PERIOPERATIVE COMPLICATIONS AND SURGICAL ONCOLOGY OUTCOMES IN AN INITIAL STUDY FROM 84 PATIENTS SUBMITTED TO LAPAROSCOPIC RADICAL CYSTECTOMY

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Summary.- OBJECTIVES: The Gold Standard treatment for a non-metastatic, invasive bladder cancer is an open radical cystoprostatectomy (ORCP). Laparoscopic radical cystoprostatectomy (LRCP) is still an experimental technique in evaluation. We describe our perioperative results defined as surgical and safety oncology variables.

METHODS: Every patient who underwent a LRCP between January 2007 and July 2011 in the urology department of the University Public Hospital was evaluated. We conducted a descriptive retrospective analysis of the variables found.

RESULTS: We evaluated 84 patients, 72 males and 12 females, with a mean age of 68 (44-79). A Bricker diversion was performed in 80 patients, a Camey II bladder replacement was performed in 3 patients, and a Studer bladder replacement was performed in 1 patient. Seventeen patients (20.23%) presented with previous abdominal surgery, and 6 patients (7.14%) presented a medical history of urological surgery. The mean surgery time was 257.57 minutes (180-420). The mean hospital stay was 11.875 days (standard deviation (SD): 6.28). The onset of tolerance to surgery occurred after 3.7 days (SD: 2.21). The transfusion rate after surgical intervention was 20.2%. The mean number of nodes removed, by means of ilio-obturator lymphadenectomy, was 17 (13-19).

There were no intraoperative complications. Early complications (less than 1 month after the intervention) occurred in 28 patients (33.3%). There were no postoperative deaths. There were late complications (starting one month after the intervention) in 7 patients (8.3%).

CONCLUSIONS: Our study demonstrated that LRCP is safe and reproducible and represents a minimally invasive option for patients with infiltrative bladder cancer.

Keywords: Bladder cancer. Treatment. Laparoscopic cystectomy.

Resumen.- OBJETIVO: La cistectomía radical abierta es el estándar oro para el tratamiento del cáncer vesical infiltrante. La cistectomía radical laparoscópica (CPRL) continúa siendo una técnica experimental en eva-
INTRODUCTION

Bladder cancer represents 2% of all malignant tumours and ranks second, in terms of frequency, among urinary system cancers (1,2). The standard treatment for a non-metastatic, invasive bladder cancer is an open radical cystoprostatectomy (ORCP) in addition to pelvic lymphadenectomy. Moreover, a laparoscopic radical cystoprostatectomy (LRCP) is performed in some cases of superficial high risk tumor, although it is not the standard treatment.

Minimally invasive surgery has been established as a safe option for the treatment of renal and prostate cancer has attracted an interest in the use of the laparoscopic technique for bladder cancer.

In the field of urology, excellent perioperative and long-term results for the treatment of renal and prostate cancer have provoked interest in using a laparoscopic technique for bladder cancer. Surgical techniques acquired through experience with laparoscopic prostatectomy have facilitated the use of LRCP (5-7).

The safety, the ability to reproduce this technique and the perioperative aspects of these treatments has led some urologists to consider the use of laparoscopy and substitute LRCP for ORCP. However, there are no large studies that demonstrate the advantages. However, there are no full-scale studies available to demonstrate the advantages and efficacy of this minimally invasive alternative for conventional surgery (8-10).

Therefore, the goal of this study is to describe our initial results using LRCP for the treatment of muscle invasive bladder cancer.

MATERIAL AND METHODS

All patients who underwent an LRCP intervention in the urology department of our hospital between January 2005 and July 2011 were included in this study. 84 patients in total fulfilled the criteria to be included in the study. The criteria necessary to proceed with LRCP was the presence of invasive bladder cancer, T2 without metastasis, and T1G3 that had not responded to treatment using Bacillus Calmette-Guerin (BCG), with a score equal or superior to 50 in the Karnofsky scale. Early complications were defined as those occurring within the first 30 days after surgery, and late complications as those occurring 30 days after surgical intervention.

SURGICAL TECHNIQUE

Patient preparation

The patient was hospitalised the day before the intervention. Two cleansing enemas and oral antibiotic therapy with tobramycin and metronidazole and prevention therapy with low molecular weight heparin is administered one hour before the surgical intervention.

Transperitoneal access is achieved using 5 trocars, two of which are 10mm wide and the remaining three, 5mm wide, are arranged as they appear in Figure 1.

