Introduction

Until 1990 various renal diseases were treated by open radical nephrectomy. In 1991 Ralph Clayman reported the first laparoscopic radical nephrectomy for removing a renal oncocytoma using a transperitoneal approach [1]. Since then the technical aspects of the laparoscopic renal extirpation procedure have been refined and improved. Gaur was one of the pioneers who started developing the retroperitoneal approach using a balloon for dissection in order to prepare the retroperitoneal space [2,3].

Starting with 1994 the use of hand-assisted techniques for laparoscopic surgery has been reported [4]. It is partly meant to overcome the difficulty of learning conventional laparoscopy. Hand assistance through a hand port device during laparoscopy allows the surgeon to use his tactile sense which can be very helpful in a difficult situation or if the surgeon has limited experience.

Nowadays, the laparoscopic radical nephrectomy is a standard procedure for renal lesions and is often indicated when nephron sparing nephrectomy cannot be performed [5]. During the early development of laparoscopic radical nephrectomy small sized T1 tumors were the classic indication for LRN [5]. As surgeons continuously gained experience performing the procedure these indications expanded, including T2 and even T3a stage tumors [6]. A number of studies have been conducted in order to compare the influence of the approach on surgical morbidity, tumor control and oncologic outcome [7-9].

Lately, more experienced surgeons have evaluated the feasibility of laparoscopic radical nephrectomy in very large T2 tumors [10,11].

Objectives

• To evaluate whether the type of approach has any effects on the perioperative outcomes, complications and morbidity.
• To evaluate the feasibility of LRN for large T2 tumors in terms of outcome, intraoperative and postoperative complications.
• To discuss the oncologic effectiveness in terms of margin status, development of metastatic disease and long–term patient survival of the minimally
invasive approach after performing laparoscopic radical nephrectomy.

Summary of articles
In order to evaluate the possible discrepancy of outcomes (in terms of complications) when using a transperitoneal, a retroperitoneal or a hand-assisted approach we have chosen to compare five studies that we considered to be most significant in terms of power of prediction and significance of the results.

1. Desai et al. conducted a prospective randomized study comparing transperitoneal to retroperitoneal laparoscopic radical nephrectomy [12].

Between 1999 and 2001, 102 patients were prospectively randomized to undergo laparoscopic radical nephrectomy with intact specimen extraction. Group one consisted of 50 patients undergoing TLRN and group two consisted of 52 patients undergoing RLRN. The groups were matched by BMI (29 versus 28, p=0.89), age (63 vs 65 years, p=0.69) ASA class (2.7 vs 2.8, p=0.37), laterality and mean tumor size (5.3 vs 5.0 p=0.73). Exclusion criteria were a BMI> 35 or prior abdominal surgery in the quadrant of interest.

Results
Retroperitoneal laparoscopic radical nephrectomy was associated with a shorter total operative time (207 vs 150 minutes, p=0.001), shorter time to renal artery control (91 vs 34 minutes, p <0.0001) as well as quicker time to renal vein control (98 vs 45 minutes p<0.0001). Open conversion wasn't necessary in either group.

The two approaches were similar in terms of blood loss (180 TLRN vs 242 mL. RLRN, p=0.82), intraoperative complications (10% vs 7.7%, p=0.30), postoperative complications (20% vs 13.5 %, p=0.14), length of extraction incision (6.5 vs 7 cm, p=0.82), duration of hospitalization (43 vs 45 hours, p=0.55)analgesia requirements (27 vs 26 mg of morphine sulfate equivalent, p=0.13) time to resumption of oral intake (1.1 versus 1.2 days, p=0.82) time to ambulation (1 vs 1.1 days, p=0.82) and complete convalescence (4.3 vs 6 weeks p=0.29). Ileus was the most common complication. It occurred in 5 patients from the TLRN and 3 patients from the RLRN group.

None of the specimens showed positive margins for cancer.

3 Patients from the transperitoneal group developed systematic metastatic disease during a mean follow up of 15 months and 1 patient from the retroperitoneal group developed systematic metastatic disease during a mean follow up of 13.5 months.

