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Original

Efficacy and Safety of an Ultrasonically Activated Device for Sealing the Bile Ducts During Liver Resection

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Abstract: The use of ultrasonically activated devices (USADs) in hepatic resections may be associated with an increased rate of complications, such as postoperative bile leaks. Nonetheless, the safety of USADs for sealing bile ducts during liver surgery has not yet been established. The purpose of this study was to assess the efficacy of a USAD for sealing bile ducts. In animal experiments, the common bile duct of ten anesthetized dogs was individually occluded using a USAD. Additionally, using the prospective liver surgery database from a single institution, we identified 45 consecutive patients who underwent hepatic resection using a USAD (USAD group) and 45 similar patients who underwent hepatic resection without the use of a USAD (NUSAD group). In the occluded and harvested canine bile ducts, the mean burst pressure was 280 mmHg, and the lumen of the bile duct was completely sealed morphologically. In the clinical study, there was no significant difference in postoperative mortality or complications between the two groups, and biliary leakage was observed in only one patient (0.7%) in the USAD group. These data demonstrate that the USAD is a safe, efficient, and practical instrument for use during liver surgery to achieve complete hemobiliary stasis.

Key words: Bile duct sealing, ultrasonically activated device, liver resection

Introduction

The number of patients undergoing hepatic resection for hepatic malignant neoplasm has increased significantly. The development of anesthetic and surgical techniques has contributed to the safety of liver surgery[1-3], and the availability of hi-tech surgical devices has further facilitated the technique of parenchymal transection during hepatectomy to evolve from the classic clamp crushing technique to a combination of different techniques[4, 5]. Most hepatic parenchymal transections are performed using a combination of instruments and techniques[6-12]. Ultrasonically activated devices (USADs), such as the harmonic scalpel (HS; Ethicon Endo-Surgery Inc., Cin-

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cinnati, OH, USA), have been introduced in liver surgery because of their simultaneous hemostatic and coagulating effects[13, 14]. These devices facilitate the local hemostasis of vessels of up to 3–4 mm, with minimal injury to surrounding tissues[15]. Previous publications have described the usefulness of USADs for hemostasis, reporting less blood loss and shorter operative times compared to conventional hemostasis[13, 14]. Several reports evaluating the use of USADs during cholecystectomy, particularly for the cystic duct, have been published[16–18]. These studies suggest that a USAD can be used to safely seal not only vessels but also the biliary tract. Conversely, an increased rate of complications, such as postoperative bile leaks, has been described following hepatic resection performed using USADs[19]. Moreover, in a study by Matthews *et al*, the USAD was not recommended for biliary surgery[20].

To address this issue, we used a canine model to investigate whether the USAD is a safe and effective modality to resect the bile duct with complete sealing. Moreover, we examined postoperative mortality and complications, particularly biliary complications, after liver resection using a USAD.

Materials and methods

Animal experiment

The animal study was approved by the Committee on Animal Ethics in the Care and Use of Laboratory Animals of the Showa University Medical School.

Ten male adult beagles weighing 10～15kg were used. Five medium-diameter bile duct segments (4.0–6.0 mm ; classified on the basis of outer diameter measurements) of the common bile duct (each 4 cm in length) were harvested from each dog. After isolation of each segment and before collection, the end of the bile duct was occluded in situ using the harmonic scalpel (HS) set at power level 3 for sealing the bile duct. The HS occluded the bile duct with mechanical pressure, and the scalpel was subsequently activated to seal and simultaneously transect the bile duct. All the bile duct segments were separated from the common bile duct by transection with the scalpel blade, and they were subsequently placed in labeled cassettes and immersed in a water bath (37°C) for testing within 4 hours of collection. A cannula was inserted into the bile duct through the end opposite the occluded stump and the cannulation site was closed by clamping. The cannula was connected to both a syringe and a digital manometer (Nippon Koden, Tokyo, Japan). The bile duct, digital manometer, syringe, and connection tubes were filled with 0.9% saline mixed with indigo carmine solution and sealed to form a closed system (Fig. 1). By slowly pushing the piston of the syringe, the intraluminal pressure of the bile duct increased until the occluded biliary stump burst or the ligature was displaced. The resulting pressure curve was recorded using the manometer. The peak of the curve was defined as the burst pressure.

