Abstract: More than 60 percent of patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) experience chronic abdominal or flank pain over the course of their lifetime. Individual enlarging cysts can cause pain through stretching the renal capsule and/or compression of surrounding structures. This pain is most often localized to the anterior abdomen. The usual strategy with laparoscopic cyst decortication (LCD) has been to excise/unroof as many cysts close to the surface of the kidney as possible. However, this provides lasting relief in only 50 to 60 percent of the treated patients, is associated with prolonged operative times, and causes significant post-operative complications such as urinary leaks leading to formation of urinomas. Of particular concern is the potentially detrimental effect of the procedure on renal function. Here, we describe a systematic approach for employing this technique for cyst related pain in ADPKD: 1) Patient must be able to provide single finger pinpoint location of chronic reproducible pain lasting at least 6 months. This pain must be consistently moderate to severe in intensity (more than 5 on a 10-point visual analog scale) despite maximal conservative therapy not including chronic opioid analgesic use. 2) The area of maximal pain/ tenderness is identified using a skin marker. 3) Ultrasonography is used to identify “culprit cysts” that are at least 4 cm in size and are located directly underneath the marked skin area. 4) Our team urologist experienced in surgical management of ADPKD employs the LCD technique, never unroofing more than three cysts. We document successful use of this approach achieving excellent and lasting pain control, while minimizing operative times and other adverse effects in three patients who underwent a total of four procedures.

Keywords: Laparoscopic cyst decortication, Marsupialization, Unroofing, Polycystic Kidney Disease, PKD, Cyst pain, Chronic Pain, Pain Management, Review.
Abbreviations:
- **ADPKD**: Autosomal Dominant Polycystic Kidney Disease
- **LCD**: Laparoscopic Cyst Decortication
- **Cr Cl**: Creatinine Clearance
- **VAS**: Visual Analog Scale
- **MRI**: Magnetic Resonance Imaging
- **USG**: Ultrasonography
- **CKD**: Chronic Kidney Disease
- **eGFR**: Estimated Glomerular Filtration Rate
- **JP**: Jackson-Pratt
- **POD**: Post Operative Day

Introduction:

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common inherited cystic renal disease; it affects 1 in every 400 to 1000 individuals and is the underlying etiology in approximately 5% of the patients who initiate dialysis every year in the United States. Pain is a common early symptom in the course of ADPKD. More than 60 percent of the patients are affected by abdominal and/or flank pain in their lifetime, often decades before renal insufficiency sets in.\(^1,2\) Additionally, chronic pain is a complaint in almost half the patients even before the diagnosis is established and represents the most common symptom leading to the diagnosis.\(^3\)

Renal cysts cause two distinct types of pain in ADPKD:

1. **Pain due to overall increased renal mass**: Enlarging cysts cause an increase in abdominal girth that, over time, leads to progressive maladaptive postural changes, including an exaggerated pelvic tilt and increased lumbar lordosis.\(^4\) Resultant mechanical strain on the lumbosacral muscles ultimately leads to hypertrophy of these muscles and progressive degenerative spine disease. In a personal observation by one of the authors (TIS), in 10 patients with ADPKD average lumbodorsal muscle thickness at L4-S1 level on abdominal MRI done to assess cyst volume was 38.7 mm, in contrast to 31.3 mm in ten matched individuals without ADPKD undergoing MRI for unrelated reasons.\(^4\) Typical presentation is chronic back pain that is usually made worse by standing or walking. Non-pharmacologic measures such as back strengthening exercises to counteract lumbar lordosis, avoidance of improper postural and movement habits (for example, with Alexander technique), heat and cold packs, and massages are the first line of management. If these are not effective, a slow and step-wise approach to systemic analgesics is needed. However, since this is a manifestation of increased renal mass and is not attributable to individual cysts, cyst decortication procedure has limited to no role in management of this type of pain.

2. **Pain directly related to enlarged renal cysts**: Individual expanding cysts can directly cause pain. This can be due to stretching of the renal capsule, traction on the renal pedicle or compression of nearby structures. Pain severity does not always correlate with cyst size; relatively small cysts can be a source of significant pain and sometimes very large cysts produce no or minimal discomfort. This pain is often localized to the anterior abdomen, and less frequently to the back. Since a single or few underlying cysts are responsible, pain is well localized and patients are often able to provide a finger-point localization of the epicenter of pain. Focal tenderness is usually appreciated in the same area. These cysts may be amenable to drainage, which can effectively control pain while avoiding the side effects of systemic analgesics (in particular, the detrimental effects of non-steroidal anti-inflammatory drugs on renal function and central nervous system effects of narcotic analgesics).

