

Is laparoscopic hepatectomy superior to open hepatectomy for hepatocellular carcinoma?

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Author contributions: Zhong JH and Peng NF contributed equally to this work; Zhong JH and Zheng MH designed the study and wrote the manuscript; all authors reviewed the manuscript and approved publication.

Conflict-of-interest statement: The authors declare no conflicts of interest regarding this manuscript.

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Manuscript source: Invited manuscript

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Received: August 30, 2016

Peer-review started: September 1, 2016

First decision: September 29, 2016

Revised: October 21, 2016

Accepted: December 7, 2016

Article in press: December 9, 2016

Published online: February 8, 2017

Abstract

The low perioperative morbidity and shorter hospital stay associated with laparoscopic hepatectomy have made it an often-used option at many liver centers, despite the fact that many patients with hepatocellular carcinoma have cirrhosis, which makes the procedure more difficult and dangerous. Type of surgical procedure proves not to be a primary risk factor for poor outcomes after hepatic resection for hepatocellular carcinoma, the available evidence clearly shows that laparoscopic hepatectomy is an effective alternative to the open procedure for patients with early-stage hepatocellular carcinoma, even in the presence of cirrhosis. Whether the same is true for patients with intermediate or advanced disease is less clear, since laparoscopic major hepatectomy remains a technically demanding procedure.

Key words: Hepatocellular carcinoma; Laparoscopic hepatectomy; Open hepatectomy

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Core tip: Type of surgical procedure proves not to be a primary risk factor for poor outcomes after hepatic resection for hepatocellular carcinoma, the available evidence clearly shows that laparoscopic hepatectomy is an effective alternative to the open procedure for patients with early-stage hepatocellular carcinoma, even in the presence of cirrhosis.

Zhong JH, Peng NF, Gu JH, Zheng MH, Li LQ. Is laparoscopic hepatectomy superior to open hepatectomy for hepatocellular carcinoma? *World J Hepatol* 2017; 9(4): 167-170 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v9/i4/167.htm> DOI: <http://dx.doi.org/10.4254/wjh.v9.i4.167>

Table 1 Propensity score studies comparing open and laparoscopic liver resection for hepatocellular carcinoma

Ref.	Country	Included period	Open/laparoscopic					P value	
			Sample size, n	Minor hepatectomy, %	Single tumor, %	Perioperative morbidity, %, P value	Perioperative mortality, %, P value	Overall survival	Disease free survival
Ahn <i>et al</i> ^[12]	South Korea	2005-2013	51/51	94/96	100/100	9.8/5.9, 0.470	0/0, 1.000	0.173	0.519
Cheung <i>et al</i> ^[11]	China	2002-2015	330/110	88/90	89/91	4.8/1.8, 0.266 ¹	1.8/0, 0.342	0.033	0.141
Han <i>et al</i> ^[13]	South Korea	2004-2013	88/88	68/65	80/76	20.4/12.5, 0.042	1.1/1.1, 1.000	0.944	0.944
Han <i>et al</i> ^[14]	South Korea	2002-2012	198/99	85/84	87/93	24.7/13.1, 0.020	-	0.086	0.701
Kim <i>et al</i> ^[15]	South Korea	2000-2012	29/29	100/100	83/97	13.8/37.9, 0.018	-	0.267	0.929
Meguro <i>et al</i> ^[17]	Japan	2003-2011	35/35	-	83/80	25.7/25.7, 1.000	-	0.672	0.954
Sposito <i>et al</i> ^[20]	Italy	2006-2013	43/43	100/100	81/86	48.8/18.6, 0.004	0/0, 1.000	0.802	0.990
Takahara <i>et al</i> ^[18]	Japan	2000-2010	387/387	79/77	-	13.0/6.7, 0.003	1.0/0.3, 0.178	0.358	0.422
Tanaka <i>et al</i> ^[19]	Japan	2007-2014	20/20	-	85/90	45.0/0, 0.001	0/0, 1.000	0.606	0.533
Yoon <i>et al</i> ^[16]	South Korea	2007-2011	174/58	88/93	100/100	22.4/6.9, 0.020	-	0.480	0.31

¹With complication of Clavien-Dindo grade IIIA or above.

