Enhanced Recovery after Implementation of Surgery Protocol in Living Kidney Donors: The ISMETT Experience

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ABSTRACT

Introduction. Laparoscopic living donor nephrectomy (LLDN) has become the standard procedure for living kidney transplantation. Enhanced recovery after surgery (ERAS) is a multimodal perioperative management aimed at facilitating rapid patient recovery after major surgery by modifying the response to stress induced by exposure to surgery. This association can further reduce hospital stay, surgical stress, and perioperative morbidity of living kidney donors.

Material and methods. In this retrospective analysis conducted at our institute, we compared the first 21 patients who underwent LLDN enrolled with the ERAS protocol with 55 patients who underwent LLDN with the fast-track protocol in the 5 years prior to ERAS protocol implementation.

Results. We evaluated 76 consecutive patients. After ERAS protocol implementation, elderly living donors had a shorter hospital stay and a faster return to normal life compared with the same age group of patients in the previous period. There were no major differences in median postoperative hospital stay and no meaningful differences in the percentage of complications after surgery and hospital readmissions.

Conclusions. The introduction of the ERAS protocol for patients undergoing LLDN compared with the traditional protocol led to a reduction in postoperative hospitalization in elder donors, without determining a raise in the number of hospital complications and readmissions.

KIDNEY transplantation is the only effective therapy for patients with end-stage renal disease on hemodialysis treatment. Living donor kidney transplantation has better results for the recipients than deceased donor transplantations [1]. In order to reduce the gap between the donor pool and patients on the waiting list, living donation has been implemented through laparoscopic living donor nephrectomy (LLDN). To improve living donation at our institute, we modified our perioperative management by introducing the enhanced recovery after surgery (ERAS) protocol, as previously introduced in our general surgery experience [2]. Since its introduction in general surgery in 2001, the ERAS protocol has proven to reduce postoperative stay and complication and readmission rates [3]. In this retrospective analysis, we investigated and compared the outcomes after implementing ERAS as perioperative management in living kidney donors with our previous model, fast track (FT). We describe our outcomes, comparing the first 21 patients enrolled in the ERAS arm with 55 patients enrolled in the FT group (Fig 1).

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0041-1345/19
https://doi.org/10.1016/j.transproceed.2019.04.089

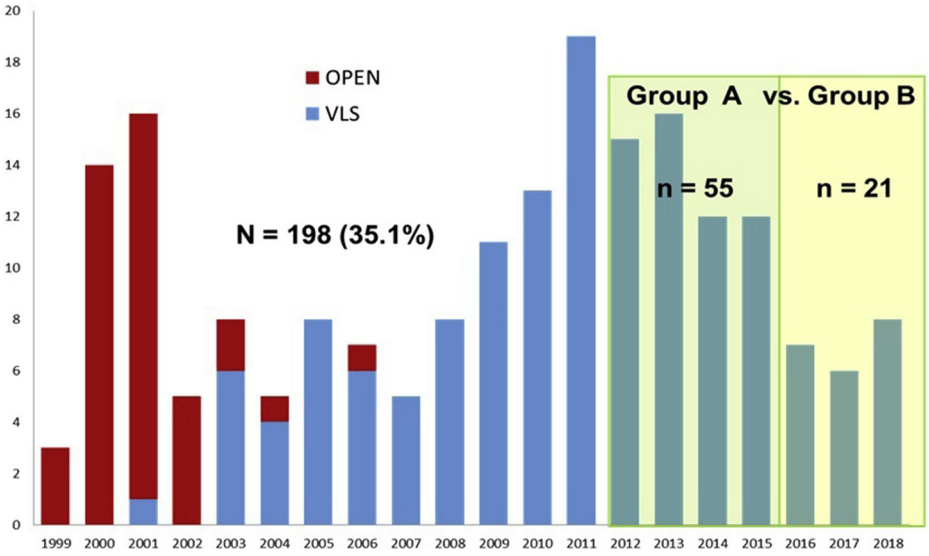

Fig 1. Study group. Group A: fast track protocol patients; Group B: ERAS protocol patients. ERAS, enhanced recovery after surgery; VLS, video laparoscopic surgery.

PATIENTS AND METHODS

From 1999 to 2018, we performed 196 living donor nephrectomies. From 1999 to 2002, all the donor nephrectomies were performed with the open technique. We began using the laparoscopic approach in 2003. Over the following 3 years, we switched fully to the mini-invasive technique. As regards perioperative management, from 1999 to 2012 we used a standard protocol. The ERAS protocol was introduced in out institute in 2 steps: in January 2013, we changed our perioperative management from the standard protocol to FT, while in June 2016, we changed from FT to the ERAS protocol. A multidisciplinary team involving anesthesiologists, surgeons, skilled nurses, and physical and respiratory therapists were involved in both the FT and ERAS protocols. Our experience with conventional, FT, and ERAS pathways are described elsewhere [2,4].

