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Vessel sealing system *vs.* conventional knot-tying for hilar dissection during living donor hepatectomy: a prospective, randomized, double-blinded study

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Abstract. – OBJECTIVE: LT has become the gold standard treatment for many liver diseases, especially chronic liver disease. A commonly seen problem, even in donors who do not develop any major complications after living donor hepatectomy (LDH), is the persistent drainage of lymphatic fluid from the hepatectomy site drain, which causes extensive hospitalization and consequent loss to the workforce. To our knowledge, no study has yet been published comparing LVSS and conventional knot-tying methods for hilar dissection, which is an important stage of the LDH procedure. We aimed to prospectively compare the outcomes of these two treatment methods.

PATIENTS AND METHODS: Donor candidates were divided into two groups: conventional suture tying (conventional knot-tying group; n=34) and Ligasure vessel sealing system (LVSS; n=34). A simple randomization method of drawing lots was used to assign the patients to each group. The following parameters were analyzed for all patients: age, gender, BMI, duration of surgery, postoperative drainage amounts, drain removal times and complications, length of hospital stay, morbidity, and mortality.

RESULTS: There were no significant differences in terms of operative times, postoperative drainage levels, hospital stay or drain removal times.

CONCLUSIONS: In this study, the use of LVSS in LDH was found to be safe, although it did not offer any advantage over conventional methods. Nevertheless, it seems probable that the use of LVSS could reduce operative time and amounts of lymphatic drainage, especially in centers with minimal experience with LDH, such as new LDH centers.

Key Words:
Transplantation, Lymphatic, Ligation, Hemostasis, Seromas.

Introduction

Since Starzl et al[1] performed the first successful liver transplant (LT) in 1967, LT has become the gold standard treatment for many liver diseases, especially chronic liver disease. In following years, the idea of living donor liver transplantation (LDLT) came to the fore for various reasons, particularly the insufficiency of the donor pool and the need for small-sized liver grafts in pediatric patients, and the first successful LDLT was performed in 1989 by Strong et al[2]. When compared to deceased donor liver transplantation (DDLT), LDLT has certain important advantages, such as shorter wait-time, shorter cold ischemia time, and a better chance of finding grafts in emergency transplant situations. However, there are significant disadvantages including the risk to donor safety and a far more complex surgery. In the past, the prospect of subjecting completely healthy individuals to the major surgery entailed in liver resection, as living donor candidates, has deterred western countries from widespread adoption of LDLT, and this reluctance still continues to a certain extent. Intraoperative and postoperative complications, secondary to donor hepatectomy, are among the most important reasons for this distanced stance and the literature includes many examples of living donor candidates who develop mortality as a result of these complications. However, in Turkey and many countries in Asia and the Middle East, where cadaveric donor pools are insufficient, LDLT remains a good option[3,4]. In fact, LDLT constitutes the majority of liver transplants performed at our center, one of the most important centers for liver disease in Turkey and Europe[5].

A commonly seen problem, even in donors who do not develop any major complications after living

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donor hepatectomy (LDH), is the persistent drainage of lymphatic fluid from the hepatectomy site drain, which causes extensive hospitalization and consequent loss to the workforce. The hepatoduodenal ligament is rich in lymphatic pathways through which almost all lymphatic flow reaches the liver. Therefore, if any lymphatic vessels are left open or inadequately ligated during hilar dissection, prolonged postoperative lymphatic drainage may occur. In order to minimize this problem, transplant surgeons prefer to close the lymphatic pathways during hilar dissection using conventional ligation methods and/or a vessel sealing system (VSS). There is no consensus as to which of these two methods is superior. The Ligasure vessel sealing system (LVSS), which has been used in clinical practice for nearly 20 years, is a vessel closure device that uses a combination of pressure and bipolar electrothermal energy. Theoretically, the use of vessel closure systems should save time and shorten operation time. Saiura et al[6] found that the use of ligasure in hepatectomies reduced both operation time and blood loss, without increasing morbidity. Ligasure has also been shown to be reliable in lymphatic dissection[7]. To our knowledge, no study has yet been published comparing LVSS and Conventional Knot-Tying methods for hilar dissection, which is an important stage of the LDH procedure. We aimed to prospectively compare the outcomes of these two treatment methods.

