



Privileged indication of anatomical resection for the hepatocellular carcinoma with microportal invasion?

Koo Jeong Kang, Keun Soo Ahn

Division of Hepatobiliary & Pancreatic Surgery, Department of Surgery, Keimyung University, Dongsan Medical Center, Daegu, Republic of Korea
Correspondence to: Koo Jeong Kang, Department of Surgery, Keimyung University School of Medicine, Dongsan Medical Center, 56 Dalseong-ro, Jung-gu, Daegu, 700-712, Republic of Korea. Email: kjkang@dsmc.or.kr; kjkang415@gmail.com.

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Comment on: Hidaka M, Eguchi S, Okuda K, *et al.* Impact of Anatomical Resection for Hepatocellular Carcinoma With Microportal Invasion (vp1): A Multi-institutional Study by the Kyushu Study Group of Liver Surgery. *Ann Surg* 2018. [Epub ahead of print].

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We have read the article with special interest on the impact of anatomical resection (AR) for hepatocellular carcinoma with microportal invasion (vp1) reported by Hidaka *et al.*, (electronically published in July 2018) (1). Even though the study is retrospective analysis, the key message in their article by propensity score matched analysis is that the AR did not influenced on the recurrence free survival and overall survival.

Survival benefit of AR of the hepatocellular carcinoma has been paid attention by hepatic surgeons for recent three decades, initiated on the hypothesis that the tumor is spread via centrifugal direction of the portal venous flow, proposed by Dr. Makuuchi. Portal blood may flow back and forth when the liver parenchyma changed to be stiff and cirrhosis. So, there may be higher chance of tumor spread in the same territory of portal tributary as the hepatic parenchyma is changed to fibrotic or cirrhotic provoked by portal hypertension. Liver tumors are thought to invade the portal venous branches, allowing tumor cells to be carried to other regions of the liver in the portal venous flow. These disseminated tumor cells grow into microscopic tumor thrombi and then into daughter nodules (2). Therefore, according to this theory, resection of the entire hepatic segment of the tumor bearing portal tributary should be better in survival outcome, especially reduce local recurrence. However, although several literatures have been published regarding values of AR, the oncologic benefits of AR are still debated (3). Several studies including well

designed case control studies have shown no benefit for AR in terms of recurrence free survival (4–6). While a few article has shown positive result of AR (7,8), those results are criticized as the differences are confounded by case selection bias including underlying liver function and tumor factors.

Although proving the superiority of AR over NAR for oncologic benefits with overcoming several biases is difficult, we can overcome this limitation by focusing on the key points of concept of AR, microportal invasion. However surprisingly, no research has so far focused on it. In this aspect, the paper reported by Hidaka *et al* which selected the patients who has the tumor with microportal invasion, neither macroportal nor microvenal invasion, should be distinguished from other previous researches, even though it is a retrospective study and there remains a question about the surgical procedure is standardized among institutions.

We can expect that the selected group with microportal invasion might have higher chance of intrasegmental portal metastasis than the patients with microvascular invasion, the recurrence free survival rate of the AR group would be significantly better than non-anatomical resection (NAR). So, presence of microportal invasion (vp1) may be privileged indication of AR for the hepatocellular carcinoma. However, the result was out of our expectation. There was no survival benefit in overall or recurrence free survival in propensity score matched analysis, moreover in the simple comparison even though the AR group have

better liver function in comparison to the NAR group. At this point, we need to remind that the hypothesis of HCC being spread via centrifugal direction of the portal venous flow has not been proved yet. This theory was established on presence of microportal invasion in small HCC (<5 cm) (2). However, there has been no evidence showing microscopically invaded tumor thrombus grow into proximal portal branch and this paper could not show the validity of this hypothesis. Nevertheless, AR looks a kind of art and satisfying procedure for surgeon, while remaining questions whether it provide really best interest to the patients. Does AR really provide better oncologic results to patients?

Another interesting point of this paper is that subsegmentectomy showed significantly lower recurrence rate in the same segment in comparison to the NAR group (2.2% vs. 13.3%). The authors interpreted this result as issue of resection margin and suggested wide resection might be better than NAR. However, we cannot know whether lower recurrence rate in the same segment in patients with subsegmentectomy resulted from wide margin or effect of AR because there was no surgical margin information. According to Hidaka's paper, oncologic effect of AR might be very limited. Even if the hypothesis regarding AR is correct, it is only applicable in limited circumstances, in small area of 'subsegment'. It means that if tumor locates beyond subsegment territory, advantage of AR would be diminished. Even in this situation, NAR with enough margin may be feasible. In addition, we also interested in how many percentage of microportal invasion of the entire microvascular invasion in the entire cohort. In the tumor located in the 'subsegment', would microvascular (microvenous) invasion also have survival impact on AR as microportal invasion?

In apart, regardless of the oncologic benefit of AR for the patients, as advancement of surgical skill and technology for minimal invasive surgery, increasing proportion of liver resections has been performed laparoscopically by expert hands. Laparoscopic anatomical segmentectomies are still highly demanding technically. On the basis of published papers including this article, where there is no survival benefit with AR or obscure of the reality, we can choose less invasive laparoscopic NAR for the patients who have small HCC in damaged liver can result in limited adhesion. If the patient needs salvage transplantation because the tumor recurred or liver function changed to decompensated later on, the patients who did laparoscopic hepatectomy can be provided with easier procedure finally better interest.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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