

These indications and timing of nephrectomy in ADPKD patients remains controversial for those undergoing renal transplant. While most ADPKD patients do not require either a unilateral or bilateral nephrectomy to facilitate kidney transplant, the size of the kidneys and associated symptoms in some cases provide sufficient

indications for surgery. Some authors advocate for native unilateral or bilateral nephrectomy prior to transplant; others promote unilateral or bilateral native nephrectomy at the time of transplant, and others suggest doing the native nephrectomy following the transplant^[14]. Another method described is the "sandwich technique", where the most severely affected native kidney is removed prior to transplant and the other native kidney is removed subsequently^[15]. All these approaches have been described with open surgical techniques, but lately, some centers have published their experience with laparoscopy showing promising results^[16].

Arterial embolization and secondary shrinkage of very enlarged kidneys has been proposed as an alternative to nephrectomy in selected cases, with the sole objective of making anatomical space for transplant or treating symptoms related to kidney volume^[17].

All of the above methods show advantages and disadvantages.

The aim of this review is to evaluate the indications, optimal timing and outcomes of native nephrectomy and other techniques in patients with ADPKD as related to kidney transplant.

MATERIALS AND METHODS

A literature review was conducted using the PubMed and Epistemonikos databases. Keywords for pre-transplant surgical management of polycystic kidneys were: Transplant, treatment and polycystic kidney disease. Keywords for pre-treatment embolization of PKD were: Embolization, transplant and polycystic kidney disease. The inclusion criterion was all articles found using this search method. The exclusion criterions were articles found to include bias and not attending pre-transplant treatment options. As a result of our search, 15 articles were found for surgical treatment and included in our final analysis. Ten articles were found in the embolization search with 3 reviews subject for final analysis. The reviews were divided into pre transplant and intra transplant treatment for the surgical treatment of PKD. All articles meeting inclusion criteria were thoroughly analyzed by 2 independent reviewers. A third independent reviewer was consulted if the reviewers did not agree about the inclusion or exclusion of a specific article. No statistical analysis was carried out.

RESULTS

Fifteen articles present results of surgical treatment in ADPKD and renal transplant. They vary with regard to the technique used (open or laparoscopic), laterality (single or bilateral) and temporality with respect to renal transplant (pre-transplant or simultaneous to transplant). Table 1 shows the results of these series.

Unilateral or bilateral nephrectomy simultaneous to renal transplant

The majority of series incorporate this modality. This

Table 1 Summary of the nephrectomy series results

Author	Year	n	Technique Open/ laparoscopic	Side Uni/Bilateral	Relation with trasplant Pre-trasplant/ simultaneous/posttrasplant	Transfusion (units)	Complications (%)	Mortality
Song	2011	31	Open	Bilateral	Simultaneous	4.68 ± 1.51	32	No
Glassman	2000	10	Open	Bilateral	Simultaneous	2.3	20	No
Tabibi	2005	13	Open	7 UI/6 bilat	Simultaneous	ND	ND	No
Skauby	2012	78	Open	Bilateral	Simultaneous	1.6 (0-11)	30	No
Kramer	2009	20	Laparoscopic	Bilateral	Simultaneous	3.3 (0 - 8)	20	No
Dunn	1999	11	Laparoscopic	7 UI/2 bilateral	Pre-trasplant	ND	55	No
Nunes	2007	16	Open	Unilateral	Simultaneous	1.81	6.3	No
Lucas	2010	42	Laparoscopic	18 UI/24 bilateral	Pre/posttrasplant	ND	25	No
Desai	2007	13	Laparoscopic	5 UI/7 bilateral	Pre/posttrasplant	0.9	60	No
Krol	2006	20	Open	Bilateral	Pretrasplant	3.2	45	No
Neeff	2012	100	Open	Unilateral	Simultaneous	ND	22	No
Wagner	2006	32	Open	Bilateral	17 simultaneous/15 pretrasplant	2.2	70 (simultaneous) 75 (pretrasplant)	No
Kirkman	2010	35	Open	10 UI/10 bilateral	Pretrasplant	ND	35	Yes (2 patients, bilateral group)
Tyson	2013	2368	Open	Bilateral	271 simultaneous/2097 pretrasplant	ND	ND	Yes (1.1% simultaneous-15.8% pretrasplant)

procedure does not show major risks when compared to renal transplant exclusively^[18-25].

