RESEARCH COMMUNICATION

Recurrence after Anatomic Resection Versus Nonanatomic Resection for Hepatocellular Carcinoma: A Meta-analysis

JZ Ye[1], ZG Miao[1], FX Wu[1], YN Zhao[2], HH Ye[3], LQ Li[4]*

Abstract

The impact of anatomic resection (AR) as compared to non-anatomic resection (NAR) for hepatocellular carcinoma (HCC) as a factor for preventing intra-hepatic and local recurrence after the initial surgical procedure remains controversial. A systematic review and meta-analysis of nonrandomized trials comparing anatomic resection with non-anatomic resection for HCC published from 1990 to 2010 in PubMed and Medline, Cochrane Library, Embase, and Science Citation Index were therefore performed. Intra-hepatic recurrence, including early and late, and local recurrence were considered as primary outcomes. As secondary outcomes, 5 year survival and 5 year disease-free survival were considered. Pooled effects were calculated utilizing either fixed effects or random effects models. Eleven non-randomized studies including 1,576 patients were identified and analyzed, with 810 patients in the AR group and 766 in the NAR group. Patients in the AR group were characterized by lower prevalence of cirrhosis, more favorable hepatic function, and larger tumor size and higher prevalence of macrovascular invasion compared with patients in the NAR group. Anatomic resection significantly reduced the risks of local recurrence and achieved a better 5 years disease-free survival. Also, anatomic resection was marginally effective for decreasing the early intra-hepatic recurrence. However, it was not advantageous in preventing late intra-hepatic recurrence compared with non-anatomic resection. No differences were found between AR and NAR with respect to postoperative morbidity, mortality, and hospitalization. Anatomic resection can be recommended as superior to non-anatomic resection in terms of reducing the risks of local recurrence, early intra-hepatic recurrence and achieving a better 5 year disease-free survival in HCC patients.

Keywords: Hepatocellular carcinoma - anatomic resection - non-anatomic resection - recurrence - survival - China

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Introduction

Hepatocellular carcinoma HCC) is fifth most frequent malignant tumor in the world and the third common cause of cancer related to a mortality of 500,000 deaths globally every year (Bosh et al., 1999; Kamangar et al., 2006). Since 2000, HCC was not just common in Asia and Africa, the incidence of HCC kept on increasing in the Western world (Parkin et al., 2001). It is an aggressive tumor that usually develops in a cirrhotic liver with limited functional reserve and the dissemination of chronic hepatitis B and C virus infections, without treatment leads to a short survival time after diagnosis (Llovet et al., 1999; Llovet et al., 2003). With advances in surgical techniques and perioperative care, hepatic resection is widely accepted as the first-line therapeutic option for most hepatocellular carcinoma (HCC) patients, improving the outcomes of hepatic resection for HCC with low operative morbidity and mortality (Torzilli et al., 1999; Poon et al., 2001; Taketomi et al., 2007). Nonetheless, the postoperative long-term survival remains unsatisfactory because of the high incidence rate of recurrence after surgical resection. Till 2010, intra-hepatic recurrences were the most common that it happened in about 36.8%-78% of HCC patients (Zhou et al., 2010).

With respect to intra-hepatic recurrence, macro-portal invasion and intra-hepatic metastasis were considered to be the most strongly risk factors affected the postoperative prognosis (Adachi et al., 1996; Vauthey et al., 2002; Park et al., 2006). Intra-hepatic metastasis via vascular invasion is a key factor of recurrence that malignant HCC cells influences prognosis of HCC via spreading through the portal vein and its branches (Nakashima et al., 1986; Yuki et al., 1990; Shirabe et al., 1991). According to the description by Makuuchi (Makuuchi et al., 1985), anatomic resection (AR), defined as the systematic removal of a hepatic segment or sub-segment, which is an entire union confined by tumor-bearing portal tributaries including a major branch of the portal vein and hepatic artery. Theoretically, AR along the portal tributary may be effective in eradicating the entire cancerous functional union, including the main solitary tumor, surgical margins, its possible satellites, nodules, and the high risk area of micro-portal invasion and intra-hepatic metastasis of HCC