Discussion
The transperitoneal approach provides a larger working space and more easily identifiable anatomical landmarks but makes the access to the renal hilum more difficult. The retroperitoneal approach has a more limited working space and anatomical structures may be more difficult to identify but provides a rapid access to renal hilum. In this study the factors known to increase the difficulty of the approaches such as a BMI>35 and prior surgery in the quadrant of interest were eliminated. The study demonstrates that the retroperitoneal approach was associated with a shorter time to renal artery control, shorter time to renal vein control and shorter operative time.

Other criteria like blood loss, complications, length of hospital stay, time to oral intake, duration of hospitalization and convalescence were similar in both groups. The fact that the transperitoneal approach has been associated with paralytic ileus which leads to a longer hospital stay hasn’t been confirmed in this study. The study demonstrated comparable safety and efficacy of both approaches but the authors state that there may be specific situations in which one of the approaches has more benefit for the patients.

2. Okegawa et al. conducted a retrospective study comparing transperitoneal and retroperitoneal laparoscopic nephrectomy for renal cell carcinoma. [13]

Between August 2001 and July 2007, 100 patients with clinical stage T1—T2 renal cell carcinoma (1997 TNM classification) underwent laparoscopic radical nephrectomy performed by 2 surgeons. The choice of approach was left to each surgeon. 47 patients underwent TLRN and 53 underwent RLRN.

Results
The two groups were similar in terms of mean operative time (292 vs 267 minutes, p=0.17), estimated
blood loss (223 vs 202 mL, P=0.62), mean hospital stay (13 vs 12.3 days, p=0.07), mean analgesic requirement (1.1 vs 0.8, p=0.06), intraoperative complications (6% vs 4%), postoperative complications (6% vs 6%). One conversion was needed in the TLRN group due to bleeding from the renal vein after the transection of the renal artery by scissors. Total blood loss was 2000 mL. Other postoperative complications were wound infection in 3 patients of the TLRN group and 2 of the RLRN group. Atelectasis occurred in one patient of the RLRN group.

There was less time to oral intake in the retroperitoneal group (1.6 vs 2.5 days, p<0.01). Authors explain this, stating that this approach involves reduced bowel manipulation.

Oncologic outcomes were reviewed retrospectively. Mean follow-up was 34 months. The 5-year disease-free survival rate was 90% for both procedures. The 5-year over-all survival rates were 98% for the TLRN group and 96% for the RLRN group.

Discussion

Desai et al.[12] reported a similar time to oral intake for the two approaches which suggests that either one of the two approaches has a benefit on the time to oral intake. However, this study revealed a shorter time to oral intake for the RLRN group, suggesting a negative impact on bowel movement when using the transperitoneal approach.

There was no significant difference between the two approaches in terms of long-term oncologic outcome.

3. Bandi et al conducted a study in which they retrospectively reviewed the clinical and oncologic outcomes of patients who underwent hand-assisted laparoscopic radical nephrectomy for clinically confined RCC at the University of Wisconsin from 1996 to 2003. [14]

The study included 75 patients with pathologically confirmed RCC. Mean follow-up was 3 years. Exclusion criteria were patients with metastatic RCC who had cytoreductive HALRN.

All 75 patients underwent transperitoneal HALRN. The operation was performed by one three surgeons. A 7-8 cm midline, lower quadrant or subcostal incision was made for the hand-port device, depending on the side of the surgery and the dominant hand of the surgeon. Several handport devices were used depending on the surgeon’s preference, like the Pneumosleeve, Handport or Lapdisc. The intact specimen was placed into a LapSac and extracted through the hand-port.

The study included 52 men and 23 women with a mean age of 59 (29-83 years), median American Society of Anaesthesiology score was 2, and a mean BMI of 29 kg/m2. The mean tumor size was 5.8 (1.7-12 cm).

Results

The mean operative time was 227 (134–361) min, mean estimated blood loss was 130 (10–650 mL). The median time to tolerating a general diet was 2.5 days and the median hospital stay was 4 days. None of the patients required conversion. 4 Patients (5%) had intraoperative complications: 1 pneumothorax, 1 port-site bleeding, one adrenal vein injury and in one patient specimen extraction was difficult. There were 23 postoperative complications, 9% major and 21% minor). The most frequent minor complications were the infection of the wound (in 5 patients) and ileus (in 5 patients). Incisional hernia occurred in 2 patients. Wound dehiscence occurred in 2 patients.