Histological examination

The five bile duct segments sealed by the USAD were fixed in 10% neutral-buffered formalin. After embedding in paraffin, 3-μm thick sections were cut and stained with hematoxylin and

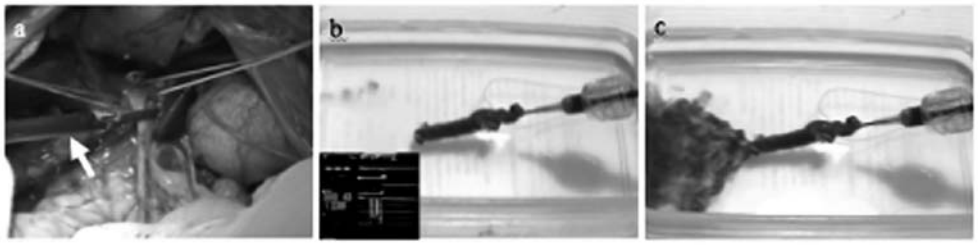

Fig. 1. Procedures of the animal experiment. (a) The canine common bile duct was harvested, occluded and transected *in situ* using an ultrasonically activated device (white arrow); (b) A cannula was inserted into the bile duct through the end opposite the occluded stump and connected to both a syringe and a digital manometer; (c) The intraluminal pressure of the bile duct was increased until the occluded biliary stump burst.

eosin and Masson's trichrome stains for histological evaluation. The bile duct was evaluated using longitudinal sections.

Patients

We searched a prospectively collected hepatobiliary surgical database for patients who underwent elective liver resection for primary and metastatic malignancy or benign disease at the Department of Surgery, School of Medicine, Showa University, Tokyo, Japan. We identified 45 consecutive patients who underwent liver resection using a USAD (USAD group) between January 2004 and March 2007, and 45 patients with similar demographic and pathologic features who underwent liver resection without the use of a USAD between January 2004 and December 2005 (NUSAD group). The four hepatobiliary surgeons who performed all the procedures introduced both techniques into their practice sequentially, beginning in January 2004. Patient demographics for both groups, as well as clinical and operative data, are presented in Table 1. The median age of the patients was 68.7 years (range, 46–80 years) and 67.1 years (range, 37–83 years) for the USAD and NUSAD groups, respectively; their respective male to female ratios were 26 : 19 and 30 : 15.

Surgical procedure

A laparotomy was performed through right subcostal and midline incisions. Following laparotomy and exploration for intra-abdominal metastases, the liver was mobilized in the standard manner. Intraoperative ultrasound was performed to assess the extent of disease and plan the parenchymal transection plane. Stay sutures were placed along the plane of the intended transection. In the USAD group, the liver tissue was divided using the HS set at power level 3 to minimize the risk of injury to the nearby structures. Both active edges of the scalpel blade were used for dissection. Parenchymal cells were easily removed by sweeping lightly, moving the ultrasonic scalpel along the length of the Glissonian branches to expose them. It is important to move quickly over several centimeters of the parenchymal tissue using a light touch to allow the Glissonian branches to be skeletonized safely and quickly. The branches were then exposed and

Table 1. Patient characteristics and pathological variables

Patient characteristics	USAD* group (n = 45)	NUSAD** group (n = 45)	*P*-value
Age, median (range), y	68.7 (46-80)	67.1 (37-83)	N.S.
Male/female, n	26/19	30/15	N.S.
Background liver status, n			
Normal/chronic hepatitis/cirrhosis	24/6/15	23/8/14	N.S.
Histology, n			
Hepatocellular carcinoma	16	17	
Cholangiocarcinoma	7	7	
Colorectal carcinoma	12	14	
Gastric carcinoma	2	3	
Other metastatic liver tumor	6	1	
Benign	2	2	
Other	0	1	
Tumor number, median (range)	1.92 (1-8)	1.73 (1-5)	N.S.
Size of largest tumor, median (range), mm	35.1 (8-72)	39.9 (4-110)	N.S.

*Liver resection with an ultrasonically activated device (USAD).
**Liver resection without the use of a USAD.
N.S., not significant.

visually confirmed. The HS was efficacious and safe in sealing and cutting Glissonian branches up to approximately 3-4 mm in diameter[15]. The Glissonian branches that were more than 5 mm in diameter were dissected using the HS controlled with 3-0 silk ties and divided sharply.

In the NUSAD group, parenchymal transection was performed using a cavitron ultrasonic surgical aspirator (Integra Life Science, Plainsboro, NJ, USA), progressive hemostasis of vessels was achieved with titanium clips or ligations, and coagulation by electrocauterization.

