Randomized Comparative Study between Using Harmonic Scalpel versus Cavitron Ultrasonic Surgical Aspirator with Bipolar Cautery in Living Donor Hepatectomy for Living Donor Liver Transplantation

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Background: Liver donation is a respectable human gift. It is essential that complications should be minimized as much as possible and must be safely performed.

Aim of the work: To evaluate feasibility and safety of using CUSA for liver resection in living donor liver transplantation (LDLT) in comparison with harmonic scalpel.

Patients and methods: This prospective study included 40 consecutive donors for LDLT held at Nasser Institute and Air Force Specialized Hospital during the period from September 2017 to September 2018.

Results: Harmonic scalpel significantly reduced operative time (p=0.000) with a reduced blood loss (p=0.016), however it caused higher rate of biliary leakage (40% vs 15% respectively). On the other hand, CUSA showed lower bile leak leading to shorter hospital stay (p=0.000).

Conclusion: Although harmonic scalpel is a faster method, CUSA is more effective and safer with a lower complication rate despite being cumbersome and need a longer learning curve.

Key words: Harmonic Scalpel, CUSA, liver resection, LDLT.

Introduction

Living donor liver transplantation (LDLT) remains the definitive management of patients with end-stage liver disease (ESLD) or patients with hepatocellular carcinoma (HCC) according to selected criteria especially in countries where deceased donor LT is not available as in Egypt.[1]

There are two stages in hepatic resection including division of liver parenchyma and perfect hemostasis. Different surgical techniques for liver transection have been developed for safe and careful transection as clamp crushing, harmonic scalpel, Habib sealer, LigaSure, cavitron ultrasonic surgical aspirator (CUSA), vascular staplers, microwave coagulators, or spray diathermy. Bipolar coagulation, ligatures, or hemoclips can do hemostasis. Until now, there are no evidences to prove the ideal method for splitting the liver of the donor.[2]

Harmonic Scalpel, HS (Johnson and Johnson Medical, Ethicon, Cincinnati, OH, USA), also known as "Ultrasonically Activated Scalpel" can cut and coagulate the liver tissue in on step causing protein denaturation by breakdown the hydrogen bonds in proteins and by production of heat in vibrating tissue, so blood vessels up to 3-4 mm in diameter are sealed.[3]

Cavitron Ultrasonic Surgical Aspirator, CUSA (Valleylab), is also known as ultrasonic dissector. The vibrating tip of the instrument causes blast of hepatocytes because of high water content and dissection of parenchyma sparing blood vessels and bile ducts. Saline solution irrigation system is used to cool the hand piece, washes the transection plane, removes the liver tissue, and permits visualization, but it has no role in tissue sealing and careful ligation is needed to avoid bleeding or bile leakage. Thus, establishment of rapid hemostasis is critical.[3]

The bipolar (BIP) sealer was tested to seal blood vessels in soft tissue and cut bone while keeping the surface temperature at less than 100 C. It works by generating radiofrequency from a standard electrosurgical generator with saline irrigation to transmit thermal energy without producing smoke or burning tissue.[4]

The aim of this study is to evaluate the feasibility, safety and effectiveness of using CUSA & bipolar diathermy for liver resection in living donor liver transplantation (LDLT) and its short-term benefits with follow up evaluation in comparison with using harmonic scalpel alone.

Patients and methods

This prospective study included 40 consecutive right lobe donors who underwent liver resection in context of LDLT. The study population was divided into two groups according to the method of liver transection: group A by harmonic scalpel (HS) and group B by CUSA/bipolar diathermy combination. The surgical procedures were held at two centres: Nasser Institute of Health & Research and Air Force Specialized Hospital during the period from September 2017 to September 2018.

All donors were accepted according to the same liver transplantation protocol applied in the two units with the following criteria: Age 21-45 years, matched blood group, no previous major abdominal operation, medically free and BMI less than 28. Patients with left liver graft and paediatric liver transplant group were excluded from the study.

Preoperative evaluation included: Full history taking and clinical examination, routine blood investigations including viral markers and tumour markers (AFP, CEA and CA19.9), radiological assessment by abdominal ultrasound and triphasic abdominal CT with hepatic venography, arteriography, portography and magnetic resonance cholangio-pancreatography (MRCP) and residual liver volume must be more than or equals to 35%.

The following outcomes were evaluated: operative data (Operative time, intraoperative blood loss and requirements for blood transfusion, changing operative plan). Postoperative outcome (Bile leakage, postoperative bleeding, ICU and hospital stay and mortality).

