GUIDELINE RECOMMENDATIONS*

a. We recommend that clinicians should include the evaluation of pain in patients with autosomal dominant polycystic kidney disease during clinic visits (1D).
b. We recommend that patients be involved in the management of their pain, non-pharmacological treatments be emphasized in the first instance (1D).
c. We suggest that surgical interventions for cyst decortication may be warranted in individuals with severe ongoing pain (2C).

*Criteria used for recommendations and levels of evidence (1,2;A-D) are described in more detail in Tables 1 and 2 of Rangan G, Savige J. Introduction to the KHA-CARI Guidelines on ADPKD. Semin Nephrol.2015;35:521-3 in this issue.

UNGRADED SUGGESTIONS FOR CLINICAL CARE

- An initial assessment (detailed history, psychosocial assessment, and physical examination) should be performed to determine the most likely basis of chronic pain in patients with autosomal dominant polycystic kidney disease (ADPKD). The initial evaluation should attempt to distinguish between acute pathology (often due to cyst infection, stones, or bleeding) and chronic pathology (caused by cyst expansion or mechanical back pain from increased kidney mass). Thus, pain due to cyst infection is typically localized and associated with fever, elevated inflammatory markers, positive urine cultures, and positive magnetic resonance imaging or fluorodeoxyglucose–positron emission tomography imaging.

- The initial assessment, and ongoing monitoring, should indicate the appropriate management of chronic pain in ADPKD. Management should be stepwise, involving non-pharmacological, pharmacological, and possibly invasive interventions for cyst decortication, and may require the involvement of multiple disciplines (radiology, urology, physiotherapy, and chronic pain clinics).

- We suggest that treatment goals for patients with chronic pain in ADPKD should be individualized and patients should be made aware that the time required to treat chronic pain is substantial (exercises for lumbar lordosis may require 3-6 months before any observed improvement).

- Pharmacological treatment of chronic pain in ADPKD should adhere to standard principles for managing chronic non-malignant pain, with the following exceptions:
  ○ Medication dose should be modified according to the level of renal function;
  ○ Chronic use of nonsteroidal anti-inflammatory drugs/cyclooxygenase-2 inhibitors should be discouraged;
  ○ A step-wise approach should be used.

- We suggest that analgesic therapy adhere to the following principles:
  ○ A systemic, non-opioid analgesic (such as paracetamol) should be the first-line treatment;
  ○ Severe acute-on-chronic pain, or pain that is refractory to non-opioid analgesics, may require escalation of analgesic therapy;
Invasive surgical interventions for cyst decortication to relieve chronic disease-related kidney pain may be considered if the pain is refractory to conservative medical management and can be attributed to a single dominant (>5 cm diameter) or a group of dominant cysts (3 cysts >4 cm diameter). A simple test in attributing pain to a cyst is to confirm that maximal tenderness overlies a cyst demonstrated on ultrasound imaging.

Surgical interventions can be divided into minimally invasive procedures (simple renal cyst aspiration or renal cyst aspiration with sclerotherapy), and complex surgical interventions that have a greater risk of morbidity (laparoscopic cyst decortication, renal denervation, and nephrectomy). The hierarchal approach and optimal choice of surgical intervention is not well described and depends on the clinical circumstances, and discussion with a surgeon/interventional radiologist. Thus, chronic pain due to a single cyst or multiple cysts may be amenable to aspiration, and pain due to recurrent cysts may be treated with aspiration plus sclerotherapy and/or laparoscopic cyst decortication. Alternatively, patients with severe intractable pain who have end-stage kidney disease may be suitable for laparoscopic nephrectomy.

**IMPLEMENTATION AND AUDIT**

- Assessment of chronic renal pain in patients with ADPKD attending renal clinics.
- A quality-of-life survey asking patients with ADPKD about pain control.
- Use of magnetic resonance imaging to determine whether pain is due to cyst bleeding, infection or enlargement, or to mechanical back pain.

