HHS Public Access

Author manuscript

*Transplantation*. Author manuscript; available in PMC 2017 February 01.

Published in final edited form as:

*Transplantation*. 2016 February ; 100(2): 407–415. doi:10.1097/TP.0000000000000838.

# Live Donor Renal Transplant with Simultaneous Bilateral Nephrectomy for Autosomal Dominant Polycystic Kidney Disease (APKD) is Feasible and Satisfactory at Long Term Follow-Up

**Sarwat B. Ahmad**[1],

Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Brian Inouye**[2],

[*]Correspondence: Jonathan S. Bromberg, Department of Surgery, University of Maryland School of Medicine, 29 S. Greene Street, Suite 200, Baltimore, MD 21201, ; Email: jbromberg@smail.umaryland.edu, Phone: 410 328 0008, Fax: 410 328 6343

[1]Author: Sarwat B. Ahmad, sarwatbahmad@gmail.com

Contribution: Participated in all aspects of data acquisition, analysis, and interpretation of data. Drafted article and revised it during many rounds of revision in concordance with the co-authors. Participated in final approval of the version to be published.

No funding. No conflicts of interest to disclose.

[2]Author: Brian Inouye, binouye@smail.umaryland.edu

Contribution: Conception and design, data acquisition, drafting of manuscript, final approval of version to be published.

No funding. No conflicts of interest to disclose.

[3]Author: Michael S. Phelan, mphelan@smail.umaryland.edu

Contribution: Supervision of all survey collection, conception and design, data acquisition, final approval of the version to be published

No funding. No conflicts of interest to disclose.

[4]Author: Andrew C. Kramer, Akramer@smail.umaryland.edu

Contribution: Conception and design, data acquisition, final approval of the version to be published.

No funding. No conflicts of interest to disclose.

[5]Author: Jay Sulek, Jay.Sulek@gmail.com

Contribution: Conception and design, data acquisition, final approval of the version to be published.

No funding. No conflicts of interest to disclose.

[6]Author: Matthew R. Weir, Mweir@medicine.umaryland.edu

Contribution: Conception and design, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[7]Author: Rolf N. Barth, Rbarth@smail.umaryland.edu

Contribution: Analysis and interpretation of data, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[8]Author: John C. LaMattina, Jlamattina@smail.umaryland.edu

Contribution: Conception and design of study, analysis and interpretation of data, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[9]Author: Eugene J. Schweitzer, Eschweitzer@smail.umaryland.edu

Contribution: Analysis and interpretation of data, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[10]Author: David B. Leeser, Dleeser@smail.umaryland.edu

Contribution: Analysis and interpretation of data, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[11]Author: Silke V. Niederhaus, Sniederhause@smail.umaryland.edu

Contribution: Conception and design, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[12]Author: Stephen T. Bartlett, Sbartlett@smail.umaryland.edu

Contribution: Conception and design, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

[13]Author: Jonathan S. Bromberg, Jbromberg@smail.umaryland.edu

Contribution: Supervision of all aspects of study, conception and design, interpretation of data, drafting article, critical revision of manuscript, final approval of version to be published

No funding. No conflicts of interest to disclose.

**Disclosures**: The authors declare no conflicts of interest.

Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Michael S. Phelan**[3],
Division of Urology, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Andrew C. Kramer**[4],
Division of Urology, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Jay Sulek**[5],
University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Matthew R. Weir**[6],
Division of Nephrology, Department of Internal Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Rolf N. Barth**[7],
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**John C. LaMattina**[8],
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Eugene J. Schweitzer**[9],
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**David B. Leeser**[10],
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Silke V. Niederhaus**[11],
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Stephen T. Bartlett**[12], and
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

**Jonathan S. Bromberg**[13,*]
Division of Transplantation Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA

## Abstract

**Background—**Timing of BN is controversial in patients with refractory symptoms of autosomal dominant polycystic kidney disease (APKD) in need of a renal transplant.

**Methods—**Adults who underwent LRT+SBN from August 2003–2013 at a single transplant center (n=66) were retrospectively compared to a matched group of APKD patients who underwent LRT alone (n=52). All patients received general health and polycystic kidney symptom surveys.

**Results—**SBN increased operative duration, EBL, transfusions, IV fluid, and hospital length of stay. Most common indications for BN were pain, loss of abdominal domain, and early satiety. There were more intraoperative complications for LRT+SBN (6 vs. 0, p=0.03; 2 vascular, 2 splenic, and 1 liver injury; 1 re-exploration to adjust graft positioning). There were no differences in Clavien-Dindo grade I or II (39% vs. 25%, p=0.12) or grade III or IV (7.5% vs. 5.7%, p=1.0) complications during the hospital course. There were no surgery related mortalities. There were no differences in readmission rates (68% vs. 48%, p=0.19) or readmissions requiring procedures (25% vs. 20%, p=0.51) over 12 months. 100% of LRT+SBN allografts functioned at >1 year for those available for follow-up. Survey response rate was 40% for LRT-alone and 56% for LRT +SBN. 100% of LRT+SBN survey responders were satisfied with their choice of having BN done simultaneously.

**Conclusions—**Excellent outcomes for graft survival, satisfaction, and morbidity suggest that the combined operative approach be preferred for patients with symptomatic APKD to avoid multiple procedures, dialysis, and costs of staged operations.

## Introduction

Autosomal dominant polycystic kidney disease (APKD) occurs in 1 out of every 500 to 1000 live births and is the most common cause of inherited renal failure [1]. APKD can cause a variety of clinical symptoms related to cyst burden and renal failure, including flank or abdominal pain, bleeding, infection, loss of abdominal domain, nephrolithiasis, anemia, and hypertension. APKD accounts for up to 10% of ESRD cases, and up to 50% of these patients progress to needing renal replacement therapy or transplantation by 70 years of age [2]. In patients with symptomatic APKD who have ESRD and anticipate renal replacement therapy or renal transplant, native nephrectomy is often indicated [3].

The approach to native nephrectomy in this group of patients has been variable. Nephrectomy can be performed open versus laparoscopically; uni- or bi-laterally; and before, after, or simultaneous with renal transplant. In a patient undergoing live donor renal transplant (LRT), timing of nephrectomy is especially controversial, since addition of nephrectomy can increase operative risk for an otherwise elective operation that not only has excellent outcomes, but also involves a graft donated from a healthy individual. Nephrectomy prior to transplant may subject a pre-dialysis patient to dialysis, anephric state, and risk sensitization to HLA antigens due to blood transfusions, thus precluding subsequent LRT. Transplantation prior to nephrectomy may be difficult due to loss of abdominal domain. For these reasons, most centers do not offer simultaneous BN and LRT.

