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and Other Interventional Techniques

Hepatic resections by means of electrothermal bipolar vessel device (EBVS) LigaSure V: early experience

R. Campagnacci,[1] A. De Sanctis,[1] M. Baldarelli,[1] M. Di Emiddio,[1] L. Organetti,[1] M. Nisi,[1] G. Lezoche,[2] M. Guerrieri[1]

[1] Clinica di Chirurgia Generale e Metodologia Chirurgica, Ospedali Riuniti, University of Ancona, Ancona, Italy
[2] 2nd Department of Surgery, "Paride Stefanini," II Clinica Chirurgica, University "La Sapienza", Rome, Italy

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Abstract
Background: Many techniques and devices are available for performing liver resection, such as clamp crushing, Cavitron Ultrasonic Surgical Aspirator (CUSA), Hydrojet and dissecting sealer, ultrasonic shears, and, more recently, electrothermal bipolar vessel sealing system (EBVS). In this prospective trial we sought to evaluate the impact of EBVS on hepatic resections.
Methods: From March 2004 to December 2005, 24 patients from our consecutive liver resection series were enrolled in the present study. There were 17 males and 7 females with a mean age of 59.6 years (range = 41–80) who had colonic cancer metastases (18), hepatocarcinoma (3), angioma (2), and intrahepatic lithisasis (1). Patients were prospectively randomized to undergo liver resection via EBVS LigaSure V (12 patients, group A) or ultrasonic shears harmonic scalpel (HS) (12 patients, group B). Hepatic procedures did not differ significantly between the two groups and were as follows: right hepatectomy (2), left hepatectomy (1), bisegmentectomy (14), and segmentectomy (7).
Results: There was no mortality in either group. The mean operative time was 136.7 min (range = 90–210) in group A and 187.9 min (range = 130–360) in group B. The Pringle maneuver was done in five patients in group A [mean time = 11.4 min (range = 6–12)] and in four patients in group B [mean time = 16 min (range = 9–26)]. The mean blood loss, total bile salts, and hemoglobin concentration from drained fluid on the second postoperative day were 205.8 vs. 506.7 ml, 0.6 vs. 1.1 mmol/L, and 1.0 vs. 2.1 g/L ($p < 0.05$) for groups A and B, respectively. Mean postoperative hospital stay was 6.1 vs. 7.8 days. In group B a patient who underwent right hepatectomy for colon cancer metastases had transient hepatic failure. No patients received blood transfusions in group A, while two or more blood units were administered in two cases in group B.
Conclusions: In the present study EBVS proved to be safe and effective for liver resection. By means of this device, statistically significant benefits concerning blood loss, total bile salts, and hemoglobin postoperative leakage were found.

Correspondence to: R. Campagnacci

Key words: Liver — Laparoscopic hepatectomy — EBVS device — Liver transection — RCT

Liver surgery continues to be a demanding procedure in which intraoperative and postoperative complications are challenges not yet completely overcome. As a matter of fact, perioperative or late outcomes after hepatic resection are influenced by many factors inherent in essential surgical skills and available technology. Liver surgeons in high-volume centers have emphasized that the restriction of bleeding as much as possible during a hepatectomy is a significant factor in determining improvement of both postoperative and and late outcomes [1, 2]. Indeed, 30 years ago hemorrhage during major hepatic resections represented roughly 20% of deaths [3]. On the other hand, blood loss and heterologous blood transfusion subsequently became known risk factors for a higher complication rate and a worse postoperative course and, in malignancy, reduced cancer disease-free survival. Since the early 20th century, in an attempt to avoid major bleeding episodes during liver resections, the liver surgeon's attention moved toward hepatic inflow restriction by means of the Pringle maneuver or more physiologically challenging techniques such as liver total vascular exclusion or low central venous pressure anesthesia, among other things. Thereafter, however, adverse effects related to inflow liver occlusion, based on both ischemic and reperfusion damage, emerged, arousing a greater interest in techniques aimed at improving hemostasis in liver surgery. Currently, there are various instruments, based on distinct concepts, that are used in hepatic surgery, such as