*[1]Guangxi Tumor Institute & Affiliated Tumor Hospital of Guangxi Medical University, [2]Department of Hepato-Billiary Surgery, [3]Affiliated Minzu Hospital of Guangxi Medical University, [4]Affiliated Tumor Hospital of Guangxi Medical University *For correspondence: lilqchina@126.com*

(Regimbeau et al., 2002; Sakon et al., 2002; Shigeki et al., 2010), rather than just remove a portion of parenchyma behind, which is done with nonanatomic resection (NAR), providing more favorable prognosis with low local recurrence or preventing recurrence, and leading an ideal long-term survival of HCC patients. Although some authors have described the potential superiority of AR that may provide better overall survival and disease-free survival (Kosuge et al., 1993; Luiet et al., 1995; Fusteret et al., 1996; Imamura et al., 1999; Regimbeau et al., 2002; Hasegawa et al., 2005; Wakai et al., 2007), others have failed to detect and demonstrate the benefits (Suh et al., 2005; Yamashita et al., 2007) of preventing intra-hepatic and local recurrence. These studies are not completely consistent and are unable to acquire conclusion about the efficacy of these two types of liver resection. Hence, the superiority of preventing intra-hepatic and local recurrence of AR versus NAR is still controversial.

Therefore this meta-analysis of nonrandomized studies based on published studies aimed to evaluate the available evidence comparing the oncologic outcomes, clinical efficacy and safety of anatomic resection with nonanatomic resection performed as a primary treatment for HCC patients.

Materials and Methods

A systematic review was conducted to identify all relevant studies that compared prognosis (overall intra-hepatic recurrence, local recurrence, 5 years overall survival, and 5 years disease-free survival) of HCC patients after anatomic resection versus nonanatomic resection. The Pudmed, medline, Cochrane Library, Embase, Ovid, and Science Citation index for all the English studies published from January 1990 to April 2011 were systematically searched. The Mesh terms were "anatomic resection", "nonanatomic resection", "systematic resection", "limited resection", and "hepatocellular carcinoma". "Related articles" was used to broaden the research as possible as we can. Furthermore, the wildcard ("*") character was also used for truncated search. All the articles, studies, reports and relevant references were also identified via manual searching. Moreover, all abstracts and citations were reviewed.

Data extraction

Two reviewers (Ye JZ and Wu FX) independently extracted the following information from each study: 1. first author and year of publish; 2. study population characteristics; 3. study design, inclusion and exclusion criteria; 4. number of subjects operated on each type of resection technique and follow-up; 5. therapy prognosis, overall intra-hepatic recurrence, early intra-hepatic recurrence, late intra-hepatic recurrence, local recurrence, and all of other relevant data, text, tables, figures. To avoid the inaccuracy of extraction and minimize subjective errors, discrepancies between the two reviewers were resolved through discussion and consensus.

Inclusion

All included studies in this meta-analysis must fulfill the criteria as below:

1. Compared the two techniques of liver resections of AR with NAR for the HCC patients, regardless of the differences in viral hepatitis, cirrhotics, or other liver diseases.
2. Reported on at least one of the prognosis (local intra-hepatic recurrence, overall survival, and disease-free survival, or other outcomes of therapy) for a special period after liver resection.
3. Clearly document indications for both AR and NAR.
4. Two or more studies were reported by the same institution and/or author, either one of higher quality or the most recent publication.

Exclusion

Any studies or reports would be excluded if it failed to fulfill the criteria as below:

1. Non-comparative studies and reports, including abstracts, letters, editorials, expert opinions, cases, review without original data, were excluded.
2. Those studies of comparison between AR and NAR were not clearly reported were excluded.
3. Those studies of cholangiocellular carcinoma or liver metastases patients were excluded.
4. Those studies it was impossible to extract or calculate appropriate data from the published results were excluded.