**BACKGROUND**

Pain is very common in ADPKD, occurring in up to 60% of patients at some time.\(^3\) Renal pain is found in 40% of dialysis patients with ADPKD but only in 2% with other diseases \((P = .0001)\).\(^7\) Seven percent of patients with ADPKD reported taking pain medication within 1 month of evaluation and these individuals had a lower score on the physical well-being component of the Short Form 36 questionnaire.\(^5\)

Pain may be short-lived, or long-term and disabling. It is most often located in the lower back, or abdomen, but may include headache and leg pain.\(^6\) Sometimes pain from polycystic kidneys is referred to the chest or perineum. Severity is typically 4 to 5 out of 10 on a visual acuity scale.\(^6\)

Chronic pain in ADPKD may disturb sleep, daily activity, mental well-being, and social relationships.\(^7\) Renal pain tends to occur early and correlate poorly with total kidney volume. Its evaluation is complex, and its characteristics (frequency, onset, duration, quality, localization) and causes change with time in any individual.\(^8\) Chronic pain may relate to an individual cyst or to mechanical back pain. Pain from a cyst is focal and located in the flank or abdomen, but the area indicated by the patient does not always correlate with the largest cysts on imaging.\(^5\)

Pain may be due to renal cyst enlargement, rupture, hemorrhage, infection, or nephrolithiasis. Enlarging cysts increase abdominal girth and also cause abdominal wall muscle hypertrophy, exaggerated pelvic tilt, and subsequent stress on lumbodorsal muscles, lumb lordosis,\(^8\) and degenerative disc disease.\(^6\) Enlarging cysts may compress surrounding tissue, causing traction on the renal pedicle and a distended renal capsule. This tends to occur gradually with growth of the kidneys and typically results in a steady nagging discomfort, exacerbated by standing and walking.

Headache does not occur more often in patients with ADPKD than in the general population, and does not necessarily indicate the presence of an intracranial aneurysm.\(^6\) In a series of 40 patients with severe recurrent headaches, none had a cerebral aneurysm on magnetic resonance angiography.\(^6\)

Magnetic resonance imaging helps differentiate mechanical low back pain caused by cyst enlargement, cyst rupture, or infection. If stone disease is likely, then pain should be investigated with abdominal computed tomography scan or ultrasound.

Pain due to infection, bleeding, or stones is treatable, but may recur. Pain due to cyst enlargement is more challenging and there is no optimal approach to management. The severity of pain from cyst enlargement varies between patients and a combination of approaches is most useful. The goal of therapy is for the individual to find the pain bearable, since complete resolution may not be possible. Treatment is achieved using pharmacological, nonpharmacological, and surgical measures. Patients should be involved as much as possible in the management of their pain.

Surgical interventions include renal cyst decompression, with or without sclerotherapy, open or laparoscopic renal cyst decortication (unroofing and collapse of cysts or fenestration and marsupialization), and nephrectomy.
SEARCH STRATEGY

Databases Searched

Medical Subject Headings (MeSH) terms and text words for autosomal dominant polycystic kidney disease were combined with the MeSH terms and text words for chronic pain. This was then combined with further searches using the MeSH and text words for pain relief, nonpharmacological interventions, and pharmacological interventions. Animal studies were specifically excluded. The search was carried out in Ovid MEDLINE (1946 to June 2014), Embase (1974 to May 23, 2014), PsyCINFO (1806 to June 2014), and the Cochrane Database of Systematic Reviews and the Cochrane Database of Clinical Trials (inception to June 2014).

Date of search: June 2014.

WHAT IS THE EVIDENCE?

Supplementary evidence Tables are available online.

Nonpharmacological Agents for Kidney Pain

The optimal nonpharmacological approach for managing chronic pain due to ADPKD is not known, but may include simple interventions (heat, ice), psychological behavioral modification, physical techniques (exercises, thermotherapy, transcutaneous electrical nerve stimulation, hydrotherapy), mind-body techniques (acupuncture, Alexander technique), or a combination of these.