Table 1. Anagraphic and clinical patient data

	EBVS group A	HS group B
Gender (Male:Female)	8:4	9:3
Age (years)	mean = 60.9 (range = 39–79)	mean = 58.2 (range = 42–81)
ASA	I = 3 II = 5 III = 3 IV = 1	I = 2 II = 7 III = 2 IV = 1
Malignant	10	11
Benign	2	1

Cavitron Ultrasonic Surgical Aspirator (CUSA), ultrasonic dissector, argon, Jet-Cutter, ultrasonic shears, and mono/bipolar cautery. At any rate, liver parenchyma division always involves some moderate blood loss and is a cause of sudden bleeding in major resections, depending on the resection type and patient characteristics. In addition to bleeding, another aspect pertinent to liver resections is bile leakage, which occurs in 5%–15% of cases [4] and is a challenging complication *ipso facto* or is becoming a late biloma. On the basis of our favorable previous and current experiences using EBVS in solid organ removal and hollow viscous procedures, in this randomized study we aimed to evaluate the impact and pros and cons of EBVS used in patients undergoing liver resection.

Methods

Patient selection

Twenty-four hepatic resections were performed in all eligible patients enrolled during a 21-month period in our department (March 2004 to December 2005). There were 17 males and 7 females in whom liver resection was performed for 21 cases of malignancy [colon cancer metastases (18) and hepatocarcinoma (HCC) (3)] and for 3 cases of benign lesions [angioma (2) and intrahepatic lithisasis (1)]. Preoperative imaging workup included computed tomography (CT) or/and magnetic resonance imaging (MRI). HCC affected two cirrhotic hepatitis C patients and one noncirrhotic nonhepatitis case. Patients suffering from cirrhosis were classified as class A using the Child-Pough classification scheme in the absence of significant signs of portal hypertension. Hepatic resection was defined based on Coinaud's liver segmentation. Anagraphic and clinical data of the patients are summarized in Table 1. Procedures were performed by a surgical team who had done at least 50 hepatectomies.

Randomization

Exclusion criteria were cirrhosis, Child-Pough B-C classification, preoperative concrete suspicion of extrahepatic disease or multiple hepatic disease that is not amenable to complete curative resection, and ASA greater than stage III. The procedure was discussed with eligible patients in order to obtain their consent and they were randomized into group A (EBVS LigaSure V) or group B (ultrasonic shears harmonic scalpel) and assigned a randomly generated number. Hepatectomies were performed or supervised by two expert surgeons (GM and CR) who were blinded with respect to a patient's group until operating day, following a single blind trial format. Twelve patients were assigned to be operated on using EBVS LigaSure V [(Tyco Valleylab, Boulder, CO, USA) (group A)] and 12 were assigned to HS (harmonic scalpel; Ultracision Ethicon Endo Surgery, Cincinnati, OH, USA) (group B)]. Of the 24, two procedures (one in each group) were performed by laparoscopic access (left lateral bisegmentectomy and V segmentectomy). The following data were analyzed: operating time, intraoperative and postoperative blood loss, postoperative bile salts and hemoglobin leakage, morbidity, and length of hospital stay. Intraoperative or postoperative (within 30 days) complications included events that negatively influenced the clinical course such as bleeding, pneumonia, or liver failure.

Statistical analysis

There were a number of parameters that summarized the main end points of this trial, represented by a comparison of the effectiveness rate of the two instruments used for liver parenchyma transection. Differences between groups were determined with unpaired Student's t test. A p value less than 0.05 was considered statistically significant. In case of clinically significant differences, but not statistically significant, a t test for means *a priori* analysis determining the sample size was performed. Usually, the larger the sample size, the larger the power. For the power calculation of a study, the power should be reasonably high to detect significant departures from the null hypothesis. A target of 80% of power is correlated to an increasing sample size to make it statistically large enough. Therefore, an appropriate sample size was calculated, i.e., the number of cases required to detect differences between groups A and B on a specific variable, assuming $\alpha = 0.05$, $\beta = 0.2$, and power = 80%. All calculations were done using Primer Biostatistic for Windows (McGraw-Hill, New York, NY, USA) and G*Power Analysis (Faul-Erdfelder, 1992, Bonn, Germany) for Windows software.

