CLINICAL SCIENCE

COMPARATIVE AND PROSPECTIVE ANALYSIS OF THREE DIFFERENT APPROACHES FOR LIVE-DONOR NEPHRECTOMY

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PURPOSE: Living donor nephrectomy is usually performed by a retroperitoneal flank incision. Due to the significant morbidity and long recovery time for a flank incision, anterior extra peritoneal sub-costal and transperitoneal video-laparoscopic methods have been described for donor nephrectomy. We prospectively compare the long-term results of donors as well as functional recipients submitted to these three approaches.

MATERIALS AND METHODS: A total of 107 live donor renal transplantations were prospectively evaluated from May 2001 to January 2004. Donors were compared with regard to operative and warm ischemia time, postoperative pain, analgesic requirements, and complications. Recipients were compared with regard to graft function, acute cellular rejection, surgical complications, and graft and recipient survival.

RESULTS: The mean operative and warm ischemia times were longer in the video-laparoscopic group ($p<0.001$), whereas patients of the flank incision group presented more postoperative pain ($p=0.035$), required more analgesics ($p<0.001$), had longer hospital stays ($p<0.001$), and suffered more pain on the 90th day after surgery ($p=0.006$). In the sub-costal and flank incision groups, there was a larger number of paraesthesias and abdominal wall asymmetries ($p<0.001$). Recipient groups were demographically comparable and presented similar acute tubular necrosis incidence and delayed graft function. The incidence of acute cellular rejection was higher in the video-laparoscopic and flank incision groups ($p=0.013$). There was no difference in serum creatinine levels, surgical complications, or recipient or graft survival between groups.

CONCLUSIONS: The video-laparoscopic and sub-costal approaches proved to be safe, and to provide donor advantages relative to the flank incision approach. Among recipients, the complication rate, graft survival, and recipient survival were similar in all groups.

KEYWORDS: Donor nephrectomy; Kidney transplantation; Laparoscopy; Surgical approaches; Outcomes.

INTRODUCTION

The aim of donor nephrectomy is to achieve an adequate graft with the lowest morbidity to the donor. During recent decades, the best approach has been a large flank incision with a rib resection. Although this is a safe procedure, it is associated with high morbidity due to incision pain and abdominal asymmetry.[1] Sub-costal abdominal incision may produce less pain, because it causes less damage to the muscles and nerves of the abdominal wall and can potentially prevent abdominal wall weakness. The laparoscopic approach offers less postoperative pain and a more rapid return to daily activities. Although effective, the learning curve for the laparoscopic approach is steep and requires a trained team along with proper equipment.

In this study, a prospective analysis of the flank incision (FI), extra-peritoneal sub-costal incision (SC), and transperitoneal video-laparoscopic (VL) methods for donor

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nephrectomy was performed to evaluate the outcomes of both donors and recipients.

METHODS AND MATERIALS

From May 2001 to January 2004, 109 live renal transplants were evaluated. Donors and recipients were properly oriented before signing the informed consent forms. Two patients refused to enroll, and a total of 107 pairs of donors and recipients were studied in three groups: 38 VL, 32 SC, and 37 FI. The criteria for the surgical approach were as follows. The VL approach was used in all left nephrectomies because of the larger extension of the left renal vein. For the right kidney, either the FI or SC approach was performed, allowing for use of the entire extension of the right vein with the aid of a vascular clamp on the inferior vena cava.

A single surgical team performed all open nephrectomies, while a team experienced with the minimally invasive approach executed the laparoscopic procedures. FI nephrectomies were performed with the patient in lateral decubitus with partial resection of the 12th rib. In the SC approach, the patient was positioned in a 30º oblique supine position and the incision made from the tip of the 12th rib to the rectus abdominis muscle. In the laparoscopic approach, the patient was also positioned in a 30-45º lateral decubitus using a maximum intracavitary pressure of 15 mmHg. The renal vessels were controlled with a Hem-O-Lok ® (Weck Closure Systems, Research Triangle Park, NC, USA) device. The kidney was extracted in an adequate retrieval bag through a transverse supra-pubic incision. Warm ischemia time was measured from renal arterial occlusion to immersion of the organ in the cold perfusion solution. All donors underwent the same follow-up protocol regardless of surgical approach.