Cyst drainage can be achieved by any of the following approaches: needle aspiration, open surgical decortication/marsupialization or laparoscopic cyst decortication (LCD). Percutaneous aspiration is the least invasive. However, fluid
frequently re-accumulates leading to recurrence of symptoms and hence, it is not recommended for management of cyst-related pain. In the marsupialization/decortication procedure, a slit is made in the wall of the cyst and the wall is excised or the edges of the slit are sutured to the external surface; the site remains open and drains freely. As a result, fluid is not allowed to re-accumulate and symptoms are less likely to recur. Surgical marsupialization of renal cysts for pain management was first described over a century ago. Several case series documented efficacy of this procedure in achieving pain control. However, reports of deterioration of renal function after undergoing this procedure led to a diminished enthusiasm for this treatment modality for many decades. In particular, Bricker and Patton published in the New England Journal of Medicine in 1957 a report of two ADPKD cases whose creatinine clearance (Cr Cl) values decreased immediately after surgery for cyst decompression, and remained reduced at one year follow up. Based on these observations and recent evidence at that time that cystic nephrons in ADPKD retain functional activity, they concluded that destruction of a large number of affected nephrons in a polycystic kidney (even with diminished reserve) will further compromise its functional ability, thereby discrediting the procedure as potentially detrimental. The procedure was resurrected in the 1980s when He et al and Ye et al documented that this procedure could be used safely and effectively for pain control in ADPKD, without any acceleration of decline in renal function. The use of a laparoscopic approach for cyst decortication for cyst-related pain in ADPKD patients was first reported by Teichman and Hulbert in 1995 in a report of six patients all of whom had failed to achieve pain control with percutaneous aspiration. Advantages of using a laparoscopic approach over open surgery include less post operative pain, shorter hospital stay, quicker recovery and improved cosmetic outcomes with equivalent pain relief. As such, once the decision to pursue treatment with invasive measures is made, LCD is the preferred technique.

Our guidelines for proceeding with LCD, which differ from prior reports, are noted below and address which cysts and how many cysts should be targeted. The role of underlying renal insufficiency should factor into this decision making. In the literature, the usual approach has been to decorticate as many of the larger cysts as possible and to puncture and drain as many of the smaller cysts as possible. Short term and long term limitations of this approach are noteworthy: first, pain relief is maintained at 2 years duration in only a little over 50% of the patients. In one prospective study of 30 ADPKD patients undergoing open cyst reduction surgery, only 62% were pain free at 2 year follow up. More recently, similar results have been reported with LCD. We postulate that lack of sustained relief from pain observed in a large percentage of the patients undergoing LCD may be, at least in part, due to sub-optimal implementation of this technique:

- Inappropriate selection of candidates: When the pain is related to the mechanical effects of an overall increase in total kidney volume (as opposed to individual cysts), these procedures are unlikely to yield significant benefit.
- Poor localization of “culprit cysts” responsible for symptoms.

Secondly, anywhere from 200 to 600 cysts are usually treated at each time. This blind and extensive decortication and drainage increases the total operative time as well as the likelihood for intra-operative and post-operative complications. Dunn et al reported an analysis of 15 patients with ADPKD who underwent a total of 21 LCDs; mean number of cysts marsupialized per procedure was 204 (range 11 to 635) and mean operative time was 5.5 hours (range 4.5 to 6.6 hours). At a mean follow up of 2.2 years, 11 patients (73%) reported an average of 62% improvement in pain, with only transient or no improvement/worsening in the other 4 (27%). Average inpatient time after the procedure was 3.2 days. Three patients in this series developed en-
capsulated collections of extravasated urine (also known as ‘urinomas’) postoperatively, warranting more procedures. In another series by Lee et al of 35 LCD procedures in 29 ADPKD patients, every detectable cyst within 2 mm of the renal surface was treated. Mean operating time was 4.9 hours (range 2.6 to 6.6 hours); average number of cysts treated per patient was 220 cysts (range 4 to 692). More than 50% improvement in pain was noted in only 52% of the treated patients at 24 months follow up. Urinomas developed in three patients necessitating ureteral stent placement in all of them. Whether there is any benefit from such extensive decortication, particularly at the expense of these complications has not been evaluated.

Thirdly, data regarding impact of LCD on natural progression of renal insufficiency are mixed. Many uncontrolled case series document that Cr Cl is unchanged after LCD. Other studies have shown a vulnerability to renal function decline, particularly if there is baseline impairment of kidney function. In the study of 29 ADPKD patients mentioned earlier, all five patients with a preoperative Cr Cl of less than 30 ml/min experienced worsening of renal function post operatively, and one patient with normal renal function at baseline had a 22% drop in Cr Cl at 24 months follow up. Whether LCD itself alters the progression of renal insufficiency remains an open question. However, if the decline in renal function is a consequence of the procedure itself, it is conceivable that doing more targeted and less extensive decortications will improve renal outcomes. This is especially relevant if renal insufficiency is already present, where all renal compensatory mechanisms are already being fully employed and there is little remaining reserve.

