Cyst Decompression Surgery for Autosomal Dominant Polycystic Kidney Disease

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ABSTRACT

A prospective study was undertaken to evaluate the efficacy of surgical cyst decompression for retarding the progression of renal failure and for the management of chronic pain associated with autosomal dominant polycystic kidney disease (ADPKD). Thirty patients with ADPKD and pain (14 patients), renal insufficiency (4 patients), or both (12 patients) underwent unilateral (19 patients) or bilateral (11 patients) cyst reduction surgery. The patients were monitored for 21 ± 2 months postoperatively. The probability of being painfree was 80% at 1 yr and 62% at 2 yr. Preoperative and 1- to 3-month postoperative serum creatinine levels and GFR (clearance of inulin or (125I) iothalamate) were not significantly different (2.2 ± 0.3 versus 2.2 ± 0.3 mg/dL and 49 ± 8 versus 54 ± 9 mL/min/1.73 m², respectively). One-year serum creatinine levels remained unchanged in patients with normal preoperative renal function (1.0 ± 0.07 versus 1.0 ± 0.05 mg/dL), whereas those with preoperative progressive renal insufficiency had no difference in the mean slope of reciprocal serum creatinine plots preceding and after surgery (−0.008 ± 0.001 versus −0.009 ± 0.002 mL/mg/month). In patients who underwent unilateral surgery, split function isotope scans showed no change in function of the operated kidney when compared with the nonoperated kidney. Surgical cyst decompression provides effective relief of chronic pain without compromising renal function. However, the data in this article do not support the use of this procedure to slow progression of renal insufficiency in ADPKD.

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tosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary disorder resulting in progressive renal failure, accounting for approximately 10% of cases of end-stage renal disease (1). Although the pathogenesis of renal failure in ADPKD remains to be elucidated, it is widely believed that progressive azotemia is due, at least in part, to compression and distortion of adjacent noncystic renal parenchyma by the expanding cysts (2–5). This point of view is supported by the fact that only 1 to 2% of nephrons in ADPKD are actually affected by cystic changes (5). Moreover, scanning electron microscope evaluation of kidneys from patients with ADPKD has convincingly demonstrated compression of tubules adjacent to cysts (5). Data derived from clinical studies indicate that renal impairment in ADPKD directly correlates with cyst size (3,6), and similarly, the presence of pain, which may be disabling, appears to correlate with the extent of cyst expansion (7). For example, over 50% of symptomatic patients have at least one cyst greater than 3.0 cm in diameter, compared with only 20% of asymptomatic patients (7).

Such observations provide a rational basis for attempts at cyst volume reduction as a means of preserving renal function and providing pain relief in patients with ADPKD. We have previously shown in a small number of patients that percutaneous cyst aspiration or open surgical reduction can provide effective pain relief without deleterious effects on renal function (8). Therefore, we undertook a prospective study in an attempt to evaluate the efficacy of surgical cyst decompression in slowing the rate of progression of renal impairment and in the management of chronic pain in patients with ADPKD.
with the more prominent symptoms was chosen. In 11 patients with bilateral chronic kidney pain, both kidneys were operated on simultaneously via a transperitoneal midline approach (8). Edges of the unroofed cysts were coagulated. Persistent bleeding was controlled by suture ligatures.

When symptoms recurred postoperatively in two patients, a second procedure was performed. In one patient, this consisted of a bilateral operation 13 months after the prior unilateral procedure. The other patient underwent unilateral cyst reduction on the side of recurrent pain 27 months after a bilateral operation. Thus, in total, 32 cyst decompression operations involving 44 kidneys were performed in these 30 patients. It was estimated that, on average, between 100 to 200 cysts per kidney were unroofed in each surgical session, which lasted 2 to 3 h.

Follow-Up

Renal function and blood pressure were monitored at regular intervals postoperatively. The interval until recurrence of pain was recorded. In patients from distant areas, follow-up was dependent on communications with referring physicians, along with regular telephone contact with the patient. With respect to the symptomatic response to surgery, data were censored in three patients at the time they attained renal insufficiency severe enough to require dialysis (at 11, 12, and 36 months). Otherwise, symptomatic outcomes were tabulated up to the closing date for this analysis, which was January 1991.

