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Original Communications

Does anatomic resection improve the postoperative outcomes of solitary hepatocellular carcinomas located on the liver surface?

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ABSTRACT

Background. It is unclear whether anatomic resection achieves better outcomes than nonanatomic resection in patients with hepatocellular carcinoma. This study aimed to compare the outcomes of anatomic resection and nonanatomic resection for hepatocellular carcinoma located on the liver surface via one-to-one propensity score-matching analysis.

Methods. Data from all consecutive patients who underwent liver resection for primary solitary hepatocellular carcinoma at Nara Medical University Hospital, Japan, January 2007– December 2015 were retrieved. Superficial hepatocellular carcinomas were defined as hepatocellular carcinoma that extended to a depth of < 3 cm from the liver surface and measured < 5 cm in diameter. The prognoses of the patients with superficial hepatocellular carcinoma who underwent anatomic resection and nonanatomic resection were compared.

Results. In this study 23 patients with superficial hepatocellular carcinoma underwent anatomic resection and 70 patients who underwent nonanatomic resection. The recurrence-free survival rate of the patients who underwent anatomic resection was better than that of the patients who underwent nonanatomic resection ($P = .006$), while no such difference was observed for nonsuperficial hepatocellular carcinoma. After the propensity score-matching procedure, the resected liver volume and operation time were the only background or clinical characteristics to exhibit significant differences between the anatomic resection (n = 20) and nonanatomic resection groups (n = 20). The recurrence-free survivial rate of the patients who underwent anatomic resection was significantly than that of the patients that underwent nonanatomic resections ($P = .030$), but overall survival did not differ significantly between the groups ($P = .182$).

Conclusion. Anatomic resection decreases the risk of tumor recurrence and improves recurrence-free survival compared with nonanatomic resection in patients with superficial hepatocellular carcinoma.

Background

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide. It is more prevalent in Asia and Africa, but the rates of HCC in Western countries are increasing.[1] Liver resection and radiofrequency ablation (RFA) are currently the only potentially curative treatments for HCC. Regarding solitary primary HCC, several retrospective studies have reported that liver resection has a prognostic advantage over RFA.[2-4] Liver resection includes anatomic resection (AR) and nonanatomic resection (NAR). Theoretically, AR can remove tumor-bearing portal territories and prevent the development of intrahepatic metastases through the portal vein. Several retrospective studies and meta-analyses have reported that AR produces superior outcomes to NAR.[5-9] In contrast, other retrospective studies have reported that AR was not superior to NAR.[10-13] Thus, it remains unclear which of these procedures should be recommended as a surgical treatment for HCC.

No clear definition of NAR has been established, but a definition should include both enucleation and nonanatomic, wide resection. In NAR, the amount of liver parenchyma resected is influenced by the location of the tumor. In cases involving HCC located on the liver surface, NAR is easy to perform and involves resecting less liver parenchymal tissue than AR, because such tumors can be identified clearly and are located far from the main Glissonian pedicle. In contrast, NAR for HCC located in the deep liver parenchyma often requires extensive resection of the liver parenchyma, as is the case in AR. Thus, we expect that the differences among the

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outcomes of AR and NAR will be greatest in cases involving HCC located on the liver surface.

In this study, we analyzed the perioperative outcomes and prognoses of HCC located on the liver surface and we examined whether AR was superior to NAR, using an analysis of one-to-one propensity score matching.

Methods

Study population

Data for all consecutive patients who underwent liver resection for primary solitary HCC at Nara Medical University, Japan, January 2007–December 2015 were retrieved from a prospective database for this retrospective study. At our institution, NAR was used to treat HCC located on the liver surface January 2007—December 2011. But the institution employed a new director, which led to AR becoming the treatment of choice for such tumors January 2012—December 2015. As for laparoscopic liver resection, NAR was usually performed during such procedures, because AR was not included in the Japanese national medical insurance system until April 2016. HCCs located on the liver surface (superficial HCCs) were defined as those which extended to a depth of < 3 cm from the liver surface and measured < 5 cm in diameter. The depth of each HCC was measured from the normalized liver surface. The prognoses of patients with superficial HCC and patients with other types of HCC (nonsuperficial HCC) were compared. In each group, we compared the prognoses of patients who underwent AR and of patients who underwent NAR.