The potential benefits of bilateral nephrectomy (BN) in conjunction with LRT are appealing: relief of symptoms, convenience, fewer operations and hospital admissions, and avoidance of dialysis. We previously reported excellent outcomes for simultaneous BN (SBN) [4] in terms of patient and graft survival in 20 patients, although follow up of recipients was

limited. In one of the largest cohorts (n=79) Skauby et al. report similarly good outcomes of SBN and LRT, but that review encompassed an earlier era (1989–1998) of transplant medicine [5]. Significant strides have been made in immunosuppression and surgical experience over the last two decades. We re-examined outcomes for this operation in a larger, contemporary cohort of patients over a 10-year period. We addressed both short and long term outcomes with a focus on relevant metrics of patient satisfaction and readmission rates.

## Methods

Our institution's kidney transplant database was searched to obtain medical records for all adult patients with a diagnosis of APKD who had undergone LRT from August 2003 to August 2013. These were further stratified into those who had also undergone unilateral or bilateral nephrectomy either simultaneously or on a different day from living donor transplantation. Electronic medical records including anesthesia and operative reports, pathology reports, discharge summaries, and progress notes were reviewed to collect the following information: age, race, sex, body mass index (BMI), American Society of Anesthesiology (ASA) class, presence of diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, or other comorbidities, dialysis status, operative time, estimated blood loss (EBL), transfusion requirements, hospital length of stay, timing of nephrectomy, indications for nephrectomy, specimen mass, ICU stay, intraoperative complications, postoperative complications, and details of readmissions to our hospital system. Perioperative complications were graded based on the Clavien-Dindo Classification System [6].

Over the past decade, our transplant center has instituted the following 3-stage approach to coordinating the LRT and SBN. The recipient bilateral nephrectomy (Stage 1) and live kidney procurement (Stage 2) begin concurrently in adjacent operating rooms. Transplant surgeons perform a laparoscopic donor nephrectomy, while a urological team performs the bilateral nephrectomy through a long, midline, transperitoneal incision. A circulating nurse facilitates communication between the two rooms, alerting the surgical teams of any delays and confirming successful completion of BN prior to committing the donor allograft to an irreversible step. Once the backtable preparation of the allograft is complete, the transplant surgeon implants it intraabdominally into the donor iliac fossa (Stage 3). Cold ischemia time rarely exceeds 45 minutes.

A validated 36-item Short Form Health Survey (RAND Corporation, Santa Monica, CA) [7] and additional APKD-specific questionnaire modified from a previously published outcomes survey [8] were mailed in paper and electronic form (Tables 7, 8) including a letter of consent and statement explaining the optional nature of the survey. These documents were sent with instructions to submit responses via return mail or electronically via online survey software. All study components were approved by The University of Maryland School of Medicine Institutional Review Board for Protection of Human Subjects.

### Statistical Analysis

For each clinical parameter, we determined the mean +/− standard error of the mean. Significance was analyzed using Student's t-tests or Wilcoxson rank sum test for numerical data and Chi-squared and/or Fisher's exact test for categorical variables. Patient survey variables were assessed based on 3, 5, 6, and 11-point Likert scales. Significance was defined as $p<0.05$. Software used for analysis was GraphPad Prism, version 5.0c (GraphPad Software, Inc. La Jolla, CA).

## Results

### Group Demographics

A total of 118 patients with APKD underwent LRT between August 2003 and 2013. Fifty-two out of 118 underwent LRT alone (Group LRT-alone). Of these, 2 had a prior LRT; 1 had prior LRT and deceased donor renal transplant; 4 received BN prior to LRT; and 2 underwent BN post-transplant. 66 out of 118 underwent LRT and SBN (Group LRT+SBN); 63 were bilateral, 2 were horseshoe kidneys, and 1 was unilateral due to difficult dissection of the left native kidney with an intraoperative decision made to leave it in place. In each group there was one patient lost to follow up, while all other patients had follow-up data available to assess graft outcomes at 1–3, 3–6, 6–12, and >12 month time points (if applicable).

Patient characteristics (age, self-reported race, sex), comorbidities (diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, BMI and ASA class), and renal status (pre-emptive vs. on dialysis) were not different between the two groups (Table 1). Indications for nephrectomy were often multiple for each patient. Incidences of indications are summarized in Table 2. Most commonly, patients reported pain (75%) and early satiety (35%), and surgeons indicated loss of abdominal domain (33%), as indications for nephrectomy. Of the 4 patients in Group 1 who underwent nephrectomy prior to transplant, there was an average 13 month interval of the anephric state prior to transplant, and indications for nephrectomy included pain in 3, loss of abdominal domain in 3, and recurrent urinary tract infection with hematuria in 1. Of the 2 patients who underwent post-transplant BN, the indications were pain, infection, and cyst rupture in the first patient; and pain and hematuria in the second patient.

### Short term operative outcomes

All SBN cases were performed in an open fashion through a long midline laparotomy incision, and renal allografts were placed intra-abdominally in the iliac fossa through the same midline incision. As expected, Group LRT+SBN had significantly increased operative duration (381 vs. 204 min, $p<0.0001$), blood loss (1251 vs. 425 mL, $p<0.0001$), red blood cell transfusion requirements (60 vs. 12 patients, or 3.4 vs. 0.46 PRBC units/patient, $p<0.0001$), intravenous fluid administration (10.4 vs. 5.9 L, $p<0.0001$), and hospital length of stay (6.6 vs. 4.8 days, $p<0.0001$) (Table 3). Supplementary Digital Content 1 describes the 6 patients who had a staged nephrectomy in Group LRT-alone. For this subset, the additional length of stay was an average of 9.8 days for all additional symptom-related

admissions, including the nephrectomy admission. Therefore, for staged nephrectomy, the average total hospital length of stay was 14.6 days versus 6.6 days for Group LRT + SBN.

Postoperative complications were categorized into early postoperative (prior to hospital discharge) and late postoperative (after discharge) events. For comparison, these were graded using the Clavien-Dindo Classification for postoperative complications. The incidence and type of intraoperative and early surgical complications of the two groups are summarized in Table 4. Consistent with previous studies, there was a higher incidence of intraoperative complications with LRT+SBN (6 vs. 0, p=0.03). Specifically, there were two vascular injuries (to IVC and graft renal artery), two splenic injuries, one liver injury, and one immediate re-exploration to reposition the graft. All injuries were immediately recognized and managed with hemostasis and/or repair by the primary surgeon and/or with intraoperative assistance from vascular or hepatobiliary consultants. One of these complications (renal vascular injury) was associated with minor delayed graft function, which resolved prior to discharge.