Patients and Methods

Study Design and Patient Selection

This single-center, prospective, randomized, double-blind study included donor candidates who applied to be living liver donors between January 2022 and May 2022 and were found to comply with the preoperative donor preparation algorithm. The donor preparation algorithm used in our Liver Transplant Establishment has previously been published[8]. Sample size and power analyzes were performed using the G*Power 3.1.9.7 package program to determine the minimum number of patients to be included in the study. As a result, the ideal number of patients for each group was determined as 34 (Tails: two, effect size=0.7, α=0.05, power=0.80). Therefore, donor candidates were divided into two groups: conventional suture tying (conventional knot-tying group; n=34) and LVSS (n=34). A simple randomization method of drawing lots was used to assign the patients to each group. The following parameters were analyzed for all patients: age, gender, BMI, duration of surgery, postoperative drainage amounts, drain removal times and complications, length of hospital stay, morbidity, and mortality. The patients were comprehensively informed about both surgical procedures and written informed consent was obtained from each patient. All surgical procedures were performed by experienced surgeons who had conducted over 100 living donor hepatectomy surgeries. The study was carried out in accordance with the principles of the Helsinki Declaration. Ethics committee approval was received for this study from the University Clinical Trials Ethics Committee (2022-3382).

Surgical Technique

The right left and left lateral LDH procedures performed in our clinic have been described in detail, previously[5]. To summarize, 1 gram of cefazolin sodium was administered intravenously while patients were on the operating table. A laparotomy was performed on all patients using a modified Makuuchi incision, extending the midline incision to above the umbilicus and laterally to the right. The right hepatic artery, right portal vein, and right biliary tract were exposed during hilium dissection in right-side LDH surgery, while the left hepatic artery, left portal vein, and left biliary tract were revealed in left-side LDH. A cholecystectomy was carried out on all patients prior to dissection, with intraoperative cholangiography performed by administering contrast material through the cystic duct, thus revealing the bile duct junction. In the conventional suture ligation group, both lymphatic channels and cellular tissues were ligated with 4/0 silk thread. In the Ligasure group, they were closed directly with a vessel-closure sealing device without using any suture material. The remaining stages of the surgical procedure were similar in both groups. The duration of the operation was determined as the time period between the first skin incision and the closure of the surgical site. The amount of lymphatic drainage was measured every morning. The criterion for removal of drains was less than 30 cc of ascitic fluid per 24 hours without biliary contamination.

Statistical Analysis

The statistical analyzes were performed using licensed IBM SPSS Statistics v25.0 (Statistical Package for the Social Sciences, Corp., Armonk, NY, USA). The quantitative variables were expressed as Median, Minimum-Maximum and 95% confidence interval (CI). The qualitative variables were reported as number and percentage (%). Kolmogorov-Smirnov test was used to assess the normality of the distribution of quantitative variables. Nonparametric Mann-Whitney U test was used to compare quantitative variables. Pearson's chi-square test was

Table I. Demographic data.

Target gene	Knot-tying	Vessel sealing system	p
Number of patients	32	32	
Age (year)	27 (18-45)	30 (18-53)	0.208
Female	15	15	1
BMI*	24 (17-29)	25 (17-32)	0.821

*Body mass index.

used to compare qualitative variables. $p \leq 0.05$ was considered a statistically significant value.

Results

Two patients from each group had to be excluded from the study because their drainage data could not be reached, and therefore the number of patients included in the analysis was reduced to 32 in both groups. Patient demographic data can be seen in Table I. Demographically, the groups were similar, with no significant difference in terms of operative times, postoperative drainage levels, hospital stay or drain removal times (Table II). Right hepatectomy was performed in 50 patients, left lateral hepatectomy in 10 patients, and left hepatectomy in four patients. No intraoperative complications or postoperative mortality developed in any of the donors included in this study.

Discussion

LDLT, a surgery first developed approximately 35 years ago, has become an accepted alternative to cadaveric liver transplantation in end-stage liver disease. Although its main goal is to offer curative treatment to patients with liver disease, LDLT differs from other surgical procedures due to the vital importance also placed on ensuring the safety of the living donor. LDLT is by definition a more complex and difficult procedure than cadaveric liver transplantation; however, with developments in medical care and surgical technique, it can nowadays be implemented with less risk of morbidity. Although it is a relatively safe surgery when carried out in experienced transplant centers, there are still risks for complication in the completely healthy donor. According to the literature, morbidity and mortality rates after LDH are between 8.7%-16.1% and 0.2%, respectively[9-11]. In our own institute, a previous study comprising five hundred living donors found the donor complication rate to be 18.6%[5], with only 64 donors not developing any complications of Type 2 or greater according to Clavien-Dindo classification.