One-to-one propensity score-matching analysis of superficial HCC

The baseline characteristics and perioperative outcomes of patients with superficial HCC who underwent AR (the AR group) were compared with the outcomes of patients who underwent NAR (the NAR group). One-to-one propensity score matching was performed. We calculated propensity scores for each patient, using logistic regression analysis involving the following covariates: the presence or absence of positivity for hepatitis C virus antibodies; the preoperative platelet count, serum albumin level, and prothrombin time; the Child-Pugh score; tumor size; and tumor depth.

Operative procedures

AR included segmentectomy, sectionectomy, hemihepatectomy, and trisectionectomy. This study focused on HCC located on the liver surface and segmentectomy, which was defined as the complete removal of one Couinaud segment, was the most common AR procedure among the study population. Segmentectomy was carried out as follows: Indigo carmine dye was injected into the root of the relevant portal vein under ultrasonographic guidance to detect the boundary of the target Couinaud segment. Then, parenchymal dissection was performed along the segmental border, landmark veins were exposed on the cut surface of the liver, and the corresponding portal branches were ligated at the root of the segment. NAR was defined as resecting the tumor together with a margin of 1–10 mm without regard to segmental, sectional, or lobar anatomy. Perioperative management and other operative procedures were performed as described previously.[14-16]

Postoperative outcomes

Postoperative complications were stratified according to the Clavien-Dindo classification.[17] Major complications were defined as those of grade IIIa or above. Bile leakage was defined according to the definitions of the International Study Group of Liver Surgery (ISGLS).[18] Surgical site infections were defined according to the Centers for Disease Control guidelines.[19] Liver failure was diagnosed according to the ISGLS definition.[20]

Follow-up

The patients were followed-up every 4 months for up to 5 years after initial operation and then every 6 months thereafter. Recurrence was defined as the appearance of a new lesion that exhibited radiologic features compatible with HCC. Initial recurrence was classified into the following 2 patterns: (1) recurrence within the Couinaud segment that contained the primary tumor in the NAR group (localized recurrence), and (2) recurrence outside of the Couinaud segment that contained the primary tumor (nonlocalized recurrence).

Statistical analyses

Continuous data are expressed as medians and ranges. Qualitative variables are expressed as frequencies (percentages). The Student *t* test or Mann-Whitney *U* test was used for intergroup comparisons of quantitative variables as appropriate; whereas the χ^2 test or Fisher exact test was used to compare categorical data. We used 2-sided *P*-values of < 0.05. A survival analysis was conducted using the Kaplan-Meier product-limit method, and the significance of differences between survival curves was determined using the log-rank test. Multivariate comparisons of survival distributions were carried out using Cox proportional hazard models. All statistical analyses were performed using SPSS for Windows v. 22.0 (SPSS Inc, Chicago, IL).

Results

Prognoses of the patients with superficial and nonsuperficial HCC

In this study cohort, 93 patients had superficial HCC and 81 patients had nonsuperficial HCC. Figs 1A and 1B show representative cases of superficial HCC and nonsuperficial HCC, respectively. Fig 1C shows the recurrence-free survival (RFS) and overall survival (OS) rates of patients with superficial HCC and patients with nonsuperficial HCC. The RFS and OS rates of patients with superficial HCC were better than those of patients with nonsuperficial HCC (*P* = .010 and < .001, resp).

The prognoses of the patients with superficial HCC who underwent AR or NAR

In this study cohort, 23 patients with superficial HCC underwent AR and 70 patients with superficial HCC underwent NAR. The RFS rate of patients who underwent AR was better than that of patients who underwent NAR (*P* = .006), while OS did not differ between these groups (*P* = .260) (Fig 2).

The prognoses of the patients with nonsuperficial HCC who underwent AR or NAR

In this study cohort, 56 patients with nonsuperficial HCC underwent AR and 27 patients with nonsuperficial HCC underwent NAR. The RFS and OS rates of patients who underwent AR were not different from those of patients who underwent NAR (*P* = .937 and .888, respectively) (Fig 3).

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