For early postoperative complications prior to hospital discharge, there were no significant differences in Grade I or II complications (self-limited or requiring pharmacologic intervention or transfusion, respectively) between Group LRT-alone vs. LRT+SBN (39% vs 25%, p=0.12) (Table 4). There were also no differences between the groups in Grade III or IV complications (life or graft-threatening, requiring surgery; 7.5% vs 5.7%, p=1.0) during the hospital course. There were no surgery related mortalities for either group. LRT+SBN patients had 97% immediate graft function. Two cases of delayed graft function, defined by no fall in creatinine by >10% in 48 hours and/or need for dialysis after transplant, resolved prior to discharge. Of note, two of the LRT-alone grafts had primary renal artery thrombosis requiring transplant nephrectomy in the immediate post-operative period. One of these patients was found to have a hypercoagulability disorder and underwent successful re-transplantation at a later time with appropriate perioperative anticoagulation. The other patient is receiving hemodialysis and is currently awaiting deceased donor renal transplant. For both of these recipient operations, the surgeons specifically noted that there was no evidence of compartment syndrome, kinking, or other anatomic abnormalities. There were two immediate re-laparotomies in Group LRT+SBN due to concern for bleeding in patients who had hypotension and a drop in hematocrit. In both cases, only self-limited residual oozing from the nephrectomy beds was found. Each group required one re-exploration to adjust positioning of the allograft in order to improve renal perfusion (Table 4). There were no differences in episodes of acute rejection during the transplant hospitalization (n=3 LRT-alone, n=2 LRT+SBN).

## Long-term outcomes

Mean follow up times were 5.1 years for Group LRT-alone and 3.8 years for Group LRT +SBN. There were no significant differences in the overall incidence of late postoperative complications as measured by readmission rates (68% vs. 48% of patients per group, p=0.19) (Table 5A). Group LRT+SBN had a total of 96 readmissions, 53 (55%) of which occurred during the first post-transplant year. Group LRT-alone had 82 total readmissions, 44 (53%) of which occurred during the first year. 40% of LRT-alone patients were re-

admitted more than once within the first year versus 30% of LRT+SBN patients, but this difference was not statistically significant. Over 10 years, 44 out of 66 patients in Group LRT+SBN required readmission versus 29 of 52 patients in Group LRT-alone (67% vs. 56%, p=0.19). Of note, Group LRT+SBN had more readmissions for dehydration or hypotension (10% vs. 0%, p=0.02) over 10 years. Despite the inclusion of a midline incision and intraperitoneal dissection, we did not observe a statistically significant difference in small bowel obstruction (6% vs. 0%, p=0.06) or ventral hernia repair (7.5% vs. 3.8%, p=0.46) over 10 years of follow up. Over the first 12 months, the overall rate of readmissions resulting in invasive, procedural or operative interventions was not significantly different between the two groups (25 vs 20%, p=0.51). Group LRT-alone had 5 post-operative lymphoceles (9%) requiring percutaneous drainage and/or fenestration within the first year. Since LRT+SBN allografts were placed intra-peritoneally, there were no postoperative lymphoceles. The incidence of urinary tract infection was similar in both groups (25% vs. 21%, p=0.66) over 10 years. Readmissions for a variety of medical reasons, such as drug toxicity, electrolyte disturbances, cardiac issues, or other infectious diseases were similar between the two groups (38% vs 39%, p=0.88) within the first year. Readmissions beyond 1 year were also similar (33% vs. 34%, p=0.46), and the details of readmissions per post-operative year are provided in Tables 5A-B, Supplementary Digital Content 2.

There was a single patient in each group for whom post-operative laboratory data were unavailable due to loss of follow up. For the remaining patients, graft survival was excellent for both groups at 1–3 months, 3–6 months, and 12 months. Graft survival was 100% in Group LRT+SBN vs. 96% in Group LRT-alone at 1 year due to the 2 episodes of renal artery thrombosis and immediate graft loss (Table 6). Of note, Group LRT+SBN had significantly fewer episodes of acute rejection in the first year (7.5% vs. 23% of patients, p=0.03). All acute rejection episodes resolved with high dose steroids or intravenous antibody therapy. There was no significant difference in serum creatinine on postoperative day 1, day of discharge, and up to 12 months (Table 6). There was no surgery-related mortality for the 10-year period.

## Patient Satisfaction

All patients were mailed a health questionnaire and satisfaction survey (Tables 7 and 8). 37 (56%) of Group LRT+SBN and 21 (40%) of Group LRT-alone responded. Of Group LRT-alone responders, two had staged nephrectomy for symptomatic native kidneys, and 19 had never had a nephrectomy.

Patients were asked to grade severity of the following six symptoms both pre- and postoperatively: difficulty with clothes, shortness of breath, infection, pain, change in eating habits, and bleeding (Table 7). For Group LRT+SBN, all six parameters decreased in severity by an average two points after the operation. On a scale of 0–10, with higher numbers corresponding with increased severity, LRT-alone patients differed significantly from LRT+SBN patients in terms of preoperative difficulty with clothes (2.3 vs. 6.1; $p = 0.001$), shortness of breath (2.7 vs. 4.8; $p = 0.038$), presence of kidney or abdominal pain (1.9 vs. 4.7; $p = 0.004$), and difficulty eating (1.2 vs. 4.7; $p < 0.0001$).

Post-operatively, LRT+SBN patients took longer to stop pain medication (p=0.005). However, there was no difference in time taken to eating a normal diet, walking without difficulty, resuming driving, or resuming normal activities (Table 7). There were also no differences in their perception of postoperative complications, where 5 (14%) of LRT+SBN patients reported moderate to severe pain (score 6–11) or presence of a general or incisional complication following their procedure, compared to 2 (10%) and 5 (24%) of LRT-alone patients reporting incisional pain/complications and general complications, respectively. 97% of LRT+SBN patients responded with a 2 or less when asked to score current pain level on a scale of 0–10.

On the SF-36 health questionnaire (Table 8), both groups of patients considered their current post-operative health to be above average (4 ± 0.71 vs. 3.8+/−0.9, with 5 being excellent). The only difference on this survey was that more LRT-alone patients felt that they “seem to get sick a little easier than other people” (p=0.04). Neither group believed that post-operative physical and emotional health interfered with social activities. Patients agreed with feeling “full of pep” and disagreed with feeling “blue”.