Outcome of interest

The primary outcomes were intra-hepatic and local recurrence. According to the time of recurrence, early or late intra-hepatic recurrence was defined as recurrence within or after 2 years after the initial liver resection (Shirabe et al., 1991; Takayama et al., 2000; Imamura et al., 2003). Regarding the site of recurrence, recurrence in the remnant liver was classified as marginal recurrence, recurrence in the same segment, recurrence in the same section, recurrence in the same hemiliver, recurrence in a distal segment, and multisegmental recurrence. Recurrence was defined as local when it arose in the same section as that where the primary tumor had been located (Regimbeau et al., 2002; Kobayashi et al., 2008). Regimbeau All cases of intra-hepatic recurrence, either early or late recurrence, and local recurrence were the primary interests of this study. Secondary outcomes were 5 years overall survival (which is defined as time since the first liver resection till death or last follow-up) and 5 years disease-free survival (which is defined as time since the first liver resection till diagnosis of tumor recurrence or last follow-up). Moreover, morbidity, mortality and other patients' characteristics were also evaluated.

Statistical methods

The meta-analysis was performed by applying the Review Manager (Revman) software, version 5.0. We analyzed dichotoucous variable by odds ration (OR) with a 95% confidence interval (95% CI) and continuous variables by weight mean difference (WMD) with a 95% CI. This ration represents the odds of an outcome event occurring in the AR group compared with NAR group.

Overall OR was analyzed by utilizing either fixed-effects model or random-effects model. Fixed-effects

Table 1. Baseline Characteristics of Studies Included in the Meta-analysis

Author (year)	Country	Inclusion criteria	Group	No. of patients	M/F	Mean age (years)	ICG15%	cirrhosis	Child-Pugh A/B+C	HBsAg and/or HCVA[b]	Tumor size (cm²)	Macrovascular invasion (yes/no)
Regimbeau 2002	France	1.Cirrhosis 2.Solitary single tumor≤4cm	AR	30	6/24/12	60±11	-	30	30/0	18	3±1	9/21/12
		3.Resection margin > 1cm 4. Without Macrovascular invasion	NAR	34	7/27/12	61±9	-	34	34/0	25	3±1	8/26/12
Kaibori 2006	Japan	Positive for HCVAb and negative for HBsAg	AR	34	5/29/12	65.1±7.4	15.6±6.02	10	7/27/12	34	3.26±2.27	16/18
			NAR	213	163/50	65.9±7.2	20.34±9.52	115	130/83	213	4.06±2.07	61/152
Wakai 2007	Japan	pT1-T2 HCC	AR	95	69/26	66(29-80)	13.3(3-43)	44	Oct-85	78	3.5(1.12-17.0)	30/65
			NAR	63	45/18	64(35-79)	17.4(4.3-48)	42	49/14	48	3.0(1.0-12.0)	8/55
Tanaka 2008	Japan	Solitary tumor within two segments	AR	83	58/25	66(41-77)	13.4(4.5-37.9)	32	Feb-81	78	-	-
			NAR	42	Jul-35	65(41-80)	15.9(5.8-38.3)	22	Feb-40	36	-	-
Nanashima 2008	Japan	Solitary tumor within one segment	AR	49	Oct-39	65±9	-	19	-	49		-
		Without Macrovascular invasion	NAR	64	43/21	64±9	-	27	-	64		-
Kobayashi 2008	Japan	Solitary tumor	AR	103	75/31	65(21-83)	15(5-30)	25	102/4	91	3.0(1.1-14.0)	31/73
			NAR	127	93/34	67(33-88)	21(2-58)	69	112/15	117	2.8(1.0-14.5)	36/84
Tanaka 2009	Japan	Without Macrovascular invasion	AR	128	150/57[#]	-	-	-	186/21[#]	140[#]	<3cm 65	63/144
			NAR	79		-	-	-			≥3cm 142	
Yamazaki 2010	Japan	Solitary tumor≤5cm	AR	111	87/24	64.8±11.1	-	61	5.2±0.4[&]	98	3.1±0.9	93/18
			NAR	98	66/32	66±8.5	-	68	5.5±0.7[&]	82	2.7±1.1	76/22
Karim 2010	USA	Single HCC	AR	28	7/21/12	62.18±12.09	-	8	3/25/12	28	5.9±2.8	9/19/12
			NAR	25	7/18/12	57.4±11.06	-	10	5/20/12	25	4.1±1.7	7/18/12
Arii S 2010	Japan	Without Macrovascular invasion	AR	128	150/57[#]	-	-	-	186/21[#]	140[#]	ns	ns
			NAR	79		-	-	-				
Chang Moo Kang 2010	Korea	Cirrhosis	AR	146	8/13/12	51.2±9.8	11.9±10.2	16	-	-	2.9±0.9	2/19/12
		Solitary single tumor≤4cm	NAR	21	112/34	52.3±9.8	10.2±9.9	80	-	-	2.8±0.8	22/124