After that, the dissection of the ureters is carried out then they are sectioned using hem-o-
Figure 1. Position of trocars in LRCP.

lock® and tied to threads of different colours. This maneuver for identifying the ureters with threads of different colours, a process developed in this hospital, is important since it serves to identify each of the ureters once they have been exposed. The distal tip from each ureter is sent to pathological anatomy for an intraoperative biopsy. One proceeds by opening the base of the Douglas sack, sectioning the lateral pedicles and the lateral prostate pedicle of the bladder with Ligasure®. The Retzius space is opened; the urethra is dissected and sectioned between two hem-o-locks. (The procedure concludes once the piece is bagged and subsequently removed.)

The ilio-obturator lymphadenectomy frees up the iliac vessel from the common iliac artery to the (obturator fossa).

The terminal ileum loop is selected, and the peristaltic direction is marked with a suture stitch using black thread clamped to some clips.

The structures are exposed and identified by the thread color. The piece and the ileal loop are extracted from a 4 cm infraumbilical minilaparotomy (Figure 2).

**Cutaneous bypass**

Both ureters are reconstructed by Bricker technique. The tip of the ileal handle is marked with a black stitch that will be used later for the ileostomy.

**Intestinal neobladder**

Following extracorporeal placement of the Camey II ileal reservoir, the neobladder is introduced into the abdominal cavity, performing the anastomosis to the urethra with two semi continuous sutures by laparoscopic route. A number 20 Ch urinary catheter is left in place.

**Cystectomy in women**

In addition to the bladder, the uterus and both ovaries are extracted through the vagina.

**Postoperative management**

The redon suction drain is removed on the first or second postoperative day depending on the outcome. Both ureteral catheters are removed 21 days after surgical intervention without the need for a radiological test previously. Anticoagulation with low molecular weight heparin is maintained for 15 days after the intervention.

**RESULTS**

Table 1 shows the characteristics of the patients. The mean age was 68 years (44-79). Additionally, many of the patients had had a prior surgery, with 17 (20.23%) presenting with a history of abdominal surgery; of these, 6 (7.14%) had a history of urological surgery, with an adenomectomy in 2 cases and left nephrectomy in another 2 cases, 1 case of radical prostatectomy, and 1 case of transurethral resection of the prostate.

We should note that none of the patients in this clinical trial who underwent an LRCP had
to be re-converted to open surgery was used. The mean surgical time was 257.57 minutes (180-420); the mean hospital length of stay after the surgical intervention was 11.875 days (standard deviation (SD): 6.28), and the mean onset of tolerance was 3.7 days (SD: 2.21). No patient in this study required analgesia with major opioids, either intraoperatively or postoperatively.

Tumor staging was based on the 2009 TNM classification. Staging before LRCP taken from the transurethral resection was T1G3 in 15 cases (17.8%), T2 in 65 cases (77.3%), T3 in 1 case (1.1%), sarcoma in 1 case (1.1%) and carcinoma in situ in 2 cases (2.3%). Staging later LRCP was T0: 8 cases (9.5%), T1: 9 cases (10.7%), T2: 19 cases (22.6%), T3: 35 cases (41.6%), T4: 11 cases (13%), and carcinoma in situ: 2 cases (2.3%) (Figures 3 and 4). 17 Patients (20.2%) required a blood with an average of 2 concentrates of blood per patient.

There were no intraoperative complications. Early complications occurred in 28 patients (33.3%). In 18 cases, the complication was due to a paralytic ileus, there was also one case of a urinary fistula, one cerebral ictus, and one intestinal obstruction. One patient experienced complications due to incorrect placement of the right catheter. There were no postoperative deaths. There were late complications in 7 (8.3%) patients, who required the placement