A closed suction drain was routinely used along the transection surface. Anesthetic technique, transfusion policy, and postoperative management were not modified during the study period.

Postoperative monitoring

Patients were monitored for the development of postoperative fluid collection and/or biliary fistulas. Bile leakage was estimated by evaluating the drainage fluid color and confirmed by assaying the total bilirubin level in the drainage fluid; a level greater than 5 mg/dl in patients with normal serum bilirubin was considered diagnostic. Grading of bile leakage after liver resection was assessed according to the definition of the International Study Group of Liver Surgery[21].

Statistical analysis

Values were expressed as means ± standard deviations. Statistical analysis by *t*-tests was conducted using Stat View 5.0 (SAS Institute, Cary, NC, USA). All *P* values less than 0.05 were considered statistically significant.

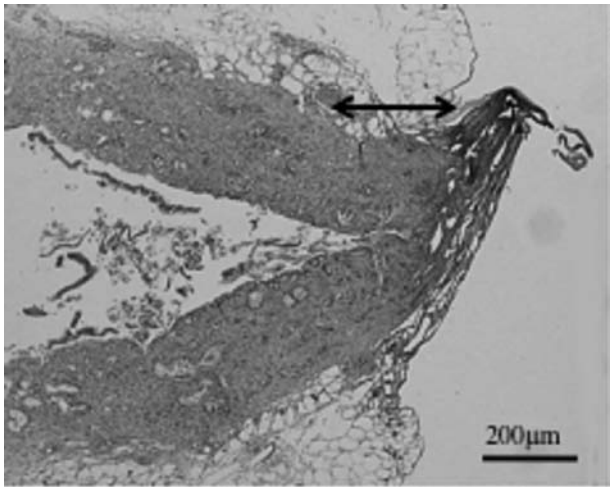

Fig. 2. Microscopic view of a canine bile duct occluded by an ultrasonically activated device at power level 3. The lumen was sealed using a welding process because of complete protein degradation. Arrow indicates the sealing zone. Hematoxylin and eosin staining.

Results

Burst pressure and morphological features of the canine bile duct sealed by a USAD

Fig. 2 shows morphological features of the canine common bile duct sealed by a USAD. Longitudinal sections of the bile duct clearly showed sealing of the lumen with loss of the biliary epithelium in the sealed area. All morphological changes were found within 1,000 μm of the USAD cutting edge. The burst pressure of the sealed bile duct was calculated to be 291 ± 20.1 mmHg.

Liver resection

Table 1 shows an equivalent distribution of the demographic and pathologic variables between the two patient groups, including tumor number and tumor size. There were no procedures in which gross positive margins were seen. The overall mean blood loss was less in the USAD group than in the NUSAD group (data not shown)[22]. The operation time for hepatectomies was also shorter in the USAD group compared to the NUSAD group (data not shown). We observed no significant difference in the number of complications between the two groups (Table 2). There were no perioperative deaths in either group, and no patients required re-exploration. One patient in each group required percutaneous drainage for fluid collection and/or biliary fistula. In each case, the collection or fistula resolved following a short course of percutaneous drainage and, when indicated, antibiotic therapy.

Discussion

Previous reports have described the usefulness of USADs in liver surgery for hemostasis, with less blood loss and shorter operative times than with conventional hemostasis[13, 14]. With recent advances in the field of hepatobiliary surgery, various energy devices are now commonly used.

Table 2. Morbidity of patients undergoing liver resection

Patient characteristics	USAD* group (n = 45)	NUSAD** group (n = 45)
Death	0	0
Wound infection	3	2
Pleural effusion	4	5
Pneumonia	1	1
Bile leakage (ISGLS Grade A)	1	1
Abdominal abscess	1	2
Postoperative bleeding	0	0
Persistent ascites	1	1
Hyperbilirubinemia	0	1
Overall complications (%)	11 (24.4)	13 (28.9)

*Liver resection with an ultrasonically activated device (USAD).
**Liver resection without the use of a USAD.
ISGLS, International Study Group of Liver Surgery.

Therefore, it is beneficial for surgeons to understand the mechanism by which USADs seal biliary branches. This study evaluated the efficacy of USADs in sealing biliary ductal structures for possible use in liver resection.

