

Surgery for Colorectal Cancer in Sri Lanka: Open to Laparoscopy

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Introduction

Colorectal cancer (CRC) is the third commonest cancer and the fourth most common cancer cause of death throughout the world with an estimated 1.2 million new cases and 600,000 deaths every year [1, 2]. In Sri Lanka colorectal cancer accounts for 7% of all malignancies with about 810 new cases diagnosed annually. It is the fourth commonest malignancy in males and fifth among females [3]

Traditionally, CRC was treated by open (conventional) surgery until Jacobs performed the first laparoscopic assisted colon cancer resection in 1991 [4]. The enthusiasm for laparoscopic colorectal resections for cancer suffered a setback when, in 1993, Alexander et al (4) reported the first case of wound recurrence three months after a right colectomy. Since 2002 four large RCTs have been published confirming the oncologic safety of laparoscopic compared with open colon cancer resection [5-8].

We performed the first laparoscopically assisted (LA) procedure for CRC in 2008 using basic laparoscopy instruments. In the beginning, most laparoscopic procedures that we undertook were laparoscopic assisted. However, as we gained experience and more advanced facilities were introduced, we progressed to perform total laparoscopic procedures (TL) for CRC.

The three main aims of our study were; to analyze the clinico-pathological aspects of CRC in our patients, to assess our overall result of surgical treatment for CRC, and to compare the surgical and oncologic outcomes between open and laparoscopic approaches for CRC in our patients.

Materials and methods

The study population comprised 270 patients managed by a single surgeon from August 1998 up to March 2016 at two tertiary care centers.

Definitions of access

Open surgery: A procedure that was performed with a formal midline skin incision as planned.

Laparoscopic-assisted resection (LA) involved laparoscopic mobilization of the colon, visualization of critical structures, and standard total mesorectal excision (TME) for rectal cancer. A small transverse abdominal incision was required to complete the procedure for vascular ligation when 'haemolock' or vascular staplers were not available, and to remove the specimen.

Total laparoscopy (TL): For the purpose of this study TL was defined as where the entire procedure, except the intra-corporeal anastomosis, was performed by the laparoscopic method.

Conversion is where the incision used was longer than a planned incision that was used to deliver the specimen in a laparoscopic procedure or where the incision was different to that planned.

Surgical technique

All procedures were performed according to standard techniques and lymph node dissection was carried out according to the "Guidelines and General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus" by the Japanese Research Society for Cancer of the Colon and Rectum [9].

Collection of data

Data was collected from personally kept patient records, and operation records were analysed retrospectively. Pathology data were collected from the operation register maintained in the unit.

Statistical analysis

Categorical data are presented as percentage and compared by the chi-square test. Continuous data are presented as mean (standard deviation) and median (range). All analyses were performed using the SPSS software (SPSS Inc., Chicago, IL, USA).

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Results

Of 270 patients, 10 were excluded from the study (not operated= 6, lost after neoadjuvant therapy= 1, inadequate data= 3). Thus, data were analyzed in the remaining 260 patients; 159 male (59 %) and 111 female (41%), median age 59; range 25 to 90 years.

Clinico-pathological features

Aetiology:

First degree relatives with a history of CRC were found among 8 patients (n= 142; 5.6%). In 5 patients (3.5%), CRC developed on a background of familial adenomatous polyposis (FAP) and two other patients (1.4%) developed CRC in long standing ulcerative colitis.

Presentation:

Twenty eight patients (n= 175; 16%) presented with sub-acute intestinal obstruction. The mode of presentation in other patients is shown in Table 1.

Duration of symptoms in 132 patients who were analysed varied from 1 to 24 months; median – 3 months.

Pathology:

The site of distribution of cancers in 243 patients is shown in Table 2. Also, the composition in the stage of presentation of CRC over the 15-year period (n= 217) from 2001 is shown in Figure 1. Forty two of 252 (17%) patients analysed had distant metastases at presentation. Histopathology data in 127 patients revealed well differentiated adenocarcinoma in 83 (65 %), moderately differentiated adenocarcinoma in 43 (34 %) and poorly differentiated adenocarcinoma in 1(1%) patient. There were 6 (5%) mucinous carcinomas.

