

## ANSWERING REVIEWERS

**Reviewer's code:** 01560494

**1. The cases of the paper is less. There are a lot of the same papers on publishing.**

This paper is single center experience in middle east, with high incidence of liver cirrohsis

**2. The manuscript contains less new innovations or insight**

There are many areas of debate:

\*value of preoperative biliary drainage

\*value of caudate lobe resection

\*Impact of major hepatic resection on long term outcome

\*This study will add evidence of prognostic factors affecting long term outcome especially in middle east countries

**Reviewer's code:** 03254227

**1. In materials and methods authors stated that patients' recruitment was starting from 2002, in results from 1995. Dates should be corrected.**

Ok

**2. There is no mention for treatment protocol including liver transplantation; these should be added in discussion -**

OK

**3. No explication are reported to explain why age is a good prognostic factor.**

Five-year survivors were younger at diagnosis than those surviving less than 5 years with a mean age ( $50.47 \pm 4.45$  versus  $54.59 \pm 4.98$ ,  $P=0.001$ ). Because in young patient, surgeon can perform major resection and provide R0 in HCC

without medical or anesthetic restriction.

#### **4. Had these survivors patients a better survival because an earlier diagnosis?**

Univariate analysis demonstrated nine variables (Young age, serum CA19-9, non cirrhotic liver, major hepatic resection, resection of caudate lobe, well differentiated tumour, lymph node status, R0 resection margin and early postoperative LCF) to be significantly associated with long term survival > 5 years. These nine factors identified in univariate analysis were further analyzed in multivariate analysis. Liver status, resection of caudate lobe, Lymph node status, R0 resection and serum CA19-9 were demonstrated to be independent risk factors for long term survival.

**Reviewer's code: 02439777**

**1. The study period is between January 2002 and April 2013, which exceeds 11 years. Was caudate lobectomy performed during the initial stage of surgery? Also, how many surgeons performed surgery on the patients included in this study? Were there any differences in their methods of operation and preference?**

		< 5 years survival	> 5 years survival	p-value
Segment resection	1	79 (37.79 %)	23 (67.64 %)	0.006

As the caudate lobe is infiltrated by HC either directly due to the close anatomic relationship or by invading the biliary branches, routine caudate lobe resection should be performed for curative treatment of HC [15,29-31]. Better R0 resection rate and long term survival are achieved by caudate lobe resection in treating cases of HC [15, 29-34]. Nimura et al found that 98% of caudate lobe resection were pathologically confirmed to be tumour positive in

cases of HC [33]. However, other authors showed that the caudate lobe was infiltrated by HC in 25-40% of cases. Caudate lobe resection contributed to improvement of DFS and OS in type III hilar cholangiocarcinoma [15,33-35]. Segment 1 resection represents a significant factor affecting survival (P = 0.006) in our study. In the initial period of the study Caudate lobe resection was performed only when infiltrated, but now it is performed routinely in all cases of HC.

All surgeons performed surgery on the patients included in this study. All surgeons participated in the study are expertise hepatobiliary and pancreatic surgeon (at least doing more than 50 hepatobiliary and pancreatic surgeries and assists in more than 100 hepatobiliary and pancreatic surgeries). There were no any differences in their methods of operation and preference

**2. Was preoperative drainage performed for all patients? Was there an influence on the long-term outcome with respect to preoperative drainage?**

The role of preoperative biliary drainage (PBD) in the management of HC remains controversial. But, no evidence that routine PBD facilitate resection, decrease postoperative morbidity or increase survival rate[27-28]. Some studies concluded that biliary drainage is required in the following conditions, planned portal vein embolization because of inadequate liver remnant volume by CT volumetry. Although PBD didn't represent a significant factor affecting long term survival, it is mandatory in cases of preoperative cholangitis, bad general condition and it improves the postoperative course of patients with serum bilirubin level more than 20 mg/dL[15,26]. PTD may has potential risk of cholangitis or tumour seeding (kloek JJ et al 2010)

	< 5 years survival	> 5 years survival	p-value
Preoperative biliary drainage	209	34	
	90 (43.06)	18 (52.9%)	0.38

No preoperative biliary drainage	119 (66.94)	16 (47.1)	
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**3. What about the patients' TNM stage and bismuth type? Did they influence prognosis?**

	< 5 years survival	> 5 years survival	p-value
Bismuth corlette classification			
Type I, II	63 (30.14 %)	11 (32.35 %)	0.68
Type III	146 (69.85 %)	23 (67.64 %)	
Type IV	0	0	

**4. Hepatic recurrence occurred in two places with 51 and 8 patients, respectively. For patients with hepatic recurrence, a comparison should be made for types R0 and R1. Moreover, it would be recommendable to discuss whether the recurrence occurred only with the R1 type. The details regarding this issue should be described under Results.**

Safety Margin			
R0	93 (44.5%)	28 (82.35 %)	<0.0001
R1	116 (55.5 %)	6 (17.6 %)	
Recurrence			
Hepatic recurrence	51 (24.4 %)	8 (23.52 %)	0.88
* Local recurrence	27 (12.9 %)	6 (17.64 %)	

Hepatic recurrence occurred in 51 (24.4%) patients in < 5 years survival group, 40 of them (78.4%) had R1 while hepatic recurrence occurred in 8 (23.52%) patients in > 5 years survival group, 4 of them (50%) had R1

**5. The information in Figure 1 and Figure 2 is thoroughly described under Results. Therefore, it would be recommendable to delete these diagrams**

Ok