This study was approved by the ethics committee of Ain Shams University Hospital and informed consent was taken from all donors participated in this study. The LDLT operation was approved by the transplantation ethical committee of both centres & the supreme committee of organ transplantation, Ministry of Health, Egypt and all donors were operated by the same surgeon.

Surgical technique

The procedure was performed through a right inverted J-shaped incision. Following laparotomy, liver mobilization and piggyback were done in the standard technique then an intra-operative ultrasound and cholangiogram were done to define the major biliary system anatomy and vasculature.

Transection of the liver parenchyma started from the anterocaudal liver surface toward the hepatic veins. The line of parenchymal transection was mapped about 1 cm to the right of the middle hepatic vein (MHV) using intraoperative Doppler ultrasound. The clearly exposed vessels (More than 5mm) were ligated by 4/0 or 5/0 polyprolene or clipped with preservation of V5 and V8.

In-group A the harmonic scalpel (Ethicon Endo-Surgery, Johnson & Johnson, New Jersey, USA) was set at a high power, and blood vessels or bile ducts up to 3-4 mm in diameter were coagulated for 5-6 seconds.

In group B Cavitron Ultrasonic Surgical Settings Aspirator (CUSA) with standard tip was used for parenchymal transection with the following Settings; 23 kHz, 70 Watt, and continuous irrigation at rate of 4-6 ml/min with normal saline and the vessel coagulation was performed by the bipolar sealer (Valleylab force FX electrosurgical generator, Medtronic, Minneapolis, USA), the power was used at 50 Watt coagulation.

Following completion cholangiogram, open-suction silicon drain was placed into the subphrenic and subhepatic spaces close to the cut surface of the liver before abdominal wound closure.

Blood loss during parenchymal transection and immediately after hepatectomy until completion of the procedures was included and estimated by the volume of blood suctioned and subtraction of rinse fluids and/or weighting the swabs that were used during transection, (Every 1 mL of blood is equivalent to 1 g increase in the swab weight).

Postoperative bile leakage was diagnosed once bile was detected from the wound or the drain or drained intra-abdominal collection with total bilirubin level in the fluid more than 3 times that in the serum.

The liver resection time was defined as the duration from the beginning of parenchymal transection until the completion of transection with complete achievement of haemostasis from the liver cut surface.

Post-operative management

All patients were admitted to the ICU for early post-operative care. Post-operative parameters of hepatic recovery, including serum total bilirubin, ALT, AST, prothrombin time, albumin, was measured daily until discharge from ICU then every other day till discharge.

The drain was removed when the amount drained was less than 100 mL/day and no bile leak and discharge from the hospital was based on the patient's general condition, clinical parameters, complications and abdominal ultrasound.

Follow-Up

Upon discharge, all patients were followed once weekly with abdominal ultrasound together with routine laboratory data for at least 1 month.

Statistical analysis

Continuous variables were described as means and standard deviations or as medians with ranges for continuous data. Categorical variables were expressed using frequency distributions. A P value of <0.05 is statistically significant. Independent Student's t test was used to compare continuous variables and chi-squared test for categorical variables. Statistical analysis was done with the help of SPSS v. 24.

Results

This study included 40 consecutive donors for LDLT, age ranging from 18 to 38 (Average 26.7). Male to female sex was 33 to 7 respectively with a mean BMI 24.48 (Range 21-27). All donors were medically & surgically free except one donor with history of open appendectomy.

According to the donor selection and preparation protocol; Factor V Leiden mutation was done routinely and any deviation from normal finding haematological consultation was done, only ten donors were heterozygous and were accepted for donation with the same prophylactic postoperative protocol of low molecular weight heparin as the rest of the normal donors.

After stratifying the donors into two groups according to the method of resection used and comparing the demographic data, there was no statistically significant difference found between harmonic group (G1) & CUSA-Bipolar group (G2) regarding age, sex, BMI, residual liver volume, Factor V Leiden mutation and surgical or medical history **(Table 1)** (p-value 0.600, 0.212, 0.571, 0.381, 0.465 and 0.311 respectively).

Upon comparing the two groups as regard the operative details, G1 showed statistically significant shorter operative time and time needed to complete the liver resection than G2 (the mean operative time was 6.07 vs 7.59 hours and the mean resection time was 1.61 vs 2.76 hours) **(Table 2)** with p-value <0.001 and <0.001 respectively.

