Laparoscopic Hepatic Resection

Laparoscopic hepatic resection (LHR) was performed by one of three experienced surgeons. Surgical methods were determined based on tumor size, location, and surgeon preferences [1,2]. After creating a pneumoperitoneum of 11–12 mm Hg, the intraperitoneal structure was evaluated using a flexible laparoscopic camera. Intraoperative sonographic examination was performed whenever needed to evaluate the exact tumor location in relation to the major intrahepatic blood vessels. Parenchymal dissection and bleeding control were performed using various energy devices (Sonison, Medtronic; Harmonic Ace, Ethicon; or Ligasure, Medtronic), advanced bipolar devices, and/or cavitron ultrasonic surgical aspirator (CUSA® EXcel, Valleylab). In general, bleeding from small vessels was controlled by bipolar coagulation, and larger vessels were clipped or electively stapled. During anatomical resection, the liver was resected by clamping the Glissonean capsule. Anatomic resection was defined as the resection of the tumor together with the related portal veins and corresponding surrounding tissue, whereas non-anatomical resection was defined as resection with an adequate resection margin (≥ 1 cm) [3].

Laparoscopic Radiofrequency Ablation

One of the interventional radiologists assessed whether percutaneous radiofrequency ablation (RFA) was feasible using planning ultrasound (US) in which fusion imaging of real-time US and pre-acquired CT/MRI was used [4]. Subcapsular tumors were defined as those located within 1 cm of the liver capsule [5]. Among those considered to be challenging for percutaneous US-guided RFA, laparoscopic RFA (LRFA) was attempted under general anesthesia by one of three radiologists with more than 3 years of experience in RFA for hepatic tumors. Three to four trocars were introduced through the sub-umbilical and subcostal areas by the surgeons. The excision of the falciform ligament was performed whenever required. The patient’s position was appropriately tilted for RFA needle insertion. If the index tumor abutted the gallbladder, laparoscopic cholecystectomy was performed before the procedure.

When the index tumor was broadly attached to the anterior liver capsule, it could be localized based on its different color on laparoscopy. As the subcapsular tumors were well visualized on laparoscopy, RF electrodes were inserted based on laparoscopic findings without direct tumor puncture. Either single (Proteus RF Electrode, STARmed) or separable clustered electrodes (Octopus electrode, STARmed) were used based on tumor size or location. In general, centripetal or no-touch RFA using multiple electrodes were preferred to ensure a sufficient ablative margin. If the tumor was not visualized on laparoscopy, laparoscopic US was also used to localize the tumor. Upon localizing the index tumor on US images, the liver capsule was cauterized on top of the index tumor before RF electrode placement as the index tumor was very close to the liver capsule. During electrode placement, the position of the electrode in relation to the index tumor was assessed using laparoscopic US. Both laparoscopy and US monitoring were used to determine whether the index tumor was entirely covered by the RFA zone. After the procedure, tract ablation was performed during electrode removal.

Contrast-enhanced CT was performed to evaluate the treatment response or any complications on the operation day. If the index tumor was considered to be covered entirely by the RFA zone on CT images, the treatment was considered a technical success [6]. When a residual tumor was detected on a CT image, a second RFA session was attempted the following day.

Follow-Up

All patients underwent follow-up contrast-enhanced CT/MRI, chest radiography, serum alpha-fetoprotein, and liver function tests 1 month after initial treatment, every 3–4 months during the first 2 years, and every 4–6 months. When LTP (defined as the appearance of enhancing tumor foci at the margin of the resection or RFA zone), intrahepatic distant recurrence, or extrahepatic recurrence developed during the follow-up period, optimal second-line treatment was performed according to the consensus of the multidisciplinary tumor board.

A major complication was defined as an event that led to substantial morbidity and disability, increasing care level, which resulted in hospital admission or substantially lengthened hospital stay. All others were considered minor complications [6].
Supplementary Results

Comparison of Cumulative LTP Rates before PS Matching
During follow-up, LTP developed in two of 60 patients (3.3%) in the LHR group and one of 29 patients (3.4%) in the LRFA group. The cumulative LTP rates at 1, 3, and 5 years were estimated to be 0.0%, 3.5%, and 3.5%, respectively, for the LHR group and 3.5%, 3.5%, and 3.5%, respectively, for the LRFA group ($p = 0.900$) (Fig. 2A).

Comparison of RFS and OS before PS Matching
By May 31, 2020, four of 69 patients (5.8%) in the LHR group and two of 29 patients (6.9%) in the LRFA group died. The RFS rates at 1, 3, and 5 years were 91.5%, 77.8%, and 72.1%, respectively, for the LHR group and 75.3%, 60.8%, and 42.5%, respectively, for the LRFA group ($p = 0.010$) (Fig. 2B). The OS rates at 1, 3, and 5 years were 100%, 94.8%, and 94.8%, respectively, for the LHR group and 100%, 92.7%, and 92.7%, respectively, for the LRFA group ($p = 0.900$) (Fig. 2C).