AR, anatomic resection; NAR, nonanatomic resection; ICG15, indocyanin green retention rate at 15 min; M, male; F, female; HBsAb, Hepatitis B surface antigen; HCVAb, Hepatitis C virus anti-body; [#]total number of two groups; [&]Child-Pugh score

Table 2. Baseline Characteristics of Patients

variables	No. of studies furnishing data	Results AR	Results NAR	OR/WMD/95%CI	P
Cirrhosis	9(18,25,30,34,36-40)	39.30%	55.90%	0.46 (0.34,0.63)	P<0.0001
Child-Pugh A/B+C	9(17-18,25,30,35-36,38-40)	86.10%	71.50%	2.15 (1.26,3.66)	P=0.005
ICG15%	5(25,30,34,36,40)	14.97+/-7.96	19.61+/-8.45	-5.77 (-6.04,-5.51)	P<0.001
Hepatitis virus infection (HBV+HCV)	10(17-18,25,30,35-40)	85.20%	84.60%	1.04 (0.64,1.70)	P=0.88
Tumor size	10(17-18,25,30,34,35,37-40)	3.41+/-0.37	3.15+/-0.22	0.34 (0.18,0.40)	P=0.031
Macrovascular invasion	8(18,25,30,34,35,38-40)	46.50%	35%	1.58 (1.12,2.23)	P=0.009

AR, anatomic resection; NAR, nonanatomic resection; ICG15, indocyanin green retention rate at 15 min; HBsAg hepatitis B virus santigen; HCVAb anti-hepatitis C virus antibody

model was used if heterogeneity isn't exit, which meant there was no variance among studies and reports, and we can assume that all of the studies come from the same population. While any heterogeneity was detected, the random-effects model would be utilized instead of fixed-effects model. This model supposed that a random group of studies were selected from all the pooled studies. Therefore, this random group of studies results in wider CI than fixed-effects model. DerSimonian and Laird methods was applied to calculate the random-effects model, including both within-study and between-study variation (DerSimonian et al., 1981). Cochran's chi-squared test was used to assess the statistical heterogeneity among studies. χ^2 and I^2 were used to estimate the heterogeneity. When the I^2 >50% or P<0.05, heterogeneity was considered to be significant.

Assessment of the quality of the study

The quality of studies was assessed by the Newcastle-Ottawa Scale (NOS) with some modifications to match the needs of this study (Wells et al., 2005), and was evaluated by three factors: patient selection, comparability of AR group with NAR group, and evaluation of prognosis.

Results

Selection of studies

Twenty-three relevant studies were systematically searched. 12 studies were excluded: 11 studies didn't provide comparative data between AR and NAR; one study (Takano et al., 2009) focused on comparative data on different types of liver resection. Studies conducted by Tanaka et al. (2009) and Arii et al (Shigeki et al., 2010) were published by the same research team with overlapping study populations. Finally, a total of 11 retrospective and nonrandomized studies comparing the recurrence after AR versus NAR published from 2002 to 2010 matched the selection criteria and were included in this meta-analysis (Regimbeau et al., 2002; Wakai et al., 2007; Kobayashi et al., 2008; Tanaka et al., 2009; Shigeki et al., 2010).

Patient characteristic

Eleven studies included in the meta-analysis were reasonably conducted. None of the studies was randomized control trial (RCT). Analysis was performed on a total of 1,576 patients: 810 patients in the AR group and 766 patients in the NAR group. The sample size of each study differed from 53 to 247 patients. Characteristics of each study are shown in the Table 1.