All specimens had negative inked margins for neoplasm. There were no port-site recurrences.

65 of the patients had a follow-up of more than 3 years. At a mean follow-up of 46 months, 13 patients died. The overall survival-rate was 80%. Five patients developed recurrent disease; three developed metastatic disease and died from RCC. The 5 year cancer-specific survival-rate was 94.4% and the 5 year disease-free survival rate was 90.2%.

4. Gill et al conducted a single-surgeon, single-center study in which they evaluated the oncologic adequacy of laparoscopic radical nephrectomy from a technical standpoint, comparing it to the oncologic efficacy of open radical nephrectomy [15]

The authors present the data regarding 100 laparoscopic radical nephrectomies, with intact specimen extraction in all cases, performed between September 1997 and August 2000. The study included 55 males and 45 females, with a mean age of 61.8 years (29–89 years), mean BMI of 29.9 (17–63), American Society of Anaesthesiologists (ASA) score of 3 (2–4). The mean tumor size was 5.1 cm (1.7–14 cm). Retroperitoneal laparoscopic nephrectomy was performed in 73 patients, and 27 patients underwent transperitoneal laparo-
scopic radical nephrectomy. Data was entered prospectively into a data bank and follow-up information was obtained telephonically or by review of patient charts. Histopathologic and radiologic (CT scan) data was compared to 40 ORN cases performed since February 1996, which all fulfilled similar inclusion criteria on preoperative CT–scan: tumor size less than or equal to 14 cm, no evidence of local invasion into surrounding organs, and no involvement of the inferior vena cava.

Results

The mean surgical time was 2.8 hours (45 minutes-5.5 hours), the mean estimated blood loss was 212 mL (10-3000mL), mean specimen weight as 554.3 g (76-1328 g). The mean incision length was 6.5 cm (1.5-12 cm). The mean postoperative requirement of narcotics was 22.2 mg of morphine sulfate equivalent (0-460 mg). The average hospital stay was 1.6 days ( <1 day-8 days). Surgical margins were negative in all cases. Complications occurred in 14 patients (14%), 3 were major and 11 minor. Renal artery haemorrhage occurred in 2 patients. In one of them a branch renal artery clip became dislodged necessitating open conversion. Another patient undergoing hemodialysis required open conversion due to generalized oozing caused by elevated plasma thromboplastin time. During open surgery a splenic capsular injury occurred, the patient necessitating splenectomy. Total open conversion rate was 2%. Minor complications were cutaneous hyperesthesia (4 patients), port site infection/ dehiscence (2 patients, one of which was located at the extraction incision), paralytic ileus (2 patients), atelectasis (one patient), postoperative hematoma (2 patients).

Compared to the ORN group, the surgical time of LRN proved to be similar (175 vs 185 min, p=0.40). It is worth mentioning that the surgical time of the minimally invasive procedure tended to decrease between September 1997 and August 2000 with increasing experience. The mean surgical time for the first 50 patients was longer compared to the second half (175.1 +–SD 53.1 vs 163.3 +–SD 60.1, p=0.02). Concomitantly with the decrease in surgical time, there was a slight increase in tumor size, (4.8 cm vs 5.4 cm) and a slight increase of the weight of the excised specimen (497 vs 609 g), and still, the second half of the LRN has a shorter mean operative time. The LRN group decreased blood loss (187 mL vs 670 mL, p<0.001), and a shorter hospital stay (1.5 days vs 5.6 days, p<0.001). The authors also state that the LRN group had decreased morbidity, reduced analgesic requirements, shorter convalescence and superior cosmetic results, but without providing the data for the ORN group.

The primary focus of the study was to evaluate the oncologic efficacy of the minimally invasive method compared to the open procedure. For this purpose, the authors compared the radiologic (CT–scan) data and the histopathologic data of the two groups. Preoperative CT revealed a tumor size of 5.1 cm in the laparoscopic group vs 5.4 in the open surgery group, p=0.50. The tumor was located in the middle of the kidney (36% vs 58%, p=0.33). Mean pathologic tumor grade was 2 in the LRN group vs 2.4 in the ORN group (p=0.07). 75 % of the patients from the LRN group had clinical T1N0M0 disease, compared to 58% in the ORN group (p=0.09). 64 % of the patients from the LRN group had clear cell carcinoma vs 73% in the open surgery group, (p=0.45).

