REVIEW ARTICLE

Renal transplantation and polycystic: Surgical considerations☆

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Abstract

Background: The indication and timing of nephrectomy in patients with autosomal dominant polycystic kidney disease (ADPKD) remain controversial, especially in patients who are candidates to renal transplantation (RT). The main surgical options such as unilateral vs. bilateral nephrectomy, nephrectomy before vs. after RT, or simultaneous nephrectomy and transplantation, are herein discussed.

Objective: Evidence acquisition of the best surgical management available for ADPKD in the context of kidney transplantation.

Acquisition of evidence: Systematic literature review in PubMed from 1978 to 2013 was conducted. Articles selected included: randomized controlled trials and cohort studies. Furthermore, well designed ADPKD reviews were considered for this study.

Synthesis of evidence: Laparoscopic nephrectomy in ADPKD is a safe procedure with an acceptable complication rate. Unilateral nephrectomy has advantages over the bilateral one regarding the perioperative complication rate. Although the timing of nephrectomy is controversial, it seems that simultaneous nephrectomy and renal transplantation neither increase surgical morbidity nor affect graft survival.

Conclusions: Simultaneous nephrectomy and RT appear to be an acceptable alternative to conventional two-stage procedure without any increased morbidity, in the context of ADPKD. Furthermore, laparoscopic nephrectomy performed in experienced centers is a safe alternative to conventional approach.

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Keywords

Autosomal dominant polycystic kidney disease; Nephrectomy; Transplant

Trasplante renal y poliquistosis: consideraciones quirúrgicas

Resumen

Contexto: La indicación y el momento de realizar una nefrectomía en pacientes con poliquistosis renal autosómica dominante (PQRAD) continúa siendo en la actualidad un tema controvertido, especialmente en aquellos pacientes candidatos a trasplante renal (TR). La nefrectomía unilateral o bilateral, el realizar la nefrectomía antes o después del TR, y la realización de la nefrectomía y el TR en el mismo acto son las principales opciones en la actualidad.

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Objetivo: Realizar una revisión de las diferentes opciones de manejo quirúrgico de la PQRAD en el contexto del TR, adaptada a la evidencia científica actual, y de otros aspectos que rodean la indicación.

Adquisición de la evidencia: Se realizó una revisión sistemática en PubMed (1978-2013), que incluye revisiones previas, estudios clínicos aleatorizados controlados y estudios de cohortes de los aspectos quirúrgicos de la PQRAD.

Síntesis de la evidencia: La nefrectomía laparoscópica en la PQRAD constituye una técnica segura y con un aceptable porcentaje de complicaciones. La realización de una nefrectomía unilatera presenta ventajas respecto a la bilateral en cuanto a un menor porcentaje de complicaciones perioperatorias. Aunque existe controversia en cuanto al momento en el que realizar la nefrectomía, parece que la realización en un mismo acto del TR y la nefrectomía no incrementa la morbilidad quirúrgica ni la supervivencia del injerto.

Conclusiones: En el contexto de la PQRAD, la realización de nefrectomía y TR simultáneo puede ser llevado a cabo sin que exista una morbilidad añadida con respecto al TR convencional. En caso de ser necesario la nefrectomía laparoscópica realizada en centros con experiencia es una alternativa segura al abordaje convencional.

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### Background

Autosomal dominant polycystic kidney disease (ADPKD) is a multisystem, monogenic disease characterized by the development of cysts in both kidneys and other extrarenal manifestations such as cysts in other organs and vascular, cardiac, digestive and musculoskeletal abnormalities, which develop at variable degrees. ADPKD has a prevalence of 0.1–0.25% and is responsible for 10% of all cases of end-stage renal failure (ESRF). ADPKD is a genetically heterogeneous disease in which 2 genes are involved: PKD1 (chromosome 16p13.3), responsible for 85% of cases, and PKD2 (chromosome 4q21-23), responsible for 15% of cases. Patients with PKD1 mutations have a more serious clinical presentation and have a higher tendency of developing ESRF at an earlier age (mean, 54 years). In contrast, individuals with PKD2 mutations develop ESRF later (mean, 74 years). Cysts are present in 17% of cases at age 29–39 years and in 75% of those aged 70 years or more. Overall, 50% of affected individuals progress to ESRF.