Technique

As is our habit, an abdominal exploration and a preliminary liver intraoperative ultrasound (6.5-MHz probe) were performed at the beginning of all procedures, whether open or laparoscopic, to exclude preoperatively undetected hepatic lesions or extrahepatic disease and to confirm preoperative imaging data, paying close attention to the relationship of the tumor with major intrahepatic vascular and biliary structures. Right hepatectomy and left lateral bisegmentectomy (II-III) were performed by making hilar and suprahepatic pedicle control/closure before parenchymal transection. For mono- and bisegmentectomies that were not left lateral, we did not use this preliminary vascular exclusion. To limit blood transfusions as much as possible, Pringle maneuver hepatic inflow vascular occlusion was used in all resections whose bleeding exceeded 300 ml. Concerning this, we pursue to limit the Pringle length of time within 30 min in all cases. A drain was left near the hepatic transection area in all patients for at least 48 h. Analgesia via ketorolac or tramadol was given during the first 24 h postoperatively and thereafter at the request of the patient. At 24 and 48 h postoperatively, the fluid drained was completely retrieved and processed by remixing to avoid bias from blood and derivate sedimentation. Then, a sample in a standard 5-ml test tube was analyzed. Clinical and chemical laboratory tests were required to determine the value of bile salts (sodium glycocholate and sodium taurocholate) and hemoglobin. This value, expressed as concentration/volume ratio, was adjusted proportionately with the total volume of fluids drained within 24 h.

EBVS LigaSure V

Based on the identification by ultrasound of the limits of the resection, or the emergence of ischemia after vascular flow exclusion, the Glisson capsule of liver was incised via electrocautery. Then the parenchyma was divided by use of LigaSure V. This device fuses vessels up to 7 mm in diameter and tissue bundles, providing a combination of pressure and energy to create vessel fusion by melting the collagen and elastin in the vessel walls. A feedback-controlled response system automatically discontinues energy delivery when the seal cycle is complete. The LigaSure V, with a stem measuring about 30 cm of length, is a device we use usually in laparoscopy. Despite its length, this instrument did offer significant advantages in open surgery as well, as for instance the anatomically favorable tips shape or the ergonomic hand controls. During transection, vessels estimated to be larger than 7 mm, including hilum and suprahepatic vessels, were ligated before division.

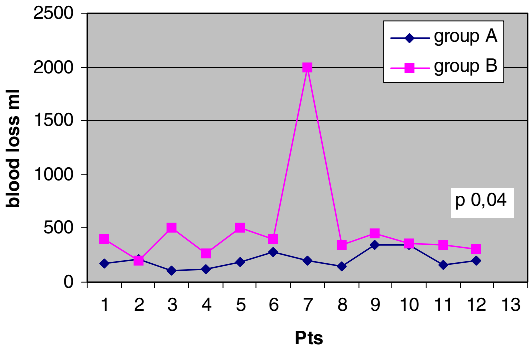

Fig. 1. Blood loss comparing group A and B liver resections.

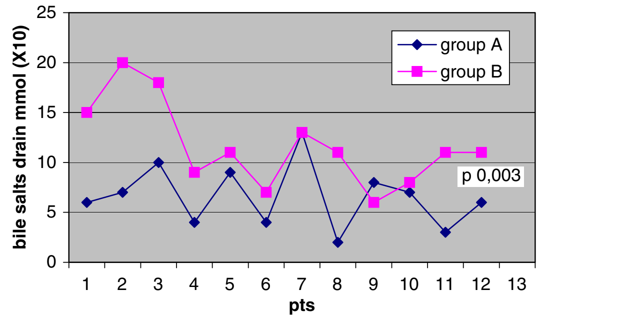

Fig. 2. Bile salts drain concentration at postoperative day 2 among groups A and B.