With respect to patients' characteristics, The Table 2 shows the significant differences between the AR group and NAR group. No significant differences of the mean age and the proportion of the male patients between AR group and NAR group. Patients in the AR group were characterized by lower prevalence of cirrhosis (OR 0.46; 95% CI-0.34, 0.63; P<0.0001), more favorable liver function reserve (OR -5.77; 95% CI-6.04, -5.51; P<0.0001), larger tumor size (OR 0.34; 95% CI-0.18, 0.40; P=0.031), and higher prevalence of macrovascular invasion (OR 1.58; 95% CI-1.12, 2.23; P=0.009) compared with the patients in NAR group.

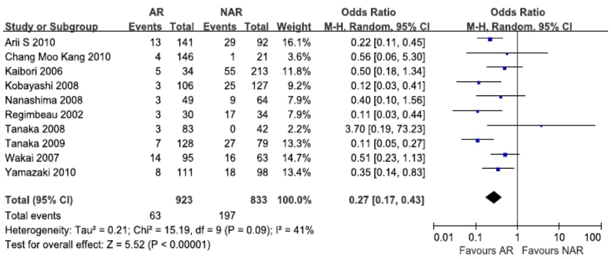

Figure 1. Results of the Meta-analysis on Local Intra-Hepatic Recurrence

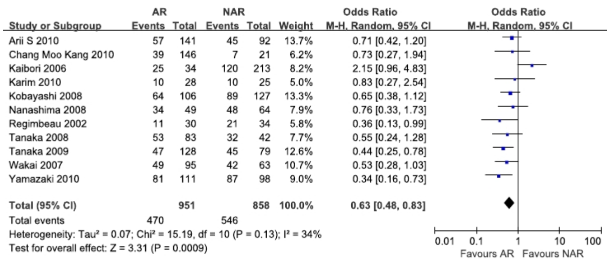

Figure 2. Results of the Meta-analysis on Overall Intra-hepatic Recurrence

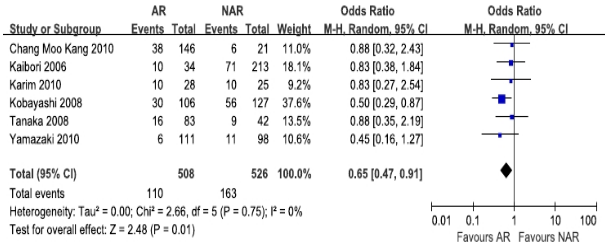

Figure 3. Results of the Meta-analysis on Early Intra-hepatic Recurrence

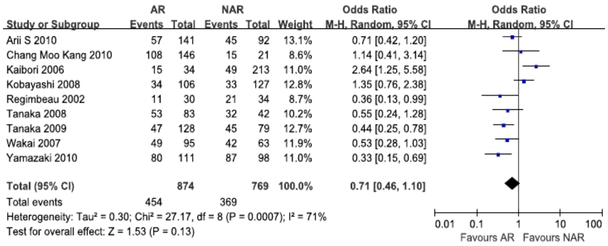

Figure 4. Results of the Meta-analysis on Late Intra-hepatic Recurrence

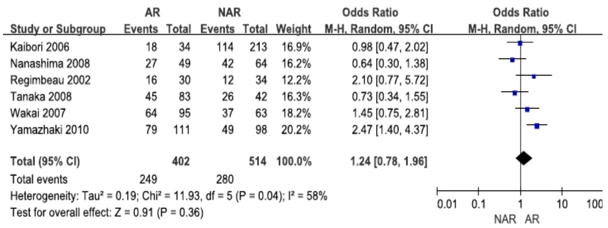

Figure 5. Results of the Meta-analysis on 5 Years Overall Survival

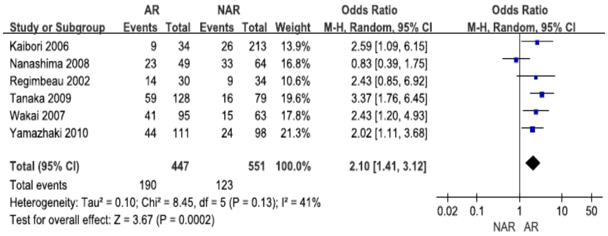

Figure 6. Results of the Meta-analysis on 5 Years Disease-free Survival

There was heterogeneity among the studies: different oncologic characteristics (tumor size, cirrhosis, macroportal invasion); different liver function reserve; and different duration of follow-up varied from study to study. Sometimes the follow-up time differed from individual to individual in the same study. Although the random effects model was applied instead of fixed effect model, the differences still might affect the respective studies and contribute to intra-study heterogeneity in this meta-analysis.