The effect of surgery on renal function was evaluated by multiple parameters. First, the short-term impact of surgery per se was assessed by comparing preoperative serum creatinine values with those obtained at 1 to 3 months postoperatively. Values were unavailable at this early time period in one referred patient with normal preoperative renal function. In addition, GFR determinations were compared preoperatively and postoperatively in the 14 patients who were able to return between 1 and 3 months for clearance studies. Secondly, the long-term effect of surgery on renal function was assessed at 1 yr. Of the 14 patients with unimpaired renal function before surgery, 11 had achieved 1yr of follow-up and their preoperative and 1-yr S\textsubscript{cr} values were compared. In the 16 patients with preoperative renal insufficiency (S\textsubscript{cr} >1.4 mg/dL), the effect of surgery on renal function was evaluated by determining the regression lines derived from the reciprocal of S\textsubscript{cr} (1/S\textsubscript{cr}) plots preceding and up to 12 months after surgery for each patient. The mean slope of these lines was calculated in deciliters per milligram per month. A minimum of three S\textsubscript{cr} values were required for construction of the regression line in each period (mean ± SE, 4.9 ± 0.6, preoperative; 5.3 ± 0.5, postoperative). With two patients, the number of values was

METHODS

Patients

During the period from November 1986 to September 1990, 30 patients (10 men, 20 women) with ADPKD underwent surgical cyst decompression. Their mean (±SE) age was 41 ± 2 yr (range, 19 to 62 yr). The diagnosis of ADPKD was confirmed in all patients by a computerized tomographic scan. The protocol was approved by the Institutional Review Boards of the Oregon Health Sciences University and the Mayo Clinic. Patients were referred from multiple areas of the country by physicians aware that this protocol was available.

After written informed consent was obtained, a baseline measurement of GFR was obtained by the renal clearance of inulin or [125I]iothalamate, and values were corrected to 1.73 m\textsuperscript{2} of body surface area. In addition, unilateral function was estimated by the differential kidney uptake of \textsuperscript{99m}Tc-dimercaptosuccinic acid (DMSA) as an index of the relative effective RPF between the two kidneys. The renal uptake of DMSA has been found to be a reliable index of renal function (9,10).

Blood pressure measurements were made with the patient seated, and at least three readings on successive days were averaged. Patients were classified as hypertensive if blood pressure was above 140/90 mm Hg or if there were a previous diagnosis of hypertension, controlled with the current use of antihypertensive medication. DMSA uptake in each kidney was determined at 24 h with correction for background and renal depth (11).

Surgery

Surgical indications were the presence of chronic pain in 14 patients (2 men, 12 women); chronic renal insufficiency, defined arbitrarily as a serum creatinine (S\textsubscript{cr}) level in excess of 1.4 mg/dL, in 4 patients (1 man, 3 women); and the presence of both pain and renal functional impairment in 12 patients (6 men, 6 women). The mean (±SE) S\textsubscript{cr} concentration in the 16 patients with renal insufficiency was 3.2 ± 0.3 mg/dL (range, 1.6 to 6.0 mg/dL). Among the 26 patients with chronic pain, 12 were regular (daily) users of narcotic analgesics.

Nineteen patients underwent unilateral cyst reduction operations as previously described (8). Surgical exposure was accomplished through a vertical lumbotomy incision in 12 patients and through a flank incision, to allow intrasurgical sonographic guidance, in 6 patients. In one patient, a midline abdominal approach was used at the time of simultaneous segmental hepatectomy for symptomatic polycystic liver disease (12). In asymptomatic patients, the operated kidney was chosen at random; otherwise, the side
Inadequate, and a third patient was excluded because of a postoperative increase in $S_{cr}$ secondary to hemorrhagic hypotension (see Results), leaving 13 patients for analysis. Finally, among those patients who underwent a unilateral procedure, postoperative split-function DMSA scans were available at 2 to 4 and/or 12 to 18 months in 14 patients, thereby allowing comparison of the operated kidney with the non-operated contralateral kidney serving as a control.

The mean follow-up was 21 months (range, 4 to 44 months). Three of the 30 patients studied were lost to follow-up; they had been observed for 18, 19, and 19 months.