### Pathogenesis

The polycystin-1 (PC1) and polycystin-2 (PC2) proteins, which are associated with the membrane, are encoded by PKD1 and PKD2, and their main function is the regulation of intracellular calcium. In the primary cilium, the polycystin complex receives and translates the mechanical stimulation into a calcium influx, which triggers an increased release of calcium from the endoplasmic reticulum. The reduction of one of the 2 polycystins below a critical level results in a phenotypic change that is characterized by the inability to maintain cell polarity, an increase in the rate of proliferation and apoptosis, the expression of a secretary phenotype and the remodeling of the extracellular matrix. The molecular mechanisms involved in these phenotypic changes include an alteration in intracellular calcium homeostasis, the activation of cyclic adenosine monophosphate (cAMP), tyrosine-kinase receptors, mammalian target of rapamycin (mTOR), the canonical Wnt pathway and other intracellular signaling mechanisms. The formation of cysts occurs as a result of dilation of renal tubules. In the initial phases, the renal parenchyma presents a normal appearance, but in the final phases the kidneys are very large and have a distorted collecting system and numerous fluid-filled cysts. AHT is the most common clinical manifestation and the main contributing factor to the disease progression. In addition, there is associated abdominal pain in 60% of cases. Other forms of presentation include recurrent urinary infections, early satiety and hematuria. Overall, 50% of cases will present ESRF at 60 years of age, with a loss of 4.4–5.9 mL/min in the GFR. Patients with PKD1 will experience ESRF at a lower mean age than patients with PKD2 (54.3 vs. 74.0).

The purpose of current treatments is to limit morbidity and mortality due to complications of the disease. Kidney transplantation (KT) is the treatment of choice for ESRF in patients with ADPKD. The majority of patients with ADPKD do not require nephrectomy (unilateral or bilateral); however, in cases where there are space restrictions or symptoms, nephrectomy is required to facilitate KT. The timing and indication for nephrectomy in patients with ADPKD continues to be a controversial subject. Traditionally, nephrectomy before transplantation has been reserved for patients with a history of infected cysts, frequent hemorrhaging or a massive increase in size.

### Acquisition of evidence

A systematic review was performed in PubMed (1978–2013), which included prior reviews; randomized, controlled clinical studies; and cohort studies of the surgical aspects of ADPKD. The controversial issues that were assessed were the justification for nephrectomy, unilateral or bilateral nephrectomy and the timing of the nephrectomy (before, during or after the KT).

### Justification for nephrectomy

Only 20% of the patients with ADPKD will require a nephrectomy. The justification for indicating this procedure is based on the potential risk of presenting renal...
and extrarenal complications (infection of the cysts, hematuria, and lithiasis) or a conflict in space for placing the graft. It has been postulated that the overall risk of performing nephrectomy is lower than the potential derived complications, including graft loss. In addition, maintaining the polycystic kidneys once the transplantation has been performed could increase the risk of infections associated with immunosuppression and cause vascular and ureteral damage to the graft due to mechanical compression. Sulikowski et al. published a rate of 40% for post-kidney transplant nephrectomies due to complications. However, nephrectomy in ADPKD has been associated with high morbidity resulting from the surgery, as well as the possibility of presenting sequelae resulting from the anephric state. Yarimizu et al. in a classic publication, analyzed a retrospective series of 305 patients with ADPKD who underwent bilateral nephrectomy in preparation for transplantation. They reported an overall mortality of 3.6%, which reached 11% in the patients older than 50 years. The overall morbidity of the series was 58.7%. Sanfilippo et al. have reported that in cases of graft failure, patients who had been previously nephrectomized showed a greater incidence of serious anemia (50% vs. 39%) and death (58% vs. 25%). Mendelsohn et al. also associated bilateral nephrectomy prior to transplantation with higher morbidity and with no effect on graft survival.

Knispel et al. analyzed 47 patients with ADPKD who underwent transplantation without prior nephrectomy. All complications were resolved medically, and no posttransplant nephrectomy was required. When comparing the graft survival with those of the control patients, there were no differences. However, with the development of laparoscopy and minimally invasive surgery, the morbidity of nephrectomy in ADPKD has declined significantly. In patients in whom nephrectomy is considered imperative due to complications or space restrictions, this procedure can be performed (in centers with experience) with lower morbidity and hospital stay than in the published series of open surgery (Table 1). Gill et al. compared the laparoscopic approach to the open approach in a retrospective series of 20 patients and found significant differences in favor of laparoscopy in terms of reduced bleeding, fewer days for nasogastric intubation and shorter hospital stays.