Pathological data showed that the tumors from the laparoscopic group were 12% smaller in size and 18% smaller in volume but the overall specimen weight was comparable in the two groups.

Surgical margins were negative for neoplasm in all patients of both groups.

No macroscopic tumor fracture was noted in any instance during mobilization of the specimen. A small, superficial tear in a renal tumor was noted during retroperitoneoscopic mobilization, without any noticeable macroscopic spillage. No local or distant recurrences were noted during a 14-month follow-up.

Follow-up

Mean follow-up was 16.1 month (1-36 months). No local or port site recurrences were reported. Two patients with pT1N0M0 disease and dialysis-dependent renal failure developed distant metastases. One patients developed hepatic metastases 12 months after the operation. One patient had multiorgan tumors (bilateral renal cell carcinomas, prostate adenocarcinoma, and synchronous transitional cell carcinoma of the bladder). He developed regional lymphadenopathy 8 months after surgery. He died 11 month postoperatively. Overall mortality rate was 1%.

Discussion

The laparoscopic technique for radical nephrecto-
my duplicates established open surgical principles. The primary aim of this study was to evaluate the oncologic adequacy of laparoscopic nephrectomy from a technical point of view and whether the minimally invasive technique fulfils the technical requirements of an oncologically adequate procedure. The documented negative surgical margins in both groups demonstrate that the laparoscopy provides an efficacious technique for obtaining oncologic safety. Over a mean follow-up period of 16.1 months, no port site or local tumor recurrences were noted.

The authors evaluated the learning curve in order to see whether there was any change in the data obtained from the first 50 operated students compared to the last 50 patients. Surgical time tended to decrease for the second half of the LRN group, despite the fact that the mean tumor size and the mean specimen weight tended to be somewhat larger. Also, the two major complications, leading to open conversion occurred during the second half of the group. The complication rate was lower during the second half (20% vs 10%) and the hospital stay was shorter (1.7 days vs 1.4 days, p=0.68), without being statistically significant.

5. Hemal et al conducted a study in which they prospectively evaluated the feasibility, safety and long-term outcome of LRN for large renal tumors (T2N0M0) comparing it to ORN. [11]

112 patients included in the study underwent LRN for clinical stage T2N0M0 renal cell carcinoma between 1998 and 2006. 41 patients underwent laparoscopic radical nephrectomy and 71 underwent open surgery. The choice of procedure depended on the patient and surgeon preference and experience. Only experienced surgeons performed laparoscopy while the open procedure was performed by all surgeons. Retroperitoneal LRN was used in 15 cases and 26 patients were operated using the transperitoneal approach. All specimens were removed intact. They were either placed in an entrapment device or a simple sterile plastic bag and some of them were removed directly.

The two groups were comparable in terms of mean age (52.5 RLRN vs 52.7 TLRN, p=0.94), mean BMI (29.4 vs 29, p=0.62), mean ASA (American Society of Anesthesiologists) score (1.95 vs 1.75, p=0.23) and mean tumor size (9.9 vs 10.1, p=0.69)

Results
Mean operative time was significantly longer in the LRN group (180.8 ± 21.5 SD vs 165.3 ± 40.9 SD, p=0.029). The mean estimated blood loss was lower in the LRN group (245 ± 125.13 SD vs 537.3 ± 139.99 SD, p=0.001). Patients from the LRN group received transfusions compared to 23 from the ORN group (14.63% vs 32.4%, p=0.04). Mean analgesic requirement (mg morphine equivalent) was significantly lower for the LRN group (16.4 ± 5 SD 3.35 vs 35.0 ± 8.01 SD, p<0.001). The mean hospital stay and the mean convalescence were also significantly lower for the LRN group: (3.6 vs 6.6 days, p<0.001), and (1.56 vs 3.3 weeks, p<0.001). Transperitoneal procedures were successful in all 26 patients. 4 complications occurred in the RLRN group, 2 of which necessitated open conversion, 1 due to bleeding from the renal artery secondary to clip dislodgement and the other because of bleeding from the renal vein. Bowel injury occurred in 1 patient from the LRN group and it was managed by intracorporeal suturing. Bowel injury occurred in 3 patients from the open surgery group and it was managed by primary repair. There was no statistical difference between the number of intraoperative complications between the two groups (9.75% LRN vs 11.26% ORN, p=0.94). Postoperative complications occurred in 5 (12.19%) of the patients from the LRN group and 11 (15.49%) of the patients from the ORN group, without being statistically significant. Nevertheless, the incidence of wound infection was higher in the ORN group, occurring in 5 patients compared to 1 patient from the LRN group. Ileus occurred in 1 patient treated laparoscopically and 2 who underwent open surgery.