Statistics

Where appropriate, data are reported as the mean ± SE. For those patients with chronic pain, the probability of remaining pain free after surgery was estimated by using a time-to-event analysis by the method of Kaplan and Meier (13). For patients undergoing a bilateral operation for pain, each kidney was considered separately, yielding a total of 39 painful kidneys. In analyzing the effect of surgery on renal function, a paired t test was used to assess statistical significance, except when comparing the regression lines for 1/S$_{cr}$, in which case a regression analysis of variance model for repeated measures was used. Differences were considered significant for $P < 0.05$.

RESULTS

Effect on Symptoms

Figure 1 shows the probability of being pain free after cyst reduction surgery in symptomatic patients. The probability of being free of pain at 12 months postoperatively was 80 ± 7%. This probability declined to 62 ± 10% at 24 months. Two patients (three kidneys) had recurrence of pain within the first postoperative month and were considered to have failed surgical treatment. In one of these patients, decompression was limited to fewer than 10 cysts because of the presence of extensive adhesions resulting from previous surgery. As mentioned above, two patients underwent repeat operations when symptoms recurred and a computed tomographic scan revealed the presence of several large cysts. Both patients experienced resolution of their pain after the repeat procedure; at 17 months after the second procedure, one patient had recurrence of pain and the other remains pain free.

Among the eight patients who experienced relapse of their pain during the period of observation, the pain was often of a lesser intensity than that present preoperatively such that only three patients, two of whom had failed surgical treatment, used narcotic analgesics on a regular basis (compared with 12 patients preoperatively).

Effect on Renal Function

There was no short-term effect on the operation on renal function as assessed by $S_{cr}$ concentrations and GFR at 1 to 3 months postoperatively compared with baseline values (Table 1). This observation was also true when only the group that had undergone a bilateral procedure was considered. It should be noted that included in this analysis is a single patient in whom surgery was complicated by hemorrhagic hypotension requiring transfusion with 3 U of packed red blood cells. Perioperative $S_{cr}$ in this patient rose from 1.8 to 3.4 mg/dL, subsequently declining to 2.5 mg/dL at 2 wk postoperatively, whereas GFR dropped from 33 preoperatively to 21 mL/min/1.73 m$^2$ 1 yr after surgery.

In assessing the long-term outcome of renal function among the 11 patients with normal preoperative renal function monitored for 1 yr, $S_{cr}$ remained unchanged (1.0 ± 0.05 versus 1.0 ± 0.07 mg/dL). In

![Figure 1. Kaplan-Meier time-to-event curve showing the probability of being pain free after cyst reduction surgery. The numbers at the bottom of the figure indicate the number of kidneys under observation at each period.](#)
patients with progressive renal insufficiency before surgery, comparison of the regression lines for \(1/\text{Scr}\) revealed no statistical difference in the mean value of their slopes before and after surgery (slope \(1/\text{Scr}\) before surgery, \(-0.008 \pm 0.001\) versus \(-0.009 \pm 0.002\) dL/mg/month after surgery; Figure 2), indicating that cyst reduction surgery did not significantly influence the course of progressive chronic renal failure due to ADPKD.

DMSA scans done before and after unilateral cyst reduction surgery in 14 patients to compare isotope uptake by the operated kidney with that of the contralateral kidney failed to reveal any consistent effect of surgery on renal function. Eight patients showed
an increased DMSA uptake by the operated kidney, with a mean increase of 8%, whereas six patients demonstrated decreased uptake, the mean decrease being 6% (Figure 3).

Effect on Blood Pressure

Hypertension was present in 22 of the 30 patients (73%) before surgery, 21 of whom were maintained on antihypertensive medication. A reduction in blood pressure was observed during the early postoperative days in most patients. However, this effect was short lived as evidenced by the fact that by the third postoperative month 12 patients had been returned to their baseline antihypertensive regimen and only 4 previously hypertensive patients remained normotensive off of drug therapy. At 1 yr, these numbers were 17 and 1, respectively, with the remaining patients on reduced dosages of antihypertensive medication. Thus, cyst decompression did not result in a sustained reduction of blood pressure in the majority of patients.

One previously normotensive patient developed hypertension requiring drug therapy 1 month after a unilateral procedure. After undergoing a bilateral procedure 13 months later for recurrent pain, she remained normotensive off antihypertensive therapy for 1 yr, after which she again developed hypertension.

Complications

The mean duration of hospitalization was 6.5 ± 0.5 days—5.5 ± 0.5 days after a vertical lumbotomy or a flank incision and 7.9 ± 0.6 days for patients undergoing a midline abdominal approach.