### Table 1  Summary of published data on laparoscopic ADPKD nephrectomy.

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Operative time (min)</th>
<th>Blood Loss (ml)</th>
<th>Hospital stay (days)</th>
<th>Mean kidney size (g)</th>
<th>Conversion rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desai et al.</td>
<td>12</td>
<td>214</td>
<td>164</td>
<td>4.2</td>
<td>2311</td>
<td>0</td>
</tr>
<tr>
<td>Mak et al.</td>
<td>3</td>
<td>208</td>
<td>100</td>
<td>10.6</td>
<td>2037</td>
<td>0</td>
</tr>
<tr>
<td>Patel et al.</td>
<td>3</td>
<td>NC</td>
<td>NC</td>
<td>5</td>
<td>NC</td>
<td>0</td>
</tr>
<tr>
<td>El-Gallery et al.</td>
<td>26</td>
<td>222</td>
<td>175</td>
<td>3</td>
<td>1768</td>
<td>22</td>
</tr>
<tr>
<td>Lipe et al.</td>
<td>18</td>
<td>315</td>
<td>350</td>
<td>4.7</td>
<td>717</td>
<td>0</td>
</tr>
<tr>
<td>Whitten et al.</td>
<td>18</td>
<td>194</td>
<td>203</td>
<td>NC</td>
<td>2029</td>
<td>0</td>
</tr>
</tbody>
</table>

Unilateral/bilateral nephrectomy

Based on the studies that consider bilateral nephrectomy to increase the risk of serious anemia and death, as well as other complications resulting from the anephric state, unilateral nephrectomy can be considered as an alternative. The majority of studies show that performing a unilateral or bilateral nephrectomy is similar in terms of morbidity and mortality. Brazda et al. have published that unilateral nephrectomy prior to transplantation in ADPKD increased patient and graft survival compared with patients without nephrectomy. Sulikowski et al. analyzed 183 patients divided into 3 groups: the pretransplant nephrectomy group, the during transplantation group and the group that did not undergo nephrectomy. They concluded that unilateral nephrectomy prior to KT reduces the number of posttransplant complications, especially those resulting from graft compression. Lucas et al. compared the complications resulting from unilateral and bilateral nephrectomies and found significant differences only in surgical time, favoring unilateral nephrectomy.

### Timing of the nephrectomy

Although the majority of patients with ADPKD will not need a unilateral or bilateral nephrectomy during the follow-up, some patients will require the procedure due to the large size of the kidneys or the onset of associated complications. The timing of the nephrectomy is still a subject of significant debate. There are those that support performing the nephrectomy prior to transplantation and others that prefer to perform it after the transplantation (Table 2). One of the reported procedures is the sandwich technique, where the native kidney in poorest condition is extracted before transplantation and the other extracted after transplantation. Nephrectomy with simultaneous transplantation through a single incision represents another option for consideration.

### Nephrectomy prior to transplantation

Schillinger et al. published a short series of 10 patients who had undergone bilateral nephrectomy prior to transplantation without complications. The authors concluded that this was a safe method for ensuring space for the graft and reducing complications resulting from the cysts. They emphasized that replacement therapy can successfully compensate for the sequelae of the anephric condition. Krol et al. analyzed a series of 18 patients who underwent bilateral nephrectomy prior to transplantation; 45% of the patients presented complications resulting from the surgery. Ten patients (55%) were ultimately transplanted...
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Table 2  Summary of main studies comparing the timing of nephrectomy in ADPKD.