LRT+SBN patients were extremely happy with their decision for the simultaneous procedure (9.6 ± 1.69 on a 10-point scale), with a score of 9 ± 2.07 (10-point scale) for satisfaction with the overall process, including financial burden and emotional stress. The lowest satisfaction score concerned cosmetic outcome (7.4 ± 3.16 on 10-point scale). Despite the cosmetic outcome, moderate to severe pain in 14% of patients, and the low percentage of patients who were able to return to normal activities within 2 weeks, 100% of patients agreed that if they had to undergo the operation again, they would choose simultaneous nephrectomy and transplant versus transplant alone or staged nephrectomy. Of the LRT-alone group, two staged nephrectomy patients responded, and both stated they would rather have had a simultaneous BN. However, this sample size was too low for meaningful comparison to the SBN group. Five non-staged LRT-alone patients reported worsening of polycystic kidney symptoms after their LRT procedure, and a retrospective desire to have had either a staged nephrectomy (n=3) or simultaneous BN (n=2).

## Discussion

Our institution performed 66 SBN comprising 55% of the APKD patients who underwent LRT over a 10 year period. This is higher than the national incidence of nephrectomy for ESRD for APKD, which is approximately 20% [9], possibly due in part to patients choosing our center that is known for this approach. In earlier eras, up to 85% of these patients had BN, and the decrease in the current era is likely due to advances in antibiotics, analgesics, imaging and minimally invasive procedures to control hemorrhage and pain [10]. Despite an increased incidence of intraoperative complications, which were in keeping with the increased magnitude of the operative intervention, the addition of BN did not worsen postoperative morbidity or mortality. There was 100% graft and patient survival. Moreover, patients reported improvement of symptoms post-operatively and expressed satisfaction of their choice to have the simultaneous procedure.

Surgeons are wary of accepting simultaneous BN as a standard of care for symptomatic APKD on the same day as a live donor renal transplant to avoid increased perioperative morbidity for the patient and graft. In addition to increased operative time, there are increased blood and fluid losses, transfusion requirements, and overall fluid administration. These larger fluid shifts may lead to metabolic derangements, blood pressure lability, or pulmonary complications. Indeed, in our study, there were 7 patients who had received simultaneous BN (10%) who were readmitted with dehydration or hypotension, requiring adjustments in blood pressure medication within the first few weeks of surgery. The extensive dissection required during removal of the large, cystic kidneys, some with scarring due to chronic infection or inflammation, was associated with more intraoperative complications such as damage to major vessels, liver, and spleen. These complications (n=6, 9%) were recognized and managed immediately, with no lasting effect on graft or patient survival. BN was also associated with 2 emergent re-operations for self-limited bleeding at the nephrectomy bed, requiring no further intervention, and with both patients recovering normally thereafter. Increased blood transfusions have been associated with adverse effects, such as allergic reactions, infection, immunosuppression, transmission of pro-inflammatory mediators, transfusion related acute lung injury, increased mortality in patients undergoing cardiac surgery (11), and allosensitization, placing the transplant patient at increased risk for acute kidney injury, acute rejection and graft loss. Interestingly, even though the patients who underwent simultaneous BN in our study received more blood transfusions, they had a lower rate of total acute rejection episodes than those who received LRT alone.

Other disadvantages of nephrectomy include increases in hospital length of stay, postoperative pain, delay in return to ambulation, and prolonged ileus. The intra-abdominal portion of BN commonly causes a post-operative ileus. In our practice, patients return to the surgical ward NPO with a nasogastric tube for decompression until passage of flatus or stool. On average, they tolerated a regular diet and were fully ambulatory by postoperative day 4. No patient in this series had an ileus lasting greater than 7 days. All BN patients were managed with a patient-controlled analgesia pump post-operatively. Despite the large midline incision and dissection, ventral hernia or small bowel obstruction occurrence was not significantly increased in this group compared to LRT alone. Patients who underwent LRT alone were advanced to regular diet and ambulating by hospital day 2–3, with an overall average length of stay of 4 days.

Laparoscopic unilateral or bilateral nephrectomy for APKD may potentially mitigate some of the morbidities, although the operative length is significantly increased, particularly for extremely large polycystic kidneys [12]. The laparoscopic approach is not routinely performed at our institution, but several other studies have reported that laparoscopic BN is safe, feasible, and reduces hospital stay, blood loss, and time to recovery in the hands of experienced surgeons [17, 18, 19, 20, 21].

Patients who underwent staged BN expressed that given their experiences they recommend to others the simultaneous over the staged operation [22]. We believe that the prolonged hospital length of stay for open SBN is advantageous when compared to the multiple readmissions required to manage ongoing clinical symptoms of retained kidneys, as well as another admission and operation for native nephrectomy. In our study, the average overall

increased length of stay experienced by the 6 patients who had a staged nephrectomy was 9.8 days on top of the average 4.8 days for LRT alone. Changes in total length of stay were also noted by Wagner et al., for a total 11.8 days for the staged cohort versus 6.9 days for concurrent nephrectomy [24]. The simultaneous procedure not only reduces overall hospital costs incurred by multiple hospital admissions, but also avoids the cost of interim dialysis sessions.

Dialysis has been associated with multiple adverse effects such as accelerated atherosclerosis [25, 26, 27, 28] and elaboration of pro-inflammatory factors that may compromise both patient and graft survival post-transplantation [29]. SBN avoids the anephric state rendered by a pre-transplant staged nephrectomy, which can lead to hyperkalemia, anemia, congestive heart failure, and osteodystrophy [31, 32]. SBN also avoids the possibility of sensitization to HLA occurring as a result of blood transfusion at the time of pre-transplant BN.

At a rate of 6 out of 66 (9%), our study's intraoperative complication rates were not significantly different from the series published by Kramer et al, who reported 1 out of 20 (5%) intraoperative complications, or Skauby et al. (10 of 78 patients, 12%) [4, 5]. Notably, only 3 out 6 of these complications were related to the additional BN procedure (injury to spleen and liver). These injuries occurred in cases noted to require extensive operative dissection due to perinephric inflammation and fibrosis, as well as poor visualization due to concomitant liver cysts. Less surgical morbidity has been seen with BN performed through bilateral flank incisions, however our current midline transabdominal approach is more appropriate for performing simultaneous LRT. As in other studies, our rates of post-operative complications and reoperation rates were not different for SBN versus LRT alone. Patient and graft survival for Group LRT+SBN were excellent (100%) at up to 12-months follow up, commensurate with other reports (5, 24). Readmission rates were not reported in earlier studies; however, the incidence of readmission within the first year for all renal transplant recipients is typically about 40% (34). For this study, readmission rates were slightly higher at 53% and 55% for LRT-alone and LRT+SBN, respectively, within 1 year.