Complications after cyst reduction surgery are listed in Table 2. Two patients sustained injury of the upper urinary collecting system. In one instance, this was repaired by stented ureteroureterostomy. The stent was removed after 5 days without sequela. The other patient had a renal fistula that was managed conservatively and successfully with the placement of an indwelling bladder catheter and continuance of the perinephric flank drain. The urine leak resolved spontaneously by the 11th day. Urinary infection occurred in 2 patients at 12 days and 2 months. The causative organism was Escherichia coli, and both patients responded to appropriate antibiotics. Transfusion of 2 U of blood was done in two patients, and as described above, a third patient received 3 U of blood. In two patients, a ventral hernia developed at the incisional site. Finally, one patient was readmitted to the hospital with partial small bowel obstruction necessitating resection of 50 cm of distal ileum adherent to the anterior abdominal wall closure.

DISCUSSION

The surgical drainage and deroofing of renal cysts for the relief of symptoms was reported first by Rovsing in 1911 (14). Subsequently, several authors confirmed favorable outcomes, including the relief of pain and prolonged renal survival, although controlled patient groups and definitive renal function studies were lacking (15-21). The procedure fell out of favor in the 1960s, after careful observations in two patients who suffered a decline in their GFR after surgery (22). This raised concerns that the destruction of functioning cystic nephrons might be detrimental to renal function. These concerns were supported by two subsequent studies on a total of nine patients who underwent differential renal function studies before and after unilateral decompression of a polycystic kidney (23,24). In most instances, the decompressed kidney showed a postoperative reduction in function. However, these studies are open to criticism because the procedures were often complicated by infection and because the rate of the renal functional decline before surgery was not considered. It has been argued that the number of cystic nephrons destroyed is insignificant in terms of the total number of functioning nephrons present in each kidney. Furthermore, in most cases of ADPKD, the cysts become detached from their tubular segment of origin and therefore no longer participate in whole-kidney excretory function (5).

The pattern of progression of ADPKD is characterized by good preservation of renal function for decades, only to be followed by a second phase of rapid deterioration leading to end-stage failure within a decade or so (3). According to the model of Franz and Reubi (3), this pattern can be explained by assuming that the radius of the cyst increases at a constant rate, resulting in an accelerated increase in cyst volume and an accelerated reduction in the volume of the residual functioning tissue.

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of Patients</th>
</tr>
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<tbody>
<tr>
<td>Upper urinary collecting system injury</td>
<td>2</td>
</tr>
<tr>
<td>UTI†</td>
<td>2</td>
</tr>
<tr>
<td>Hemorrhagic hypotension</td>
<td>1</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td></td>
</tr>
<tr>
<td>2 U</td>
<td>2</td>
</tr>
<tr>
<td>3 U</td>
<td>1</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>2</td>
</tr>
<tr>
<td>Small bowel obstruction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
</tbody>
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† UTI, urinary tract infection.
On the basis of the aforementioned observations suggesting that renal insufficiency in ADPKD is the result of pressure exerted by the steadily enlarging cystic nephron on normal parenchyma, there has been a resurgence of interest in cyst decompression procedures in an attempt to arrest or retard renal deterioration. Indeed, Shangzhi and associates (25) performed thorough cyst deroofing operations in 52 patients, reporting stabilization or improvement in renal function in most instances. Moreover, the procedure afforded prolonged pain relief and control of hypertension. Similarly, Bennett et al. (8) found that percutaneous cyst aspiration or surgical cyst decompression alleviated symptoms without adversely affecting renal function in all 11 of their patients suffering from severe pain. With percutaneous aspiration, however, pain relief was usually temporary. More recently, a preliminary report showed a significant improvement in GFR, measured by isotope clearance techniques, immediately after percutaneous cyst puncture (26). Other authors have emphasized the symptomatic and antihypertensive responses after the operation (27). Although uncontrolled, these studies nonetheless challenged the concept that cyst decompression surgery accelerated deterioration of renal function.