Recently, a large propensity score study comparing laparoscopic and open hepatectomy for treating hepatocellular carcinoma (HCC) was published in *Ann Surg*^[1]. This parallel comparison comes at an important time, because technical and procedural improvements have led to increasing use of laparoscopic hepatectomy, including for more extensive hepatectomy and particularly in cases of left lateral sectionectomy^[2]. In fact, the low perioperative morbidity and shorter hospital stay associated with laparoscopic hepatectomy have made it an often-used option at many liver centers^[3-8], despite the fact that many patients with HCC have cirrhosis, which makes the procedure more difficult and dangerous. The long-term benefits of laparoscopic hepatectomy remain controversial, and this study^[1] provides the first evidence that it is associated with better long-term overall survival (OS) than open hepatectomy ($P = 0.033$).

Our own clinical experience and evidence in the literature suggest that mortality risk following liver resection depends primarily not on the type of surgical procedure but on tumor-related factors^[9-11]. In order to examine this possibility in more detail, we reviewed all randomized controlled trials and other studies involving propensity score analysis comparing laparoscopic and open hepatectomy published in 2014-2016. We identified 10 studies involving 2275 patients, comprising one from China^[1], five from South Korea^[12-16], three from Japan^[17-19], and one from Italy^[20] (Table 1). Across these 10 studies, 90% of patients had single tumors and 84% underwent minor hepatectomy. This means that most patients had early-stage HCC and surgical procedures were relatively straight forward. In 7 of 10 studies (accounting for 73% of all patients), laparoscopic hepatectomy was associated with a significantly lower rate of perioperative morbidity. None of the studies found significant differences in perioperative mortality or disease-free survival (DFS) between the laparoscopic and open procedures. Eight of the 10 studies (accounting for 86% of all patients) reported 5-year OS and DFS^[1,12-15,17-19]. Meta-analyses based on these eight studies revealed that patients in the laparoscopic group had significantly higher 5-year OS than those in the open group [risk ratio (RR) = 0.91,

95% confidence interval (95%CI): 0.86-0.95, $P < 0.001$; $I^2 = 39\%$; Figure 1A], but similar 5-year DFS (RR = 0.96, 95%CI: 0.87-1.06, $P = 0.440$; $I^2 = 0\%$; Figure 1B). Similar results were obtained when the study by Cheung *et al*^[11] was excluded.

Thus, substantial evidence suggests that laparoscopic hepatectomy is associated with significantly better long-term OS than open hepatectomy. It is possible that this reflects less tissue manipulation - and therefore less hematogenous dissemination of malignant tumor cells - in "no-touch" anterior-approach laparoscopic hepatectomy^[1]. However, the two techniques were associated with similar DFS, indicating similar rates of tumor recurrence, which is the main cause of death among HCC patients. In fact, patients in the two groups across all 10 studies showed similar tumor characteristics, including diameter, number, vascular invasion, and New Edmondson grade. Since these characteristics are the main risk factors of tumor recurrence, the available evidence appears to be consistent with the idea that mortality risk following liver resection depends on tumor-related factors and not on type of surgical procedure.

To examine this hypothesis rigorously, at least two questions must be answered. One is whether differences in blood loss and surgical complexity may help explain the difference in OS. Six of the 10 studies^[1,13,16-19] reported significantly less blood loss in the laparoscopic group, yet the studies did not report whether tumors were close to the hepatic vein or portal hepatis, which would make the surgery more complex and increase risk of blood loss. Another question is whether economic differences may help explain the OS difference. Since laparoscopic hepatectomy costs substantially more than open hepatectomy, it stands to reason that patients opting for the laparoscopic procedure may be in a better financial position. This raises the possibility that such patients also receive better postoperative therapies, such as antiviral therapy, liver-protecting therapy, and/or psychological intervention. Such patients may also receive more extensive and/or more aggressive therapy after tumor recurrence. All these factors may explain the observed long-term OS advantage of laparoscopic hepatectomy

