

## ORIGINAL ARTICLE

# Clamp–crush technique vs. radiofrequency-assisted liver resection for primary and metastatic liver neoplasms

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## Abstract

**Background:** Several techniques for liver resection have been developed. We compared radiofrequency-assisted (RF) and clamp–crush (CC) liver resection (LR) in terms of blood loss, operating time and short-term outcomes in primary and metastatic tumour resection.

**Methods:** From 2002 to 2007, 196 consecutive patients with primary or metastatic hepatic tumours underwent RF-LR ( $n = 109$ ; group 1) or CC-LR ( $n = 87$ ; group 2) in our unit. Primary endpoints were intraoperative blood loss (and blood transfusion requirements) and total operative time. Secondary endpoints included postoperative complications, mortality and intensive care unit (ICU) and hospital stay. Data were collected retrospectively on all patients with primary or secondary liver lesions.

**Results:** Blood loss was similar ( $P = 0.09$ ) between the two groups of patients with the exception of high MELD score ( $>9$ ) cirrhotic patients, in whom blood loss was lower when RF-LR was used ( $P < 0.001$ ). Total operative time and transection time were shorter in the CC-LR group ( $P = 0.04$  and  $P = 0.01$ , respectively), except for high MELD score ( $>9$ ) cirrhotic patients, in whom total operation and transection times were shorter when RF-LR was used ( $P = 0.04$ ). Rates of bile leak and abdominal abscess formation were higher after RF-LR ( $P = 0.04$  for both).

**Conclusions:** Clamp–crush LR is reliable and results in the same amount of blood loss and a shorter operating time compared with RF-LR. Radiofrequency-assisted LR is a unique, simple and safe method of resection, which may be indicated in cirrhotic patients with high MELD scores.

## Keywords

Liver resection, radiofrequency-assisted technique, Kelly clamp–crush technique, MELD score

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## Introduction

Liver resection remains the reference standard for the treatment of both primary and metastatic liver tumours.<sup>1–5</sup> Excessive blood loss and blood transfusion contribute to poor short- and long-term outcomes,<sup>6–8</sup> although they may not represent the most important factors associated with unfavourable results after hepatectomy.

Multiple approaches have evolved to reduce bleeding during the parenchymal transection phase.<sup>9,10</sup> In the late 1980s several groups

popularized the technique of liver division under low retrograde hepatic vein flow, with inflow occlusion to minimize blood loss during transection of liver parenchyma.<sup>9,11,12</sup> Inflow occlusion (Pringle manoeuvre) can be performed with or without vascular preconditioning.<sup>11</sup> However, notwithstanding the manoeuvre's effectiveness in reducing blood loss, it is important to note that intraoperative ischaemia can occur in cases of marginal liver function.<sup>13,14</sup> More precisely, there are circumstances in which the Pringle manoeuvre is undesirable, such as in a small liver remnant, underlying liver disease, advanced age, steatosis, preoperative

jaundice and prolonged chemotherapy.<sup>13,14</sup> Ischaemic preconditioning and intermittent clamping of the portal triad are the only strategies that have been clinically established to protect against liver injury.<sup>15,16</sup>

Recent efforts have used vessel-sealing devices for parenchymal transection in order to accomplish bloodless liver resection and reduce intraoperative ischaemia.<sup>13,17–24</sup> Since its landmark description by Weber and associates,<sup>23</sup> the concept of bloodless liver resection has driven hepatobiliary surgeons to establish the ideal approach. Lesurtel *et al.*<sup>10</sup> concluded that the traditional clamp–crush technique was the most effective overall, after comparing four different transection strategies in a prospective randomized study.

More recent studies have shown that the Cavitron ultrasonic surgical aspirator (CUSA)<sup>25</sup> and other sealing devices,<sup>12</sup> when combined with the clamp–crush (CC) technique or bipolar forceps,<sup>25</sup> may constitute the ideal approach. The CUSA is very precise in liver dissection and theoretically avoids the need for inflow occlusion. However, despite this theoretical precision in its ability to divide vessels, Lesurtel *et al.* found that one-third of patients undergoing liver transection with CUSA required the Pringle manoeuvre.<sup>10,25</sup>

Dissection in the right plane is mandatory in order to achieve satisfactory tumour resection with minimal blood loss and damage to the liver remnant. Intraoperative ultrasound (IOUS) can be very helpful in delineating the proper transection plane.<sup>12</sup>

The purpose of this report is to compare radiofrequency-assisted liver resection (RF-LR) with the traditional KCC technique for parenchymal division in terms of blood loss, operating time and postoperative outcomes, in the setting of both primary and metastatic liver lesions.