Transcutaneous electrical nerve stimulation may be helpful when used intermittently, especially for dull aching pain.6 A 2-week trial indicated individuals in whom this treatment was effective. Spinal cord stimulation with permanent electrodes implanted in the epidural space was required much less often but may be effective too. Acupuncture and electrical stimulation of acupuncture points produced pain relief through activation of the gate control system by which large fibers were stimulated and small fibers were suppressed.9

Pharmacological Agents for Kidney Pain

The management of pain in ADPKD involves the use of analgesics, but there is no evidence for any specific type. Recent studies with disease-modifying agents, such as tolvaptan and somatostatin analogues, suggested that a reduction in cyst size may prevent chronic pain. Treatment of patients with ADPKD (glomerular filtration rate > 60 mL/min, total kidney volume > 750 mL) with tolvaptan for 3 years was associated with a reduction in kidney volume and a decrease in kidney pain (five events in the tolvaptan and seven in the placebo group per 100 person-years; P = .007). The reduction in pain occurred soon after starting tolvaptan and was sustained throughout the study.10 Although there is recent evidence for octreotide in reducing cyst enlargement, pain improvement was not assessed.17

Other medications for pain relief include paracetamol, and the judicious use of nonsteroidal agents, tramadol, and codeine-based analgesics including fentanyl patches. Some of these agents have the potential for abuse. There is no specific evidence for gabapentin and pregabalin in ADPKD, but both agents are useful in other forms of neuropathic pain involving the genitourinary tract.12

Renal Cyst Aspiration With or Without Sclerotherapy

Common surgical treatments for pain in ADPKD are percutaneous drainage of the affected cyst and, if unsuccessful, open surgical decortication. Cyst aspiration alone is ineffective because fluid reaccumulates following the procedure, and it is difficult to identify the cyst causing the pain. The approach may be laparoscopic.13,14 Cyst decompression has been reported to result in lasting pain relief and improved renal function,15,16 but in other studies to have no effect on renal function or hypertension.6

Pain due to enlarged cysts has been treated with cyst ablation plus sclerotherapy (using either absolute ethanol or N-butyl cyanoacrylate/iodized oil). Usually one or several large cysts (> 5 cm diameter) only are ablated.17 Ablation with 99% ethanol in a cohort of 15 individuals was successful in all 15, with complete resolution of the cysts in 13 and recurrence in 2.17 The indication for the procedure in this series was “severe flank pain,”17 and the mean age of the patients was 35 years with an average cyst size of 7.3 cm. Pain was significantly reduced but the serum creatinine increased (pretreatment 1.89 versus post-treatment at 1 year 2.1 mg/dL; P < .05), but the study had no control group.17 Repeat cyst aspiration and sclerotherapy was performed in three cases.17 Complications included nephrectomane fistula in one individual and urinary tract infection in another.17

Surgical Cyst Decortication

All studies of surgical cyst decortication have demonstrated an improvement in pain.6 However, a systematic review of surgical renal cyst decortication reported worsening renal function, especially where the initial creatinine clearance was less than 45 mL/min/1.73 m2.18

In a single-center series, 29 individuals with chronic pain underwent laparoscopic decortication.19 Each cyst within 2 mm of the renal surface was treated. The mean operating room time was 4.9 hours (range, 2.6-6.6 h), with no patient requiring open surgery. An average of 220 cysts were treated per patient (range, 4-692), and 73%, 52%, and 81% of patients noted a greater than 50% improvement in their pain at 12, 24, and 36
months, respectively. Their creatinine clearance changed $+4\%$, $+7\%$, and $-2\%$ at 12, 24, and 36 months, respectively. In another series, cyst decortication was performed with a harmonic scalpel and was complicated by postoperative bleeding in two of seven patients and by ileus in a further individual. Pain was reduced from 7.4 to 2.3 out of 10 after a mean of 14 months (range, 2-29 mo; $P < .0001$), but recurred in one patient at 4 months. In another study of cyst decortication in 19 patients with ADPKD, 67% reported more than a 50% improvement in pain after a mean of 10.9 years (range, 6.4-16.9 y). Ten patients progressed to end-stage kidney disease and there was no difference in blood pressure control at 10 years. Preoperative estimated glomerular filtration rate was a strong predictor of postlaparoscopic cyst decortication progression to end-stage kidney disease.

In a series of six patients who underwent laparoscopic renal cyst marsupialization, all six reported less pain after a follow-up period of 6 to 40 months. The indication for the procedure was failure of conservative management (analgesia, percutaneous aspiration) and as an alternative to open surgical decortication. Mean blood loss was 140 mL, and mean length of hospital stay was 3 days.