Mata-analysis of efficacy

Intra-hepatic recurrence including early (≤2 years) and late (>2 years) recurrence, and local recurrence were the primary end points. The pooled analysis of 11 studies providing data shows that local intra-hepatic recurrence was significantly reduced after anatomic resection compared with non-anatomic resection (OR 0.27; 95% CI-0.17, 0.43; P<0.00001) (Figure 1). Overall intra-hepatic recurrence (OR 0.63; 95% CI-0.48, 0.83; P=0.0009) (Figure 2) and early intra-hepatic recurrence (OR 0.65; 95% CI-0.47, 0.91; P=0.01) (Figure 3) were marginally lower in the AR group than that in NAR group. No difference of late intra-hepatic recurrence was found between AR group and NAR group (OR 0.71; 95% CI-0.46, 1.10; P=0.13) (Figure 4).

Regarding to overall survival and disease-free survival, six studies shows AR did not achieved a better 5 years overall survival significantly (OR 1.24; 95% CI-0.78, 1.96; P=0.36) (Figure 5). However, six studies shows AR improved the disease-free survival significantly at 5 years (OR 2.10; 95% CI-1.41, 3.12; P=0.0002) (Figure 6).

Mata-analysis of safety

Seven studies reported the overall postoperative morbidity and mortality (Table 2). Overall postoperative morbidity and mortality were described in 29.9% and 2% of patients who underwent anatomic resection, compared 30.7% and 2.2% of patients who underwent nonanatomic resection. No significant differences of overall postoperative morbidity (OR 0.92; 95% CI-0.66, 1.28; P=0.62) and mortality (OR 0.90; 95% CI-0.31, 2.59; P=0.84) were found between AR group and NAR group. Moreover, there was No significant difference of the length of hospitalization between AR group and NAR group (Table 2).

Discussion

The results of this meta-analysis show that anatomic resection significantly reduced the risk of local recurrence in patients with HCC after the initial surgical procedure compared with nonanatomic resection. Overall intra-hepatic recurrence and early intra-hepatic recurrence were slightly decreased after anatomic resection versus nonanatomic resection. It is noted that patients in AR group were characterized by lower prevalence of cirrhosis, larger tumor size, more favorable liver function reserve, and higher prevalence of macrovascular invasion. Moreover, anatomic resection improved 5 years disease-free survival significantly. However, AR did not provide a better overall survival at 5 years and reduce the late intra-hepatic recurrence. No statistical differences of morbidity, mortality and the length of hospital stay were found between AR group and NAR group. In view of these included studies were retrospective, we should analyze the results carefully.

Hepatic resection is the valid first-line therapeutic option and potentially curative treatment for HCC patients. Despite the intricate correlations of liver cancer and underlying liver diseases in most patients, a considerable portion of them still can undergo safe hepatic resection with good oncologic results and low morbidity (Fan et al., 1999). However, a high rate of intra-hepatic recurrence after surgical procedure led to late death of HCC patients that the long-term survival remains unsatisfactory (Fan et al., 2010). Intra-hepatic metastasis and macroinvasion were considered to be the strongly risk factors lead to postoperative recurrence (Adachi et al., 1996; Vauthey et al., 2002; Park et al., 2006). Either intra-hepatic metastasis from the primary tumor or a de novo multicentric tumor can cause intra-hepatic recurrence (Poon et al., 2001). Residential intra-hepatic metastasis from HCC spreading through the portal vein and its branches, which could not be detected before and during surgery (Kobayashi et al., 2008), is the key factor of local recurrence (Nakashima et al., 1986; Yuki et al., 1990; Shirabe et al., 1991). Therefore, anatomic resection defined as systematic removal of a hepatic segment or subsegment confined by tumor-bearing portal tributaries, is theoretically effective for eradication of entire cancerous functional union, including the main solitary tumor, surgical margins, possible satellites, nodules, the high risks area of intra-hepatic metastasis and micro-portal invasion of HCC (Regimbeau et al., 2002; Sakon et al., 2002; Shigeki et al., 2010). The fact that in this current study, local recurrence and overall intra-hepatic recurrence were found to be infrequent after AR than NAR, indicating that AR is effective for eradicating the intra-hepatic metastasis by resecti time of recurrence occurred after the initial surgical procedure, recurrences were classified into early (≤2 years) and late (>2years) intra-hepatic recurrence (Shirabe et al., 1991; Takayama et al., 2000; Imamura et al., 2003). The current study also suggested that anatomic resection significantly reduced the risk of early intra-hepatic recurrence compared with nonanatomic resection. This finding is in accordance with the theory that intra-hepatic metastasis spreading through the portal vein and its branches is the main route of early intra-hepatic recurrence (Poon et al., 2009).