Here, we describe a systematic approach to using LCD for management of cyst-related pain in ADPKD, and illustrate its successful use in 3 patients who underwent a total of 4 procedures. The steps of this approach are outlined below:

1. To be eligible for this procedure, careful history and physical examination are required to establish whether the pain is related to individual cysts and is severe and long-standing enough to warrant invasive therapy:

   i) The ADPKD patient must be able to provide a single finger pinpoint location of reproducible chronic pain, usually in the anterior abdomen, for at least 6 months in duration.
   ii) The area of maximal tenderness is at the pinpoint location.
   iii) Pain must be moderate to severe and impacts the daily quality of life. A visual analog scale (VAS) of pain is more than 5/10 (averaging 7/10 in our cohort).
   iv) Maximal conservative therapy regimens have failed, but not including chronic narcotic use. Patient’s ability to tolerate various analgesics should factor into decision making.

2. The area of maximal pain/pinpoint tenderness is identified using a skin marker in conjunction with ultrasonography (USG). The aim of the radiologic evaluation is communicated to the radiologist prior to the procedure.

3. Abdominal USG is used to identify the culprit cyst(s) that are directly beneath the marked skin area and measure at least 4 cm in the biggest dimension. In certain instances, additional computed tomography/magnetic resonance imaging (MRI) may be required for better delineation prior to proceeding with LCD.

4. Following this, an experienced urologist who is familiar with the nuances of surgical management in ADPKD patients employs the LCD technique, never unroofing more than three cysts at a time.

**Case 1:**

45 year old male with ADPKD and stage IV chronic kidney disease (CKD) with estimated glomerular filtration rate (eGFR) of 27 ml/min/m² presented with localized right upper quadrant pain. The pain had been present for at least 3 years, and had been getting worse over the preceding 6 months. It was described as constant and non-radiating, and graded at 7 on 10-point VAS. Pain relief with acetaminophen and tramadol was inadequate. Chronic use of non-steroidal anti-inflammatory drugs was contraindicated due to underlying renal insufficiency. Given his teaching responsibilities, he was unable to tolerate narcotic analgesics during the daytime due to their sedative effects. Physical examination was notable for bilaterally palpable kidneys; the right lower pole was extremely tender to light anterior palpation
with only mild tenderness on the left side. Using USG, two
cysts were identified in lower pole of the right kidney (5.0
cm & 6.5 cm in the biggest dimension), directly beneath the
area of marked maximal discomfort. Only these two cysts
were decorticated using the LCD technique. Jackson-Pratt
(JP) drain was removed on post operative day (POD) 1 and
he was discharged to home on POD 2. The procedure result-
ed in complete relief of pain on the right side that was main-
tained at his last follow up at 34 months. The repeated and
sustained VAS at each visit was 1-2/10, down from 7/10.

He presented a year and a half after the initial procedure
with focal pain in left upper abdominal quadrant that was
characterized as constant, non-radiating and 8/10 in severity
on the VAS. The marked skin area of tenderness corre-
sponded to the site of pain. USG identified one cyst 4.7 cm
in largest dimension directly below this area. A JP drain was
not required and patient as discharged to home on POD 2.
Again, LCD directed at this single cyst resulted in complete
resolution of pain; patient remained pain free (VAS 1/10) at
his last follow up at 15 months.

No differences were seen between pre-operative and
post-operative serum creatinine values on either of two in-
tances. However, he has had progressive CKD consistent
with the natural course history of ADPKD, with the most re-
cent eGFR 12 ml/min/1.73m² and is undergoing evaluation
for renal transplantation.

**Case 2:**

51 year old male with left-sided dominant ADPKD and nor-
mal renal function with serum creatinine of 1 mg/dL pre-
sent with worsening pain and discomfort on the left side
of two years duration. Pain severity was rated at 5/10-point
VAS; this was associated with a sensation of constant ab-
dominal fullness and increased abdominal girth. Bending
forward and sleeping on his left side worsened this discom-
fort. A large (21 cm x 16 cm) cyst originating from the lower
pole of the left kidney was visualized on USG; this was sig-
ificantly enlarged compared with his MRI from three years ago when he had no pain. This large cyst was excised
(drained a total of 1.7 L of straw-colored fluid). Additionally,
two adjacent large cysts were also unroofed. He tolerated
the procedure well, was discharged to home the day after
surgery and remained symptom free at his last follow up
10 months after the procedure (repeated VAS 1/10). Pa-
tient’s renal function was not affected; serum creatinine 10
months after the procedure was 0.9 mg/dL.