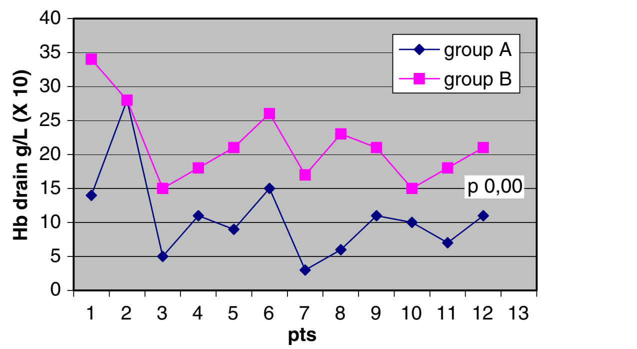

Fig. 3. Hemoglobin drain concentration at postoperative day 2 among groups A and B.

Ultrasonic shears

Ultrasonic shears ultracision followed closely the sequence of maneuvers in EBVS, incising the liver capsule with cautery and inserting the ultrasonic tips into the parenchyma. Vibrating 55,500 times per second, the active blade denatures protein in the tissue to form a sticky coagulum. Pressure exerted on tissue with the blade surface collapses blood vessels and allows the coagulum to form an hemostatic seal. Cutting and coagulation is controlled by the surgeon by adjusting the power level, blade edge, tissue traction, and blade pressure. The EBVS series vessels more than 5 mm in diameter were ligated before division.

Experience before trial

Because our goal is to keep bleeding during a hepatectomy to a minimum, before the present trial we dealt with this kind of surgery using several devices and/or techniques for parenchyma transection, such as clamp crush, hydrodissection, bipolar, ultrasonic, and EBVS. Indeed, since recording progressive favorable impressions with respect to the advantages of EBVS application for gastrointestinal procedures, this tool was increasingly preferred for hepatectomy in terms of time required to perform the task and reducing bleeding. Nonetheless, considering previous hepatectomy series, HS and EBVS were used in a similar number of procedures, even though in our practice we used EBVS later than HS.

Results

The mean operating time was 136.9 min (range = 90–210) in group A and 183.6 min (100–360) in group B [($p = 0.08$) power = 0.38]. The operating time of the two groups was evaluated by using a larger sample size based on Student's t test for means *a priori* analysis and calculated with an assumed power of 80% two-tailed and $\alpha = 0.05$. In this particular instance, the total sample size for $\alpha = 0.05$ should be 34 patients (effect size $d = 1$, critical $t[32] = 2.03$, and $\delta = 2.91$), i.e., a slightly higher number of cases (Fig. 1). Hepatic pedicle inflow occlusion during resection was done in five cases in group A, with a mean time of 12.2 min (range = 6–22), and in four cases in group B, with a mean time of 16 min (range = 9–26). In resection for malignancy, all specimens in which the lesion seemed to be close to the margin were inspected by the surgeon to detect macroscopically at least 1 cm of malignancy-free margin. The specimens in these cases were examined by the pathologist who, by a frozen section of margin, confirmed that the margin was microscopically free as well. There was no mortality in either group. The mean intraoperative blood loss was 210 ml (range = 90–450) and 485 ml (100–2000) for groups A and B, respectively [($p < 0.05$) power = 0.93] (Fig. 2). On the second postoperative day, total bile salts and hemoglobin concentration from drainage fluid were 0.6 and 1.1 mmol/L and 1.0 and 2.1 mmol/L [($p < 0.05$) power = 0.83 and 1, respectively] in groups A and B (Figs. 3 and 4). Patients in whom was found more than 1.5 mm/L of bile salts in drained fluids had initial clinical evidence of uncomplicated biliary fistula, while in the remaining cases bile leak was subclinical. In group B, after a right hepatectomy for metachronous metastases of colon cancer, a patient had transient hepatic failure that required a prolonged hospital stay of over 20 days. No patients in group A received a blood transfusion, while for two cases in group B, 5 and 2 blood units were administered. Postoperative hospital stay was 6.1 days (range = 4–9) and 7.8 days (4–26) for groups A and B, respectively ($p > 0.05$). A larger sample size, based on a Student's t test for means *a priori* analysis, was used for postoperative hospital stay as was done for operating time for the two groups. The total sample size set for $\alpha = 0.05$ and power = 0.80 two-tailed did result in 32 patients (effect size $d = 1.03$, critical $t[30] = 2.04$, and $\delta = 2.93$) (Fig. 5). Patients who underwent hepatectomy for malignant disease, primary or metastatic, were referred to and followed up in conjunction with an oncologist. Imaging follow-up by means of CT and MRI was negative for signs of recurrence both at the resection's margins and at the remaining liver parenchyma at a mean of 12.6 months (range = 6–32).