It has been shown that the USAD uses high-frequency mechanical energy to offer the surgeon controlled and precise incision and hemostasis[15]. Because of its simultaneous hemostatic and coagulating effect, with minimal injury to the surrounding tissues, it may theoretically offer a considerable advantage over electric coagulation. Although blood vessels up to 5 mm in diameter can be sealed by coagulation with the scalpel blade, Matthews et al reported that USAD is not recommended for biliary surgery[20]. They evaluated various energy sources, such as the USAD and the electrothermal bipolar vessel sealer, for sealing ductal structures for possible use in liver or gallbladder surgery by measuring the burst pressure. In their ex vivo study, the mean cystic duct burst pressure was 621 mmHg with surgical clips and 482 mmHg with the electrothermal bipolar vessel sealer; however, the mean cystic duct burst pressure after using a USAD was 278 mmHg, which was significantly less than the other methods[20]. Therefore, they concluded that a USAD should not be used for the transection of the cystic duct or major hepatic ducts during hepatobiliary surgery. On the other hand, Hüscher *et al* demonstrated that a USAD may divide both blood vessels and the cystic duct, with no need for further ligatures, and possibly reduce the risk of thermal injuries[16]. They calculated the burst pressure of the sealed cystic duct to be higher than 320 mmHg in the first 50 cases. Although our experiment was not the same as the above animal experiments, we showed that a USAD could effectively seal a bile duct of less than 4～6 mm in diameter at power level 3, withstanding *ex vivo* burst pressures of up to 290 ± 20.1 mmHg. The mean basic common bile duct pressure is 15 mmHg (range, 5–35 mmHg) and increases to 135 mmHg (range, 95–195 mmHg) during phasic contractions of

the sphincter (4 times/min). Therefore, any sealing method that leads to bursting pressures of the cystic duct greater than 195 mmHg could be reasonable[22]. Examination of morphological features in the animal experiment showed that the bile ducts were sufficiently sealed. However, a possible problem of our study is the lack of short- and long-term *in vivo* follow-up after sealing to reveal whether corrosion by bile in the sealed bile ducts causes leakage. Thus, further trials are still required to evaluate the long-term safety of USADs.

Another advantage of using a USAD in liver surgery is that it allows the surgeon to skeletonize a Glissonian branch easily. If the USAD is moved quickly along several centimeters of the parenchymal tissue using a light touch, then the Glissonian branches are safely and quickly skeletonized. The Glissonian and venous branches can then be occluded and divided by ultrasonic protein coagulation. The USAD provides both effective isolation and coagulation functions during liver transection. In the USAD group, the operation time was shortened and significantly less blood loss was seen in patients undergoing liver resection, when compared to patients in the NUSAD group[23]. Therefore, the USAD is a safe and simple instrument for use during the skeletonization and isolation of vessels during liver parenchymal transection.

Bile duct injury, including bile leakage, can lead to significant morbidity and even mortality; such injury often needs additional treatment. Kim *et al* reported that the use of a USAD alone has been associated with a significant increase in the incidence of postoperative bile leaks[19]. On the other hand, another study by Westervelt[24] demonstrated that the USAD provides complete and reliable hemobiliary stasis in most patients undergoing laparoscopic cholecystectomies. He reported that there were no clinically apparent immediate or remote postoperative bile leaks, even when closure and division of the cystic duct was achieved solely by a USAD[24]. Our findings are in agreement with this report by Westervelt and similar previous studies. In our study, there was no significant difference in postoperative complications between the USAD and NUSAD groups. In particular, the rate of bile leakage was the same in both groups.

As patients in the USAD group experienced no more complications than those in the NUSAD group, we believe that the USAD is as safe and effective as the commonly used clip and cavitron ultrasonic surgical aspirator technique for achieving safe closure and division of the Glissonian branches during liver resection. Further research is required to investigate the efficacy of biliary branch closure using this approach in patients undergoing liver resection compared with conventional and other approaches.

In conclusion, the USAD is a safe, efficient, and practical instrument to use during liver resection.

Conflict of interest disclosure

The authors have no financial support to disclose. This work has not been presented or published previously.

References

1) Jarnagin WR, Gonen M, Fong Y, *et al*. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. *Ann Surg*. 2002;**236**:397-406.