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Male</td>
<td>72 (85.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (14.3%)</td>
</tr>
<tr>
<td>Mean age</td>
<td>68 years (44-79)</td>
</tr>
<tr>
<td>Medical history of abdominal surgery</td>
<td>17 (20.23%)</td>
</tr>
<tr>
<td>Medical history of urological surgery</td>
<td>6 (7.14%)</td>
</tr>
<tr>
<td>Preoperative risk (ASA physical status scale)</td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>12 (14.3%)</td>
</tr>
<tr>
<td>Class II</td>
<td>57 (67.9%)</td>
</tr>
<tr>
<td>Class III</td>
<td>14 (16.7%)</td>
</tr>
<tr>
<td>Class IV</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Urinary diversion</td>
<td></td>
</tr>
<tr>
<td>Bricker’s technique</td>
<td>80 (95.2%)</td>
</tr>
<tr>
<td>Camey II technique</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>Studer’s technique</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Mean surgical time</td>
<td>257.57 minutes (180-420)</td>
</tr>
<tr>
<td>Analgesia during surgical intervention</td>
<td></td>
</tr>
<tr>
<td>Metamizol</td>
<td>65 (77.4%)</td>
</tr>
<tr>
<td>Minor opioids</td>
<td>18 (21.4%)</td>
</tr>
<tr>
<td>Analgesia after surgical intervention</td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>2 (2.4%)</td>
</tr>
<tr>
<td>Metamizol</td>
<td>64 (76.2%)</td>
</tr>
<tr>
<td>Minor opioids</td>
<td>18 (21.4%)</td>
</tr>
<tr>
<td>Mean hospital length of stay</td>
<td>11.875 days (standard deviation: 6.28)</td>
</tr>
<tr>
<td>Mean onset of tolerance</td>
<td>3.7 days (standard deviation: 2.21)</td>
</tr>
<tr>
<td>Transfusion after surgical intervention</td>
<td>17 (20.2%)</td>
</tr>
<tr>
<td>Mean number of resected lymph nodes</td>
<td>17 (13-19)</td>
</tr>
<tr>
<td>Rate of reentries in the first 3 months after the surgery</td>
<td>19 (22.6%)</td>
</tr>
</tbody>
</table>
of bilateral nephrostomies due to stenosis of the ureteroileal anastomosis.

With a median follow up of 41 months (from 18 months to 61 months), 23 patients have died (27.3%), all of them due to cancer. Of the 61 patients (72.6%) who are currently alive, 35 patients are free of disease (57.3%), 3 (4.9%) present with a local pelvic relapse, 17 (27.8%) present with metastasis in the inguinal and pelvic lymph nodes, and 6 (9.8%) present with distant metastases. A curve to show the survival rate of patients is drawn and presented in Figure 5 and 6.

**DISCUSSION**

Radical cystectomy has been accepted as the gold standard procedure for the treatment of invasive bladder cancer because it provides excellent local control of the cancer.

Open radical cystectomy, despite being performed by experienced surgeons, is associated with significant morbidity. A prolonged hospital stay is common, largely due to paralytic ileus related to the lengthy exposure of the peritoneum.
Thus, LRCP appears to be a minimally invasive alternative to conventional surgery and has the potential to decrease perioperative morbidity without compromising oncological results (11,12).

Table III shows results from several published studies of laparoscopies with a minimum of 30 patients. As far as we know, the largest clinical trial of LRCP available, by Cathelineau et al. (13) that used 84 patients, coincides with the number of patients used in our study.

Our blood transfusion rate was similar to that of Castillo et al. (14), at 20%. In the study by Hemal et al. (16), the transfusion rate was greater at 44%. In contrast, this rate is very low in other studies; for example, in Cathelineau et al., the transfusion rate is only 5%, Gerullis et al. (15) had a rate of 5.9% and Wang et al. managed a rate of 9.7%.

The mean hospital stay in our hospital was 11.8 days long, similar to the Cathelineau study, in which the hospital stay was longer, with a duration of 19.7 days, and the Hemal et al. study, in which the hospital stay was 10.2 days. In the study by Wang et al. (17), the mean hospital stay was greater, with duration of 19.7 days.

In our study, the rate of early and late complications was 33.3%. The rates of complications in other studies were similar to that in our study. The rate of complications was 30% in the study by Castillo et al., 28.1% in the study by Wang et al., and 27% in the study by Hemal et al.

In the study by Cathelineau et al., the rate of early complications was 18%, which is lower than in our study. However, 20% of our patients presented with a history of abdominal surgery, which suggests greater surgical difficulty and the possibility for complications. Additional information includes our rate of reentries, 3 months after surgical intervention (22.6%) in accordance with the rate of complications in this medical trial.

Table II. Published LRCP series with more than 30 patients.