These series have longer surgical times, higher transfusion and complication rates when compared to renal transplant alone. However, they all coincide on favorable long-term results of renal graft function and global survival. These series do not show mortality rates.

Song *et al*^[18] reports that 32 patients with ADPKD who were transplanted without nephrectomy had a greater incidence of hypertension (91% vs 66%) and urinary tract infection (31% vs 6.4%) compared to a similar group where simultaneous bilateral nephrectomy and renal transplant was performed.

Glassman reports that in nine transplanted patients, postoperative creatinine was 2.2 vs 1.6 in the simultaneous nephrectomy and transplant group. This study incorporates a non-validated user satisfaction survey: 70% of patients submitted to the double procedure were satisfied. In patients submitted to transplant exclusively, 7 out of 9 would have preferred simultaneous nephrectomy^[19].

Neeff *et al*^[24] presents a series of 100 patients with ADPKD submitted to nephrectomy with a prolonged unilateral midline Gibson incision. Only 12% of patients presented postoperative complications (linfocele, hernia, hematoma, haemorrhage). Four percent of patients had to be operated due to one of these complications. Overall renal graft survival was of 96% and 80% in years 1 and 5, respectively. Graft survival rates are similar to series without nephrectomy. This study does not present a control group.

Fuller at UCLA presents 32 patients submitted to nephrectomy at all times. Seven patients underwent nephrectomy before transplant, 16 simultaneous with renal transplant and nine post-transplant. There were no differences in terms of complications. This study suggests performing unilateral or bilateral nephrectomy

simultaneous to transplant, especially in the live donor setting^[25].

Other authors study results in patients submitted to bilateral nephrectomy; some patients were also transplanted simultaneously. In these series, surgical times and complications rates in the compared groups were similar^[16,26,27].

Wagner *et al*^[26] reports shorter hospitalization stay in patients with simultaneous nephrectomy and transplant (6.9 d) vs differed nephrectomy and transplant (11.8 d for both hospitalization periods).

Tyson *et al*^[27] presents the analysis of the Nationwide Inpatient Sample Database, demonstrating lesser mortality in the nephrectomy and transplant (OR = 0.06) compared with the bilateral nephrectomy without transplant group. This difference is not found when analyzing high volume centers only.

Martin *et al*^[16] reports better postoperative creatinine values in patients submitted to laparoscopic bilateral nephrectomy and simultaneous transplant compared to differed transplant (1.6 vs 2.3 mg/dL).

Pre-transplant bilateral nephrectomy

Two authors present very small series with pre-transplant nephrectomy with differed transplant. Both show the highest postoperative complications rate and mortality.

Kirkman analyzes outcomes of patients submitted to unilateral or bilateral nephrectomy before or after transplant. Mortality is present in this series. In the pre transplant bilateral nephrectomy group 2 of 10 patients died, while in the bilateral differed nephrectomy group 1 of 10 patients died. All deaths were due to colonic ischemia leading to multiorgan failure. There is no statistical analysis for this difference^[14].

Król *et al*^[28] presents 20 patients in hemodialysis submitted to open bilateral nephrectomy. Postoperative complications were present in 9 of 20 patients (45%).

Table 2 Serum creatinin at discharge in transplant and nephrectomy series

Author	Year	Creatinin at discharge	
		Transplant	Transplant + nephrectomy
Wagner	2006	2	1.6
Lucas	2010	1.6	1.5
Nunes	2007	1.79	1.6
Kramer	2009	2	1.6
Tabibi	2005	1.2	1.3
Glassman	2000	2.2	1.6
Wagner	2007	2	1.6
Martin	2012	2.3	1.6

Complications described include hernia, chronic abdominal pain, peptic ulcer and ileum. This series does not present mortality.

Laparoscopic nephrectomy

Two authors present small laparoscopic nephrectomy series, with no control group. There is a lesser complication, transfusion, pain and hospital stay rate as compared to cohorts with open surgery. There is no mention of graft function or survival with this technique^[29,30].