Although response rates were suboptimal (40% for LRT-alone and 56% for LRT+SBN) with a discrepancy between the two response rates, this is the largest series to date that attempts to measure patient satisfaction along with outcomes. In addition to an overall reduction in symptoms, 100% of the patients who responded stated that they would choose to have the BN done simultaneously if they had to do it again. This included 2 of the patients who had a major intraoperative complication. The groups did not score their post-operative complications differently. Of note, the two staged nephrectomy responders said they would have rather had a simultaneous procedure, and 5 (11% of non-staged, LRT-alone patients) stated they would have had some type of nephrectomy.

Our study had a high follow up rate, but is limited by its retrospective nature, lack of randomized control study design, sample size, and potential for non-response bias. This study is likely underpowered to detect significant differences. Future studies should compare outcomes of LRT+SBN with a larger number of staged nephrectomies (we only had 6 out of 118 patients). However, considering the high patient satisfaction rates revealed in this study,

our recommendation is to perform BN simultaneously for end stage APKD patients with medically refractory symptoms, taking into account that this approach may only be suitable for transplant centers with the staffing and expertise available to coordinate the simultaneous operations. A thorough risk-benefit analysis should be discussed with these patients in light of the higher risk of intraoperative morbidity.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

**Funding**: None

## Abbreviations

| | |
|---|---|
| **APKD** | autosomal dominant polycystic kidney disease |
| **ASA** | American Society of Anesthesiologists Classification System |
| **BMI** | body mass index |
| **BN** | bilateral nephrectomy |
| **EBL** | estimated blood loss |
| **LOS** | length of stay |
| **LRT** | live donor renal transplant |
| **NPO** | nil per os |
| **UTI** | urinary tract infection |

## References

1. Chang MY, Ong AC. Autosomal dominant polycystic kidney disease: recent advances in pathogenesis and treatment. Nephron Physiol. 2008; 108:1–7.
2. Mochizuki T, Tsuchiya K, Nitta K. Autosomal dominant polycystic kidney disease: recent advances in pathogenesis and potential therapies. Clin Exp Nephrol. 2013; 17(3):317–26. [PubMed: 23192769]
3. Freed SZ. The present status of bilateral nephrectomy in transplant recipients. J Urol. 1976; 115(1): 8–11. [PubMed: 1107603]
4. Kramer A, Sausville J, Haririan A, et al. Simultaneous bilateral native nephrectomy and living donor renal transplantation are successful for polycystic kidney disease: the University of Maryland experience. J Urol. 2009; 181(2):724–8. [PubMed: 19091353]
5. Skauby MH, Oyen O, Hartman A, et al. Kidney transplantation with and without simultaneous bilateral native nephrectomy in patients with polycystic kidney disease: a comparative retrospective study. Transplantation. 2012; 94(4):383–8. [PubMed: 22828736]
6. Dindo D, Demartines N, Clavien P. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240(2):205–13. [PubMed: 15273542]

7. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ. 1993; 306(6890):1437–1440. [PubMed: 8518639]
8. Barth R, Phelan M, Goldschen L, et al. Single-port donor nephrectomy provides improved patient satisfaction and equivalent outcomes. Ann Surg. 2013; 257(3):527–533. [PubMed: 22968070]
9. Patel P, Horsfield C, Compton F, et al. Native nephrectomy in transplant patients with autosomal dominant polycystic kidney disease. Ann R Coll Surg Engl. 2011; 93(5):391–395. [PubMed: 21943464]
10. Fuller TF, Brennan TV, Feng S, et al. End stage polycystic kidney disease: Indications and timing of native nephrectomy relative to kidney transplantation. J Urol. 2005; 174(6):2284–2288. [PubMed: 16280813]
11. Engoren M, Habib R, Zacharias A, et al. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thorac Surg. 2002; 74(4):1180–6. [PubMed: 12400765]
12. Dunn MD, Portis AJ, Elbahnasy AM, et al. Laparoscopic nephrectomy in patients with end stage renal disease and autosomal polycystic kidney disease. Am J Kidney Dis. 2000; 35(4):720–725. [PubMed: 10739795]
13. Sulikowski T, Tejchman K, Ziętek Z, et al. Experience with autosomal dominant polycystic kidney disease in patients before and after renal transplantation: a 7-year observation. Transplantation Proc. 2009; 41(1):177–180.
14. Rozanski J, Kozlowska I, Myslak M, et al. Pretransplant nephrectomy in patients with autosomal dominant polycystic kidney disease. Transplant Proc. 2005; 37(2):666–668. [PubMed: 15848495]
15. Drognitz O, Kirste G, Schramm I, et al. Kidney transplantation with concomitant unilateral nephrectomy: a matched-pair analysis on complications and outcome. Transplantation. 2006; 81(6):874–880. [PubMed: 16570011]
16. Mitchell TS, Halasz N, Gittes RF. Renal transplantation: selective preliminary bilateral nephrectomy. J Urol. 1973; 109:796. [PubMed: 4573108]
17. Lipke MC, Bargman V, Milgrom M, et al. Limitations of laparoscopy for bilateral nephrectomy for autosomal dominant polycystic kidney disease. J Urol. 2007; 177(2):627–631. [PubMed: 17222647]
18. Gill IS, Kaouk JH, Hobart MG, et al. Laparoscopic bilateral synchronous nephrectomy for autosomal dominant polycystic kidney disease: the initial experience. Clin Urology. 2001; 165(4): 1093–1098.
19. Ismail HR, Flechner SM, Kaouk JH, et al. Simulataneous vs sequential laparoscopic bilateral native nephrectomy and renal transplantation. Transplantation. 2000; 80(8):1124–1127. [PubMed: 16278596]
20. Desai MR, Nandkishore SK, Ganpule A, et al. Pretransplant laparoscopic nephrectomy in adult polycystic kidney disease: a single center experience. BJU Int. 2008; 101(1):94–97. [PubMed: 17922857]
21. Bendavid Y, Moloo H, Klein L, et al. Laparoscopic nephrectomy for autosomal dominant polycystic kidney disease. Surg Endosc. 2004; 18:751–754. [PubMed: 15026905]
22. Glassman DT, Nipkow L, Bartlett ST, et al. Bilateral nephrectomy with concomitant renal graft transplantation for autosomal dominant polycystic kidney disease. J Urol. 2003; 164(3):661–664. [PubMed: 10953121]
23. Brazda E, Ofner D, Riedmann B, et al. The effect of nephrectomy on the outcome of renal transplantation in patients with polycystic kidney disease. Ann Transplant. 1996; 1(2):15–18. [PubMed: 9869924]
24. Wagner MD, Prather JC, Barry JM. Selective, concurrent bilateral nephrectomies at renal transplantation for autosomal dominal polycystic kidney disease. J Urol. 2007; 177(6):2250–4. [PubMed: 17509331]
25. Huysmans K, Lins RL, Daelemans R, et al. Hypertension and accelerated atherosclerosis in end-stage renal disease. J Nephrol. 1998; 11:185–195. [PubMed: 9702869]
26. London GM, Drueke TB. Atherosclerosis and arteriosclerosis in chronic renal failure. Kidney Int. 1997; 51:1678–1695. [PubMed: 9186855]
27. Wheeler DC. Cardiovascular disease in patients with chronic renal failure. Lancet. 1996; 348:1673–1674. [PubMed: 8973424]