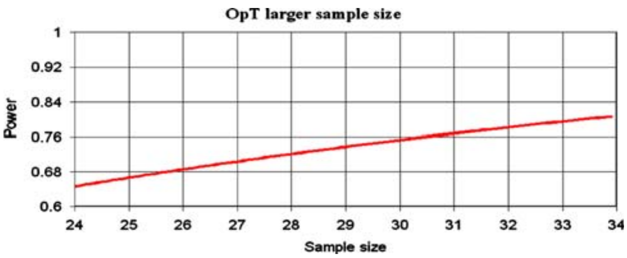

Fig. 4. Larger sample size power calculation for operating time.

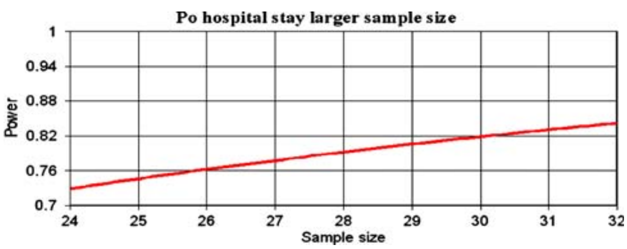

Fig. 5. Larger sample size power calculation for postoperative hospital stay.

Discussion

Much has been done in the technology field with respect to surgery, both laparoscopic and open, but much more must be done. In 2005 Lesurtel et al. [5] reported his results of evaluating four different liver transection strategies—clamp crushing, CUSA, Hydrojet, and dissecting sealer—in 100 consecutive patients. In short, CUSA is an ultrasonic dissector (flush = 4 ml/min at 23 kHz and 70-W cauter). Hydrojet, which produces a pressurized water jet (30–40 bar), washes the soft liver tissue, leaving only more resistant vessels and bile duct that are then ligated or clipped. Dissecting sealer (TissueLink) couples radiofrequency with a conductive fluid to seal liver tissue to precoagulate parenchyma and isolate intrahepatic structures. The same surgical team, with experience of at least 30 liver resections and assisted by the same anesthesia team, performed a standardized resection. In this series, the Pringle maneuver was done only in the clamp crushing technique. Overall mean blood loss was 326 ml.

The main result of this study was the 3–5-fold lower blood loss in the clamp series compared with that of other devices. Nonetheless, no differences were registered among the four strategies in overall rate of bile collections within three months [5]. Blood loss and blood transfusions in hepatic surgery have been thoroughly examined in a number of trials. For instance, in 2003, Kooby et al. [6] reported their 15 years of experience with more than 1300 patients who underwent hepatic resection with curative intent for the treatment of liver metastasis from colorectal cancer. When following up the patients who had been transfused, it was found that they had twice as high a chance of developing major complications and a higher risk of infectious complications. Moreover, transfused subjects were more likely to die in the immediate postoperative period. Interestingly, patients who received only one or two allogenic or autologous transfusions were associated with more overall and high-grade complications but they did not have any negative effect on long-term survival. The mechanism of both a worse postoperative survival and a disease-free survival seems to be related to the adverse effect on immune function. Transfusion suppresses host immunity, reducing natural killer activity and the number of T cells and the cytotoxic T-cell function with a decrease in the T4-to-T8 ratio. In liver cancer cases, transfusions cause an increase in CD8 lymphocytes and a reduction in phytohemoagglutinin (PHA) response, effects that are thought to be related to the number of leukocytes in packed red blood cells [6]. Poon et al. [7] and other authors reported noteworthy conclusions on a series that included more than 1200 liver resections over two decades. Their conclusions pointed out that transfusions are a factor in increasing perioperative morbidity and mortality and in the worsening of the long-term survival of patients with hepatic malignancies. As a consequence, they recommended that each liver surgeon should pursue the zero blood transfusion rate [7, 8].