REFERENCES
1. Kim JM, Kim S, Rhu J, Choi GS, Kwon CHD, Joh JW. Elderly hepatocellular carcinoma patients: open or laparoscopic approach? *Cancers (Basel)* 2020;12:2281
2. Kim JM, Kwon CHD, Yoo H, Kim KS, Lee J, Kim K, et al. Which approach is preferred in left hepatocellular carcinoma? Laparoscopic versus open hepatectomy using propensity score matching. *BMC Cancer* 2018;18:668
3. Kim JM, Kwon CHD, Joh JW, Na BG, Lee KW, Choi GS, et al. Nonanatomical resection is comparable with anatomical resection in solitary hepatocellular carcinoma <5cm in the right posterior section. *Medicine (Baltimore)* 2016;95:e5382
4. Lee MW, Rhim H, Cha DI, Kim YJ, Lim HK. Planning US for percutaneous radiofrequency ablation of small hepatocellular carcinomas (1-3 cm): value of fusion imaging with conventional US and CT/MR images. *J Vasc Interv Radiol* 2013;24:958-965
5. Worakitsitisatorn A, Lu DS, Lee MW, Asvadi NH, Moshksar A, Yuen AD, et al. Percutaneous thermal ablation of subcapsular hepatocellular carcinomas: influence of tumor-surface contact and protrusion on therapeutic efficacy and safety. *Eur Radiol* 2020;30:1813-1821
6. Ahmed M, Solbiati L, Brace CL, Breen DJ, Callstrom MR, Charboneau JW, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria--a 10-year update. *Radiology* 2014;273:241-260
## Supplementary Table 1. Univariable Analysis for Survival Outcomes for All 89 Patients

| Variable                                           | Recurrence-Free Survival | Overall Survival |
|----------------------------------------------------|--------------------------|-----------------|
|                                                   | HR (95% CI) | P     | HR (95% CI) | P     |
| **Treatment type [LHR]**                           | 2.36 (1.32–4.23) | 0.016 | 1.16 (0.28–4.86) | 0.862 |
| **Age at enrolment**                               | 1.00 (0.97–1.04) | 0.902 | 1.00 (0.92–1.09) | 0.921 |
| **Sex [male]**                                     | 0.71 (0.29–1.74) | 0.794 | 1.80 (0.33–9.87) | 0.500 |
| **Cause of liver disease [HBV]**                   |             |      | 0.222 |       | 0.195 |
| HCV                                                | 0.63 (0.37–5.91) | 0.390 | 0.68 (0.01–24.64) | 0.683 |
| Others                                             | 0.69 (0.92–4.13) | 0.078 | 1.50 (0.97–25.97) | 0.055 |
| Both HBV and HCV                                   | 0.33 (0.01–10.24) | 0.826 | 2.51 (0.09–151.90) | 0.219 |
| **AFP**                                            | 1.00 (1.00–1.00) | 0.695 | 1.00 (0.99–1.01) | 0.524 |
| **PIVKA-II**                                       | 1.00 (1.00–1.00) | 0.118 | 1.00 (1.00–1.00) | 0.865 |
| **ALBI grade [grade 1]**                           | 1.66 (0.68–4.06) | 0.263 | 1.26 (0.15–10.82) | 0.832 |
| Platelet count, x 10^9/L                            | 0.99 (0.99–1.00) | 0.109 | 1.01 (0.99–1.02) | 0.325 |
| **Total bilirubin, mg/dL**                         | 1.53 (0.75–3.13) | 0.243 | 0.81 (0.13–5.05) | 0.826 |
| Albumin, g/dL                                      | 0.78 (0.33–1.85) | 0.579 | 1.03 (0.15–7.27) | 0.978 |
| Prothrombin time, INR                              | 9.57 (0.27–336.91) | 0.214 | 110.21 (0.09–136367.65) | 0.196 |
| Creatinine, mg/dL                                  | 0.96 (0.71–1.29) | 0.794 | 0.63 (0.02–16.63) | 0.783 |
| **Tumor size, cm**                                 | 0.81 (0.41–1.62) | 0.556 | 1.36 (0.28–6.53) | 0.700 |
| **Tumor abutment of liver capsule**                | 1.58 (0.48–5.20) | 0.453 | 8.29 (1.51–45.39) | 0.015 |
| **Tumor distance from capsule, cm**                | 5.75 (0.21–159.23) | 0.302 | 674.14 (8.29–54838.56) | 0.004 |
| **Tumor location (Couinaud segment) [II]**         | 0.660 |       | 0.362 |       |
| **Complication [presence]**                         | 0.93 (0.28–3.05) | 0.899 | 0.58 (0.03–12.96) | 0.728 |
| **Hospital stay, days**                            | 0.94 (0.81–1.09) | 0.410 | 0.91 (0.64–1.30) | 0.623 |

The numbers in parentheses are 95% CIs. A univariable Cox proportional hazards model for recurrence-free survival and overall survival was used. The reference category for each categorical variable is in square brackets in the first column. AFP = alpha-fetoprotein, ALBI = grade albumin-bilirubin grade, CI = confidence interval, HBV = hepatitis B virus, HCV = hepatitis C virus, HR = hazard ratio, INR = international normalized ratio, LHR = laparoscopic hepatic resection, PIVKA-II = protein induced by vitamin K absence-II