Table 1. Mode of presentation

Presentation	Number	%
Bleeding per rectum	75	42.8%
Change of bowel habits	30	17.1%
Abdominal pain	23	13.1%
Anemia	07	4%
Other	12	6.8%

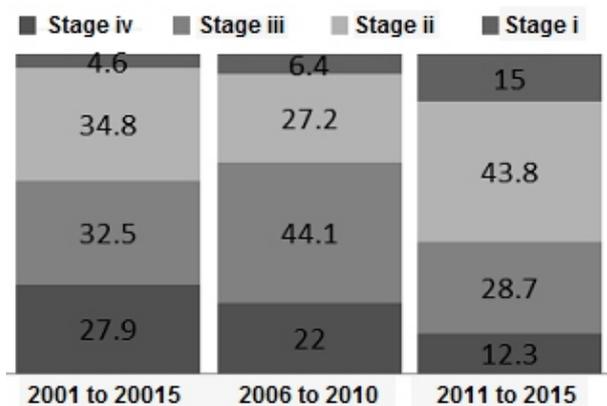


Figure 1. Tumour stage at presentation

Surgical procedure:

Two hundred and sixty patients had surgical intervention during the study period. Furthermore, 25 had only a palliative procedure (resectability 90%), an emergency surgical procedure was required in 26 (10%) patients for intestinal obstruction. In nine patients, tumour was not resectable.

Analysis of data from patients who underwent surgical resection (n= 235) showed that 66 patients were treated with neoadjuvant therapy. This includes 50 of 101 with rectal cancer (49%) who received chemo irradiation, of which eight (16%) were complete responders.

Surgical access:

One hundred and sixty-eight patients underwent open surgery (O) compared with 67 patients who underwent laparoscopic surgery. The laparoscopy group comprised 43 laparoscopic assisted (LA) and 24 total laparoscopic (TL) procedures. The overall conversion rate for laparoscopic procedures was 16 %.

Surgical technique:

Group I lymph nodes were included in the dissection (D1 dissection) in 32 patients and 143 patients underwent N2 nodal dissection (D2 dissection). Only 2 patients had N3 nodal (D3) dissection. In the remaining patients (n= 58) nodal dissection status could not be determined (Dx).

To achieve tumour clearance combined organ resection was performed in 11 patients. A sutured colorectal anastomosis was performed in 73 patients (51 %) and stapled anastomosis was performed in 71 patients. In 27 (34%) who underwent anterior resection of the rectum, we created a proximal diverting loop ileostomy.

Quality indicators in surgical procedures:

The AR: APR ratio was 1.5:1. The operating time for each procedure is shown in Table 3. Table 4 shows the volume of blood loss during the procedures.

All resected specimens (n= 235) had negative proximal and distal margins. The circumferential resection margin was reported only in later pathology reports and therefore the data were insufficient for analysis. Lymph node (LN) harvest could be determined in 92 patients (36.5 %). Twelve or more LNs were examined in 27 % patients. The node positivity was 15 %. Table 5 indicates the lymph node harvest in 92 procedures. Also, the number of lymph nodes harvested in our unit has been increasing and had almost reached the recommended standard over the last two years (Figure 2)

Post-operative complications:

There were 93 complications (40%), of which, thirteen (5.5%) were major surgical complications. Seven of 185 patients had anastomotic leaks (4%); five followed AR (leak rate following AR is 6.3%). Other major complications were abdominal wound dehiscence (n= 5; 2.1 %) and post operative