28. Zimmermann J, Herrlinger S, Pruy A, et al. Inflammation enhances cardiovascular risk and mortality in hemodialysis patients. Kidney Int. 1999; 55:648–658. [PubMed: 9987089]
29. Lowrie EG. Acute-phase inflammatory process contributes to malnutrition, anemia, and possibly other abnormalities in dialysis patients. Am J Kidney Dis. 1998; 32(Suppl):S105–S112. [PubMed: 9892376]
30. U.S. Renal Data System. USRDS 2013 Annual Data Report: Atlas of Chronic Kidney Disease and End-stage Renal Disease in the United States. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases; 2013.
31. Harnett JD, Foley RN, Kent GM, et al. Congestive heart failure in dialysis patients: prevalence, incidence, prognosis and risk factors. Kidney Int. 1995; 47:884–890. [PubMed: 7752588]
32. Fournier A, Oprisiu R, Hottelart C, et al. Renal Osteodystrophy in Dialysis Patients: Diagnosis and Treatment. Artificial Organs. 1998; 22:530–557. [PubMed: 9684690]
33. Darby CR, Cranston D, Morris PJ. Bilateral nephrectomy before transplantation: indications, surgical approach, morbidity and mortality. Br J Surg. 1991; 78(3):305–7. [PubMed: 2021844]
34. Matas AJ, Smith JM, Skeans MA, et al. Annual Data Report: Kidney. Am J Transplant. 2014; (Suppl 1):11–44. [PubMed: 24373166]
35. Kirkman MA, van Dellen D, Mehra S, et al. Native nephrectomy for autosomal dominant polycystic kidney disease: before or after kidney transplantation? BJU Int. 2011; 108(4):590–4. [PubMed: 21166760]
36. Lucas SM, Mofunanya TC, Goggins WC, et al. Staged nephrectomy versus bilateral laparoscopic nephrectomy in patients with autosomal dominant polycystic kidney disease. J Urol. 2010; 184(5): 2054–9. [PubMed: 20850813]

**Table 1**

Patient Characteristics

| | LRT-alone mean ± SEM | LRT + SBN mean ± SEM | P-value |
|---|---|---|---|
| **Total (n)** | 52 | 66 | |
| **Age (years)** | 52 ±1.4 | 50 ± 1.1 | 0.41 |
| **Race (self-reported)** | 48 White<br>3 Black<br>1 Hispanic | 53 White<br>9 Black<br>3 Hispanic<br>1 Asian | 0.07 |
| **Sex (M:F)** | 26: 26 | 34: 32 | 0.87 |
| **Body mass index (kg/m$^2$)** | 28 ± 0.7 | 28 ± 0.7 | 0.95 |
| **ASA class** | 3.02 ± 0.03 | 3.02 ± 0.05 | 1.0 |
| **On Dialysis** | 19 | 21 | 0.95 |
| **Previous transplants** | 4 | 0 | |
| **Staged Nephrectomy (n)** | | | |
| Pre-transplant | 6 | 0 | |
| Post-transplant | 4 | | |
| Post-transplant | 2 | | |

**Table 2**

Indications for Nephrectomy

| | LRT-alone % of n=6 | LRT+SBN % of n=66 |
|---|---|---|
| Pain | 83 | 76 |
| Early satiety/weight loss | | 39 |
| Loss of abdominal domain | 50 | 33 |
| Infection | 33 | 20 |
| Shortness of breath | | 18 |
| Bleeding | 33 | 14 |
| Cyst rupture | 17 | 8 |
| Nephrolithiasis | | 8 |
| Lethargy | | 4 |
| Weight gain/girth | | 3 |
| Obstructive uropathy | | 3 |
| Diminished mobility | | 1 |

* may be more than one per patient

**Table 3**

Perioperative Clinical Parameters

| | LRT-alone mean ± SEM | LRT+SBN mean ± SEM | P-value |
|---|---|---|---|
| **Operative duration (min)** | 204 ± 10 | 381 ± 10 | **<0.0001** |
| **Estimated blood loss (mL)** | 425 ± 48 | 1251 ± 104 | **<0.0001** |
| **PRBC units/patient** | 0.46 ± 0.1 | 3.4 ± 0.3 | **<0.0001** |
| **# patients transfused (%)** | 12 (23) | 60 (90) | **<0.0001** |
| **Intravenous fluids (mL)** | 5,908 ± 295 | 10,440 ± 425 | **<0.0001** |
| **Mass of kidneys removed (gm)** | n/a | L 2,125<br>R 2,067<br>Horseshoe 4448 | |
| **Length of stay (days)** | 4.8 ± 0.3 | 6.6 ± 0.3 | **<0.0001** |

## Table 4

Intraoperative and Early Surgical Complications

| | LRT-alone mean ± SEM | LRT+SBN mean ± SEM | P-value |
|---|---|---|---|
| **Major surgery-related intraoperative complications** | 0 | 6 (9%; injuries to IVC, renal a, spleen [2], liver; allograft repositioning) | **0.03** |
| **Grade I or II early complications** | 13 (25%) | 26 (39%) | 0.12 |
| Electrolyte imbalances | 3 | 3 | |
| Post-operative bleeding not requiring surgical intervention | 2 | 2 | |
| Pneumonia | 0 | 1 | |
| Delayed graft function * | 3 | 2 | |
| Acute rejection | 3 | 2 | |
| *Clostridium difficile* colitis | 0 | 1 | |
| Neuropathy | 1 | 0 | |
| **Grade III or IV early complications (life or graft threatening, requiring surgery or other emergent management)** | 3 (5.7%) | 5 (7.5%) | 1.0 |
| Primary renal artery thrombosis leading to graft failure and transplant nephrectomy | 2 | 0 | |
| Seizure from hyponatremia | 0 | 1 | |
| Anaphylactic reaction requiring intubation | 0 | 1 | |
| Surgical re-exploration to control bleeding | 0 | 2 | |
| Surgical re-exploration to adjust positioning of allograft | 1 | 1 | |