## Materials and methods

Between January 2002 and March 2007, a total of 196 patients underwent hepatic resection for primary or metastatic liver carcinoma in our department. Radiofrequency-assisted LR was used in 109 patients (group 1) and the CC technique was applied in 87 (group 2). The decision about which technique should be used was based on the tumour characteristics of each patient. The CC method was used in patients in whom tumours were closer to the major vasculature.

Major hepatectomy was defined as the resection of three or more liver segments. Primary endpoints were blood loss and total operating time in both groups. Secondary endpoints included postoperative morbidity, mortality, intensive care unit (ICU) and hospital stay and degree of liver damage, assessed by measurement of serial postoperative bilirubin, prothrombin and transaminase levels. Patient characteristics in both groups are presented in Table 1. There was no statistically significant difference regarding ASA (American Society of Anesthesiologists) scores or demographics in the groups and subgroups selected (Table 1).

Resections were performed under low central venous pressure (CVP) anaesthesia (0–5 mmHg) and under the supervision of two

**Table 1** Patient characteristics in the clamp–crush (CC-LR) and radiofrequency-assisted (RF-LR) liver resection groups

	KCC-LR	RF-LR	P-value
Patients, <i>n</i>	87	109	
Demographics			
Gender, male/female	59/28	73/36	0.63
Age, years	62 ± 2.4	59 ± 2.2	0.79
Body mass index, kg/m <sup>2</sup>	24.8 ± 1.2	25.6 ± 1.2	0.72
Preoperative risk evaluation			
ASA score 1/2/3	30/57/0	35/72/2	0.59
Indication for resection			
Hepatocellular carcinoma, <i>n</i>	37	46	0.64
Colorectal liver metastases, <i>n</i>	50	63	
Type of liver resection			
Major (≥3 segments)	40	39	0.72
Minor (<3 segments)	47	70	
Non-tumorous liver parenchyma characteristics			
Steatosis	21	20	0.65
Preoperative chemotherapy, %	46	58	0.82
Cirrhosis, MELD score ≤9	23	32	0.79
Cirrhosis, MELD score >9	10	12	

hepatobiliary and pancreas surgeons (SD, CD). Each patient underwent IOUS to establish the tumour location and its relation to major vascular structures. Vascular control for major resections was mainly extrahepatic. In five patients intra-parenchymal dissection was performed in response to firm adhesions from previous operations, which made pedicle dissection impossible.

Radiofrequency-assisted LR was performed using the Radiofrequency Cool-Tip device (Radionics Division, Tyco Healthcare Group, Burlington, MA, USA) with a single 3-cm needle (17-gauge adapted with a 20-cm electrode). The technique for RF-LR is reported elsewhere.<sup>26,27</sup> Briefly, liver resection is performed by inserting the entire non-insulated tip of the electrode, parallel to the liver surface, into the liver parenchyma. Radiofrequency energy is applied and coagulative desiccation progresses upwards from the inserted non-insulated tip of the electrode to the liver surface, causing the colour of the tissue to become pale as a result of coagulative necrosis. After a cylinder of desiccated liver tissue has been achieved, the electrode is left in place while the desiccated tissue is cut with a surgical scalpel all the way to the non-insulated tip of the electrode.<sup>26,27</sup> The Pringle manoeuvre was not applied when RF-LR was performed.

In CC-LR, a small, vascular angle Potts clamp was used. Small vessels (<2 mm) were coagulated with monopolar forceps and bigger structures were ligated or clipped. A stapler device was used to transect the hepatic veins in some cases. Intermittent clamping was applied in all patients with CC transection. Intermittent portal triad clamping (Pringle manoeuvre) was performed in cycles of inflow occlusion for 10 min followed by reperfusion for 5 min.