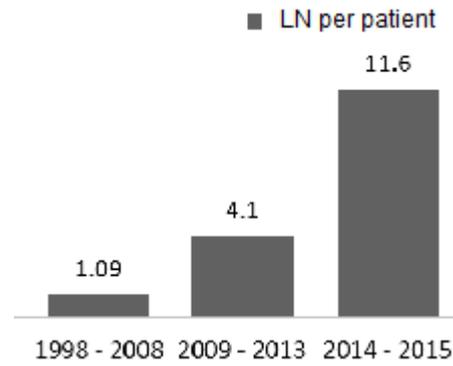


Figure 2. Lymph node harvest-1998 to 2015

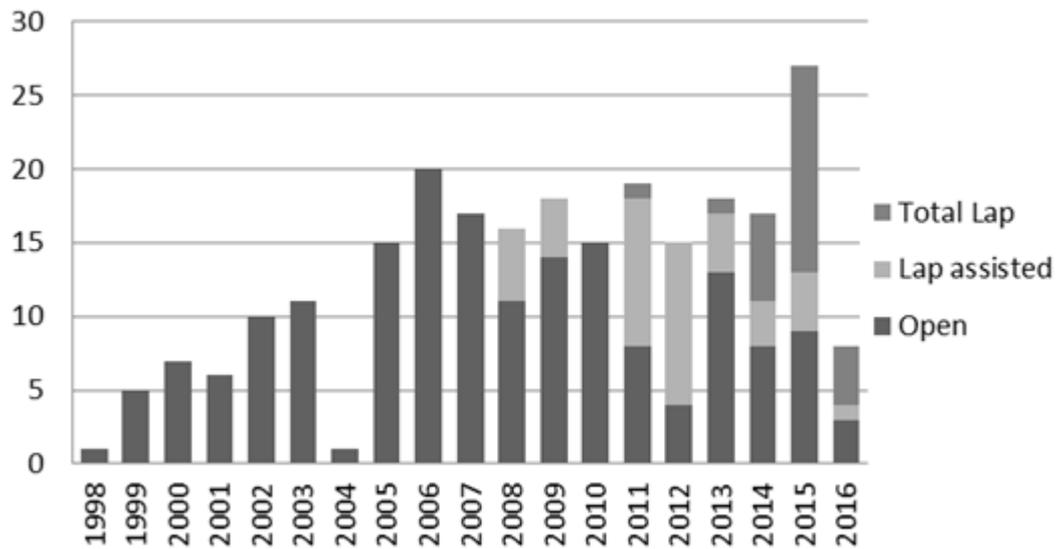


Figure 3. Transition from open to laparoscopic colorectal resection

Table 2. Distribution of Colorectal cancer

Site	Number	%
Caecum	03	1.2 %
Ascending Colon	20	8.2 %
Transverse Colon	18	7.4 %
Descending Colon	09	3.7 %
Sigmoid Colon	63	25.9 %
Recto sigmoid junction (Rs)	24	10.2 %
Upper Rectum (Ra)	32	13.1 %
Lower Rectum (Rb)	66	27.1 %

Table 3. Operating time (overall)

Procedure	Range (Hrs)	Median (Hrs)
Right hemicolectomy (n=11)	1 to 4.5	2.2
Extended right hemicolectomy (n= 11)	1.75 to 6.5	3
Left hemicolectomy (n=8)	2.5 to 4	2.7
Sigmoid colectomy (n= 32)	2 to 4.5	2.7
Anterior resection (AR) (n= 68)	2.5 to 6.5	4
Abdomino perineal resection (APR) (n= 36)	2 to 7	4
Sub-total colectomy (n= 2)	3.5 to 3.7	3.6
Procto-colectomy (n= 4)	3.5 to 9	4
Hartmann's procedure (n= 9)	1.5 to 4.5	2.5

Table 4. Blood loss (overall)

Procedure	Range (ml)	Median (ml)
Right hemicolectomy (n= 18)	50 to 700	275
Extended right hemicolectomy (n= 10)	100 to 700	700
Left hemicolectomy (n= 08)	50 to 500	325
Sigmoid colectomy (n= 46)	100 to 2000	300
Anterior resection (AR) (n= 37)	300 to 3000	450
Abdomino-perineal resection (APR) (n= 37)	300 to 3800	925
Subtotal colectomy (n= 3)	350 to 2000	650
Procto colectomy (n=3)	100 to 950	500
Hartmann's procedure (n =8)	50 to 500	275

Table 5. Operative parameters open vs. laparoscopy

Parameter	Open	Lap assisted (LA)	Total lap (TL)	LA + TL
Median operating time (hours)	3 (1 to 6.5)	4.6 (3 to 9)	4 (2.5 to 5.5)	4 (2.5 to 9)
Median blood loss (ml)	500 (50 to 3800)	461 (100 to 950)	150 (50 to 300)	200 (50 to 950)
LN harvest (median) (range)	8.44 (1 to 28)	7.1 (1 to 15)	10.0 (3 to 16)	8.7 (1 to 16)
Conversion	NA	12 (17.9 %)		
Median Hospital stay(d)	8 (4 to 30)	8.1 (4 to 38)	5 (3 to 12)	5 (3 to 38)