Laparoscopic marsupialization in 15 individuals with normal renal function involved an average of 204 cysts per kidney (range, 11-635) that were decorticated or drained. The average time of surgery was 5.5 hours, and the mean hospital stay was 3.2 days. After a follow up of 2.2 years, pain was decreased by 62% (range, 30%-90%) in 11 cases (73%). One patient demonstrated no improvement, and one had worsening pain. Pain recurred at 4 and 36 months postoperatively. Hypertension did not change in 40%, improved in 20%, and worsened in 33%, requiring further antihypertensive agents. Individuals who underwent bilateral procedures had better long-term pain relief but were more likely to develop hypertension. The effect on pain appeared to be long-lasting.

Surgical cyst decompression in a series of 30 individuals where 26 had pain resulted in 80% being pain-free at 1 year, and 62% being pain-free at 2 years. There was no effect on renal function, and serum creatinine was the same at 1 and 3 months compared with preoperative levels.

Renal Denervation

Twelve patients aged 8 to 19 years (mean age, 12.4 y) with pain due to ADPKD that was refractory to narcotic analgesics underwent laparoscopic denervation of 16 kidneys. All 12 were pain-free after a mean of 25.5 months. Three patients had further episodes of pain, associated with pyelonephritis, stones, or hemorrhage. Renal denervation can be performed laparoscopically, thoracoscopically, or using catheter-based techniques. Celiac axis block is increasingly used for chronic nonmalignant pain after a trial of local anesthetic with or without steroids under fluoroscopic guidance.

Nephrectomy

Nephrectomy is useful for managing chronic intractable pain if renal function is already significantly impaired and renal transplantation is considered.

Arterial Embolization

This technique has been used for the management of pain in patients with ADPKD, and involves embolization of the renal arteries. It is effective in abdominal pain with chronic renal failure. Currently, only case reports of arterial embolization are published.

SUMMARY OF THE EVIDENCE

Pain from polycystic kidneys can be caused by cyst infection, bleeding, or stone disease. Chronic pain is usually related to increased cyst size and mechanical back pain due to increased kidney or liver volume. Currently, there is limited evidence for nonpharmacological, pharmacological, or surgical interventions, and the optimal management of chronic pain in patients with ADPKD is not known. Studies conducted so far have been limited by small sample size and heterogeneity of inclusion criteria, length of follow-up and end points, as well as by the lack of a control group.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendation.
UK Renal Association: No recommendation.
Canadian Society of Nephrology: No recommendation.
European Best Practice Guidelines: No recommendation.
International Guidelines: No recommendation.
Spanish Guidelines:

The cause of chronic pain should be evaluated and corrected if possible.

a) Mechanical back pain or pain due to renal enlargement should be managed symptomatically (D).
b) Narcotic analgesics should be reserved for acute episodes (D).
c) Invasive procedures may be considered in the presence of intractable pain due to cyst enlargement (D).
SUGGESTIONS FOR FUTURE RESEARCH

- Determination of the incidence and prevalence of pain in patients with ADPKD.
- Assessment of the effectiveness and best method of delivering various nonpharmacological approaches in the management of chronic pain in patients with ADPKD.
- Determination of the clinical and radiological risk factors for developing pain due to enlarged renal cysts. The clinical utility of monitoring kidney cyst size using imaging in patients with ADPKD.
- Inclusion of an assessment of chronic pain, as a patient-related outcome, in all randomized controlled clinical trials testing the efficacy of treatments in slowing renal cyst growth.
- Assessment of the role of somatostatin analogues in reducing cyst size and treating chronic pain in patients with ADPKD.

APPENDIX A. SUPPLEMENTARY INFORMATION

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.semnephrol.2015.10.013.