Clips, sutures and ligatures were used selectively during parenchymal transection with both techniques.

Total operating time was recorded as time from the start of anaesthesia to completion of the operation.

Transection time was defined as time from the beginning to the end of parenchymal transection.

Total blood loss incurred during the whole operation was estimated taking into account suction volume after subtraction of rinse fluids.

The indication for transfusion was a haemoglobin level  $<8$  g/dl within 48 h of surgery.

A bile leak was defined by the occurrence of: (i) bilious drainage into operatively placed drains for  $>7$  days after the hepatic resection, or (ii) postoperative imaging demonstrating a fluid collection confirmed to be bile with percutaneous drainage.

All patients with hepatocellular carcinoma (HCC) had underlying Child A cirrhosis and normal platelet counts. The presence of cirrhosis was evaluated by the Ishak fibrosis score<sup>28</sup> and the degree of steatosis was graded as 0 (no steatosis or  $<10\%$ ) and 1 (steatosis  $>10\%$ ).

### Statistical analysis

Statistical analysis was performed with SPSS (Version 10.0; SPSS, Inc., Chicago, IL, USA). Categorical variables were analysed with Fisher's exact test and chi-squared test and continuous variables with Mann-Whitney *U*-test. Differences were considered significant at  $P < 0.05$ .

### Results

A total of 39 major and 70 minor hepatectomies were performed in group 1 (RF-LR). Forty major and 47 minor hepatectomies were performed in group 2 (CC-LR). The results are shown in Table 2.

Blood loss was significantly higher in cirrhotic patients with MELD (*model for end-stage liver disease*) scores  $>9$ , when the CC technique was used to perform LR ( $P < 0.001$ ). The KCC method was significantly faster than RF-LR in terms of median total operation time ( $P = 0.04$ ) and median transection time ( $P = 0.01$ ) in all patients except cirrhotic cases with high MELD scores ( $>9$ ), in whom RF-LR was significantly faster than KCC ( $P = 0.04$ ).

Patients who developed biliary fistula were managed conservatively. Those who developed intra-abdominal abscess were successfully treated with computed tomography (CT)-guided drainage.

The RF-LR group showed higher rates of both bile leak and infectious complications (Table 2).

One patient died on postoperative day 8 as a result of hepatic insufficiency. This patient had undergone RF-LR.

All patients had a postoperative increase of liver enzymes which normalized within 7 days. Median peak postoperative serum bilirubin level was 1.17 mg/dl (range 0.49–3.48 mg/dl) in the RF-LR group and 1.01 mg/dl (range 0.45–2.34 mg/dl) in the CC-LR group.

Resected specimens were carefully examined for depth of tissue coagulation along the transection margin. Depth of tissue coagulation was 3–5 mm in the RF-LR group and provided an additional tumour-negative margin at the resection border.

### Discussion

Bleeding after liver resection remains a significant factor affecting prognosis.<sup>6–8</sup> The clamp–crush technique with inflow occlusion is a reliable method of liver resection, reported by several groups in the literature.<sup>10,29–32</sup>

Although vascular occlusion techniques have been proven effective to control intraoperative bleeding, the pathophysiologic effects have been only poorly analysed and are difficult to predict in patients with decreased hepatic reserve.<sup>10,32</sup>

Recent efforts have aimed to achieve bloodless liver resections in the setting of parenchymal transection with new sophisticated devices.<sup>13,17,23,33</sup> The application of Radionics as a parenchymal transection device has generally evolved from experience with microwave coagulation therapy (MCT).<sup>21</sup>

Most of the blood loss during major resections with RF-LR occurred from small branches or side holes in the hepatic veins and resulted from poor visualization of these anatomic structures and the blind insertion of the sharp edge of the RF needle. These anatomic structures appeared to be more difficult to visualize with Radionics compared with the CUSA or CC techniques, which concurs with similar findings noted by Poon *et al.*<sup>21</sup>

Inadvertent injuries of these vessels can lead to serious blood loss and require additional haemostasis, which prolongs transection time. Better delineation of the transection plane with the use of IOUS can help to avoid such events. Intraoperative US can define the relationship between a tumour and the major intrahepatic vessels or bile duct pedicles. When the relationship between the tumour and the major intrahepatic structures is unknown, unexpected damage to such structures can occur during transection, leading to massive bleeding or bile duct injuries, and sometimes to tumour exposure at the transection plane.<sup>12</sup>