In order to evaluate the postoperative pain and analgesic intake, donors that did not undergo a pre-established form of anesthesia (epidural block associated with general anesthesia) as well as those who underwent surgical re-exploration were excluded from this analysis. The patients rated their pain levels using a visual numeric scale. Postoperative analgesia consisted of metamizole sodium, which was administered either intravenously (1 g) or orally (0.75 g) upon the patient's request. When metamizole sodium was insufficient, meperidine (20 mg) was used and a detailed record of administered dosages was maintained. After discharge, oral metamizole sodium was prescribed at the same dosage given during the hospital stay. Surgical re-intervention, blood transfusion, and abdominal wall infection were analyzed on the 90th day after surgery. Late postoperative complications were categorized as incisional problems, chronic pain, hypoesthesia, and abdominal wall asymmetries.

In the recipients, data regarding the terminal chronic renal insufficiency etiology, time of dialysis, level of immunological match between donor and recipient, and length of hospital stay were collected. The immunosuppression protocol was based on administration of cyclosporine, prednisone, and azathioprine or mycophenolate mofetil. Recipient surgical complications were analyzed in first- and second-time transplant recipients due to the fact that the iliac fossa was not previously manipulated. Regardless of condition, all recipients were considered for determination of the post-transplant graft and patient survival rates.

Serum creatinine was measured on the 1st, 3rd, 5th, 10th, 30th, and 90th postoperative days, and when possible it was also measured one and two years after the transplant. For the analysis of creatinine levels, patients who underwent postoperative dialysis were not included in the measurements for the following ten days. Postoperative complications were categorized as vascular and ureteral abnormalities, lymphocele, hematoma, and need for another surgical intervention.

Univariate analysis was performed using the Student's t-test for continuous parametric data, Wilcoxon rank sum test for continuous non-parametric data, Pearson's Chi-square test for categorical data, or Fisher exact test where appropriate. Within group comparisons were compared using paired t-tests. Kaplan-Meier survival curves were generated for analysis of recipient survival.

RESULTS

Demographics, surgical time, and warm ischemia time are reported in Table 1. All laparoscopic procedures were completed without open conversion. The mean warm ischemia time in the VL group was 2.7±1.3 min, which was significantly longer than that for the SC and FI groups (valor SC and valor FI, respectively).

There was one pleural opening each in the SC (3.1%) and FI (2.7%) groups. Two patients, both from the VL group (1.9%), required re-operation. One patient underwent an exploratory laparotomy showing no abnormal findings on the second day after transplantation, whereas the second patient presented with hypotension and tachycardia associated with abdominal pain two hours after nephrectomy. In surgery, active bleeding was found at a lumbar vein that had been clipped. This patient was the only one in this pool of donors (0.9%) to receive a blood transfusion. The hospital stay for the FI group was significantly longer ($p<0.001$). There was a higher frequency of late incisional problems on the

Table 1 - Donor demographics, pain scale, and analgesic use

		VL (n=38)	SC (n=32)	FI (n=37)	p-value
Age (yrs)		37.2 ± 7.0	40.2 ± 10.4	41.3 ± 12.4	p=0.528
Male (%)		21 (55.3%)	14 (43.8%)	8 (21.6%)*§	p=0.011
Related (%)		23 (60.5%)	24 (75%)	31 (83.8%)	p=0.073
BMI		27.1 ± 3.8	26.6 ± 4.1	25.6 ± 4.0	p=0.302
Operative time (min)		168.7 ± 27.0†*	138.0 ± 12.2	150.9 ± 32.2	p<0.001
Warm ischemia (min)		3.3 ± 4.1†*	1.0 ± 0.4	1.0 ± 0.4	p<0.001
Hospital stay (days)		3.1 ± 0.9	3.3 ± 0.5	3.7 ± 0.6*§	p<0.001
Post-Operative Day		VL	SC	FI	p-value
1st		3.8	5.3	5.5*	p=0.025
3rd		2.6	3.6	4.6*	p=0.004
7th		1.7	1.8	2.7	p=0.059
Pain (90th)		3 (7.9%)	6 (18.8%)	14 (37.8%)*§	p=0.006
Paresthesia (90th)		1 (2.6%)	16 (50.0%)†	14 (37.8%)*	p<0.001
Asymmetry (90th)		0	9 (28.1%)†	13 (35.1%)*	p<0.001
Drug	Consumption	VL	SC	FI	p-value
Meperidina	Number of patients	1 (2.9%)	4 (12.5%)	8 (21.6%)	p=0.060
	Mean doses per group	0.03 ± 0.17	0.16 ± 0.45	0.32 ± 0.71	p=0.057
	Mean amount per group (mg)	0.6	3.1	6.5	p=0.057
Metamizole	Number of patients	34	32	37	-
	Mean doses per group	6.7 ± 2.0	11.7 ± 3.8†	16.7 ± 3.4*§	p<0.001
	Mean amount per group (g)	6.2	10.4†	14.5*§	p<0.001

* = (FI ≠ VL). § = (FI ≠ SC). † = (VL ≠ SC)

90th postoperative day, where these were most frequently categorized as pain in the FI group and paresthesia and abdominal asymmetry in the FI and SC groups (Table 1). No deaths occurred in this group of donors. Data regarding the demographics of the 107 transplant recipients, duration of dialysis before the transplant, and post-transplant hospital stay length are shown in Tables 2 and 3.