REFERENCES

# APPENDIX

## RENAL COMPLICATIONS — CHRONIC PAIN

**Date written:** April 2015  
**Author:** Judy Savige, David J. Tunnicliffe, Gopala K. Rangan

<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study type</th>
<th>Follow-up</th>
<th>Group of interest/ experimental group</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
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<tbody>
<tr>
<td>Casale et al. (2008) [23]</td>
<td>12 (16 surgeries)</td>
<td>Interrupted time series, single center</td>
<td>Mean 25.5 (18 – 41) months</td>
<td>Patients with ADPKD &lt;19 years of age presented with chronic flank narcotic analgesics pain with intermittent severe episodes.</td>
<td>Laparoscopic renal denervation</td>
<td>• Pain relief- Wong – Baker scale</td>
</tr>
</tbody>
</table>
| Dunn et al. (2001) [22] | 15 | Interrupted time series, single center | Mean 26.4 months | Patients with ADPKD referred for laparoscopic management of chronic abdominal pain. (n=15) | Cyst marsupialization | • Pain relief- Pain analogue scale  
• Serum creatinine |
| Elzinga et al. (1992) [15] | 14 | Interrupted time series, single center | 12 - 28 months | Patients with ADPKD, surgical indication was chronic pain | Unilateral cyst decortication | • Pain relief |
| Haseebuddin et al. (2012) [21] | 19 | Interrupted time series, single center | Mean 130.8 (76.8 – 202.8) months | Patients with ADPKD who underwent laparoscopic cyst decortication. (n=19) | Laparoscopic cyst decortication. | • Pain relief- 50% improvement  
• Antihypertensive therapeutic index |
| Lee et al. (2003) [19] | 11 | Interrupted time series, single center | Mean 12 (3 – 24) months | Patient with ADPKD and abdominal or flank pain. Baseline (n=11) | Cyst ablation- largest cyst on symptomatic side after mean 12 months follow-up (n=11) | • Pain-relief- Self-reported  
• Hypertension relief |
| McNally et al. (2001) [20] | 7 | Interrupted time series, single center | 14 | Patients with end-stage kidney disease secondary to ADPKD and pain attributed to their cyst disease | Laparoscopic cyst decortication with the harmonic scalpel | • Pain relief - not reported |
| Singh et al. (2006) [17] | 15 | Interrupted time series, single center | 7 days | Patients with ADPKD- non-communicating dominant cysts (>5cm), and severe flank pain, and normal renal function (n=15) | Sclerotherapy- absolute ethanol- cyst ablation- largest cyst on symptomatic side | • Pain relief  
• Serum creatinine |
| Techman et al. (1995) [13] | 6 | Interrupted time series, single center | 6 – 40 months | Patients with ADPKD who presented with refractory cysts pain. | Laparoscopic marsupialization of ADPKD | • Pain relief- resolution of pain |
Table 2. Risk of bias- Interrupted time series- quality appraisal tool EPOC.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Independent Intervention</th>
<th>Pre-specified shape of intervention</th>
<th>Intervention effect to on data collection</th>
<th>Allocation concealment</th>
<th>Incomplete data</th>
<th>Selective reporting</th>
<th>Other risks of bias</th>
<th>Quality</th>
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</thead>
<tbody>
<tr>
<td>Casale et al. (2008) [23]</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td>Low</td>
<td>Individual pain scores not presented, recall bias concerns.</td>
<td>Low</td>
</tr>
<tr>
<td>Dunn et al. (2001) [22]</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Individual pain scores not presented, recall bias concerns.</td>
<td>Low</td>
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<tr>
<td>Haseebuddin et al. (2012) [21]</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Recall bias concerns, high loss to follow-up</td>
<td>Very low</td>
</tr>
<tr>
<td>Lee et al. (2003) [19]</td>
<td>High</td>
<td>Low</td>
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<td>Low</td>
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<td>Inconsistent follow-up times</td>
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<td>McNally et al. (2001) [20]</td>
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<td>High</td>
<td>None evident</td>
<td>Low</td>
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<tr>
<td>Singh et al. (2008) [17]</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td>High</td>
<td></td>
<td>Short follow-up</td>
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<td>High</td>
<td>Low</td>
<td>None evident</td>
<td></td>
<td>Very low</td>
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Table 3. Pain outcomes