Similarly, statistical significant finding was found when comparing the blood loss during resection in both groups (230 ml in G1 and 277.75 ml in G2) in favour of G1 with a p-value of 0.016 taking into consideration that major vascular injury did not occur in both groups. And this was reflected on the amount of blood collected and transfused by the cellsaver that was statistically highly significant in G2 (mean 486.25±95.79 mL in G2 and 365.5±79.37 mL in G1 with a difference of more than 120 mL **(Table 2)** with p-value of 0.000).

There was no statistically significant difference found between the two studied groups regarding haemoglobin level at start (measured preoperatively) and at end of surgery (measured on day one in ICU) **(Table 3)** with p-value = 0.551 and 0.518 respectively.

The incidence of bile leakage was found to be more in G1 as it occurred in eight cases (40%); four patients (20%) presented by bile from the drain & three patients (15%) presented by biloma and one patient suffered from both (5%) **(Table 4).**

Half of these patients were managed conservatively and four (20%) of them required ultrasound guided pigtail insertion **(Table 5)** with mean time of return to normal was 18.14±3.72 days.

While in G2 bile leakage occurred only in three cases; two patients (10%) presented by bile from the drain & one patient (5%) presented by biloma, only a single patient required ultrasound guided pigtail insertion and all patients had a smooth recovery with 24.33±5.13 days required to return to normal.

On comparing the above-mentioned complications in the two groups, no statistical significance was observed. We did not face any case of postoperative bleeding or intra-abdominal hematoma and mortality did not occur in the study group.

Although the postoperative complications were not significant between the two groups, both the ICU & hospital stay, were longer and statistically significant in G1 **(Table 6)** with p-value 0.033 and 0.001 respectively.

Table 1: Demographic Data

		Harmonic group	CUSA/ bipolar	Test value	P-value	Sig.
		No. = 20	No. = 20			
Age (yrs.)	Mean ± SD	27.10 ± 4.63	26.35 ± 4.33	0.529•	0.600	NS
	Range	18 – 38	19 – 33			
Sex of donor	Female	2 (10.0%)	5 (25.0%)	1.558*	0.212	NS
	Male	18 (90.0%)	15 (75.0%)			
Medical history	Free	20 (100.0%)	20 (100.0%)	NA	NA	NA
BMI	Mean ± SD	24.61 ± 1.50	24.34 ± 1.49	0.572•	0.571	NS
	Range	21 – 27	22 – 27			
Residual liver volume (%)	Mean ± SD	38.50 ± 1.54	39.00 ± 2.00	-0.886•	0.381	NS
	Range	36 – 42	36 – 43			
Factor V Leiden mutation	Hetero	6 (30.0%)	4 (20.0%)	0.533*	0.465	NS
Clexan dose postoperative	Mean ± SD	40.00 ± 0.00	40.00 ± 0.00	NA	NA	NA
	Range	40 – 40	40 – 40			
Surgical history	Free	19 (95.0%)	20 (100.0%)	1.026*	0.311	NS
	Appendectomy	1 (5.0%)	0 (0.0%)			

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS).
*:Chi-square test. •: Independent t-test.

Table 2: Operative Data

		Harmonic group	CUSA/bipolar	Test value	P-value	Sig.
		No. = 20	No. = 20			
Operative time (hr)	Mean ± SD	6.07 ± 1.00	7.59 ± 1.35	-4.041•	0.000	HS
	Range	4.3 – 8	6 – 12			
Liver resection time (hr)	Mean ± SD	1.61 ± 0.52	2.76 ± 0.95	-4.734•	0.000	HS
	Range	0.8 – 2.9	1 – 4.8			
Blood loss during resection (ml)	Mean ± SD	230.00 ± 60.87	277.75 ± 58.46	-2.530•	0.016	S
	Range	130 – 330	130 – 400			
Major vascular injury	No	20 (100.0%)	20 (100.0%)	NA	NA	NA
Cell saver transfusion (ml)	Mean ± SD	365.50 ± 79.37	486.25 ± 95.79	-4.341•	0.000	HS
	Range	200 – 500	350 – 700			

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS).
*:Chi-square test. •: Independent t-test.