Via clinical observation and evaluation, different background characteristics of patients in AR group and NAR group, especially the tumor features and preservation of hepatic function, might affect the oncologic results. Wakai et al. (2007) reported that anatomic resection can provide a better 5 years disease-free survival and reduce the intra-hepatic recurrence for HCC (pT1 or T2). Hence, patients with pT1-T2 HCC seemed to be fit for anatomic resection. Regimbeau et al. (2002) suggested that anatomic resection achieved a better 5 years disease-free survival and lower risk of local recurrence than nonanatomic resection without increasing the postoperative morbidity and mortality in patients with small HCC. Thus, patients with small HCC seemed to be good candidate for anatomic resection. Although Tanaka et al. (2009) and Arii et al. (Shigeki et al., 2010) overlapped the population, both of them certified that AR significantly reduced the risk of local recurrence in patients without macrovascular invasion. Their findings demonstrated that anatomic resection should be the first choice of HCC without macrovascular invasion. Yamazaki et al. (2010) found that anatomic resection significantly decreased the risk of local recurrence and late intra-hepatic recurrence with providing a better 5 years disease-free survival in patients with solitary tumors which diameters were no longer than 5 cm. Also, early intra-hepatic recurrence was slightly lower after AR versus NAR. AR seemed to be recommended prior to NAR for HCC with solitary tumors which diameters were no longer than 5 cm. However, Nanashima et al. (2008) reported that in his study the patients were high selection of solitary tumors located within one segment and no macroscopic venous invasion occurred. Although patients in the AR group were characterized by larger tumor size, no differences of early intra-hepatic recurrence, late intra-hepatic recurrence, local recurrence and 5 years disease-free survival were found between AR group and NAR group. Thus, when HCC just located within one segment without macrovascular invasion, AR was not supposed to be superior to NAR. Furthermore, Kaibori et al. (2006) pointed that central tumors which were near the liver hilum or major vessels should be resected by nonanatomic resection rather than anatomic resection, because it was too hard to obtain an adequate margin.

It is noted that heterogeneity was exited among the involved studies, in terms of factors such as tumor features, hepatic function, and degree of fibrosis of the noncancerous parenchyma. Besides anatomic resection would be superior from the standpoint of eradication of intra-hepatic metastasis, the patients in AR group might partly be due to a high selection of lower prevalence of cirrhosis and well-preserved liver function. However, HCC patients in NAR group may have more extensive disease that a more conservative resection was applied to preserve liver parenchyma. This might be the reason why anatomic resection achieved a better 5 years disease-free survival. Although 5 years disease-free survival was found marginally longer after anatomic resection compared with nonanatomic resection in this study, no statistical difference of 5 years overall survival was found between AR group and NAR group. Moreover, late intra-hepatic recurrence was not reduced after anatomic resection compared with nonanatomic resection. Regarding to intra-hepatic recurrence, multicentric recurrence of HCC after initial resection is another key factor other than intra-hepatic metastasis (Minagawa et al., 2003). This might be reasonable to describe why anatomic resection reduced early intra-hepatic recurrence but not late intra-hepatic recurrence. In addition, is anatomic resection decreased the remnant hepatic reserve that the adverse effects might be brought. Based on this concept, some surgeons chose nonanatomic resection as a safe and efficient surgical procedure instead of anatomic resection in HCC patients with inadequate or uncertain hepatic functional preservation.