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<tr>
<th>Study ID</th>
<th>N</th>
<th>Study type</th>
<th>Follow-up/years</th>
<th>Outcome</th>
<th>Results</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cascale et al. (2008) [23]</td>
<td>12 (16 surgeries)</td>
<td>Interrupted time series</td>
<td>Mean 25.5 (18-41) months</td>
<td>Pain-Wong-Baker scale</td>
<td>Pre surgery 6-9/10, post 0-1/10</td>
<td>Low</td>
</tr>
<tr>
<td>Dunn et al. (2001) [22]</td>
<td>15</td>
<td>Interrupted time series</td>
<td>Mean 26.4 months</td>
<td>Pain relief- Pain analogue scale</td>
<td>73% reported a 62% decrease in pain.</td>
<td>Low</td>
</tr>
<tr>
<td>Elzinga et al. (1992) [15]</td>
<td>14</td>
<td>Interrupted time series</td>
<td>12 – 24 months</td>
<td>Pain relief- self-reported</td>
<td>Pain free at 1-year follow-up 80%, pain free at 2 years 62%</td>
<td>Very low</td>
</tr>
<tr>
<td>Haseebuddin et al. (2012) [21]</td>
<td>19</td>
<td>Interrupted time series</td>
<td>Mean 130.8 (76-202.8) months</td>
<td>Pain relief- telephone interview</td>
<td>44% reported a 50% decrease in pain.</td>
<td>Very low</td>
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<td>Lee et al. (2003) [19]</td>
<td>11</td>
<td>Interrupted time series</td>
<td>Mean 12 (3-24) months</td>
<td>Pain relief- self-reported</td>
<td>64% of patients reported pain relief for 12 – 24 months</td>
<td>Very low</td>
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<tr>
<td>McNally et al. (2001) [20]</td>
<td>7</td>
<td>Interrupted time series</td>
<td>14 months</td>
<td>Pain relief- not reported</td>
<td>Pre surgery: 7.4/10 Post surgery: 2.3/10</td>
<td>Low</td>
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<tr>
<td>Singh et al. (2006) [17]</td>
<td>15</td>
<td>Interrupted time series</td>
<td>7 days</td>
<td>Pain- Mean Visual analogue scale</td>
<td>Pre surgery: 6.5/10 Post surgery (7-days): 2.3/10</td>
<td>Low</td>
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<tr>
<td>Teichman et al. (1995) [13]</td>
<td>6</td>
<td>Interrupted time series</td>
<td>6-40 months</td>
<td>Pain relief- Resolution of pain</td>
<td>100% (6/6) patients had pain resolved at end of follow-up.</td>
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Table 4. Renal function outcomes

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<th>Study ID</th>
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<th>Study type</th>
<th>Follow-up/years</th>
<th>Outcome</th>
<th>Results</th>
<th>Quality</th>
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<tbody>
<tr>
<td>Dunn et al. (2001) [22]</td>
<td>15</td>
<td>Interrupted time series</td>
<td>Mean 26.4 months</td>
<td>Serum creatinine</td>
<td>68% of patients had no change in serum creatinine post cyst marsuplization surgery</td>
<td>Low</td>
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<tr>
<td>Elzinga et al. (1992) [15]</td>
<td>14</td>
<td>Interrupted time series</td>
<td>12 – 24 months</td>
<td>Serum creatinine</td>
<td>No difference in patients serum creatinine when compared preoperatively and postoperatively</td>
<td>Very low</td>
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<tr>
<td>Singh et al. (2006) [17]</td>
<td>15</td>
<td>Interrupted time series</td>
<td>12 months</td>
<td>Serum creatinine (mean)</td>
<td>Preoperatively: 1.9 mg/dL Postoperatively 2.1 mg/dL. Significant improvement at 1 year follow-up (P&lt;0.001)</td>
<td>Low</td>
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</table>

Table 5. Blood pressure outcomes

<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study type</th>
<th>Follow-up/years</th>
<th>Outcome</th>
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<th>Quality</th>
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<tbody>
<tr>
<td>Dunn et al. (2001) [22]</td>
<td>15</td>
<td>Interrupted time series</td>
<td>Mean 26.4 months</td>
<td>Hypertension relief</td>
<td>Preoperatively recorded as normotensive or antihypertensive medication preoperatively were recorded as normotensive postoperatively</td>
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<tr>
<td>Haseebuddin et al. (2012) [21]</td>
<td>19</td>
<td>Interrupted time series</td>
<td>Mean 130.8 (76-202.8) months</td>
<td>Antihypertensive therapeutic index (ATI)</td>
<td>53% had an ATI less than or equal to preoperative ATI at follow-up</td>
<td>Very low</td>
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<tr>
<td>Lee et al. (2003) [19]</td>
<td>11</td>
<td>Interrupted time series</td>
<td>Mean 12 (3-24) months</td>
<td>Hypertension relief</td>
<td>25% of patients postoperatively hypertension was resolved</td>
<td>Very low</td>
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