Results in follow-up
The patients were followed for a similar period of time, 51. 4 months (3-78 months) for patients in the LRN group and 57.2 months (4-80 months) for patients in the ORN group. None of the patients had local or port-site recurrences. Metastasis occurred in 3 patients from the LRN group (7.3%), two of which died from the disease and 7 from the ORN group (9.85%), 4 of which died from the disease. 3 patients in the LRN group, and 4 patients from the ORN group died of noncancer related causes (stroke and myocardial infarction). The 5-year overall survival-rate was 87.8% in the LRN group and 88.7% in the ORN group (p=0.87). The cancer specific 5-year survival was 95.12% in the LRN group and 94.36% in the ORN group (p=0.79). The recurrence-
free 5-year survival was 92.6% for patients treated laparoscopically and 90.1% for patients undergoing open surgery. No significant p values resulted from the follow-up data.

Discussion

Removing large renal masses (tumors > 7 cm) laparoscopically can prove to be technically challenging. The working space can be decreased because of the presence of the specimen and orientation might be difficult because of altered anatomical landmarks, because of the likelihood of encountering parasitic vessels.

Advantages found in the outcome of patients treated minimally invasive included lower estimated blood loss resulting in a decreased need for transfusion, less need for postoperative analgesia, shorter hospital stay and shorter convalescence. All of these criteria proved to be not only clinically but also statistically significant.

The mean operative time was significantly increased in the LRN group. The authors explain this result by stating that the reason for this might be their learning curve. They included all of their cases in the study, even the initial ones. The authors also state that the increased operative time didn’t have a negative impact on the patients, nor did it have any economical consequence, being balanced by the shorter hospitalisation as well as shorter convalescence. The authors consider that it is very important to be prudent when treating larger tumors, since the dissection of the kidney is more difficult because of the parasitic vessels and the increased involvement of adjacent organs. They also believe that their success in treating T2 tumors is based on their previous experience with advanced laparoscopy.

Studies data comparison and discussions

The Bandi study [14] regarding the hand-assisted LRN had the highest complication rate of the 7ve presented (36%). Incisional hernia and wound dehiscence were complications that occurred in 4 patients.

Infection of the wound is a relatively frequent complication. It occurred in 5 patients from the HALRN group [14], 5 patients in the study conducted by Okegawa et al [13] and only 1 patient from the TLRN group in the study conducted by Desai et al [12]. It also occurred in 5 patients who underwent open surgery compared to 1 patient who was treated laparoscopically in the last study [9]. Port site infection occurred in 2 patients from the LRN group in the study conducted by Gill et al [15], one of which was located at the extraction incision. The incidence of wound infection might be higher with increasing incision length.

Prolonged postoperative ileus occurred in 5 patients treated by HALRN [14], 5 patients from the TLRN group (Desai) and 3 from the RLRN group (Desai) [12]. Still, the mean time to oral intake didn’t seem to be affected by the occurrence of ileus in the Desai study (1.1 resp. 1.2 days), whereas Okegawa showed a shorter time to oral intake in the RLRN group (2.5 vs 1.6 days) [12,13]. Median time to oral intake for patients treated by HALRN was 2.5 days [14].