Pre-transplant embolization of polycystic kidneys

There are few cohorts that show the effect of embolization of renal arteries to reduce the size of polycystic kidneys for graft space. In 2010, Cornelis *et al.*^[17] published their experience of 25 patients with ADPKD awaiting renal transplant treated with embolization. Renal size was evaluated with computed tomography scan pre embolization and at 3 and 6 mo post procedure. Thirty-six percent and 84% of patients had a reduction of renal size at 3 and 6 mo, allowing renal transplant. Mean reduction in renal size at these times was 42% and 54%. The main complication reported was post embolization syndrome in five patients. This syndrome is characterized by low fever and severe lumbar pain. Pain was managed with opioid derivatives, disappearing in 2 wk post procedure. One patient developed a pseudo-aneurism at the puncture site, managed with manual compression. These authors conclude that trans-arterial embolization prior to renal transplant is an option to nephrectomy and suggest a post-therapy pain management protocol^[17].

This same group published their results in 2014, presenting now a series of 73 patients in which 82 procedures were performed in 76 renal units. Renal artery embolization was successful in diminishing renal size by 89.5% at 5.6 mo after treatment (range 2.8 to 24.3 mo). Mean renal size reduction was 59% 3 mo post embolization. Post embolization syndrome was present in 15 procedures (18.3%). Complications described in this series include one pulmonary embolism, one iliac artery thrombosis, a pseudo aneurysm of the femoral artery and an infection of a renal cyst, all categorized as grade II complications according to the Clavien Dindo classification. This group describes 43 successful transplants with previous renal embolization^[31].

DISCUSSION

All published series present small patient cohorts. This does not allow categorical conclusions regarding pre-treatment options of very large ADPKD. The largest series, presented by Skauby *et al.*^[21] and Tyson *et al.*^[27], coincide in that there is a longer surgery time and complication rate in nephrectomy with concomitant transplant than in transplant alone. Tyson also refers to the possible better prognosis for patients that receive transplant with simultaneous nephrectomy. However, this difference could be accounted for by technical experience more than a graft-related determinant factor.

Another factor to consider is the function of the graft at the moment of hospital discharge. Reports seem to indicate that the function of the graft may be better when it is done with simultaneous nephrectomy as compared to transplant and differed nephrectomy (Table 2).

It seems that the worst moment for nephrectomy is before or after the transplant. Although these series are small, Kirkman *et al.*^[14] and Król *et al.*^[28] report higher rates of complications and mortality -up to 20%- in patients with bilateral nephrectomy without immediate transplant. The factors that may explain this are anephric time and permanence in dialysis.

Post-transplant nephrectomy, though not a central objective of our study, seems to have a greater rate of urinary tract infection due to cyst infection. This greater infection rate may be due to immune-suppression in the transplanted patient. This argument is frequently employed to perform nephrectomy pre or intra transplant.

There are few reports studying renal embolization for volume management of ADPKD. There is only one group actively working on this subject, with excellent results in terms of reduction of renal size and pain control^[17,31].

While our experience in embolization previous to transplant is limited, our results coincide with those shown previously in diminishing renal size and augmenting space for renal graft allocation. If we could suggest something it would be to use an epidural catheter for pain control after embolization. Another suggestion would be to embolize using not only coils but also ethanol to attain an adequate level of ischemia and posterior renal atrophy. We strongly believe that embolization of polycystic kidneys will have a leading role in the near future.

COMMENTS

Background

Autosomal dominant polycystic kidney disease plays a key role in chronic kidney disease. So far, the timing of the surgical procedure remains unclear, especially related to kidney transplantation.

Research frontiers

To find the best timing for kidney transplantation (before, concomitant, or after nephrectomy), comparing both living and cadaveric donors. Strong evidence supported by collaborative multi centric trials is necessary. The authors believe embolization of polycystic kidney disease plays an important role in this setting,

especially in low volume centers.

Innovations and breakthroughs

Embolization only requires an interventional radiologist that allows adequate management with a minimally invasive approach. This technique should be considered as a first line treatment instead of nephrectomy.

Applications

End stage and complicated autosomal dominant polycystic kidney disease (ADPKD).

Peer-review

The authors reviewed the literature regarding surgical approach and timing for the native nephrectomy for patients with ADPKD being scheduled kidney transplantation. The paper is well-written and provides important information regarding this aspect.

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