Data regarding pain intensity and analgesic consumption were collected for 103 of the 107 donors. Four patients (all from the VL group) were excluded from this evaluation; two of the patients were excluded because they did not receive epidural anesthesia, and two were excluded because they underwent re-operation during the postoperative period.

Data regarding the need for dialysis during the first week, delayed renal function, and immediate renal function are presented in Table 2. No statistically significant difference was noted among the three groups with regard to the immediate function of the transplanted organ (p=0.785).

Table 2 - Recipient demographics and graft function

	VL (n=38)	SC (n=32)	FI (n=37)	p-value
Age (yrs)	34.7 ± 15.8	32.7 ± 15.3	33.1 ± 15.0	p=0.879
Male (%)	17 (44.7%)	12 (37.5%)	17 (45.9%)	p=0.751
Pre-transplant dialysis time (months)	29.6 ± 24.3	23.3 ± 23.0	29.8 ± 25.5	p=0.568
Hospital stay (days)	15.1 ± 12.7	13.5 ± 11.5	12.9 ± 8.4	p=0.881
Graft function	VL (n=29)	SC (n=29)	FI (n=29)	TOTAL (n=87)
Dialysis on first week (%)	3 (10.3%)	2 (6.9%)	4 (13.8%)	9 (10.3%)
Serum Cr > 3.0, 5th PO (%)	2 (6.9%)	2 (6.9%)	2 (6.9%)	6 (6.9%)
Immediate function (%)	24 (82.8%)	25 (86.2%)	23 (79.3%)	72 (82.8%)
Total, Delayed function (%)	5 (17.2%)	4 (13.8%)	6 (20.7%)	15 (17.2%)

Table 3 - Incidence of recipient complications by surgical approach

Complication	VL (n=38)	SC (n=32)	FI (n=34)	TOTAL (n=104)
Arterial complication	1	1	2	4 (3.8%)
Thrombosis	1	1	1	3 (2.8%)
Anastomosis rupture	0	0	1	1 (0.9%)
Ureteral complication	3	2	2	7 (6,7%)
Stenosis	3	0	2	5 (4.8%)
Urinary fistula	0	2	0	2 (1.9%)
Obstructive acute abdomen	1	0	0	1 (1,0%)
Lymphocele	1	0	1	2 (1.9%)
Hematoma	1	0	0	1

The mean creatinine levels of the 87 evaluated recipients are shown in Figure 1. Nine patients were excluded from this dataset due to the need for dialysis during the first week after transplantation. There was no statistically significant difference in the creatinine levels at any time during the postoperative period, frequency of vascular (p=0.834) or ureteral complications (p=1.0), or total complication rate (p=0.570) between groups. Of the 107 transplant recipients, the 9 patient deaths (8.4%) were equally distributed among all three groups (p=0.516, Figure 2). Four patients died during their initial hospital stay, two secondary to sepsis, and two due to cardiovascular complications. The other five deaths occurred during the late postoperative period, four of which were due to cardiovascular complications.

DISCUSSION

In the last decade, approaches with lower morbidity have been proposed for living kidney donors. Approximately over a similar period VL approaches to renal surgery have been developed and tested in Brazil.[2,3] During In this study, we compared three approaches with respect to their benefits for donors and graft function. Because the VL and SC approaches were new at our institution, the first 15 nephrectomies for each procedure were not included in this study to eliminate effects due to the learning curve.[4-7] Initially, we found no evidence indicating that the VL approach was safe for kidneys with multiple arteries; when we faced such a condition, the right kidney was harvested.[8,9] In recent years, however, arterial multiplicity is no longer considered an exclusion criterion for laparoscopic donor nephrectomy.[10]

Pain intensity on an analog scale differed in all three groups, and a significant decline was noted on various postoperative days. The FI group presented the highest pain intensity during the follow-up period. A statistically significant difference in the first three postoperative days was observed in comparison to the VL group. The SC group presented lower