Recently, some studies argued about the role of ultrasonic technology or EBVS radiofrequency-based energy tools in liver surgery [9–12]. Constant et al. [13] performed nonanatomical resection using LigaSure in laparoscopic and open surgery, and resection without LigaSure by finger fracture in an animal model (swine). The liver cholescintigraphy and inspection after 48 h revealed less blood loss and absence of biliary leakage in two LigaSure groups (open and laparoscopic) compared with that of finger-fracture procedures. However, this study enrolled a low number of animal models, overall nine swine.

Romano et al. [14] in 2004 reported on 30 consecutive patients who underwent 6 major and 24 minor and non-anatomical liver resections using the EBVS LigaSure system, without Pringle routine portal triad occlusion. In their series neither hemorrhage nor bile leakage occurred postoperatively, whereas the rate of patients requiring intraoperative blood transfusions amounted to 17%, with a median blood loss of 250 ml [14]. Apart from blood vessel sealing, this study underlined the effectiveness of small bile branch sealing, significantly contributing to zero bile leakage. In fact, they highlighted how both the low trauma and the minimal lateral thermal spreading, relating to the absence of charring in the cut surface, allowed easy identification and closure of persistent bleeding and biliary patency after LigaSure. This may partly explain the favorable result gotten from LigaSure with respect to biliary fistula rate compared with HS or different devices reported in other series [15]. In these studies, intrahepatic small biliary branches, namely, subsegmental vessels, really seem well sealed and have a permanent result that significantly reduces the rate of bile leakage. In fact, in our series we did not find bile leakage after liver resections performed by EBVS. Moreover, in an attempt to avoid any misleading false negatives and to overcome failure of detecting a bile leak, not even reaching clinical evidence, we planned to sample the fluids drained after 48 h in all resections. Analyzing the results of this survey, we found a significant statistical difference when comparing the EBVS and the HS groups. This trend in favor of EBVS appeared to evaluate perioperative blood loss and hemoglobin concentration/volume ratio in the drained fluids as well. In all series the hepatic injury as a result of inflow occlusion was presumably negligible, as deduced by investigating the transaminases and bilirubin levels in the postoperative course, because the Pringle maneuver still remained abundant after 30 min, with a mean duration of 14 min.

Finally, despite that the operating time did not differ statistically for EBVS compared with HS hepatectomies, we analyzed this parameter and the postoperative hospital stay for the two groups using larger sample numbers via *a priori* analysis. In this way, by setting a statistically significant α value and power, beyond the clinical impact, the results suggested that only an additional ten cases for the number of patients were needed.

The above-mentioned data lead us to make the following conclusions about our study. First, the EBVS LigaSure V was shown to be a safe device, able to reduce both bile leakage and bleeding of liver resections, both intra- and postoperatively, with statistically significant results. Second, the EBVS results in a shorter postoperative course, a reasonable consequence of the intraoperative benefits. Third, far from jeopardizing these conclusions, additional comparative randomized studies investigating this field should be performed.

Conclusions

In our experience EBVS LigaSure V was demonstrated to be safe and effective in liver resection. This device was able to reduce blood loss, total bile salts, and hemoglobin concentrations within statistical significance. Moreover, operating time and postoperative hospital stay had clinically better results and a positive trend on analysis of a larger number of patients operated on with the EBVS device. Despite that the overall number of hepatectomies was small in this study, these results should not be underestimated, and we foresee an interesting use of this technology in hepatic surgery.

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