2) Poon RT, Fan ST, Lo CM, *et al*. Improving perioperative outcome expands the role of hepatectomy in manage-

ment of benign and malignant hepatobiliary diseases: analysis of 1222 consecutive patients from a prospective database. *Ann Surg*. 2004;**240**:698-708.
3) Cunningham JD, Fong Y, Shriver C, *et al*. One hundred consecutive hepatic resections. Blood loss, transfusion, and operative technique. *Arch Surg*. 1994;**129**:1050-1056.
4) Lin TY. A simplified technique for hepatic resection: the crush method. *Ann Surg*. 1974;**180**:285-290.
5) Takayama T, Makuuchi M, Kubota K, *et al*. Randomized comparison of ultrasonic vs clamp transection of the liver. *Arch Surg*. 2001;**136**:922-928.
6) Fan ST, Lai EC, Lo CM, *et al*. Hepatectomy with an ultrasonic dissector for hepatocellular carcinoma. *Br J Surg*. 1996;**83**:117-120.
7) Papachristou DN, Barters R. Resection of the liver with a water jet. *Br J Surg*. 1982;**69**:93-94.
8) Schroder T, Hasselgren P, Brackett K, *et al*. Techniques of liver resection. Comparison of suction knife, ultrasonic dissector, and contact neodymium-YAG laser. *Arch Surg*. 1987;**122**:1166-1171.
9) Yamamoto Y, Ikai I, Kume M, *et al*. New simple technique for hepatic parenchymal resection using a Cavitron Ultrasonic Surgical Aspirator and bipolar cautery equipped with a channel for water dripping. *World J Surg*. 1999;**23**:1032-1037.
10) Taniai N, Onda M, Tajiri T, *et al*. Hepatic parenchymal resection using an ultrasonic surgical aspirator with electrosurgical coagulation. *Hepatogastroenterology*. 2002;**49**:1649-1651.
11) Sakamoto Y, Yamamoto J, Kokudo N, *et al*. Bloodless liver resection using the monopolar floating ball plus ligasure diathermy: preliminary results of 16 liver resections. *World J Surg*. 2004;**28**:166-172.
12) Poon RT, Fan ST, Wong J. Liver resection using a saline-linked radiofrequency dissecting sealer for transection of the liver. *J Am Coll Surg*. 2005;**200**:308-313.
13) Aldrighetti L, Pulitano C, Arru M, *et al*. "Technological" approach versus clamp crushing technique for hepatic parenchymal transection: a comparative study. *J Gastrointest Surg*. 2006;**10**:974-979.
14) Ouchi K, Mikuni J, Sugawara T, *et al*. Hepatectomy using an ultrasonically activated scalpel for hepatocellular carcinoma. *Dig Surg*. 2000;**17**:138-142.
15) Bubenik LJ, Hosgood G, Vasanjee SC. Bursting tension of medium and large canine arteries sealed with ultrasonic energy or suture ligation. *Vet Surg*. 2005;**34**:289-293.
16) Huscher CG, Lirici MM, Di Paola M, *et al*. Laparoscopic cholecystectomy by ultrasonic dissection without cystic duct and artery ligature. *Surg Endosc*. 2003;**17**:442-451.
17) Tebala GD. Three-port laparoscopic cholecystectomy by harmonic dissection without cystic duct and artery clipping. *Am J Surg*. 2006;**191**:718-720.
18) Foschi D, Cellerino P, Corsi F, *et al*. Closure of the cystic duct by ultrasonic energy: an electron-microscopic and biomechanical study in man. *Surg Laparosc Endosc Percutan Tech*. 2009;**19**:34-38.
19) Kim J, Ahmad SA, Lowy AM, *et al*. Increased biliary fistulas after liver resection with the harmonic scalpel. *Am Surg*. 2003;**69**:815-819.
20) Matthews BD, Pratt BL, Backus CL, *et al*. Effectiveness of the ultrasonic coagulating shears, LigaSure vessel sealer, and surgical clip application in biliary surgery: a comparative analysis. *Am Surg*. 2001;**67**:901-906.
21) Koch M, Garden OJ, Padbury R, *et al*. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. *Surgery*. 2011;**149**:680-688.
22) Kavlakoglu B, Pekcici R, Oral S. Clipless cholecystectomy: which sealer should be used? *World J Surg*. 2011;**35**:817-823.
23) Aoki T, Murakami M, Koizumi T, et al. Skeletonization and isolation of the Glissonean and venous branches in liver surgery with an ultrasonic scalpel technology. *Int Surg*. 2015;**100**:1048-1053.
24) Westervelt J. Clipless cholecystectomy: broadening the role of the harmonic scalpel. *JSLS*. 2004;**8**:283-285.

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