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Timing of nephrectomy</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulikovsky et al.</td>
<td>183</td>
<td>N = 25 pre KT</td>
<td>40% of nephrectomies post-KT by complications</td>
</tr>
<tr>
<td></td>
<td>(50 KT)</td>
<td>N = 4 simultaneous</td>
<td></td>
</tr>
<tr>
<td>Kirkman et al.</td>
<td>35</td>
<td>N = 20 pre KT</td>
<td>Unilateral nephrectomy post-KT is the technique with the fewest complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 12 post KT</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 3 sandwich technique</td>
<td></td>
</tr>
<tr>
<td>Lucas et al.</td>
<td>42</td>
<td>N = 16 simultaneous</td>
<td>KT with simultaneous nephrectomy, same complications as KT alone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 22 post KT</td>
<td></td>
</tr>
<tr>
<td>Nunes et al.</td>
<td>159</td>
<td>N = 143 simultaneous</td>
<td>No differences in complications and graft survival</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 16 = no nephrect.</td>
<td></td>
</tr>
<tr>
<td>Neef et al.</td>
<td>100</td>
<td>N = 100 simultaneous</td>
<td>Graft survival: 97%</td>
</tr>
<tr>
<td>Fuller et al.</td>
<td>171</td>
<td>N = 32 pre KT</td>
<td>Reoperation: 12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 16 simultaneous</td>
<td>No differences in morbidity unilateral or bilateral</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 25 bilateral</td>
<td>Simultaneous KT in living-donor cases</td>
</tr>
</tbody>
</table>

Successfully. Lipke et al. published the results of 14 patients treated with radical bilateral laparoscopic nephrectomy, with 4 of these patients requiring conversion to open surgery. The authors considered that presenting a volume of more than 3500 cm³ presented a significantly high risk of conversion to open surgery. In their study, Sulikowski et al. 18 compared the performance of nephrectomy pre- and post-KT. They reported a higher number of complications (42.5%) in the group of patients who did not undergo pretransplant nephrectomy.

Postkidney transplant nephrectomy

Among the series that support nephrectomy after transplantation is the study by Kirkman et al. 31 who, after comparing both groups, suggested that pretransplant nephrectomy should only be performed in cases of clear indications (complications or conflict of space). For this group, posttransplant unilateral nephrectomy presented a lower rate of complications in comparison with the pretransplant nephrectomy, especially when bilateral.

Nephrectomy and simultaneous transplantation

The simultaneous performance of a nephrectomy and KT through a single incision, cranially expanding the Gibson incision 3–5 cm, was initially reported by Nunes et al., 37 who analyzed 159 patients with ADPKD comparing them based on the need for performing a simultaneous nephrectomy at the time of KT due to space restriction. The authors concluded that simultaneous nephrectomy is a safe process that does not affect hospital stay or graft survival. Only those patients who required nephrectomy at the time of KT had a longer surgical time and intraoperative need for crystalloid transfusion. Lucas et al. 32 conducted a follow-up of 42 patients with ADPKD. When they compared the KT group alone to nephrectomy and transplantation, they concluded that there were no differences between the two groups in terms of morbidity and graft survival. Similarly, Neeff et al. 38 published a series of 100 consecutive transplants in which a simultaneous nephrectomy was performed. The overall rate of complications was 12%, with a graft survival at 1 year and 5 years of 96% and 80%, respectively. Hazem et al. analyzed 2 groups comparing bilateral nephrectomy and KT at the same time with bilateral laparoscopic nephrectomy and deferred KT. They argued that medical advances in the use of recombinant erythropoietin and vitamin D could compensate perfectly for the time the patient remained in the anephric state. Due to the fact that bilateral nephrectomy and KT simultaneously required additional treatment in 60% of the cases, performing a pretransplant bilateral laparoscopic nephrectomy is feasible. 39 Wagner et al. compared two groups of symptomatic patients with ADPKD, one of which underwent bilateral nephrectomy and deferred transplantation from cadaveric donors and the other who had living donors and underwent KT and bilateral nephrectomy in the same act. The authors concluded that for the living-donor group the bilateral nephrectomy concurrent with the transplantation provided a reduced hospital stay without affecting graft functionality. 40

Conclusions

Laparoscopic nephrectomy in ADPKD constitutes a safe technique with an acceptable percentage of complications. Unilateral nephrectomy has advantages compared with bilateral nephrectomy in terms of a lower percentage of perioperative complications. Although there is controversy concerning when to perform the nephrectomy, it seems that the performance of KT and nephrectomy in a single act does not increase surgical morbidity or graft survival.

Conflict of interest

The authors declare that they have no conflicts of interest.
References