The shortest operative time was achieved in the RLRN group in the study conducted by Desai et al [12] (Table 1.) Compared to the transperitoneal approach they also achieved a shorter time to renal artery control (91 vs 34 min), as well as a shorter time to renal vein control (98 vs 45 min). The authors state that their preference for RLRN couldn’t have biased this result because at the time they started the study, they were well past the learning curve for TLRN. Gill et al. compared the operative time of the first 50 patients to the second half of the cohort, revealing a shorter operative time for the second half of the group (175.1 vs 163.3 min), concomitantly with a slight increase in tumor size [15]. Thus, the operative time tended to the decrease with increasing experience of the surgeon. The study conducted by Hemal et al. revealed a longer operative time for LRN compared to the ORN group [10]. The excision of a large specimen requires a certain experience and can be more time consuming than that of smaller T1 tumors. This was shown in a study conducted by Berger et al [6], where the operative time for tumors < than 7 cm turned out to be shorter than the operative time needed for treating tumors > than 7 cm (180.6 vs 209.5 min, p=0.0021).

Nadler et al conducted prospective randomized study in order to compare the three approaches [16]. 33 patients with a renal mass < 7 cm were enrolled in the study and 11 had each procedure. HALRN achieved the fastest mean operative time (139 min compared to 196 min TLRN and 185 min RLRN). HALRN had the disadvantage of the highest rate of hernia. TLRN resulted in shorter hospital stay (2.1 days compared to 3.4 days HALRN and 3.6 days RLRN, p=0.0039), shorter time to oral intake (13 hours compared to 19 HALRN and 16 RLRN). This was similar in Okegawa’s RLRN group[13]. The transperitoneal approach involves a greater
amount of intestinal manipulation which may lead to prolonged hospital stay and time to oral intake.

Still, at the present there is no strong evidence supporting the superiority of one of the three approaches. Each surgeon chooses the approach according to his experience and patients characteristics. In case of large specimens it can be easier the use the hand-assisted approach especially compared to the retroperitoneal approach in which working space is limited [16]. Also HALRN can be an alternative method to classic LRN for inexperienced surgeons[18]. Kawauchi et al. [18] conducted a study in which they evaluated whether the surgeon experience would affect patient prognosis, considering that hand-assistance is indicated for educational purposes. Their study showed that surgeon experience did not affect the oncological outcomes.

The use of minimally invasive techniques in large T2 tumors is feasible and as safe as the open procedure in terms of oncologic outcome although the perioperative and long-term outcome might be strongly connected to the surgeon’s experience [6,11]. With increasingly larger tumors, the dissection becomes more difficult, resulting in a greater risk of transgressing oncologic principles. Hemal et al state that advanced surgical skills are required in order to perform laparoscopic radical nephrectomy in case of large renal tumors [11].

**Oncologic outcome across the studies**

Several authors have recently studied the oncologic outcome of laparoscopic radical nephrectomy compared to that of open radical nephrectomy [8,11,18,19]. Oncologic outcome can be evaluated on the basis of several criteria like positive surgical margins, tumor seeding in the renal bed or the wound (local or port-site recurrence), and development of metastatic disease, disease-free survival rate and cancer-specific survival rate.

Gill et al, Bandi et al, and Desai et al confirmed negative margins for neoplasm in all specimens [15,14,12]. No local or port site recurrence occurred in the studies, except for 1 patient from the HALRN group included in the study conducted by Bandi et al, who developed a local recurrence at the nephrectomy bed at 18 months after surgery. After performing a resection he continued to be disease-free at a follow-up of 49 months [13]. (Table 2)

The 5-year disease-free survival rates and the 5-year cancer specific survival rates were similar when comparing the 5 studies [11,12,13,14,15]. Previous studies have revealed similar survival rates when comparing laparoscopic radical nephrectomy to open radical nephrectomy [8,11,19]. Permpongkosol et al also evaluates the 10 year disease-free and cancer specific survival rates (94% for LRN vs 87% for ORN and 97%for LRN and 86% for ORN) [7]. (Table 2)

Negative margins for neoplasm, the low percentage of recurrence, as well as the 5 year disease-free survival rates and the 5-year cancer-specific survival rates confirm that laparoscopic radical nephrectomy is oncologically equivalent to open radical nephrectomy [7,8,9,18,19].

**Key words:** laparoscopic radical nephrectomy, renal cell carcinoma

**Abbreviations:**

HALRN hand assisted laparoscopic radical nephrectomy

LRN laparoscopic radical nephrectomy

ORN open radical nephrectomy

RCC renal cell carcinoma

RLRN retroperitoneal laparoscopic radical nephrectomy

TLRN transperitoneal laparoscopic radical nephrectomy

**References**