Table 3: Haemoglobin difference preoperative and postoperative day 1

		Harmonic group	CUSA/bipolar	Test value	P-value	Sig.
		No. = 20	No. = 20			
Preoperative Hgb	Mean ± SD	13.98 ± 1.49	13.72 ± 1.23	0.602•	0.551	NS
	Range	11 – 17	12 – 16			
Postoperative D1 Hgb	Mean ± SD	13.72 ± 1.48	13.45 ± 1.17	0.652•	0.518	NS
	Range	10.5 – 16.8	11.8 – 15.7			

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS).
•: Independent t-test. *: Paired t-test.

Table 4: Complications

		Harmonic group	CUSA/bipolar	Test value	P-value	Sig.
		No. = 20	No. = 20			
Biloma	Yes	3 (15.0%)	1 (5.0%)	3.135*	0.077	NS
Bile leakage from wound	No	20 (100.0%)	20 (100.0%)	NA	NA	NA
Bile leakage from drain	Yes	5 (25.0%)	2 (10.0%)	1.558*	0.212	NS
Timing of bile leak (days)	Mean ± SD	12.29 ± 1.50	12.00 ± 2.00	0.253•	0.807	NS
	Range	10 – 14	10 – 14			
Intra-abdominal hematoma	No	20 (100.0%)	20 (100.0%)	NA	NA	NA
Postoperative bleeding	No	20 (100.0%)	20 (100.0%)	NA	NA	NA
Mortality	No	20 (100.0%)	20 (100.0%)	NA	NA	NA

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS). *:Chi-square test •: Independent t-test.

Table 5: Intervention for bile leakage

		Harmonic group	CUSA/bipolar	Test value	P-value	Sig.
		n=8	n=3			
Type of Intervention	Pigtail	4 (50.0%)	1 (33.0%)	2.533*	0.282	NS
	Conservative	4 (50.0%)	2 (67.0%)			
Timing to cure (days)	Mean ± SD	18.14 ± 3.72	24.33 ± 5.13	-2.180•	0.061	NS
	Range	14 – 24	20 – 30			
Success rate	Yes	8 (100.0%)	3 (100.0%)	2.133*	0.144	NS

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS). *:Chi-square test •: Independent t-test.

Table 6: ICU and Hospital stay

		Harmonic group	CUSA/bipolar	Test value•	P-value	Sig.
		No. = 20	No. = 20			
ICU stay (day)	Mean ± SD	2.85 ± 0.49	2.50 ± 0.51	2.208	0.033	S
	Range	2 – 4	2 – 3			
Hospital stay (day)	Mean ± SD	8.35 ± 1.93	6.65 ± 0.81	3.635	0.001	HS
	Range	6 – 12	5 – 8			

P-value >0.05: Non significant (NS). P-value <0.05: Significant (S). P-value< 0.01: highly significant (HS). •: Independent t-test.

Discussion

LDLT has become a widely accepted definitive modality in treating various end-stage liver diseases. This is largely because of the shortage of deceased donor organs, together with an increasing demand for liver transplantation, especially in Egypt.

Recipient outcome is important; however, donor safety has the highest priority during the entire adult LDLT process.[5]

Organ donation is a noble human gift that should be respected, this necessitates minimization of donor complications as much as possible, and the surgeons must safely perform living donor liver resection.[6]

There is evident controversy regarding which of the techniques is safe and most effective in parenchymal resection in open donor LDLT as this step has a great effect on intraoperative bleeding, blood transfusion, postoperative blood loss, bile leakage and survival, this is why this issue remains under investigation.[7]

The results of the our study showed that harmonic scalpel in the context of right hepatectomy in LTLD donor operation, significantly reduced the total operative time with a tendency toward an estimated reduced blood loss and blood transfusion, however has caused a higher rate of biliary leakage.

Also CUSA device can better identify and isolate vascular and biliary structures, which are then closed tightly with clips or ligated with a polypropylene suture showing a better results regarding bile leak that was reflected on shorter hospital stay.

According to our study the time needed to complete the resection was significantly lower in the harmonic group and this was reflected also on reduction on the operative time and this is logic because that the harmonic shear by its technique simultaneously cut and coagulate the liver parenchyma and structures in a single step.

In contrast to the other group in which the dissection was done by the CUSA and the coagulation and sealing was done by the bipolar or surgical clips then to be separated by scissors. CUSA is always said to be cumbersome and complicated and it is easy for the instrument to malfunction.