In the study presented here, we have shown that surgical cyst decompression is highly effective in the management of chronic pain related to polycystic kidneys, conferring long-term relief in the majority of patients without adversely impacting renal function. Pain is a common symptom in ADPKD, afflicting about 60% of patients (2.6). It can be severe and intractable, rendering the individual narcotic dependent or disabled. In those patients who fail conservative medical management, a surgical approach should be considered a viable option because it offers a reasonable chance for prolonged relief of symptoms. In our experience, those patients with relatively small numbers of predominantly large cysts are particularly likely to benefit from such an approach.

Surgical cyst decompression had no short-term adverse effect on renal function, as assessed by S_cr and GFR determinations. Mean S_cr concentration remained unchanged, whereas mean GFR 1 to 3 months postoperatively was numerically increased from the preoperative level, despite inclusion of the single patient who suffered a brief episode of hemorrhagic hypertension with moderate acute and residual deterioration of renal function. Although not a statistically significant difference, the observation is nonetheless important in that marked deterioration in renal function, which was the major reason that this type of operation was abandoned in the past, was not observed.

Whether surgical decompression of polycystic kidneys can alter the course of progressive renal insufficiency is more difficult to assess. The slope of 1/S_cr against time has been proposed as a convenient way to measure the rate of progression in chronic renal failure (28,29). However, there is considerable controversy about the value of 1/S_cr as a substitute for GFR determinations for this purpose. It is well known that S_cr concentrations are not sensitive reflections of decreases in GFR. Differences in tubular secretion, extrarenal elimination, and rate of generation of creatinine among patients with chronic renal failure, as well as the changing nature of these parameters in individual patients over time, may render the rate of decline in 1/S_cr an inaccurate measure of the rate of decline in GFR. Furthermore, the use of the slope of 1/S_cr against time is based on the assumption that GFR declines in a linear fashion. Such an assumption may not be valid in ADPKD (3), making it hazardous to have patients serve as their own controls in studying the effects of an intervention on progressive renal failure. Recently, other investigators have confirmed that the decline in renal function is linear in ADPKD (30). A full account of the limitations of the use of 1/S_cr to monitor progression of renal disease has recently been published (31).

An inadequate number of GFR measurements were performed in the study presented here before and after surgery for logistical reasons related to where the patients lived to allow for a meaningful analysis. Although we recognize its limitations, we adopted the rate of decline in 1/S_cr for assessment of the impact of our operation on the course of ADPKD. By using this approach, we could not demonstrate that decompression of the polycystic kidney slows the progressive decline in function in ADPKD, because there was no change in the mean of the slopes of the regression lines preceding and after surgery. This is at variance with the more optimistic report of Shangzhi et al. (25). Although their results can be criticized for their crude estimates of renal function (mainly based on measurements of plasma BUN levels), it is possible that their more extensive operation, with drainage of up to 1,000 cysts, is necessary for optimal results on renal function. Moreover, it can be argued that a real difference in efficacy, although present, may have gone unrecognized, owing to the large variability in the rates of decline among individuals, resulting in imprecision when a mean 1/S_cr slope is used. However, split-function radiologic DMSA scans also failed to demonstrate any consistent effect of surgery on the operated kidney. Indeed, most differences between sequential scans were within the range of variability of the test. Implicit in the use of DMSA scans to monitor individual kidney function is the assumption that, left untreated, the rate of functional deterioration would be similar for both kidneys. Given the marked asymmetry of function that was often present at the time of entry into the study, such an assumption may be invalid.

The initial reduction in mean arterial pressure ob-
served after cyst decompression is in agreement with results from other reports (8,19,25,27). The pathogenesis of the hypertension associated with ADPKD remains unclear. It has been proposed that the hypertensive effect of cyst decompression reflects the renin-dependent nature of the hypertension owing to cyst-induced renal ischemia causing stimulation of the renin-angiotensin-aldosterone system (32). In this study, however, long-term persistence of the antihypertensive effect of surgery was not seen.

In summary, surgical cyst decompression is very effective at providing marked relief in the majority of patients who suffer from the chronic pain and discomfort associated with polycystic kidneys. Contrary to earlier published reports, these procedures do not accelerate deterioration of renal function. The hope that this operation might preserve renal function in the presence of preexisting renal insufficiency was not realized in this study. However, until new treatment strategies to prevent the formation and growth of cysts become available (33), surgical cyst decompression offers a safe and effective therapeutic alternative for those patients suffering from chronic, disabling pain, in whom more conservative measures have failed.

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REFERENCES


