

Comparison of hydro-dissection versus ultrasonic aspirator in division of liver parenchyma in laparoscopic resection

Lap Liver Study

NCT03208192

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Study Design – Lap Liver Resection

Title of the study: comparison of water-jet dissector with ultrasonic aspirator in division of liver parenchyma in laparoscopic resection

Background: until now, there is no agreement about the safest and feasible method for liver parenchyma transection during laparoscopic liver resection.

Study design: prospective, randomized, single-center

The purpose of the study: comparison of short-term results of two methods of parenchyma liver transection during laparoscopic liver resection

Material and Methods: two groups will be compared.

Group 1: liver resection using a bipolar dissector (Erbe), ultracision harmonic scalpel (Ethicon) and water-jet dissector (ERBEJET 2).

Group 2: liver resection using a bipolar dissector (Erbe), ultracision harmonic scalpel (Ethicon), and ultrasonic aspirator (Misonix/SonaStar Ultrasonic Surgical Aspiration System)

Indication laparoscopic liver resection.

- Benign liver tumors (hemangioma, focal nodular hyperplasia, hepatocellular adenoma, biliary cystadenoma):
 - lesions of 7 cm or more and clinical manifestation with complaints of abdominal pain due to physical activity or body position.
 - Unresolved suspicion for malignancy
- Hydatid echinococcosis
- Malignant tumors (colorectal cancer metastases in the liver, hepatocellular carcinoma, intrahepatic cholangiocellular carcinoma, gallbladder cancer T1b-3NxM0)

For enlargement of the groups patients with Hydatid echinococcosis are included if total pericystectomy is performed. The surgery in those cases does not differ from liver resection for benign tumors.

Inclusion Criteria:

- Patients with benign lesions (hemangioma, focal nodular hyperplasia [FNH], hepatocellular adenoma, biliary cystadenoma, hydatid echinococcosis [only with total pericystectomy]) and malignant tumors (colorectal cancer metastases in the liver [CRLM], hepatocellular carcinoma [HCC], intrahepatic cholangiocellular carcinoma, gallbladder cancer T1b-3NxMo without invasion into bile ducts and adjacent organs), which involves laparoscopic segmental or major resection of the liver.
- Gender: both, male and female
- Minimum age 18 years
- Maximum age: 80 years
- ASA physical status I-IV
- BMI up to 40 kg/m²
- No simultaneous extrahepatic intra-abdominal procedures (bile duct resection, colon resection, partial duodenum resection)
- Total bilirubin up to 100mmol/l if jaundice presents in non-cirrhotic patients
- If cirrhosis is present, class A and B according to CTP score

Exclusion Criteria

- Difficulty index > 12 points (see below)

- Tumor invasion of IVC or portal trunk (necessity of vascular reconstruction)
- Repeated liver resection before laparoscopic resection (the single resection before is not a contraindication)
- Simultaneous extra-hepatic intra-abdominal procedures (bile duct resection, colon resection etc.)
- Age under 18 years
- Age above 80 years
- ASA physical status >IV
- BMI > 40 kg/m²
- Total bilirubin >100mmol/l if jaundice presents in non-cirrhotic patients
- If cirrhosis is present, class C according to CTP score
- Persons who are incapable of giving consent
- Pregnant or breast-feeding women
- Patients enlisted in other studies

Preoperative examination:

1. Hematology (WBC, RBC, Hb, Plt)
2. Biochemistry (CRP, TP, AST, ALT, total bilirubin, creatinine, glucose)
3. Abdominal ultrasound examination (tumor location, size and involvement of large vessels)
4. Abdominal enhanced CT (with or without MRI) (tumor location, size and involvement of large vessels)
5. Chest CT
6. The upper digestive tract endoscopic examination

Additional examination for patients with malignant tumors:

7. Colonoscopy (if last procedure >1 year)
8. Tumor markers (CEA and CA 19-9 for CRLM, AFP and CA 19-9 for primary liver tumors).

Postoperative examination.

Further evaluation will be done at PO Day 2, 4, 6, 28. On Day 7 some patients may be discharged.

If patient stays in hospital more than 30 days, evaluation (hematology, biochemistry and US examination) on PO Week 2, 3, 4 and 5 until discharge will be done. Abdominal CT should be undertaken if needed.

1. Hematology (WBC, RBC, Hb, Plt)
2. Biochemistry (CRP, TP, AST, ALT, total bilirubin, creatinine, glucose)
3. Abdominal ultrasound examination (fluid collections and liver ischemia with estimation of the size and localization, pleural effusion with estimation of side and volume)

Difficulty Index

It is mandatory to estimate the complexity of laparoscopic liver resection by calculating the difficulty index proposed by Go Wakabayashi (2014) and modified in 2016 (attachment 1). As the difficulty index includes the type of liver resection (partial resection, segmentectomy, and sectionectomy), the size and topography of the tumor, its proximity to the large vessels of the liver, the presence and stage of liver cirrhosis (CTP), all patients in each group will be divided into four subgroups according to the complexity of liver resection: low, intermediate, advanced and expert.

The comparison will be conducted between groups 1 and 2 according to difficulty of liver

resection.

Comparative analysis should include following intraoperative and postoperative factors

Primary endpoint:

Intraoperative blood loss - absolute measurement of blood loss in relation to resection size (ml/cm²)

Absolute blood loss will be calculated as the amount of blood (collected only during the parenchyma resection) in suction the container after the subtraction of all irrigating fluids and weighing operative sponges.