**Case 3:**

39 year old with ADKD and preserved renal function with
serum creatinine of 0.9 mg/dL first presented to us for eval-
uation of left flank pain of at least two to three years dura-
tion. This pain was present all the time, being 7/10-point
VAS and requiring near maximal doses of tramadol on a
daily basis. The pain episodically radiated down his back to
his left lower extremity. Tenderness on deep palpation was
appreciated in the area where the patient reported maximal
pain. Corresponding to this area, two adjacent cysts were
identified in the lower pole of the left kidney on USG (4.4
cm and 3.8 cm in largest dimension). These two cysts were
unroofed. Patient required placement of a JP drain that was
removed on POD1, following which the patient was dis-
charged. He reported complete resolution of his symptoms
(VAS 1/10), which was maintained at follow up six months
after the procedure. This has been his longest pain free in-
terval in over 3 years. Additionally, his serum creatinine re-
mained unchanged.

Additional information regarding total operative time,
length of hospitalization and complications is outlined be-
low:
Pain is a common symptom in ADPKD, often occurring early in the course of the disease and frequently leading to diagnosis. However, it is vastly under-recognized and its management remains suboptimal; this results in unnecessary suffering, decreased quality of life and lost productivity. Acute pain can occur as a result of cyst rupture and hemorrhage, pyelonephritis, cyst infection (known as pyocystis) or nephrolithiasis. As outlined earlier, chronic pain in ADPKD can be a consequence of either the effects of increased total kidney volume on the spinal column and paraspinal muscles, or stretching of the capsule, compression or pull created by the expanding cysts (resulting in irritation of nerves in the renal capsule, renal parenchyma or intrarenal collecting system). As with all other types of chronic pain, comprehensive, step-wise and personalized approach involving non-pharmacologic, pharmacologic and surgical approaches is key to achieving effective relief from pain. This article focuses on the appropriate and specific circumstance use of a LCD procedure to offer long term relief/cure from pain while avoiding the side effects of systemic medications.

<table>
<thead>
<tr>
<th>Case</th>
<th>Number of cysts decorticated/unroofed</th>
<th>Duration of procedure</th>
<th>Duration of hospitalization (from procedure to discharge)</th>
<th>Complications</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Right)</td>
<td>2</td>
<td>63 minutes</td>
<td>2 days</td>
<td>None</td>
<td>No pain at 34 months</td>
</tr>
<tr>
<td>1 (Left)</td>
<td>1</td>
<td>64 minutes</td>
<td>2 days</td>
<td>None</td>
<td>No pain at 15 months</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>98 minutes</td>
<td>1 day</td>
<td>None</td>
<td>No pain at 10 months</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>64 minutes</td>
<td>1 day</td>
<td>None</td>
<td>No pain at 5 months</td>
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</tbody>
</table>

The previous reported strategy with decortication procedures in management of cyst-related pain in ADPKD has been to drain as many cysts close to the surface of the kidney as possible. Not only has this proven ineffective in providing long term relief in a large percentage of the cases, it is associated with prolonged operative and hospitalization times, and major post-operative complications (eg., urinary leaks leading to formation of urinomas). Most concerning is the potentially detrimental effect on renal function associated with unfocused broad scale unroofing of cysts, especially in the face of pre-existing renal insufficiency where compensatory mechanisms have already been fully exhausted. A more focused and limited approach has not been reported, and no guiding principles are available regarding which and how many cysts can be safely decorticated for pain control in patients with ADPKD. To our knowledge, this case series represents the first report documenting systematic employment of LCD with specific criteria for targeting "culprit cysts." Careful history and physical examination combined with protocol-driven use of imaging are outlined to identify patients whose chronic pain is attributable to enlarging individual cysts and likely to benefit from LCD. In three patients, who underwent a total of four procedures, sustained complete resolution of pain was observed. Operative time was dramatically lower than as reported in previous studies. Blood loss was minimal. No major or minor complications were observed and patients were discharged to home within 1 to 2 days. While the patient in case 1 has had pro-
progressive chronic kidney disease over the last three years, it is notable that his renal function parameters immediately after the surgery were unchanged compared to pre-procedure. His projected slope of decline in renal function was consistent with the natural course history of his ADPKD and unaffected by surgery. Patients in cases 2 and 3 had normal renal function at baseline, and their serum creatinine values remained unchanged at last follow up.

In summary, this case series highlights that LCD is a useful tool in the armamentarium for management of chronic pain in management. Focused LCD aiming cysts responsible for patient symptoms identified through thorough clinical and radiographic evaluation can increase the success rate of the procedure while minimizing adverse effects. The importance is noted of a multi-disciplinary approach involving nephrology, urology and radiology, all committed to pain relief in those with ADPKD. Further long term studies in a large cohort are required to establish the effectiveness of this approach.

References:


