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REVIEW ARTICLE

Techniques for liver parenchymal transection: a meta-analysis of randomized controlled trials

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Abstract

Background: Different techniques of liver parenchymal transection have been described, including the finger fracture, sharp dissection, clamp–crush methods and, more recently, the Cavitron ultrasonic surgical aspirator (CUSA), the hydrojet and the radiofrequency dissection sealer (RFDS). This review assesses the benefits and risks associated with the various techniques.

Methods: Randomized clinical trials were identified from the Cochrane Library Trials Register, MEDLINE, EMBASE, Science Citation Index Expanded and reference lists. Odds ratio (ORs), mean difference (MDs) and standardized mean differences (SMDs) were calculated with 95% confidence intervals based on intention-to-treat analysis or available-case analysis.

Results: We identified seven trials including a total of 556 patients. Blood transfusion requirements were lower with the clamp–crush technique than with the CUSA or hydrojet. The clamp–crush technique was quicker than the CUSA, hydrojet or RFDS. Infective complications and transection blood loss were greater with the RFDS than with the clamp–crush method. There was no significant difference between techniques in mortality, morbidity, liver dysfunction or intensive therapy unit and hospital stay.

Conclusions: The clamp–crush technique is more rapid and is associated with lower rates of blood loss and otherwise similar outcomes when compared with other methods of parenchymal transection. It represents the reference standard against which new methods may be compared.

Keywords

liver paranchymal transection, liver resection

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Background

Blood loss is one of the most important factors affecting the perioperative outcome of patients undergoing liver resection surgery.[1–3] Various techniques have been used to reduce blood loss, including lowering the central venous pressure,[4] hypoventilation[5] or vascular occlusion.[6,7] Various methods of liver parenchymal transection have been suggested to decrease blood loss. These include the finger fracture technique,[8] sharp dissection,[9,10] Kelly's technique[11–14] (the clamp–crush technique), ultrasonic dissection (using the Cavitron ultrasonic surgical aspirator [CUSA]),[12,13,15–17] the hydrojet[13,15,17] and the radiofrequency dissecting sealer (RFDS).[11,13,14] Among these, the finger fracture technique, clamp–crush technique and sharp dissection do not require any special instruments.

The finger fracture technique and the clamp–crush technique are generally considered to represent the standard forms of liver parenchymal transection. The ultrasonic dissector (CUSA), hydrojet and RFDS are newer techniques. Randomized controlled trials have been published to assess the benefits and risks of various techniques. We were unable to identify any systematic

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reviews or meta-analyses of parenchymal transection techniques in liver resection that might provide an evidence base for the optimal technique for liver parenchymal transection during elective liver resection surgery.

Materials and methods

Identification of trials and data extraction

Randomized clinical trials comparing one method of parenchymal transection with another were reviewed, irrespective of language or publication status. Trials were included irrespective of the nature of the underlying liver, use of vascular occlusion or the method of management of the raw surface. Co-interventions (including radiofrequency [RF] ablation) were allowed, provided that they were used equally in the intervention groups. Quasi-randomized studies, in which the methods of allocating participants to a treatment were not strictly random, cohort studies and case-control studies were excluded. The Cochrane Hepato-Biliary Group Controlled Trials Register,[18] the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE, EMBASE and the Science Citation Index Expanded[19] were searched until March 2008 using the MeSH terms: liver or hepatic or segmentectomy or resection or transection or hepatectomy and blood loss or blood losses or hemorrhage or hemorrhages or haemorrhage or haemorrhages or hemostasis or hemostases or haemostasis or haemostases. A filter recommended by the Cochrane Collaboration[20] was used to exclude non-randomized studies in MEDLINE and EMBASE. The references of the identified trials were searched to identify further relevant trials. Two reviewers independently identified the trials for inclusion and extracted the following data: year and language of publication; country of study; year of study; inclusion and exclusion criteria; sample size; population characteristics, such as age, gender ratio, major or minor liver resections, normal or cirrhotic livers; method of vascular occlusion; management of the cut surface; outcomes, and methodological quality. Sample size calculations and intention-to-treat analysis are reported by the trial authors.

Outcomes

Data for the following outcomes were extracted: mortality at 30 days; mortality at maximal follow-up; perioperative morbidity (such as re-operations for bleeding, bile leakage, etc.); adverse events; clinically significant air embolism; biochemical markers of liver damage (aspartate aminotransferase [AST], alanine aminotransferase [ALT]) and markers of liver function (bilirubin, prothrombin time); blood loss during resection; total operative blood loss; blood transfusion (number of units, number of patients requiring blood transfusion); parenchymal transection time/speed; total operation time; length of hospital stay, and costs as reported by the authors.

Assessment of methodological quality

Instructions given in the *Cochrane Handbook for Systematic Reviews of Intervention*[20] and the Cochrane Hepato-Biliary Group Module[18] were followed. Because there is a risk that intervention effects in randomized trials with inadequate methodological quality will be overestimated,[21–24] the following methodological quality components were assessed: generation of allocation sequence; allocation concealment; blinding; incomplete data outcomes; selective outcome reporting; baseline imbalance; early stopping; academic bias, and sponsor bias. If the information was not available in the published report of the trial, the authors were contacted in order that the trial could be assessed correctly.

Statistical methods

Meta-analyses were carried out according to the recommendations of the Cochrane Collaboration[20] using the software package RevMan 5[25] provided by the Cochrane Collaboration. For dichotomous outcomes, the odds ratio (OR) was calculated with 95% confidence intervals (CIs). For continuous outcomes, mean differences (MDs) or standardized mean differences (SMDs) were calculated with 95% CIs. The random-effects model and a fixed-effect model were used.[26,27] In cases of discrepancy between the two models, we report both results; otherwise we report only the results from the fixed-effect model. Heterogeneity was explored by chi-squared test with significance set at a *P*-value of 0.10, and the quantity of heterogeneity was measured by I2.[28] An I2 of >30% was considered to indicate statistically significant heterogeneity. An intention-to-treat analysis[29] was performed whenever possible. Otherwise, an available-case analysis was adopted. Subgroup analyses for normal livers and chronic liver disease, liver resections vs. living donor retrievals, minor and major liver resections, different techniques of vascular occlusion and different techniques of management of the cut surface, and trials with low and high risks of bias were not performed because of the few trials included under each outcome.

Results

Description of studies

We identified a total of 887 references through the electronic searches of the Cochrane Hepato-Biliary Group Controlled Trials Register and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (n = 107), MEDLINE (n = 393), EMBASE (n = 242), and the Science Citation Index Expanded (n = 145). Of these, 288 duplicates and 591 clearly irrelevant references were excluded by reading the abstracts (Fig. 1). Eight references were retrieved for further assessment. No references were identified through scanning reference lists of the identified randomized trials. One reference was excluded[17] because randomization had been stopped because of a technical difficulty. The remaining seven references represented completed randomized trials which fulfilled the inclusion criteria.[10–16] Important details of the trials are shown in Table 1. All seven trials carried a high risk of bias as all lacked blinding of patients and outcome assessors. Figure 2 shows a methodological quality summary based on our judgements of the methodological quality

of the studies. The techniques compared, numbers of participants, percentages of major resection and use of vascular occlusion are given in Table 1.

Outcome measures

The primary outcome measures reported by all trials were perioperative mortality,[10,11,13,14,16] surgery-related complications,[10,11,13–16] air embolism,[12] blood loss,[11–16] number of patients transfused,[10,11,13,14] amount of blood transfused,[11–13,15] operating time,[10,12,14] transection time,[11–13,15,16] transection speed,[11,13,14,16] markers of liver parenchymal injury,[11,13] markers of liver dysfunction,[13] intensive therapy unit (ITU) stay[10,13] and hospital stay.[10,11,13,14] The other outcome measures reported by the trials were air embolisms detected in the heart,[12] costs[13] and tumour exposure at the resection margin.[16]

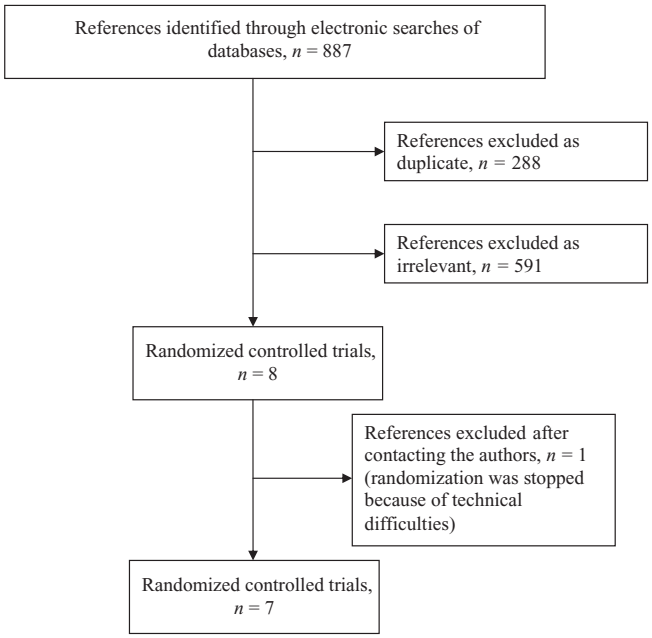

Figure 1 Flow chart of articles identified, included and excluded

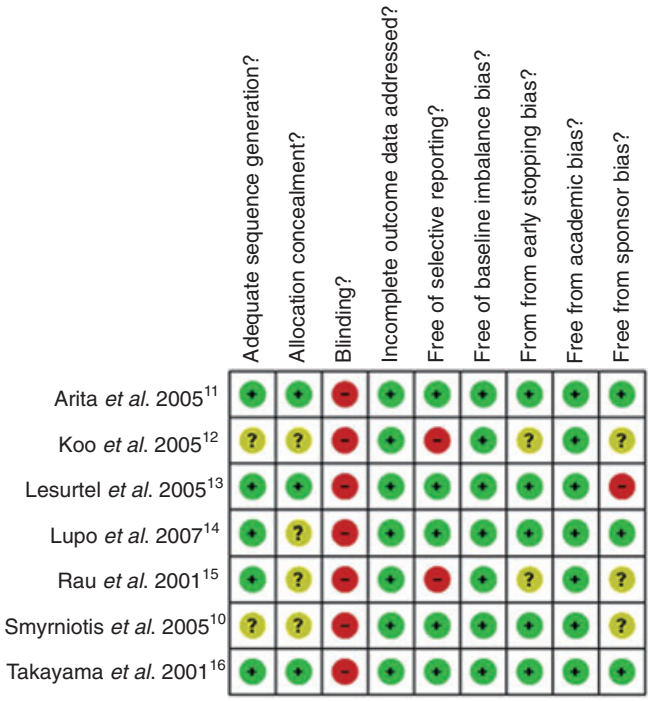

Figure 2 Methodological quality summary: review authors' judgements of each study on each methodological quality item

Table 1 Characteristics of included studies

Study (year)	Techniques compared and number of patients in each group	Major resection	Cirrhosis	Vascular occlusion
Rau *et al.* (2001)[15]	Hydrojet (*n* = 31) CUSA (*n* = 30)	24 (39.3%)	None	Intermittent
Takayama *et al.* (2001)[16]	CUSA (*n* = 66) Clamp–crush (*n* = 66)	43 (32.6%)	None	Intermittent
Arita *et al.* (2005)[11]	RFDS (*n* = 40) Clamp–crush (*n* = 40)	20 (25%)	21 (26.3%)	Intermittent
Koo *et al.* (2005)[12]	CUSA (*n* = 25) Clamp–crush (*n* = 25)	Not stated	None	No
Smyrniotis *et al.* (2005)[10]	Sharp transection (*n* = 41) Clamp–crush (*n* = 41)	60 (73%)	12 (14.6%)	Selective intermittent but equal in each group
Lesurtel *et al.* (2005)[13]	CUSA (*n* = 25) Hydrojet (*n* = 25) RFDS (*n* = 25) Clamp–crush (*n* = 25)	61 (61%)	None	Only in clamp–crush
Lupo *et al.* (2007)[14]	RFDS (*n* = 40) Clamp–crush (*n* = 40)	21 (42%)	7 (14%)	No

CUSA, Cavitron ultrasonic surgical aspirator; RFDS, radiofrequency dissection sealer

CUSA vs. the clamp–crush technique

In the three trials that compared outcomes between the CUSA and clamp–crush methods,[12,13,16] a total of 232 patients were randomized to either CUSA (116 patients) or clamp–crush (116 patients). One trial[13] compared CUSA without vascular occlusion and the clamp–crush technique with vascular occlusion and was thus considered to differ from the other two.[12,16] This trial was analysed separately.

Trials comparing the CUSA and clamp–crush techniques with vascular occlusion

There was no statistically significant difference between the techniques in mortality, morbidity, operative blood loss, median transection blood loss, amount of blood transfused, operating time or transection time. The number of patients with air embolism detected in the heart by echocardiography was significantly higher in the CUSA group (OR 24.77, 95% CI 1.34–457.61). However, none of the patients had clinically significant air embolism.

Trial of CUSA without vascular occlusion and the clamp–crush technique with vascular occlusion

Significantly more blood was lost (MD 2.50 ml/cm^2, 95% CI 1.01–3.99) and significantly more patients required blood transfusion (OR 11.29, 95% CI 1.29–98.89) with CUSA without vascular occlusion than with the clamp–crush technique with vascular occlusion. Transection speed was also significantly quicker (MD −1.60, 95% CI −2.31 to −0.89) in the clamp–crush method than in CUSA. There was no statistically significant difference between the two groups in mortality and morbidity, peak AST, ALT or bilirubin level, prothrombin activity, ITU or hospital stay between the two groups. The CUSA was between three and six times more costly than the clamp–crush technique, depending upon the number of cases performed per year, because of transection speed, blood loss and the cost of maintaining the instrument.[13]

RFDS vs. the clamp–crush technique

In the three trials that compared outcomes between the RFDS and clamp–crush methods,[11,13,14] 180 patients were randomized to either the RFDS (89 patients) or clamp–crush (91 patients) techniques. There was no mortality in either group. Infected intra-abdominal collections were significantly higher in the RFDS group than in the clamp–crush group (OR 11.02, 95% CI 1.38–88.28). The difference between the techniques in the incidence of wound infection approached statistical significance in favour of the clamp–crush technique (OR 7.58, 95% CI 0.80–68.46). Transection blood loss was higher in the RFDS group than in the clamp–crush group (MD 1.90 ml/cm^2, 95% CI 0.92–2.88). There was no difference between the two groups in the number of people requiring a blood transfusion (OR 1.19, 95% CI 0.50–2.82). The amount of blood transfused could not be estimated as no-one in the clamp–crush group underwent blood transfusion in the only trial[11] that reported on this outcome. By imputing values of 0.01 and 0.01 for mean and standard deviation (SD), instead of 0 and 0, we were able to calculate a mean difference.[30] This was statistically significantly lower in the clamp–crush method (number of units: MD 1.49, 95% CI 1.27–1.71; amount of blood transfused: MD 359.99 ml, 95% CI 307.31–412.67).

There was no statistically significant difference in AST, ALT or bilirubin levels, prothrombin activity, or ITU or hospital stay. Transection speed was statistically significantly quicker (MD 1.40 cm^2/min, 95% CI 0.57–2.23) in the clamp–crush method than in RFDS in the only trial that reported on this outcome.[13] There was no difference in median operating time between the two groups in the one trial that reported this.[14] Costs were calculated in one trial[13] based on transection speed, blood loss and the cost of maintaining the instrument. The RFDS was approximately three times more costly than the clamp–crush technique.

On exclusion of the trial, which used vascular occlusion in the clamp–crush group alone,[13] infected intra-abdominal collections favouring the clamp–crush technique and the amount of blood transfused (after imputing the mean and SD as mentioned previously) were the only outcomes for which the groups showed statistically significant differences. This was because transection speed and costs were reported only in the trial that was excluded in the sensitivity analysis.[13]

Hydrojet vs. the clamp–crush technique

Only one trial provided comparison between the clamp–crush and hydrojet techniques.[13] The hydrojet group experienced greater blood loss (MD 2.00 ml/cm^2, 95% CI 0.86–3.14) and a greater need for blood transfusion (OR 11.29, 95% CI 1.29–98.89). The clamp–crush method was statistically significantly quicker (MD 1.50 cm^2/min, 95% CI 2.33 – 0.67). There were no statistically significant differences in mortality (OR 5.43, 95% CI 0.25–118.96), morbidity, peak AST or ALT, bilirubin level, prothrombin activity, median ITU stay (1 day in both groups) or hospital stay (9 days in both groups). The hydrojet method was approximately two to four times more costly than the clamp–crush technique depending upon the number of cases operated per year based on transection speed, blood loss and the cost of maintaining the instrument.

Sharp dissection vs. the clamp–crush technique

Only one trial compared outcomes between the sharp dissection and clamp–crush techniques.[10] There was no statistically significant difference in median intraoperative blood loss (500 ml in sharp dissection vs. 460 ml in clamp–crush) or the number of people requiring blood transfusion (OR 0.80, 95% CI 0.32–2.01). Neither was there any statistically significant difference between the two groups in operative morbidity or mortality, median operating time (205 min in sharp dissection vs. 211 min in clamp–crush), median ITU stay (1 day in both groups) or hospital stay (10 days in sharp dissection vs. 11 days in clamp–crush).

Hydrojet vs. CUSA

Two trials compared outcomes between the hydrojet and CUSA techniques.[13,15] There was no statistically significant difference between the two groups in transection blood loss, intraoperative blood loss, number of people requiring transfusion or mean transfusion requirements, mortality (OR 1.00, 95% CI 0.13–7.72), morbidity, peak AST or ALT, bilirubin levels, prothrombin activity, transection time or speed, median ITU stay or median hospital stay. Costs were calculated in one study[13] based on transection speed, blood loss and the cost of maintaining the instrument. The hydrojet was approximately a third more cost-effective than CUSA.

RFDS vs. CUSA techniques

Only one trial compared outcomes between the RFDS and CUSA methods.[13] There was no statistically significant difference in transection blood loss, the number of people requiring blood transfusion, mortality (OR 5.43, 95% CI 0.25–118.96), morbidity, peak AST or ALT, bilirubin levels, prothrombin activity, transection speed, median ITU stay (1 day in both groups) or median hospital stay (9 days in both groups). Costs were calculated according to transection speed, blood loss and the cost of maintaining the instrument. Depending upon the number of cases operated, RFDS costs were approximately 50–100% of those of CUSA.

RFDS vs. the hydrojet

Only one trial compared outcomes between the RFDS and hydrojet methods.[13] There was no statistically significant difference in transection blood loss, number of people requiring blood transfusion, mortality (OR 0.18, 95% CI 0.01–4.04), morbidity, peak AST or ALT, bilirubin level, prothrombin activity, transection speed, median ITU stay (1 day in both groups) or median hospital stay (9 days in both groups). Costs were calculated based on transection speed, blood loss and the cost of maintaining the instrument. The RFDS technique cost about 25% more than the hydrojet.

Discussion

In this systematic review, no differences were found in mortality rates in liver resection surgery irrespective of the method used for parenchymal transection. However, the mortality associated with liver resection surgery is low[31] and the trials were not adequately powered to identify significant differences in mortality. This review also found no significant differences between the various techniques in morbidity, apart from in one trial, which showed RFDS to be more strongly associated with infective complications than the clamp–crush method. The reason for this difference was not clear, but the increased amount of non-viable tissue and the consequent necrosis of biliary ducts left at the resection margin may influence the rate of abscesses in RFDS.[14] No differences between the techniques were noted in markers of liver injury or length of ITU or hospital stay.

Given the similarities between the techniques in terms of morbidity and mortality rates, we must establish the optimal transection technique according to other considerations. Blood and blood products are expensive and, in larger studies, blood loss in liver surgery has been shown to correlate with both morbidity and mortality.[1–3] The clamp–crush technique resulted in the lowest blood loss and transfusion requirements. However, in the trial that compared clamp–crush outcomes with those of three other techniques (CUSA, RFDS and the hydrojet),[13] continuous portal triad clamping was used in the clamp–crush technique, but no inflow occlusion was used in the other techniques. Another trial[12] comparing outcomes between the clamp–crush technique and CUSA did not employ vascular occlusion. This trial did not find any difference in blood transfusion requirements between the two groups. The third trial[16] that compared the clamp–crush technique with CUSA employed intermittent vascular occlusion in both groups. This trial did not report on blood transfusion requirements, but did report that the median transection blood loss was similar in the two groups. Thus, it is likely that vascular occlusion played an important role in decreasing blood transfusion requirements in the clamp–crush technique in the trials in which vascular occlusion was used in the clamp–crush technique only. This may have produced a bias in favour of the clamp–crush technique in terms of blood loss and transfusion and thus the technique should be assessed as a package. The role of vascular occlusion in liver surgery and the optimal method is controversial. In a recent review,[32] intermittent vascular occlusion was shown to be safe and to decrease blood loss and blood transfusion requirements, but it did not affect morbidity. Data on other factors influencing blood loss during liver surgery, including the use of low central venous pressure, hypoventilation and drugs such as tranexamic acid, were not reported in most of the trials.

In the comparison of transection methods, transection speed is more important than operating time as this takes the resection surface area into account, which may influence both transection duration and blood loss. The clamp–crush technique is quicker than the CUSA, hydrojet or RFDS methods. Transection speeds in sharp dissection and the clamp–crush technique have not been compared, but no difference was found in operating time. On a practical level, the accuracy of the implication that the use of the faster technique could facilitate increased theatre usage, thereby allowing additional procedures to be performed on the same day and thus reducing both operating costs and waiting times for surgery, remains to be resolved.

Air embolism can be a fatal complication of liver surgery. Koo *et al.*[12] detected a significantly higher number of air emboli in the heart in their CUSA group than in their clamp–crush group. All large emboli (half or more of the right heart diameter) were found in the CUSA group.[12] However, none of the patients in either group developed clinical symptoms. The importance of this

finding in the absence of clinical symptoms is not clear, but it is likely to reflect the risk of a massive air embolism with CUSA.

Liver surgery is expensive in terms of personnel, facilities and equipment. The clamp–crush and sharp dissection techniques do not involve any additional instruments. A cost comparison between the clamp–crush technique and other techniques revealed that clamp–crush is two to six times cheaper than other methods, depending on the number of surgeries performed each year.[13] Furthermore, the clamp–crush technique may contribute to cost savings because it decreases blood loss and transfusion requirements.

This review is restricted by the small number of trials in each comparison, which makes it impossible to perform subgroup analyses. Sample size is not sufficiently powered to detect clinically significant differences in the primary outcomes. All the trials were at high risk of bias, mainly because of the lack of blinding. Although patient blinding can be easily achieved, even this was not reported in the trials and it is not safe to assume that the patients were blinded to the groups. Blinding of outcome assessors is more difficult to achieve. Bias resulting from lack of blinding can be minimized by using objective outcomes whenever feasible[13] and by involving a second team of surgeons.

In conclusion, the clamp–crush technique is more rapid and is associated with lower blood loss than other methods of parenchymal transection; it thus remains the reference standard against which new methods may be compared. There is an ongoing need for high-quality, randomized controlled trials, with sufficient sample sizes and factorial designs, to identify the effects of confounding factors, such as the method of vascular occlusion, quality of parenchyma resected (cirrhotic/post-chemotherapy), low central venous pressure, hypoventilation and methods of dealing with the cut surface of liver (e.g. tissue glue).

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Conflicts of interest

None declared.