In our study population, we included 76 consecutive patients who underwent LLDN before and after implementing our perioperative protocol to ERAS. We divided this population into 2 groups: Group A (55 patients; men 14, women 41; mean age, 50.42 $\pm$ 9.1 years) included all the patients enrolled in the FT protocol; Group B (21 patients; men 4, women 17; mean age, 55.5 $\pm$ 7.5 years) included all the patients enrolled in the ERAS protocol. For all these patients, the following data were recorded: age, sex, body mass index, American Society of Anesthesiologist classification, preoperative carbohydrate loading, and preoperative fast. Postoperative data recorded were operating time, hospital length of stay (LOS), complications recorded according to the Clavien-Dindo classification, conversion rate, epidural catheter placement, opioid avoidance, nasogastric tube removal, starting day of nutrition per os, and first mobilization after surgery. All the surgical procedures were performed by 3 surgeons experienced in both laparoscopic and open nephrectomy. Our technique for LLDN has been previously reported [4].

ERAS Protocol Pathways

Preoperative care. All the patients received information on the ERAS protocol at the outpatient clinic surgical visit. During the visit, each patient was evaluated by our nurse (patient care coordinator) as regards to nutritional status and physical performance. In particular, we explained the necessity of carbohydrate loading before surgery and the perioperative diet. We also explained to each patient the perioperative physical and respiratory rehabilitation daily program. We suggested to each patient to stop smoking at least 4 weeks before surgery and to take a 30-minute walk 2 times per day.

The day before surgery, we hospitalized and reassessed the patient. To assess the nutritional status, we applied for each patient the Malnutrition Universal Screening Tool. It is a useful and validated screening tool divided into 5 steps, which allowed, in a simple and easy way, the identification of malnourished patients or those at risk for malnutrition. For score $\geq$ 2, an electronic aware report was sent to our nutritional team to start the patient's nutritional education and further follow-up before and after surgery. To assess the patient's physical performance, we used the Blaylock Risk Assessment Screening scale, while to assess the respiratory performance, we used the Medical Research Council scale. For a score $\geq$ 11 according to Blaylock Risk Assessment Screening scale and $\leq$ 3 in the Medical Research Council scale, our rehabilitation team was alerted. The day before surgery, regular diet was administered, and the day of surgery, a preoperative carbohydrate drink (Gatorade 500.0 mL, 30.0 g carbohydrates) was administered 2 to 3 hours before the surgery. The patients were placed on *nihil per os* 2 to 3 hours before surgery.

Intraoperative care. All patients underwent epidural catheter placement immediately before induction and continuous epidural analgesic drug administration (bupivacaine 0.25%, 125.0 mg/50.0 mL; rate 9.0 mL/h) during surgery. Ultra-short antibiotic prophylaxis was administered preoperatively (ceftriaxone 2.0 g). Intraoperative normothermia was mandatory. Fluid restriction (normal saline 0.9%; rate: 1.0 mL/Kg/h) during surgery was mandatory and established together with our anesthesiology team. Heparin was administered intravenously (IV) (enoxaparin 50.0 U/kg) before clamping and cutting renal vessels in the donor. Abdominal drainage was placed for each patient, and drugs to prevent nausea and vomiting were administered at the end of surgery.

Postoperative care. As per the ERAS protocol, the donor left the operating room without a nasogastric tube, was mobilized for 2 hours the day of surgery, and then started to sip water. Intravenous fluids were administered only 24 to 48 hours after surgery (normal saline 0.9%, rate 1.0 mL/kg/h). Low-molecular-weight heparin was

started subcutaneously (enoxaparin 4000 U) on postoperative day 1 to prevent deep vein thrombosis. As regards postoperative oral diet, each patient was advanced to clear diet on day 1 after surgery, soft diet on day 2 after surgery, and regular diet on day 3. According to our rehabilitation program, patients were placed out of bed for 2 hours the day of surgery, had a ward ambulation twice a day on day 2 after surgery, and normal physical and respiratory activity on day 3. Epidural analgesia was stopped and the vesical catheter removed 48 hours after surgery. Postoperative pain was managed with continuous epidural analgesia and intravenous drugs (ie, paracetamol 1.0 g 3 times a day, ketorolac 30.0 mg IV 2 times a day) for 24 to 48 hours after surgery. After stopping the epidural analgesia, only IV drugs were administered until discharge. After discharge oral analgesic therapy was administered when indicated. Finally, the patients were discharged after fulfilling our discharge criteria (normal temperature, stable hemodynamics, at least 1 bowel movement, good pain control, and autonomous walking and eating).

Statistical Analysis

Data are expressed as mean and standard deviation or as median and interquartile range when not approximately normal. Differences between groups were tested using the Student *t* test or the Kruskal-Wallis test, as appropriate. All analyses and graphics were done in the R statistical computing environment, version 3.5.1. (R Core Team, Vienna, Austria).