* defined as no fall in creatinine >10% in 48 hours and/or need for dialysis after transplant

**Table 5A**

Overall Readmissions (over 10 years)

| | LRT-alone | LRT+SBN | P-value |
|---|---|---|---|
| **Total readmissions** | 82 | 96 | 0.29 |
| **Patients readmitted (n)** | 29 | 44 | 0.25 |
| **% of total patients** | 56 | 67 | |
| **Average readmissions per patient** | | | 0.63 |
| **mean ± SEM** | 1.6 ± 0.29 | 1.4 ± 0.21 | |
| **Small bowel obstruction (n)** | 0 | 5 | 0.06 |
| **% of total patients** | 0 | 6 | |
| **% of readmissions** | 0 | 5 | |
| **Ventral or incisional hernia (n)** | 2 | 5 | 0.46 |
| **% of total patients** | 3.8 | 7.5 | |
| **% of readmissions** | 2 | 5 | |
| **Total rejection episodes (n)** | 12 | 5 | **0.03** * |
| **% of total patients** | 23 | 7.5 | |
| **% of readmissions** | 14 | 5 | |
| **Acute venothromboembolism (n)** | 3 | 2 | 0.65 |
| **% of total patients** | 5.7 | 3 | |
| **% of readmissions** | 3.6 | 2 | |
| **Urinary tract infection (n)** | 13 | 14 | 0.66 |
| **% of total patients** | 25 | 21 | |
| **% of readmissions** | 16 | 14.6 | |
| **Dehydration or Hypotension (n)** | | 7 | **0.02** * |
| **% of total patients** | 0 | 10 | |
| **% of readmissions** | | 7 | |

## Table 5B

Readmissions within 1st year

| | LRT-alone | LRT+SBN | P-value |
|---|---|---|---|
| **Total readmissions (n)** | 44 | 53 | 0.88 |
| **% of overall readmissions** | 53 | 55 | |
| **Patients readmitted (n)** | 25 | 40 | 0.19 |
| **% of overall patients** | 48 | 68 | |
| **Readmitted more than once (n)** | 10 | 12 | 1.0 |
| **% of overall patients** | 19 | 18 | |
| **% of 1st year readmissions** | 40 | 30 | |
| **Surgery-related readmissions requiring additional procedure (n)** | 13 | 13 | 0.51 |
| **% of overall patients** | 25 | 20 | |
| **% of total 1st year readmissions** | 29 | 24.5 | |
| **Small bowel obstruction (n)** | 0 | 3 | **0.07** |
| **% of all 1st year readmissions** | 0 | 5.6 | |
| **Wound infections (n)** | 1 | 5 | 0.23 |
| **% of all 1st year readmissions** | 4.5 | 9.4 | |
| **Other medical readmissions (n)** | 31 | 38 | 0.88 |
| **% of all 1st year readmissions** | 70 (Osteomyelitis, hyponatremia, edema, drug toxicity, cellulitis, esophagitis, shortness of breath, BK nephropathy, elevated creatinine, pulmonary hypertension, gastroenteritis, abdominal pain, anasarca) | 71 (Drug toxicity, BK nephropathy, elevated creatinine, diabetes mellitus, hyperkalemia, neutropenia, leucopenia, acute pancreatitis, dizziness, atrial fibrillation, urinary incontinence, upper respiratory infection) | |

**Table 6**

Renal Function and Graft Survival

| | LRT-alone mean ± SEM | LRT+SBN mean ± SEM | P-value |
|---|---|---|---|
| **Pre-op Creatinine** | 6.25 ±0.4 | 5.76 ± 0.3 | 0.30 |
| **POD 1 Creatinine** | 3.14 ± 0.2 | 2.78 ± 0.1 | 0.21 |
| **Creatinine at Discharge** | 1.57 ± 0.1 | 1.39 ± 0.1 | 0.18 |
| **Creatinine 1–3 months** | 1.43± 0.05 | 1.36 ± 0.05 | 0.14 |
| **Creatinine 4–6 months** | 1.35 ± 0.05 | 1.39 ± 0.06 | 0.97 |
| **Creatinine 7–12 months** | 1.39 ± 0.07 | 1.38 ± 0.06 | 0.81 |
| **Graft survival at 12 months** | 96% (2 failed, arterial thrombosis) | 100% | 0.19 |

## Table 7

Polycystic Kidney Symptom Survey

| LRT-alone | | LRT + SBN | | P-Value |
|---|---|---|---|---|
| **Total Responded** | 21 (40%) | **Total Responded** | 37 (55%) | |
| **Average Symptom Pre-op (0–10)** | | **Average Symptom Pre-op (0–10)** | | |
| Difficulty with clothes | 2.3 ± 3.7 | Difficulty with clothes | 6.0 ± 3.8 | **0.001** |
| Shortness of breath | 2.7 ± 3.3 | Shortness of breath | 4.8 ± 3.6 | **0.038** |
| Infection | 1.0 ± 2.4 | Infection | 2.6 ± 3.4 | |
| Pain | 1.9 ± 3.3 | Pain | 4.7 ± 3.5 | **0.004** |
| Eating normal amounts of food | 1.2 ± 2.3 | Eating normal amounts of food | 4.7 ± 3.6 | **<0.001** |
| Bleeding in urine | 1.0 ± 2.0 | Bleeding in urine | 2.5 ± 2.9 | |
| **Average Decrease in Symptom after Simultaneous BN** * | **N/A** | **Average Decrease in Symptom after Simultaneous BN** | | **N/A** |
| | | Difficulty with clothes | 4.8 ± 4.2 | |
| | | Shortness of breath | 4.0 ± 3.6 | |
| | | Kidney infection | 2.1 ± 3.0 | |
| | | Kidney pain | 3.8 ± 3.5 | |
| | | Eating normal amounts of food | 4.3 ± 3.7 | |
| | | Hematuria | 2.4 ± 2.9 | |
| **Patients Reporting 6+ in Severity (0–10)** | | **Patients Reporting 6+ in Severity (0–10)** | | |
| General complications | 5 (24%) | General complications | 5 (14%) | 0.259 |
| Incisional complications | 2 (10%) | Incisional complications | 5 (14%) | 0.501 |
| Incisional pain | 2(10%) | Incisional pain | 5 (14%) | 0.501 |
| **Patients Regaining Following Functions in Less than 2 Weeks** | | **Patients Regaining Following Functions in Less than 2 Weeks** | | |
| Eating a normal diet | 16 (76%) | Eating a normal diet | 25 (69%) | 0.351 |
| Walking without difficulty | 17 (81%) | Walking without difficulty | 27 (75%) | 0.364 |
| Stopped pain medication | 18 (86%) | Stopped pain medication | 18 (50%) | 0.005 |
| Resumed driving | 6 (29%) | Resumed driving | 4 (11%) | 0.089 |
| Resumed normal activities | 2 (10%) | Resumed normal activities | 3 (8%) | 0.602 |
| **Current Pain Level (0–10)** | | **Current Pain Level (0–10)** | | |
| 0 – 2 | 20 (97%) | 0 – 2 | 36 (97%) | 0.597 |
| 3 – 10 | 1 (3%) | 3 – 10 | 1 (3%) | 0.597 |