References

1. Shimada M, Takenaka K, Fujiwara Y, Gion T, Shirabe K, Yanaga K *et al.* (1998) Risk factors linked to postoperative morbidity in patients with hepatocellular carcinoma. *Br J Surg* 85:195–198.
2. Yoshimura Y, Kubo S, Shirata K, Hirohashi K, Tanaka H, Shuto T *et al.* (2004) Risk factors for postoperative delirium after liver resection for hepatocellular carcinoma. *World J Surg* 28:982–986.
3. Ibrahim S, Chen CL, Lin CC, Yang CH, Wang CC, Wang SH *et al.* (2006) Intraoperative blood loss is a risk factor for complications in donors after living donor hepatectomy. *Liver Transpl* 12:950–957.
4. Wang WD, Liang LJ, Huang XQ, Yin XY. (2006) Low central venous pressure reduces blood loss in hepatectomy. *World J Gastroenterol* 12:935–939.
5. Hasegawa K, Takayama T, Orii R, Sano K, Sugawara Y, Imamura H *et al.* (2002) Effect of hypoventilation on bleeding during hepatic resection: a randomized controlled trial. *Arch Surg* 137:311–315.
6. Belghiti J, Noun R, Zante E, Ballet T, Sauvanet A. (1996) Portal triad clamping or hepatic vascular exclusion for major liver resection. A controlled study. *Ann Surg* 224:155–161.
7. Belghiti J, Noun R, Malafosse R, Jagot P, Sauvanet A, Pierangeli F *et al.* (1999) Continuous vs. intermittent portal triad clamping for liver resection: a controlled study. *Ann Surg* 229:369–375.
8. Rui JA, Wang SB, Chen SG, Zhou L. (2003) Right trisectionectomy for primary liver cancer. *World J Gastroenterol* 9:706–709.
9. Smyrniotis VE, Kostopanagiotou GG, Gamaletsos EL, Vassiliou JG, Voros DC, Fotopoulos AC *et al.* (2002) Total vs. selective hepatic vascular exclusion in major liver resections. *Am J Surg* 183:173–178.
10. Smyrniotis V, Arkadopoulos N, Kostopanagiotou G, Farantos C, Vassiliou J, Contis J *et al.* (2005) Sharp liver transection vs. clamp crushing technique in liver resections: a prospective study. *Surgery* 137:306–311.
11. Arita J, Hasegawa K, Kokudo N, Sano K, Sugawara Y, Makuuchi M. (2005) Randomized clinical trial of the effect of a saline-linked radiofrequency coagulator on blood loss during hepatic resection. *Br J Surg* 92:954–959.
12. Koo BN, Kil HK, Choi JS, Kim JY, Chun DH, Hong YW. (2005) Hepatic resection by the Cavitron ultrasonic surgical aspirator increases the incidence and severity of venous air embolism. *Anesth Anal* 101:966–970.
13. Lesurtel M, Selzner M, Petrowsky H, McCormack L, Clavien PA. (2005) How should transection of the liver be performed? A prospective randomized study in 100 consecutive patients: comparing four different transection strategies. *Ann Surg* 242:814–823.
14. Lupo L, Gallerani A, Panzera P, Tandoi F, Di Palma G, Memeo V. (2007) Randomized clinical trial of radiofrequency-assisted vs. clamp-crushing liver resection. *Br J Surg* 94:287–291.
15. Rau HG, Wichmann MW, Schinkel S, Buttler E, Pickelmann S, Schauer R *et al.* (2001) Surgical techniques in hepatic resections: ultrasonic aspirator vs. Jet-Cutter. A prospective randomized clinical trial. *Zentralbl Chir* 126:586–590.
16. Takayama T, Makuuchi M, Kubota K, Harihara Y, Hui AM, Sano K *et al.* (2001) Randomized comparison of ultrasonic vs. clamp transection of the liver. *Arch Surg* 136:922–928.
17. Rau HG, Meyer G, Jauch KW, Cohnert TU, Buttler E, Schildberg FW. (1996) Liver resection with the water jet: conventional and laparoscopic surgery. *Chirurg* 67:546–551.
18. Gluud C, Nikolova D, Klingenberg SL, Whitfield K, Alexakis N, Als-Nielsen B *et al.* (2008) Cochrane Hepato-Biliary Group. About the Cochrane Collaboration Cochrane Review Groups. Issue 4. Art. No.: LIVER.
19. Royle P, Milne R. (2003) Literature searching for randomized controlled trials used in Cochrane reviews: rapid vs. exhaustive searches. *Int J Technol Assess Health Care* 19:591–603.
20. Higgins JPT, Green S, eds. (2008) *Cochrane Handbook for Systematic Reviews of Intervention 5.0.0*. [Updated February 2008.] The Cochrane Colloboration. http://www.cochrane-handbook.org. [Accessed 15 March 2008].

21. Schulz KF, Chalmers I, Hayes RJ, Altman DG. (1995) Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 273:408–412.

22. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M *et al.* (1998) Does the quality of reports of randomized trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 352:609–613.

23. Kjaergard LL, Villumsen J, Gluud C. (2001) Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 135:982–989.

24. Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman GD *et al.* (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 336:601–605.

25. Cochrane Collaboration. (2008) *Review Manager (RevMan)*. [Computer program.] Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration.

26. DeMets DL. (1987) Methods for combining randomized clinical trials: strengths and limitations. *Stat Med* 6:341–350.

27. DerSimonian R, Laird N. (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188.

28. Higgins JPT, Thompson SG. (2002) Quantifying heterogeneity in a meta-analysis. *Stat Med* 21:1539–1558.

29. Newell DJ. (1992) Intention-to-treat analysis: implications for quantitative and qualitative research. *Int J Epidemiol* 21:837–841.

30. Sweeting MJ, Sutton AJ, Lambert PC. (2004) What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 23:1351–1375.

31. Asiyanbola B, Chang D, Gleisner AL, Nathan H, Choti MA, Schulick RD *et al.* (2008) Operative mortality after hepatic resection: are literature-based rates broadly applicable? *J Gastrointest Surg* 12:842–851.

32. Gurusamy KS, Kumar Y, Sharma D, Davidson BR. (2007) Methods of vascular occlusion for elective liver resections. *Cochrane Database Syst Rev* 17:CD006409.