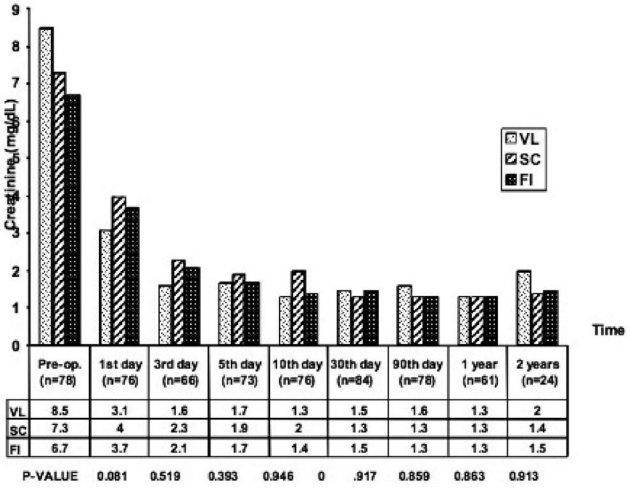

Figure 1 - Mean serum creatinine levels during hospitalization and follow-up

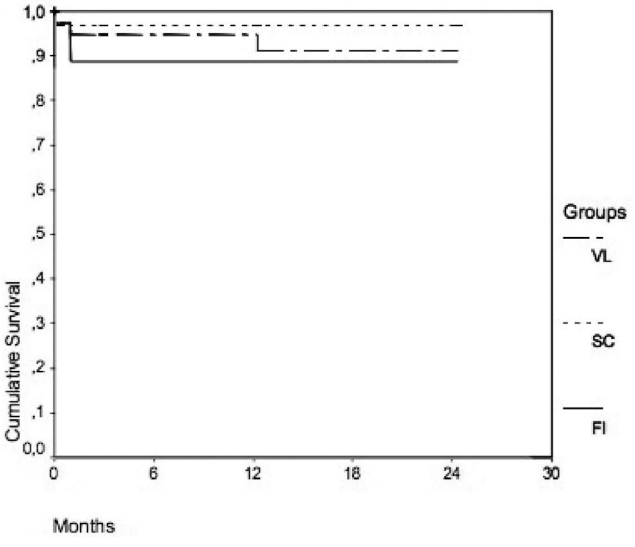

Figure 2 - Recipient overall survival according to type of nephrectomy

pain intensity in comparison to the FI group, but higher pain intensity than the VL group; however, these differences were not statistically significant. The difference in postoperative pain had a direct relationship with the amount of consumed analgesic. In the FI group, a greater number of patients required metamizole and meperidine during the hospital stay or after discharge. The hospital stay was longer in the FI group, but no difference in length was observed between the VL and SC groups. Other studies in the literature have noted similar results, with longer convalescence and longer times away from daily activities.[11]

In all groups, some late complications were related to the operative wound. In the VL group, four donors (10.5%) presented pain or paresthesia around the supra-pubic scar (Pfannestiel incision) used for organ extraction. As expected, there was no complaint or abdominal asymmetry 90 days after nephrectomy in this group. Pain, paresthesia, and/or abdominal asymmetry were observed in 19 (59.4%) and 24 (64.9%) donors from the SC and FI groups, respectively. These rates are higher than the average of 48% reported in the literature, 14. Such a high complaint and asymmetry rates are undesirable in a group of healthy kidney donor volunteers.

In the recipient group, there was no relationship between the approach used to harvest the kidney and its function in the recipient. As reported in previously published studies, this correlation shows that the longest surgical and warm ischemia times remain within a safe and reasonable range without impairment post-transplant renal function.[12,13]

Our data showed a higher rate of delayed graft function than did previous studies. We believe that this higher rate is related to intra-operative hypo-hydration. With strict adherence to a new protocol for donor hydration, this incidence was reduced to 5%. The complication rate was similar among the three groups. This data is supported by existing literature, which describe complication rates of up to 31% for the VL approach and 19% for open surgery.[14,15]

Finally, there was no difference in the graft or recipient survival rates that could be attributed to the effect of warm ischemia time or manipulation of the kidney pedicle. The causes of mortality were predominantly cardiovascular or septic complications.[14,16]

CONCLUSIONS

Donor nephrectomy performed with the laparoscopic and anterior sub-costal approaches is just as safe as that performed via the standard flank oblique incision. The former techniques offer advantages with regard to postoperative pain, hospital stay, and late morbidity from the incision. The lower morbidity in the laparoscopic and sub-costal approaches did not compromise the harvesting of an adequate organ, since graft function, surgical complications, and survival rates were similar in all groups.

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