RESULTS

There were 76 patients included in our study: 55 patients in the FT group (Group A), and 21 patients in the ERAS group (Group B). No statistically significant difference was found in the preoperative variables between the 2 groups. All the surgical procedures were performed by 3 experienced surgeons and were laparoscopic. There was no conversion to open procedure in either group. The mean operating time was 210 ± 35 minutes in both groups. There were no major differences in median postoperative hospital stay, nor significant differences in the percentage of postoperative complications and hospital readmissions. We investigated whether there were some differences in LOS in 3 subgroups of patients divided by age before and after ERAS implementation. We divided the patients into 3 subgroups: I group, from 28 to 50 years; II group, from 51 to 60 years; III group, from 61 to 72 years. Before the implementation of the ERAS protocol, there were no differences among these 3 subgroups (Fig 2). After ERAS protocol implementation, elder living donors had a shorter hospital stay and a faster return to normal life. Interestingly, looking at the time of starting rehabilitation after surgery in the ERAS group, we found that elderly donors had a shorter hospital stay when the rehabilitation was started less than 10 hours after surgery (Fig 3). No differences were detected regarding postoperative complications. There was no mortality in either group. After discharge, no urgent readmission was necessary for the patients in either group.

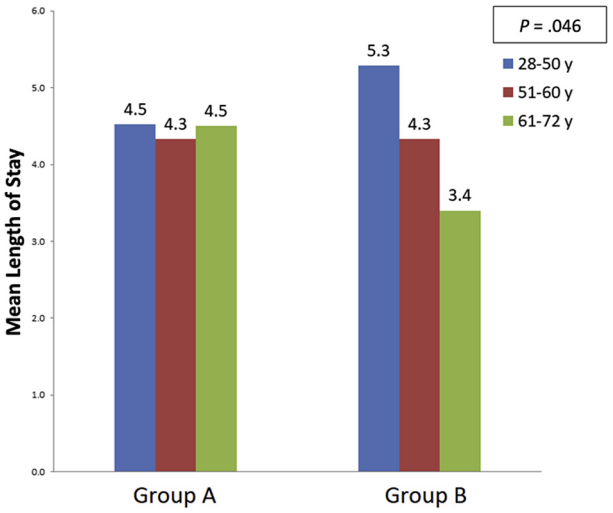

Fig 2. LOS distribution in both groups, according to donor age. LOS, length of stay.

DISCUSSION

Living donation is an important resource for kidney transplantation. In order to favor living kidney donation, over the last decade, the laparoscopic approach has spread widely in order to reduce pain, perioperative complications, and LOS. To reduce complications, achieve better results, and make living donation safer, we implemented our program by unifying the benefits of mini-invasive surgery with the advantages of the implementation of perioperative ERAS protocol.

Our procedures were all performed laparoscopically. There were no statistically significant differences in demographic data between the 2 groups, or in LOS, though this was probably secondary to the small patient cohort.

Differently from other centers [5,6], we use as a standard of our ERAS protocol epidural analgesia during and after surgery. The treatment of postoperative pain is a key point

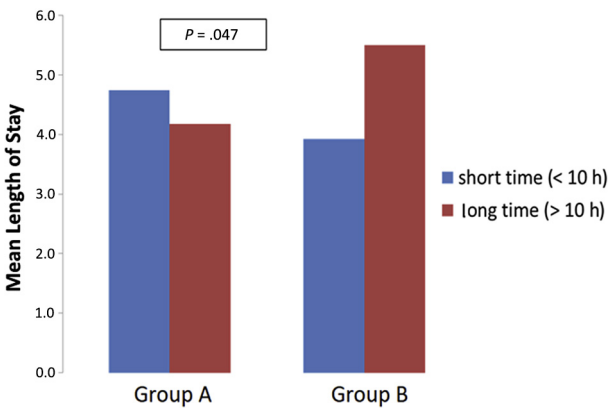

Fig 3. Different LOS according to the start of rehabilitation in both groups. LOS, length of stay.

in our study. As per our protocol, each patient in the ERAS group received a continuous epidural anesthesia for 48 hours after surgery, and no opioid drug was allowed. The patients in group B had good pain control (mean score ≤ 3 in the first 72 hours after surgery), which allowed earlier rehabilitation. The time of first mobilization was the day of surgery for all the patients in the ERAS group. Furthermore, we found that it is crucial to start rehabilitation care in the first 10 hours after surgery, perhaps suggesting that limits of living donation could be safely extended for elderly donors.

CONCLUSION

The introduction of the ERAS protocol in patients undergoing LLDN compared with the traditional protocol led to a reduction in postoperative hospitalization in elderly donors, without an increase in the number of hospital morbidities and readmissions.

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