Table 6. Cause of death

Cause of death	Number	%
Sepsis	04	1.7 %
Congestive cardiac failure	02	0.8 %
Deep vein thrombosis / Pulmonary embolism	01	0.4 %
Myocardial infarction	01	0.4 %
Bleeding due to cirrhosis of liver / DIC*	01	0.4 %
Hepato-renal syndrome	01	0.4 %
Total	10	4.2 %

*Disseminated intravascular coagulation

bleeding (n=1; 0.4%). Wound infection occurred in 31 patients (13.1%) and prolonged ileus was seen in 5 (2.1%). Myocardial infarction (3.4%) was the commonest non-surgical post-operative complication (total 9.7%). Twelve patients underwent re-exploration (5%) and the hospital re-admission rate was 2.5 % (6 patients).

30 Day post-operative mortality

There were ten post-operative deaths (overall mortality of 4.2%). However, procedure related mortality was 1.7% (n= 4). All were due to sepsis following anastomotic leaks. The causes of death are listed in Table 6.

Laparoscopic surgery

Figure 3 illustrates the transition from open to laparoscopic procedures over the study period.

Open vs. laparoscopy:

Comparison of operative parameters between the two groups is shown in table 5. Respective percentages of morbidity, anastomotic leak and mortality for the open and laparoscopy groups were 31.1% versus 30.9%, 3.1% versus 2.9% and 5.5% versus 1.8%.

Intra operative complications:

There were two intra operative complications in the laparoscopy group (3%); inadvertent injury to bowel and injury to the left ureter.

Follow up

Follow up data was available for 121 patients (58 %). The overall follow up period ranged from to 2 months to 15

years (median 1.1 years). An incisional hernia was found in 6 patients who underwent open surgery (4%). Stoma complications were detected in 6 patients who underwent APR (15%).

Oncological outcome (overall)

Local recurrence:

There were 10 patients who developed local recurrences (8 %) from 2 to 49 months (median time to recurrence 1 year); nine followed surgery for rectal cancer (n= 80; 11%). Only one patient (2.4 %) developed local recurrence after colon cancer resection (n= 41). Nine local recurrences were following open (10%) and 2 followed laparoscopic operation (6%).

Distant metastasis:

Distant metastases were detected in 20 patients (17 %) during follow up. The commonest site was the liver. There was one port site (1 %) recurrence following a lap-assisted procedure at 9 months.

Discussion

This is a study of 260 patients with colorectal cancer who underwent either standard open or laparoscopic surgery. The median age of the study group was 59 years (range 25 to 90 years), which is lower than reported in most western literature (70 years, range 28 to 95) [10]. There was no marked difference in male to female ratio, 1.4: 1, in this study compared to other published data [11, 12].

Clinico-pathological parameters

Sixteen percent presented as an emergency. One study reported emergency presentation for CRC in 13.6 % [10] whereas others have reported emergency presentations in up to 30 % [13]. All patients who presented as an emergency had intestinal obstruction. Other larger studies have reported intestinal obstruction as the commonest (78 %) mode of emergency presentation [14, 15]. Bleeding per rectum was the commonest symptom (42.8 %), which was followed by change of bowel habits (17.1 %) in those who presented to the out-patient clinic.

There is a marked variation in the duration of symptoms in developed countries (1 to 10 months; median 3.5 months) [16] and African countries (21 days to 84 months; median 22 months) [11]. In our study, median duration was 3 months (1 to 24 months).

A family history of CRC among first degree relatives was obtained in 8 (5.6 %) patients in this study and compares with the same reported by Phillip LC (5.4 %) in his study of 332 patients from Tanzania [11]. In another study, a family history of CRC was reported among 20.5 % of patients in Sweden [10]. Pooled data analysis shows a relative risk of 2.24% and 2.93% for patients with a first degree relative affected by CRC

and patients with ulcerative colitis respectively [17].

In our study group the proportion of rectal cancer (RC) was higher (40.2%) than reported (15.7 to 38.7%) in other studies [10, 11, 18]. Further, about 80 % of CRC in our patients was located on the left side making it accessible even with a flexible sigmoidoscope. Therefore, stool occult blood combined with flexible sigmoidoscopy would be an attractive option for screening of CRC in our patients. However, the cost effectiveness of this approach has to be determined by further studies.