LVSS has long been used in abdominal cancer surgery, bariatric surgery, gynecological cancer surgery, and retroperitoneal dissections, with the aim of reducing operation time and the amount of bleeding. Macario et al[12] published a meta-analysis

Table II. Comparation of patients legnth of hospital stay, surgery time and drainage volume.

	Knot-tying	Vessel sealing system	p
Operation time (min)	303 (170-602)	291 (181-427)	0.240
Length of stay (day)	9 (6-13)	8 (6-12)	0.521
Drain removal (POD)	6 (4-9)	6 (4-9)	0.512
Remnant volume (%)	33 (29-80)	33 (29-82)	0.612
POD1 (ml)	100 (0-350)	45 (0-300)	0.204
POD2	110 (0-450)	140 (0-500)	0.242
POD3	100 (0-700)	100 (0-450)	0.480
POD4	70 (0-110)	35 (0-360)	0.255
POD5	90 (0-650)	90 (0-400)	0.145
POD6	160 (0-800)	80 (0-400)	0.162
POD7	140 (0-1,110)	120 (0-800)	0.420
POD8	120 (20-1,100)	70 (0-480)	0.243
POD9	80 (0-550)	90 (0-600)	0.892
POD10	60 (0-580)	50 (0-450)	0.855
POD11	120 (0-340)	30 (0-520)	0.151
POD12	60 (0-350)	30 (0-480)	0.721

POD: postoperative day.

showing that the use of LVSS in various surgeries reduced operation time by a quarter. Although the use of LVSS in hepatobiliary surgery is relatively new, some studies have been published evaluating its success; these mainly refer to liver parenchymal dissection or recipient hepatectomy. In these studies, LVSS was found to reduce both the duration of surgery and the amount of bleeding[6,13,14]. However, in contrast to the literature, this present study evaluated the use of LVSS in LDH hilar dissection. In this study, we noted that some donor surgeries took longer than expected, either because of an unexpectedly lengthy operation on the recipient or the development of complications during the recipient operation which required extra time to manage. However, when comparing operation times, no significant difference was found between the LVSS group and the group using the conventional knot-tying technique. We hypothesize that the reason for the disparity between our results and those mentioned in the literature, may be that the surgeons included in our study had significant experience in LDH and were very familiar with both techniques. We acknowledge the possibility that the use of LVSS may shorten the duration of surgery in centers that have recently introduced LDH.

LVSS is effective in vessels up to 7 mm diameter and has a lateral thermal spread lower than ultrasound, electrocautery, or laser[15]. It is also suitable for sealing lymphatic vessels. While lymphatic vascular anatomy varies from patient to patient, significant lymphatic pathways are known to lie within the hilium of the liver. Surgical complications such as lymphorrhea, lymphocele and seroma frequently develop after lymphatic dissection resulting in delayed drain removal and prolonged hospital stay for patients, postoperatively. Many studies have reported the use of LVSS in the dissection of lymphatic channels to be easy and safe[7], reduce surgical lymphatic complications, and shorten drain withdrawal times[16,17]. However, other studies argue that these devices have no advantage over conventional methods[18]. Apart from the consequences of dissecting lymphatic vessels, complications may also arise due to the patients' age, BMI, or presence of diabetes, as well as the use of oral anticoagulants[19]. Living liver donor candidates are generally selected from young patients with no additional disease and in this study, mean donor age and BMI were similar in the two groups; neither was there any difference between the daily drainage amounts or drain withdrawal times of the patients in the two groups. Fortunately, no patients developed lymphorrhea, lymphocele or seroma at the surgical site. When the length of hospital stay was compared, no significant difference was found between the two groups.

Conclusions

In this study, the use of LVSS in LDH was found to be safe, although it did not offer any advantage over conventional methods. Nevertheless, it seems probable that the use of LVSS could reduce operative time and amounts of lymphatic drainage, especially in centers with minimal experience with LDH, such as new LDH centers.

Conflict of Interest

The authors declare they have no conflicts of interest.

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