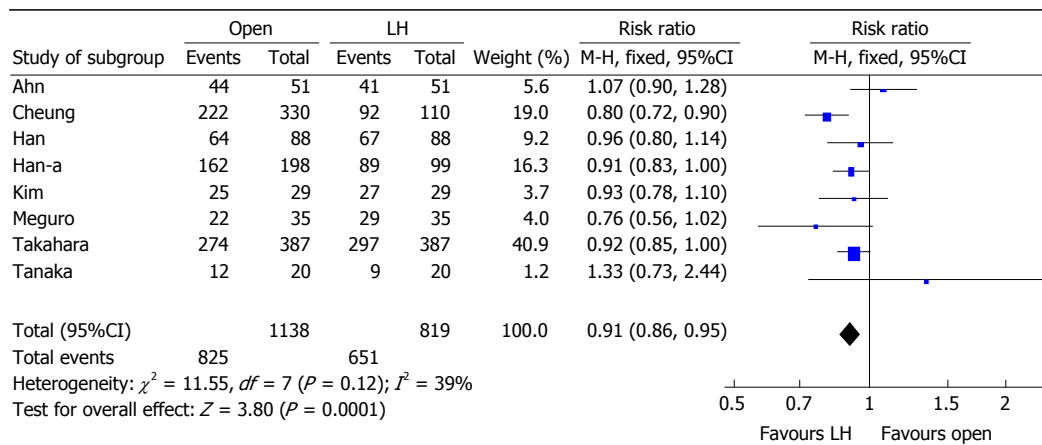
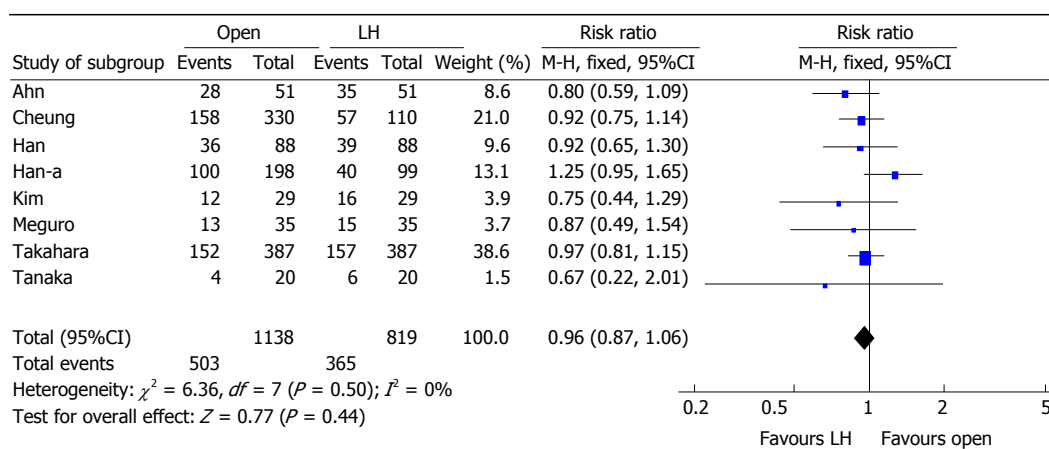
A**B**

Figure 1 Forest plots of meta-analysis comparing the efficacy of laparoscopic with open hepatectomy. A: Rate of 5-year overall survival; **B:** Rate of 5-year disease-free survival. LH: Laparoscopic hepatectomy.

over open hepatectomy. Therefore, assessing the long-term impact of this procedure requires large randomized controlled trials that take surgical complexity and patient financial condition into account. At least, comparative studies with propensity score analysis should adjust surgical complexity and financial condition between groups.

Even if, as we suspect, type of surgical procedure proves not to be a primary risk factor for poor outcomes after resection, the available evidence clearly shows that laparoscopic hepatectomy is an effective alternative to the open procedure for patients with early-stage HCC, even in the presence of cirrhosis. Whether the same is true for patients with intermediate or advanced disease is less clear, since laparoscopic major hepatectomy remains a technically demanding procedure. Even so, we agree that laparoscopic hepatectomy is an alternative choice for treatment of HCC.

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P- Reviewer: Kao JT, Yang T S- Editor: Qiu S L- Editor: A
E- Editor: Li D





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