The maintenance of low CVP remains an important adjunctive measure to reduce blood loss in liver transection.<sup>12</sup>

Blood loss and transfusion requirements were similar between the two methods (CC-LR vs. RF-LR) in our study ( $P = 0.09$ ), with the exception of the high-risk cirrhotic patients (Child A, MELD score  $>9$ ). Blood loss in this subgroup of patients was significantly higher when CC was used ( $P < 0.001$ ). The benefits of RF-LR, in terms of blood loss, in this particular subgroup of patients can be attributed to better control of capillary bleeding by coagulation of the small capillaries in cirrhotic liver tissue, which is more friable than normal tissue.

Total operating time and transection time were longer when RF-LR was used, as a result of the low transection speed of the RF device and the occasional interruption of the process for additional haemostasis. Similar findings were observed by Clavien

**Table 2** Clamp-crush (CC-LR) vs. radiofrequency-assisted (RF-LR) techniques in liver resection for colorectal liver metastases (CLM), hepatocellular carcinoma (HCC) and in the entire cohort

	Colorectal liver metastases				Hepatocellular carcinoma				CLM + HCC			
	CC-LR	RF-LR	Total	P-value	CC-LR	RF-LR	Total	P-value	CC-LR	RF-LR	Total	P-value
Patients, <i>n</i>	46	57	103		41	52	93		87	109	196	
ASA score 1/2/3	17/29	21/36		0.06	13/28	14/36/2		0.06	30/57	35/72/2		0.09
Median blood loss, ml (range)	480 (200-700)	400 (100-750)	430 (100-750)	0.06	580 (200-850)	510 (200-900)	560 (200-900)	0.09	580 (200-850)	490 (100-900)	540 (100-900)	0.09
Patients receiving RBC transfusion in the first 48 h, <i>n</i>	12	11	23 (22.3%)	0.06	16	10	26 (27.9%)	0.06	27 (31%)	22 (20.2%)	49 (25%)	0.06
Median transection time, min (range)	50 (20-100)	110 (60-160)	80 (20-160)	0.01	70 (30-120)	100 (50-180)	90 (30-180)	0.02	60 (20-120)	105 (50-180)	85 (20-180)	0.01
Median total operation time, min (range)	160 (110-240)	225 (150-270)	195 (110-270)	0.01	190 (130-290)	250 (150-300)	205 (130-300)	0.04	170 (110-290)	240 (150-300)	195 (110-300)	0.04
30-day mortality	0	1	1		-	-	-	-	-	1	1	
Abscess = 1	0	3	3 (2.9%)	0.04	1	5	6 (6.4%)	0.03	1 (1.1%)	8 (7.33%)	9 (4.6%)	0.04
Biliary fistula = 1	1	6	7 (6.8%)	0.03	0	4	4 (4.3%)	0.03	1 (1.1)	10 (9.17%)	11 (5.6%)	0.04
Pleural effusion = 1	5	7	12 (11.6%)	0.61	8	6	14 (15%)	0.05	13 (15%)	13 (12%)	26 (13%)	0.60
Patients staying in ICU for $\geq 1$ day, <i>n</i>	18	12	30 (29.1%)	0.13	15	13	28 (30%)	0.06	33 (38%)	25 (23%)	58 (29.5%)	0.15
Median hospital stay, days	7 (4-10)	9 (4-12)	9 (4-12)	0.04	8 (4-12)	10 (5-15)	9 (4-15)	0.04	7 (4-12)	9 (4-15)	9 (4-15)	0.04

RBC, red blood cell; ICU, intensive care unit

*et al.* and Petrowsky *et al.*, who reported greater blood loss and longer transection time for RF-LR than for CC-LR with intermittent vascular clamping.<sup>34,35</sup>

Complications related to the biliary tree following RF-LR have been described in the literature.<sup>33</sup> Such complications represent the main problem with major resections using RF-LR and, regardless of the ultimate advantageous function of a bloodless RF device, the liver surgical principles of hilar dissection should not be overlooked. Although the technique simplifies parenchymal transection, it should not alter the convention that such devices should only be used by experienced hepatobiliary surgeons with excellent knowledge of the regional anatomy. We must not forget that an important part of liver resection involves intraparenchymal dissection in order to allow for precise control of pedicles.