Concerning to the surgical treatment of HCC, the balance between surgical curability and preservation of hepatic function is a key factor that influencing the long-term prognosis. HCC patients were usually underlying liver disease, such as chronic hepatitis infection and cirrhosis. In these individual studies, up to 100% of the HCC developed in underlying chronic hepatitis. The underlying chronic cirrhotic liver has a limited capacity to regenerate that the extent of resection might be limited because of the possibility of postoperative hepatic failure. Thus, the balance between surgical resectability and preservation of hepatic function must be taken into consideration when operative treatment would be given to HCC patients. In HCC patients with limited hepatic functional reserve, NAR with an adequate tumor-free margin is justified as an important method of resection that preserves as much liver parenchyma as possible to decrease possibility of postoperative hepatic failure.

However, the optimum extent of operative treatment of HCC patient remains controversial whether anatomic resection can reduce the late intra-hepatic recurrence and provide better long-term survival compared with non anatomic resection. When surgical treatment is considered to given patients with HCC, surgeons must extremely note to maintain enough preservation of hepatic function. Wide resection should be careful or restrict based on the preservation of hepatic function. It also leaves a chance of a repeat resection if HCC recurred. To reduce the risk of local recurrence and early intra-hepatic recurrence after the initial hepatic resection, anatomic resection has been recommended. However, the type of hepatectomy was not selected by a restrictive policy and the extent of resection was not totally decided according to a predetermined algorithm. When surgeons consider which type of hepatectomy will be given to HCC patients, oncologic characteristics, curability and the preservation of hepatic function would be comprehensive evaluated rather than choosing mechanically. How to balance the extent of the resection with the preservation of hepatic function is the key of operative treatment for HCC. Although anatomic resection should be performed to decrease the risk of local recurrence, intra-hepatic recurrence, and increase the 5 years disease-free survival, nonanatomic resection could be still considered as a safe and efficient type of resection when AR is not appropriate, especially for patients with inadequate hepatic functional reserve.

Meta-analysis, which includes several groups of compared data from randomized or nonrandomized clinical trials, might be used when controversy remains after several trials. Although randomized clinical trials (RCT) are traditionally utilized and best confined in meta-analysis, nonrandomized studies are still valid in some clinical studies when the number and sample size of RCTs are insufficient (Mathurin et al., 2003). This study as a meta-analysis still has some limitations that must be taken into consideration. First, the results of any meta-analysis are affected by the quality of the included individual studies. None of the involved studies in this meta-analysis are RCTs. Second, it was not impossible to match all patient groups for totally the same inclusion criteria, including tumor characteristics, preservation of hepatic function, and other factors known to affect results for HCC patients. Third, not all the studies provided comparable or extractable data on local recurrence, early or late recurrence, 5 years overall survival and 5 years disease-free survival. Fourth, it is necessary to note that the results might be affected by absence of stratification according to recognized prognostic indicators regard to tumor size and hepatic functional reserve. Fifth, heterogeneity was among the included studies; thus randomized effects model was applied instead of fixed effects model. However, it is impossible to figure out all the potential bias. Finally, the risk of publication bias was always existed, especially in meta-analysis based on published studies.

In conclusion, this meta-analysis suggested that anatomic resection significantly reduced the risks of local recurrence and achieved a better 5 years disease-free survival in the HCC patients compared with nonanatomic resection. Also, anatomic resection was effective of decreasing the early intra-hepatic recurrence marginally. However, anatomic resection was not advantageous in preventing late intra-hepatic recurrence compared with nonanatomic resection. Anatomic resection might be recommended as a safe and effective surgical procedure for patients with HCC, especially in those patients with small HCC or solitary tumor within one segment and without macrovascular invasion. However, nonantomic resection is considered as an alternative resection when anatomic resection is inappropriate to be performed, especially for patients with poor preservation of hepatic function. Substantial heterogeneity among the involved studies indicated that clinic oncologic features between AR group and NAR group were different. Better designed, more qualified studies are required to investigate the effect of hepatic resection on preventing the risk of recurrence for HCC.

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