<table>
<thead>
<tr>
<th>Studies</th>
<th>Nº Patients</th>
<th>Surgical Time (Minutes)</th>
<th>Length of Hospital Stay</th>
<th>Transfusion %</th>
<th>Total Complications %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cathelineau et al. 2005</td>
<td>84</td>
<td>280</td>
<td>12</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Castillo et al. 2006</td>
<td>59</td>
<td>337</td>
<td>ND</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Gerullis et al. 2007</td>
<td>34</td>
<td>244</td>
<td>ND</td>
<td>5,9</td>
<td>0</td>
</tr>
<tr>
<td>Hemal et al. 2008</td>
<td>48</td>
<td>310</td>
<td>10,2</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>Wang et al. 2008</td>
<td>31</td>
<td>365,7</td>
<td>19,7</td>
<td>9,7</td>
<td>28,1</td>
</tr>
<tr>
<td>Hospital de León</td>
<td>84</td>
<td>257,57</td>
<td>11,8</td>
<td>20,2</td>
<td>33,3</td>
</tr>
</tbody>
</table>
The most frequent late complication in our study was stenosis of the ureteroileal anastomosis which coincides with results published in other studies, appearing in 10% of patients. Other authors have identified a high rate of this type of complication that could be related to an untidy procedure when the ureters are dissected. Nevertheless this is information that will be studied further in a comparative study against open surgery. The treatment was a permanent urinary derivation by means of a nephrostomy due to the age, and other negative factors affecting these patients.

The number of neobladders in our series is very low compared with other studies, given that it was only performed in 4 out of 84 patients. This pattern is due to the advanced age of the in our study. But to also make sure that the time spent in surgery could be kept to a minimum. Nevertheless, this result is presently changing. As our experience increases, our surgical times are becoming shorter. However, this result is presently changing. As our experience increases, our surgical times are becoming shorter.

In our study, we have analysed the use of analgesics to determine which drugs were most commonly used in patients undergoing LRCP. Analgesics belonging to the first and second step of the World Health Organization guidelines are the most widely used by these patients. Thus, we believe that the analgesic requirements might be lower due to the minimization of the incision, but however it is something that will be analyzed in a comparative study against open surgery. For this reason, we strongly suggest for the incision to be reduced as far as possible through the use of threads to expose the ureters and the intestinal handle.

This maneuver facilitates the process by keeping the incision to a minimum. We have not found information from other authors who use the above mentioned selection by means of threads. In addition, we do not thread the left ureter through the retroperitoneum. Despite this, we have not found major instances of intestinal occurrence nor sub-occurrence in comparison with other studies.

The neoadjuvant chemotherapy was was not used in our study due to the advanced age of the majority of the patients so as not to delay surgical intervention. Instead, adjuvant chemotherapy based on cisplatin was used in 28 cases (33.3%) of them.

The oncological data for LRCP are promising, although the data published to date consists of short studies with a brief follow up period.

In the majority of the studies described, disease-free survival ranges from 70 to 80% during a follow up period of approximately 3 years. In our study, 57.3% of patients are currently free of disease, with a median follow up of 41 months. Nevertheless, this average follow up period is short compared to CPRA studies. In a study by Stein et al. (20), after a follow up of 5 years, 68% of the patients were disease free, 30% of the patients developed local recurrence, 22% of the patients developed distant metastasis, and 7% of the patients developed local recurrence. These oncological results for an open surgery technique are similar to those of the laparoscopic surgery studies (21,22).

In addition, the global rate for survival in our patients intervened using CPRL was of 54.5 %, lower than the Haber and Gill clinical trial (23) that with 35 patients, reported a 63% global survival rate after a 5 year follow up period.

The difference could be due to the high percentage of patients with a superficial bladder tumor (78%) in the Haber and Gill clinical trial, when compared to our results (17.8%). Regarding lymphadenectomy, we consider it sufficient to continue until the common iliacus is reached, where we obtain a number of nodes with a median of 17, being between 10 and 15 the number of nodes needed by many authors (24), to be considered a valid oncological procedure, since to fulfill an extended lymphadenectomy up to the aortic would force technical changes, such as a change in the arrangement of the trocars.

Our study, nevertheless, is limited. We were dealing with a retrospective descriptive study, with a short follow-up period compared with the bigger clinical trials in open cystectomy. For that reason, more LRCP studies are necessary, with a long term follow-up period to establish the safety of this surgical technique in invasive bladder cancer, as well as studies comparing both surgical approaches.

CONCLUSIONS

The results collected in the study for our clinical trial indicates an early onset to tolerance, a low hospital stay, with a low rate in complications and good oncological results. We consider, therefore, that the LRCP technique is a minimally invasive alternative to ORCP. It is safe and can be reproduced for treating muscle invasive bladder cancer.
REFERENCES AND RECOMMENDED READINGS
(*of special interest, **of outstanding interest)