In this study RF-LR was associated with a higher rate of bile leak compared with CC-LR (Table 2) ( $P = 0.04$ ). This is extremely interesting because CC was used to resect tumours closer to the major liver structures and was therefore used to perform more demanding hepatectomies. It is our understanding that the RF device may not provide for efficient sealing of biliary radicals under all circumstances. Another possible explanation for the higher incidence of bile leakage and fistula formation in the RF-LR group is that these are caused by the detachment of necrotic remnant tissue on the resection surface.

In our series, the incidence of infective complications, such as intra-abdominal abscess formation, was higher in the RF-LR group than the CC-LR group ( $P = 0.04$ ). This is probably related to the higher bile leak rate and the ischaemic tissue at the transection interface.<sup>36</sup>

In our study, pathological specimens for all patients showed a tumour-free margin  $\geq 1$  cm. No statistical difference regarding the width of the tumour-free margin was identified between the two methods ( $P = 0.08$ ). It appears that the demarcation line produced by the Cool-Tip device extends further into the liver remnant, thereby increasing the surgical margin.<sup>12</sup>

However, the effect of this amount of necrotic tissue on cirrhotic patients with a limited liver remnant is not clear. High postoperative aspartate aminotransferase (AST) levels reflect the coagulation–necrosis pattern at the raw surface of the remnant liver parenchyma and maximum AST value is well correlated with the transection area.<sup>17</sup> A theoretical benefit of RF-assisted transection has been reported<sup>14,21,23,26</sup> based on the fact that parenchymal degeneration is limited to the transection surface, unlike the whole-liver ischaemic damage caused by the Pringle manoeuvre. We used the Pringle manoeuvre only in KCC-LR in cycles of inflow occlusion for 10 min, followed by reperfusion for 5 min. We found no significant difference between our two transection groups in terms of liver injury as estimated by transaminase and bilirubin levels on postoperative day 3.

As clear data for the comparison of various liver transection techniques are currently lacking, the choice of technique is often based on the individual surgeon's preference. However, certain general recommendations can be made based on existing data and

the authors' experience. Clamp crushing is a fast, low-cost technique, associated with low morbidity, but it requires substantial experience to be used effectively in liver transection, especially in the cirrhotic liver. Radiofrequency-assisted transection seems to be beneficial in high-risk cirrhotic patients. However, the risk of thermal injury to the major bile duct and the higher morbidity rate are serious concerns and its use is probably restricted to minor resection. Our study did not evaluate the impact of RF and CC liver transection on longterm outcomes, including tumour recurrence. There is growing evidence that RF causes cellular death beyond the line of transection, by affecting the enzymatic mechanism of cell division in distant cells.<sup>22</sup> As already reported, this raises exciting possibilities for tissue ablation beyond the histological margin, but further studies should be carried out to establish its clinical effectiveness.

Although bloodless RF-LR is promising, there are several associated issues worth noting. Firstly, the technique is still in development and no randomized trial evidence exists to compare bloodless liver resection with traditional approaches. Secondly, bile leak rates are generally not reported accurately because some groups use bloodless devices combined with clips or staplers and rely on intraoperative cholangiograms to carry out early diagnosis and treatment. Thirdly, although the device provides excellent coagulation and is strongly recommended for cirrhotic patients, limited experience exists in patients with advanced cirrhosis, portal hypertension and low platelet count, and, fourthly, data on outcomes of liver resection in jaundiced patients with hilar cholangiocarcinoma, in which CUSA seems to be more efficient, are insufficient.

## Conclusions

The Kelly clamp–crush technique remains a reliable method of parenchymal transection in which both transection and total operating time are reduced compared with times in RF-LR. Blood loss is similar in patients with metastatic liver cancer or HCC and good hepatic reserve. Complication rates are higher after RF-LR because of the higher incidence of infection and bile leak. The sealing of biliary radicals requires more time than sealing of vessels and therefore meticulous ablation is mandatory.

## Conflicts of interest

None declared.

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