Distant metastases were present at presentation in 16.6 % of our patients with 80.9 % of them in the liver and 4.6 in the lung. Published data shows 20 to 25 % of colon cancer and 18 % of rectal cancer patients have distant metastases at presentation with liver being the commonest site [13].

Preoperative management

Neoadjuvant therapy has been used in 64 patients out of whom 50 were for patients with RC. The use of neoadjuvant chemo-irradiation for RC became the standard practice after the trial in 2012 [19, 20]. Though 49 % patients with RC received neoadjuvant therapy sub group analysis shows a marked increase in the tendency to use neoadjuvant therapy after the year 2011 (27% before and 80 % after 2011). Simon et. al. in 2012 [22], examined the trend in the use of neoadjuvant radiotherapy among surgeons across the south west region of France and found that 62% of the patients received neoadjuvant radiotherapy for RC. A complete response to neoadjuvant chemo radiation was seen in 16% of our patients. A similar response rate has been observed (17 %) in the landmark paper published in 2004 by Habr-Gama where they adopted a “watch and wait” policy for this group of complete responders [22]. Others have reported complete response rates as high as 25 % [22].

Surgery (overall)

The overall operability among our patients (90 %) was lower than other studies (97 %) [19]. However, the operability among those patients undergoing emergency procedures was only 65 %, a finding that has not been reported earlier.

Post-operative management

The overall postoperative complication rate in this study (39.5 %) was higher than reported (26.2 %) in a similar study [11]. The commonest post-operative complication (13.2%) was wound infection. The reported incidence of wound infection is between 3 to 30% across the literature [23]. Similarly, the overall incidence of anastomotic dehiscence (3.7% in this study) ranged between 1% to 30% in the literature [24, 25]. Higher incidences of anastomotic dehiscence have been reported following rectal cancer resection versus colon resection (5% vs. 10%) [19]. However in the hands of an experienced colorectal surgeon, the reported incidence of

anastomotic dehiscence following AR has been between 3% and 6% [25]*, and it was slightly higher (6.3%) in the present study. Prolonged ileus (2.1%) contributed to longer hospital stay in our patients. One study showed a slight difference in the incidence of ileus following open surgery versus laparoscopic surgery (3.3 % vs. 2.4%) but the difference was not statistically significant [26].

The median hospital stay was 10 days (3 to 38 days) in our patients. Median hospital stay after surgery for CRC was 12 (4 to 72 days) in one study [11]. The difference is probably due to the inclusion of patients who underwent laparoscopic surgery in our study. Our re-operation rate (5.1%) was lower than the reported 12% for LA and 10% for open surgery [27]. The overall readmission rate of 2.5% in our study group is comparable to the reported 2% for LA and 12% for open surgery in the same study.

The overall 30 day mortality in our study was 4.2%. Eighty percent of deaths followed surgery for rectal cancer. Mortality as high as 13% has been reported following emergency procedures while that reported for elective procedures is around 2% [19]. In these studies it is not clear if post-operative mortality was procedure related or due to other co morbid factors. Procedure related mortality in our patients was 1.7%. Also, we observed higher mortality among patients with rectal cancer (6.6% vs. 1.7%) than those with colon cancer. Others have reported overall mortality from 8% to 10.5% for CRC [11].

The number of LN examined could be determined in only 36.5 % of patients, far less than reported in other studies [28]. In a large study of 3557 patients mean LN harvest was 13 (1 to 53), (37); in our patients we could harvest only a median of 8 (1 to 41) nodes. Lymph node positive ratio (15.1%) was also lower than reported (49.7%) [18, 29].

Follow up

Incisional hernias were found in 2.7% of patients followed up, and it was slightly higher than reported in the literature [26]. Port site hernia was observed in 1.4% of the patients by the same group but we have not encountered this complication in our patients undergoing laparoscopy thus far. Port site recurrence was seen in one of our patients (1.4%). In one study port site recurrence following laparoscopic resection of CRC was 1.2 % [30]. Other studies have reported port site recurrences between 0.7 to 1.3% following laparoscopic surgery for CRC [5, 31]. The complications related to stoma in our study (14.6%) was also higher than that reported in a similar study (4.1%) [27].

