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ORIGINAL ARTICLE

# Living donor liver transplantation for hepatocellular carcinoma: results of prospective patient selection by Kyushu University Criteria in 7 years

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## Abstract

**Background:** Expanding patient selection beyond the Milan criteria in living donor liver transplantation (LDLT) for hepatocellular carcinoma (HCC) has long been a matter for debate. We have used the Kyushu University Criteria – maximum tumor diameter <5 cm or des-γ-carboxy prothrombin <300 mAU/ml – in LDLT for HCC since June 2007. The aim of the present study was to present the results of our prospective patient selection by Kyushu University Criteria and to confirm whether or not our criteria were justified.

**Methods:** The entire study period was divided into the pre-Kyushu era (July 1999–May 2007) and the Kyushu era (June 2007–November 2014). Eighty-nine and 90 patients underwent LDLT for HCC in the pre-Kyushu era and the Kyushu era, respectively.

**Results:** In the pre-Kyushu era, there were significant differences in recurrence-free and disease-specific survival between the beyond-Milan and the within-Milan patients. In the Kyushu era, however, the differences in recurrence-free and disease-specific survival between the beyond-Milan and the within-Milan patients disappeared. The 5-year overall patient survival in the Kyushu era was 89.4%.

**Conclusion:** Our selection criteria enabled a considerable number of beyond-Milan patients to undergo LDLT without jeopardizing the recurrence-free, and disease-specific, and overall patient survival.

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## Introduction

Patient selection in living donor liver transplantation (LDLT) for hepatocellular carcinoma (HCC) has long been a matter for debate.[1–4] Although the Milan criteria has been considered a gold-standard for patient selection in liver transplantation for HCC,[5–8] a considerable number of beyond-Milan patients benefitted from liver transplantation without any sign of recurrence.[9–16] Compared to deceased liver transplantation, patient selection in LDLT is free from organ allocation systems and therefore a more liberal expanding of criteria can be applied. At present, many transplant centers have their own expanded criteria for HCC, and each criteria has exhibited satisfying results so far. We previously reported that both tumor size <5 cm and des-γ-carboxy prothrombin (DCP) level <300 mAU/ml were favorable independent factors against HCC recurrence after LDLT, and then a new selection criteria named Kyushu University Criteria – tumor size <5 cm or DCP <300 mAU/ml without gross vascular invasion or extrahepatic metastasis on imaging studies, irrespective of the number of tumors - was introduced.[13] Before the introduction of these criteria, the absolute exclusion factors in our institute were only gross vascular invasion and extrahepatic metastasis (pre-Kyushu era in Fig. 1). After the introduction of these criteria (June 2007), we had turned down candidate recipients beyond the Kyushu University Criteria because of extremely high possibility of HCC recurrence (Kyushu era in Fig. 1). In addition, since our criteria were





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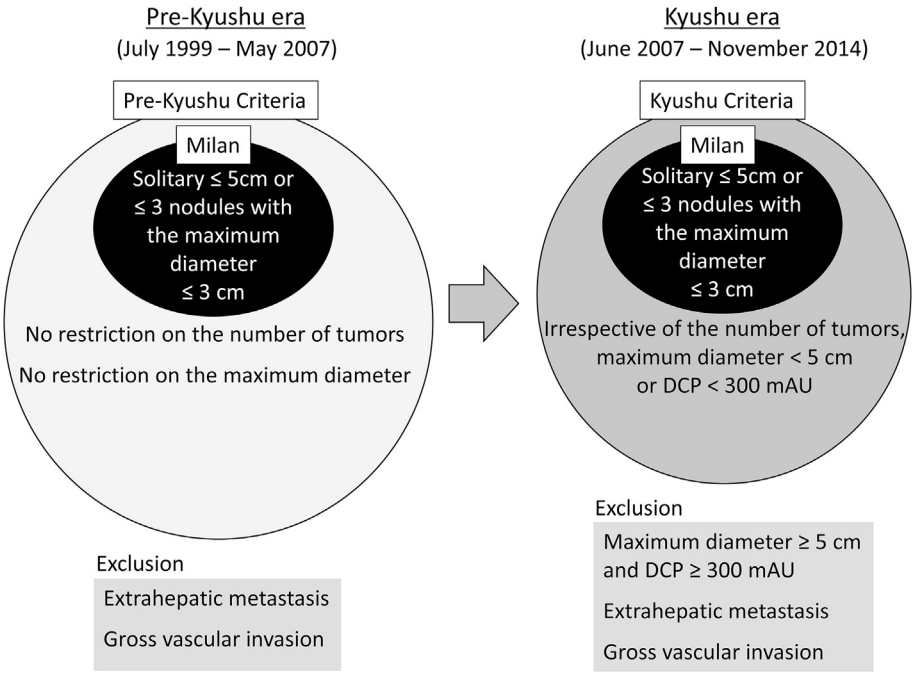


**Figure 1** **Diagrams showing the selection criteria in the pre-Kyushu era and the Kyushu era**. Note that "maximum diameter ≥5 cm and DCP ≥300 mAU" was added to the exclusion criteria in the Kyushu era. DCP, des-γ-carboxy prothrombin

presented at medical meetings, in the medical journals, and on our website, a considerable number of patients came to our hospital in order to undergo LDLT because they were turned down as candidate recipients at other hospitals due to the reason that their HCC status were beyond the criteria of those hospitals. The aim of the current study was to present the results of our prospective patient selection in LDLT for HCC in 7 years and to confirm whether or not our criteria were justified.

## Patients and methods

This study was approved by the institutional review board of Kyushu University (No. 28-202).

### Patients

Data from the medical records of 179 patients who underwent LDLT for HCC between July 1999 and November 2014 were retrospectively reviewed. The status of HCC in these 179 patients was preoperatively determined by the certified radiologists using the imaging studies that were performed according to the protocols of our hospital. Patients with incidental HCC in explanted livers or with only non-viable HCC by preoperative treatments were not enrolled in this study. The 89 patients who underwent LDLT before the introduction of the Kyushu University Criteria (July 1999–May 2007) were assigned to the pre-Kyushu group, while the latter 90 patients who underwent LDLT after the introduction of these criteria (June 2007–November 2014) were assigned to the Kyushu group. The certified radiologists of our hospital preoperatively determined the diameters of tumors, the numbers of tumors, the presence of vascular invasion, and the presence of extrahepatic metastasis by examining preoperative imaging studies and judged each tumor status as within or beyond the Milan criteria. The indications committee comprised of hepatologists, radiologists, anesthesiologists, etc. of our hospital determined the indications for LDLT and whether or not Japanese National Health Insurance coverage was applied in each patient. Japanese National Health Insurance coverage had only applied to HCC patients both whose liver was decompensated cirrhosis and whose tumor status was within the Milan criteria since the adaptation of this coverage in April 2004. Prior to April 2004, there had been no insurance coverage on any LDLT for cirrhosis with HCC. In addition, if the tumors were treated by some therapies prior to transplant, only patients who underwent LDLT with the tumor status within the Milan criteria, which was confirmed by contrast-enhanced CT or MRI taken within one month before transplant, could receive the National Health Insurance coverage (the interval between the time of this CT or MRI just before transplantation and the time of the last therapy for HCC had to be more than 3 months).

Model for End-Stage Liver Disease (MELD) scores were calculated by the MELD model, United Network for Organ Sharing modification.[17]

Perioperative patient managements, operative procedures, follow-ups of the patients were done as previously described.[13,18,19] Systemic CT or abdominal MRI examinations were taken at least once in every 6 months by the third year after




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