* Not Applicable, because they did not have simultaneous BN

## Table 8

SF-36 Health Questionnaire Responses

| | LRT-alone mean ± SEM | LRT + SBN Average mean ± SEM | P-Value |
|---|---|---|---|
| **In general, would you say your health is: (1 – 5)** | 3.8 ± 0.9 | 4.0 ± 0.7 | 0.267 |
| **Compared to one year ago, how would you rate your health in general now? (1 – 5)** | 3.5 ± 1.0 | 3.9 ± 1.1 | 0.187 |
| **Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports (1 – 3)** | 2.0 ± 0.8 | 2.2 ± 0.8 | 0.302 |
| **Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf (1 – 3)** | 2.7 ± 0.6 | 2.8 ± 0.4 | 0.376 |
| **Lifting or carrying groceries (1 – 3)** | 2.7 ± 0.6 | 2.8 ± 0.4 | 0.176 |
| **Climbing several flights of stairs (1 – 3)** | 2.6 ± 0.6 | 2.6 ± 0.6 | 0.754 |
| **Climbing one flight of stairs (1 – 3)** | 2.9 ± 0.3 | 2.9 ± 0.3 | 0.880 |
| **Bending, kneeling, or stooping (1 – 3)** | 2.6 ± 0.5 | 2.7 ± 0.6 | 0.495 |
| **Walking more than a mile (1 – 3)** | 2.6 ± 0.7 | 2.7 ± 0.6 | 0.632 |
| **Walking several blocks (1 – 3)** | 2.9 ± 0.5 | 2.9 ± 0.3 | 0.944 |
| **Walking one block (1 – 3)** | 3.0 ± 0.2 | 2.9 ± 0.3 | 0.636 |
| **Bathing or dressing yourself (1 – 3)** | 3.0 ± 0.2 | 3.0 ± 0.2 | 0.686 |
| **Cut down the amount of time you spend on work or other activities (1 – 2)** | 1.9 ± 0.4 | 1.9 ± 0.3 | 0.702 |
| **Accomplished less than you would like (1 – 2)** | 1.7 ± 0.5 | 1.8 ± 0.4 | 0.406 |
| **Were limited in the kind of work or other activities (1 – 2)** | 1.8 ± 0.4 | 1.8 ± 0.4 | 0.991 |
| **Had difficulty performing the work or other activities (for example. it took extra effort) (1 – 2)** | 1.8 ± 0.4 | 1.9 ± 0.3 | 0.584 |
| **Cut down the amount of time you spend on work or other activities (1 – 2)** | 1.8 ± 0.4 | 1.9 ± 0.3 | 0.391 |
| **Accomplished less than you would like (1 – 2)** | 1.8 ± 0.4 | 1.8 ± 0.4 | 0.650 |
| **Didn’t do work or other activities as carefully as usual (1 – 2)** | 1.9 ± 0.3 | 1.9 ± 0.3 | 0.661 |
| **Emotional problems interfered with your normal social activities with family, friends, neighbors or groups? (1 – 5)** | 4.8 ± 0.7 | 4.6 ± 0.9 | 0.357 |
| **How much bodily pain have you had during the past 4 weeks? (1 – 6)** | 4.8 ± 1.3 | 5.1 ± 1.1 | 0.397 |
| **During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (1 – 5)** | 4.5 ± 0.7 | 4.6 ± 0.8 | 0.828 |
| **Did you feel full of pep? (1 – 6)** | 4.6 ± 0.9 | 4.2 ± 1.3 | 0.157 |
| **Have you been a very nervous person? (1 – 6)** | 5.5 ± 0.7 | 5.1 ± 1.3 | 0.204 |
| **Have you felt so down in the dumps that nothing could cheer you up? (1 – 6)** | 5.3 ± 0.9 | 5.3 ± 1.2 | 0.928 |
| **Have you felt calm and peaceful? (1 – 6)** | 4.9 ± 0.7 | 4.6 ± 0.9 | 0.267 |
| **Did you have a lot of energy? (1 – 6)** | 4.8 ± 0.9 | 4.3 ± 1.1 | 0.089 |
| **Have you felt downhearted and blue? (1 – 6)** | 5.2 ± 1.0 | 5.0 ± 1.3 | 0.555 |
| **Did you feel worn out? (1 – 6)** | 4.6 ± 1.1 | 4.4 ± 1.1 | 0.532 |
| **Have you been a happy person? (1 – 6)** | 4.9 ± 0.7 | 4.8 ± 1.2 | 0.610 |
| **Did you feel tired? (1 – 6)** | 4.5 ± 1.2 | 4.1 ± 1.3 | 0.289 |
| **During the past 4 weeks, how much time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc)? (1 – 5)** | 4.5 ± 1.0 | 4.5 ± 0.8 | 0.792 |

| | LRT-alone mean ± SEM | LRT + SBN Average mean ± SEM | P-Value |
|---|---|---|---|
| **I seem to get sick a little easier than other people (1 – 5)** | 4.3 ± 1.0 | 3.7 ± 1.0 | **0.042** |
| **I am as healthy as anybody I know (1 – 5)** | 3.9 ± 1.2 | 3.6 ± 1.0 | 0.385 |
| **I expect my health to get worse (1 – 5)** | 3.9 ± 1.0 | 3.4 ± 1.4 | 0.108 |
| **My health is excellent (1 – 5)** | 3.7 ± 1.1 | 3.8 ± 0.9 | 0.804 |