Secondary endpoints:

Intraoperative factors:

1. Blood loss relative to total blood volume (%) (attachment 2)
2. Duration of liver parenchyma transaction.
3. Necessity to apply the Pringle maneuver.
4. Number of Pringle maneuver applications.
5. The total duration of Pringle maneuver.
6. Duration of the longest application of Pringle maneuver
7. Number of patients needed for banked blood transfusion
8. Number of bank blood units needed for transfusion
9. Rate of conversion to hybrid (with upper midline incision of 10 cm long), open or robotic surgery
10. Open/lap surgery before laparoscopic procedure

Postoperative factors:

1. Morbidity according to Clavien-Dindo classification (it is advisable to activate complications class II-V), as shown in attachment 3.
2. Duration of hospital stay

Bile leakage will be classified in severity according to the international study group for liver surgery (A,B,C) (attachment 4).

Since the difficulty index does not take into account the number of liver lesions (and, in fact, needs to be calculated for each of the multiple lesions), only resection of the liver lesion with the highest difficulty index must be considered when comparing groups (especially for the liver parenchyma transection).

Flow chart and CRF are attached.

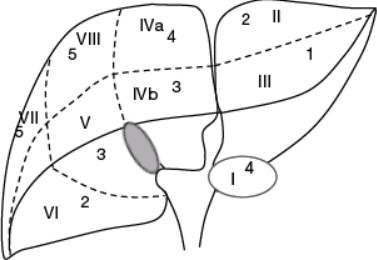
The number of patients in each group requires revision in line with the required statistical power of the study. Most likely, it requires at least 50 patients in each group (total number – not less than 100 patients).

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Attachment 1

Difficulty index score (IWATE Criteria)

IWATE Criteria													
Difficulty index	0	1	2	3	4	5	6	7	8	9	10	11	12
Difficulty level	Low				Intermediate			Advanced			Expert		
Index surgery	<div><div>Left lateral sectionectomy</div><div>Right or left hepatectomy</div><div>Simple and small partial hepatectomy in segment III</div><div>Posterior sectionectomy for segment VII tumor ≥ 3 cm</div></div>												

Scoring system																																	
Tumor location (Couinaud segment)								Tumor size																									
								Score																									
								<3 cm						0																			
								≥3 cm						1																			
<table><tr><th>Segment</th><th>Score</th></tr><tr><td>S1</td><td>4</td></tr><tr><td>S2</td><td>2</td></tr><tr><td>S3</td><td>1</td></tr><tr><td>S4a</td><td>4</td></tr><tr><td>S4b</td><td>3</td></tr><tr><td>S5</td><td>3</td></tr><tr><td>S6</td><td>2</td></tr><tr><td>S7</td><td>5</td></tr><tr><td>S8</td><td>5</td></tr></table>								Segment	Score	S1	4	S2	2	S3	1	S4a	4	S4b	3	S5	3	S6	2	S7	5	S8	5	Proximity to major vessel*					
								Segment	Score																								
								S1	4																								
S2	2																																
S3	1																																
S4a	4																																
S4b	3																																
S5	3																																
S6	2																																
S7	5																																
S8	5																																
No						Score																											
						0																											
Yes						1																											
						*Main or second branch of Glisson's tree, major hepatic vein, or inferior vena cava																											

Extent of liver resection				HALS/Hybrid		Liver function	
Score							
Partial resection	_____	0		No	0	Child Pugh A	0
Left lateral sectionectomy	_____	2		Yes	-1	Child Pugh B	1
Segmentectomy	_____	3					
Sectionectomy and more	_____	4					

The average blood volume is calculated as 75 ml/kg for men and 65 ml/kg for women, and in case of obesity 70 ml/kg for men and 60 ml/kg for women.

Source:

Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery 1962;51:224–32

[http://www.surgjournal.com/article/0039-6060\(62\)90166-6/abstract](http://www.surgjournal.com/article/0039-6060(62)90166-6/abstract)

Iijima T, Brandstrup B, Rodhe P, Andrijauskas A, Svensen CH. The maintenance and monitoring of perioperative blood volume. Perioper Med 2013;2:1–12.

<https://www.ncbi.nlm.nih.gov/pubmed/24472160>

Attachment 3

CLAVIEN-DINDO GRADING SYSTEM FOR THE CLASSIFICATION OF SURGICAL COMPLICATIONS

Grades	Definition
Grade I:	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II:	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III:	Requiring surgical, endoscopic or radiological intervention
Grade III-a:	Intervention not under general anesthesia
Grade III-b:	Intervention under general anesthesia
Grade IV:	Life-threatening complication (including CNS complications: brain haemorrhage, ischaemic stroke, subarachnoid bleeding, but excluding transient ischaemic attacks) requiring IC/ICU management.
Grade IV-a:	Single organ dysfunction (including dialysis)
Grade IV-b:	Multi-organ dysfunction
Grade V:	Death of a patient
Suffix 'd':	If the patients suffers from a complication at the time of discharge, the suffix “d” (for ‘disability’) is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication

Source:

Dindo D., Demartines N., Clavien P.A.; Ann Surg. 2004; 244: 931-937

<http://www.surgicalcomplication.info/index-2.html>

Attachment 4

A definition and grading of severity of bile leakage by the International Study Group of Liver Surgery

Definition:

Bile leakage is defined as bilirubin concentration in the drain fluid at least 3 times the serum bilirubin concentration on or after postoperative day 3 or as the need for radiologic or operative intervention resulting from biliary collections or bile peritonitis.

Grading:

- Grade A bile leakage causes no change in patients' clinical management.
- A Grade B bile leakage requires active therapeutic intervention but is manageable without relaparotomy.
- Grade C bile leakage, relaparotomy is required.

Source:

Koch et al, Bile leakage after hepatobiliary and pancreatic surgery: A definition and grading of severity by the International Study Group of Liver Surgery. Surgery Volume 149, Issue 5, May 2011, pages 680-688

<http://www.sciencedirect.com/science/article/pii/S0039606010006781>