This was similar to a study that compares the usage of CUSA and harmonic but in combination with TissueLink, the median operative time in the HS and CUSA groups was 185 and 290 min, respectively.[8]

As regard the blood loss, taking in consideration that there was no incidence of major blood vessel injury during the hepatectomy in both groups. The harmonic group showed a lower volume of blood loss and a lower amount of blood transfused by the Cellsaver, this is because it can seal vessels until 2-3mm of diameter but major vessels were controlled by surgical clips. While after using CUSA, it requires a longer time for the haemostasis of the raw surface by bipolar.

Although the difference in the amount of blood loss and the transfused blood when comparing both groups was relatively irrelevant (47 mL and 120 mL respectively), but it was statistically significant.

This finding was validated to be clinically insignificant by observing the haemoglobin level pre and postoperative showing no significant drop in either group. We were fortunate that we did not face any case of postoperative bleeding or intra-abdominal hematoma.

In a study done by Bodzin & his colleagues, he explained the decrease in estimated blood loss in the Harmonic Scalpel (HS) group over the CUSA group might be because the HS had inherent coagulating properties while the CUSA had the manual ability to coagulate at the surgeon's decision. In the same study, he retrospectively compared 47 patients performed heaptectomy with the HS or the CUSA system and showed that the HS provided an estimated reduced blood loss and a need for blood transfusion with a faster operative time.[8]

This was against the results published in a meta-analysis conducted by Kamarajah et al, who demonstrated that bipolar cautery is best for blood loss and operative time. In contrast, the Harmonic scalpel was ranked best for overall and major complications as well as overall transfusion rates.[9]

During liver resection, the complication of bile leakage had been always a distressing complication and may be affected by the technique used during hepatectomy.[8]

In our study, the incidence of bile leakage was higher in G1 group. Revisiting our data; we demonstrated 40% (n=8) biliary leak rate in the G1 and 15% (n=3) in G2 but still statistically insignificant. Our explanation for decreased bile leak by the CUSA group is that CUSA has a high degree of tissue selectivity during dissection that helps in better identification of the bile ducts offering excellent visualization so that they can be securely ligated.

Bodzin & his colleagues who noted the same tendency toward a higher rate of perihepatic collections as compared to the CUSA group noted the same. However, he did not mention that all of these collections were because of bile leakage. This is beside only 17% of the collections found in the postoperative management required drainage. This finding was related by him to the fact that the HS device produce a higher working power and a faster parenchymal cutting probably sealing the lymphatic and bile ducts insufficiently because of a faster sealing speed.[8]

In contrast to a prospective multicentre randomized study, including 212 patients in five centres, Gotohda et al., clarified the fact that energy devices allowed for less intraoperative bleeding and less bile leakage with a faster transection time.[10]

Another explanation by Romano et al., for the tendency toward a higher number of perioperative collections in the HS group that, although the HS produces no smoke and thermal injury is limited, the depth of marginal necrosis is greater than that incurred by either the water jet or CUSA. The lateral spread of the energy is 500 micrometres so the sealed tissues slough later on leading to bile leak.[11]

Takahara et al. who suggested that the ischemic changes in the bile duct might be the cause of bile leakage as thermal damage to the small vessels around the bile duct may cause ischemic changes in the bile duct also adopted this theory.[12]

Based on this, Kaibori et al. suggested that it is important to establish soft coagulation while using the bipolar system near the hepatic hilum to avoid bile leakage and this may contribute to the reduction of biliary complication in CUSA group.[13]

According to our protocol, it is allowed to discharge the donor who had bile leak as long as the drain in place and his general condition is fine for close follow up. Bile leakage occurred in both groups but it was managed successfully in all patient either by conservative management in 50% of patients with bile leak in group 1 and 67% in group 2 and the time for cure in both groups was statistically insignificant.

In the previously mentioned retrospective comparative study by Bodzin et al showed that HS provided a shorted hospital stay. The median LOS was 6.0 days (Range 2-49) in the Harmonic group compared with 7.0 days (Range 6-27) in the CUSA group.[8]

While revising the overall hospital stay, they were markedly reduced in the CUSA group and this may be because of the lower incidence of biliary complications in this group with faster capacity to return to normal activity.

Conclusion

We believe that harmonic scalpel is a faster method for resection but in context of LDLT, the CUSA is more effective and safer with a lower complication rate in spite of being less comfortable to use and need a cumbersome learning curve. We believe that our results should be taken into consideration when deciding which techniques or devices are most safe and effective.

The question of whether any alternative transection technique provides a benefit over the other needs a bigger number of cases and a longer follow up so we can provide full insights into the benefit–risk ratio of different methods for parenchymal transection.

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