Oncological outcome

The literature reveals a higher local recurrence rate for RC (10 to 20 %) compared to colon cancer (2 to 10%) [26]. In our patients, local recurrences were seen in 11.2% following RC

and 2.4% following colon cancer (overall 8.2%) and was within the reported figures. In a meta-analysis, 40 to 50 % of patients eventually developed liver secondaries following surgery for CRC within 3 years [32]. In our study 10.7% of the patients developed liver secondaries within 2 years. The incidence of brain metastases among our patients (1.6%) was within the reported range of 0.6% to 3.2% [33].

Open surgery vs. Laparoscopy

The operative time in the laparoscopy group (LA + TL) was longer than the open surgery group. In a meta-analysis of 13 trials operating time in laparoscopy was longer ($p=0.027$) in all but one (32) study. In addition, most of the studies have observed significantly lower mean blood loss following the laparoscopic approach [34]. Though our blood losses in both groups were higher (689 ml vs. 323 ml) laparoscopy group had a lower blood loss). The two intraoperative complications (2.9%) were seen within in the first 10 procedures. In most studies, the incidence of intraoperative complications were similar in laparoscopic (for RC 6.1% to 21.1 %: overall 3.7%) and open surgery [35].

Conversion rate in our study (17.9 %) was almost equal to that reported from North America (17.5%) although it is higher than the Europe (10.3%) and Asia (13.6%) [36]. However, it is within the reported range (15 to 30 %) [6, 8, 37, 38]. The reported hospital stay after laparoscopic CRC surgery is 5 to 8 days [6, 8]. In a meta-analysis of 7 trials, hospital stay after laparoscopic colon and rectal cancer resection has been analyzed separately and shown to be significantly shorter in both groups [35]. In our study the hospital stay was assessed together in both groups and was found to be lower in laparoscopy group (open 9.4 days vs. laparoscopy 6.1 days).

Postoperative complications in our study were comparable between the two groups (open 31% vs. laparoscopy 30.9%). The literature does not reveal a significant difference in postoperative complications between laparoscopic and open surgery either [35]. Anastomotic leak rate did not differ significantly between the two groups (OR 0.97) in this study. However in most published studies, including a meta-analysis of 7 trials [35], there was no significant difference in the anastomotic leakage between open and laparoscopic approach. There was no significant difference in post-operative mortality between the open and laparoscopic techniques (5.5% vs. 1.8%; OR 0.25). In a meta-analysis of six trials, mortality was below 2% in either group [35]. Though not statistically significant, open surgery group in our study showed a higher mortality (5.5%) probably because of the inclusion of the learning curve. In another randomized trial mortality was 5% for open and 4% for laparoscopic surgery [39].

Higher LN harvest in TL group could be attributed to the difference in pathological reporting rather than the surgical

technique since this group represents the most recently reported group where LN harvesting is highest.

Local recurrence after the resection of colon cancer was 28% vs. 18% in the Barcelona trial [34]. In our study local recurrence following open surgery (10.2%) was lower than Barcelona trial. Though local recurrence following laparoscopic resection was lower in our study (6%) compared with Barcelona trial, comparison cannot be made since ours is not a randomized controlled trial. Multiple factors would have contributed for the higher local recurrence rate in open surgery group. Some of the patients especially in the early part of this study did not receive neoadjuvant therapy as they underwent surgery in an era before the neo adjuvant therapy became the standard practice at least in our practice (use of neoadjuvant therapy for RC was 27% before and 80 % after 2011). Secondly, the learning curve also would have contributed to some extent. Thirdly, patients who underwent laparoscopic surgery have been followed up for a shorter period compared to open surgery group. Many randomized studies have confirmed the non-inferiority of laparoscopic over open surgery with respect to overall survival and disease-free survival [, 3, 14, , 40]. Our experience is similar despite being a non-randomized study.

Conclusion

There are differences in the clinic-pathological aspects of CRC in our patients especially with regard to age and stage at presentation. The overall operative and oncological result of this study shows that we can reach the accepted standards in colorectal surgery. Though laparoscopic surgery for colorectal cancer is more recent, despite the steep learning curve we have reached accepted international standards within a short period of time. Two aspects of our study that need attention are LN retrieval and reporting, and long term follow up. While LN harvest has shown improvement over the years, follow up reporting of patients has to be longer.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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