

ORIGINAL ARTICLE

Intention-to-treat analysis of liver transplantation, resection and thermal ablation for hepatocellular carcinoma in a single centre

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Abstract

Background: potentially curative treatment options for hepatocellular carcinoma (HCC) include liver transplantation (LT), liver resection (LR) and thermal ablation (TA). Long term intent-to-treat (ITT) analysis from a single-centre using all three modalities contemporaneously has not been published.

Methods: An ITT analysis was undertaken of all patients with HCC listed for LT, or have undergone LR or TA.

Results: 444 patients were identified; 145 were listed for LT (121 underwent LT), 190 underwent LR and 109 underwent TA. One and 3-year overall survival (OS) was similar among LT, LR and TA (88/77%, 88/64% and 95/72%) whereas 5-year OS was higher following LT than LR or TA (73% vs. 54% vs. 49%). Disease-free survival at 1- and 5-years was higher for LT (97% and 84%) than LR (66% and 35%) or TA (73%, and 19%).

Conclusion: LT offered the lowest rate of cancer recurrence and highest chance of long-term survival. Differences in outcome likely reflect a combination of cancer-related factors (AFP, micro- and macro-vascular invasion), patient-related factors (performance status, co-morbidities and psychosocial issues) and treatment type. Two thirds of patients treated by LR and three quarters treated by TA had HCC recurrence by 5 years, reinforcing the need for close long-term surveillance.

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Introduction

Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related mortality worldwide and has the fastest growing cancer mortality rate, attributable to the current hepatitis C and obesity epidemics.¹ Almost 750,000 people die from HCC each year, most within the Asia–Pacific region.² Most cases of HCC develop in the presence of underlying chronic liver disease. The routine screening of patients at risk of developing HCC has enabled the detection an early stage when curative interventions may be possible. Surgery, either replacing the whole liver by transplantation, or removing part of the liver by resection, or thermal ablation in a subset of patients with small targetable tumours, are the only treatment modalities with the potential to cure HCC.^{3,4}

Liver resection (LR) has traditionally been considered the preferred method of treatment for patients with HCC with preserved liver function and absence of portal hypertension. Unfortunately, only a minority of patients meet these criteria. Liver transplant (LT) is the treatment of choice in patients with limited HCC and poor underlying liver function.^{5,6} LT also has the advantage of lowering the risk of metachronous tumours by eradicating the underlying field defect but feasibility of LT as first-line treatment is limited by the availability of donor organs. Furthermore a proportion of patients experience tumour progression on the waiting list despite loco-regional therapies. LT is also associated with long term problems such as surgical complications, graft rejection, recurrence of primary liver disease and complications related to lifelong immunosuppression. Thermal

ablation (TA), including radiofrequency (RFA) and microwave ablation (MWA), are relatively new technologies that offer potential advantages over LT and LR, such as lower procedure-related morbidity, mortality and cost. Also, TA can be performed via a percutaneous approach, laparoscopically, or at open surgery. The chief technical limitations of TA are incomplete ablation leading to lesion recurrence, related to tumour size and proximity to major vessels, and thermal injury to important structures. Another major limitation of both LR and TA is the long-term risk of metachronous tumours arising in the remnant liver.

Many previous reports have compared LT with LR, and LR with TA, but there have not been any published studies that have analysed all three modalities contemporaneously in a single institution. The present study is an intent-to-treat (ITT) analysis of outcome for all patients with HCC treated with curative intent at a single centre, where all three modalities were available.

Patients and methods

Study design

This study was an ITT analysis of all patients, more than 18 years of age, with first presentation of HCC that were treated with curative intent at Auckland City Hospital, Auckland, New

Zealand since the inception of the New Zealand Liver Transplant Unit in February 1998, to December 2014.

All patients were discussed in a dedicated HCC multidisciplinary meeting and treatment allocation determined as follows. Patients with anatomically resectable tumours and preserved liver function with no portal hypertension, and no prohibitive co-morbidities, were offered LR as first treatment. Those with HCC within University of California San Francisco (UCSF) criteria⁶ who were not resectable either because of tumour distribution or severity of underlying liver disease, and who otherwise had no contraindications to transplantation, were offered LT as first treatment. Those with targetable lesions who were not LR or LT candidates were offered TA as first treatment. The treatment modality for patients with very early HCC (Barcelona Clinic Liver Cancer⁴ (BCLC) stage 0) that was both resectable and targetable for TA was determined by surgeon and/or patient preference.

Patients were stratified by their primary treatment modality to either LT, LR, or TA (Fig. 1). The LT group included all patients who were placed on the waiting list with the intent to undergo LT. Reasons for removing patients from the LT waitlist included tumour progression beyond transplant criteria, hepatic decompensation (died while on the waiting list), psychosocial issues (substance abuse, psychiatric illness), and co-morbidities

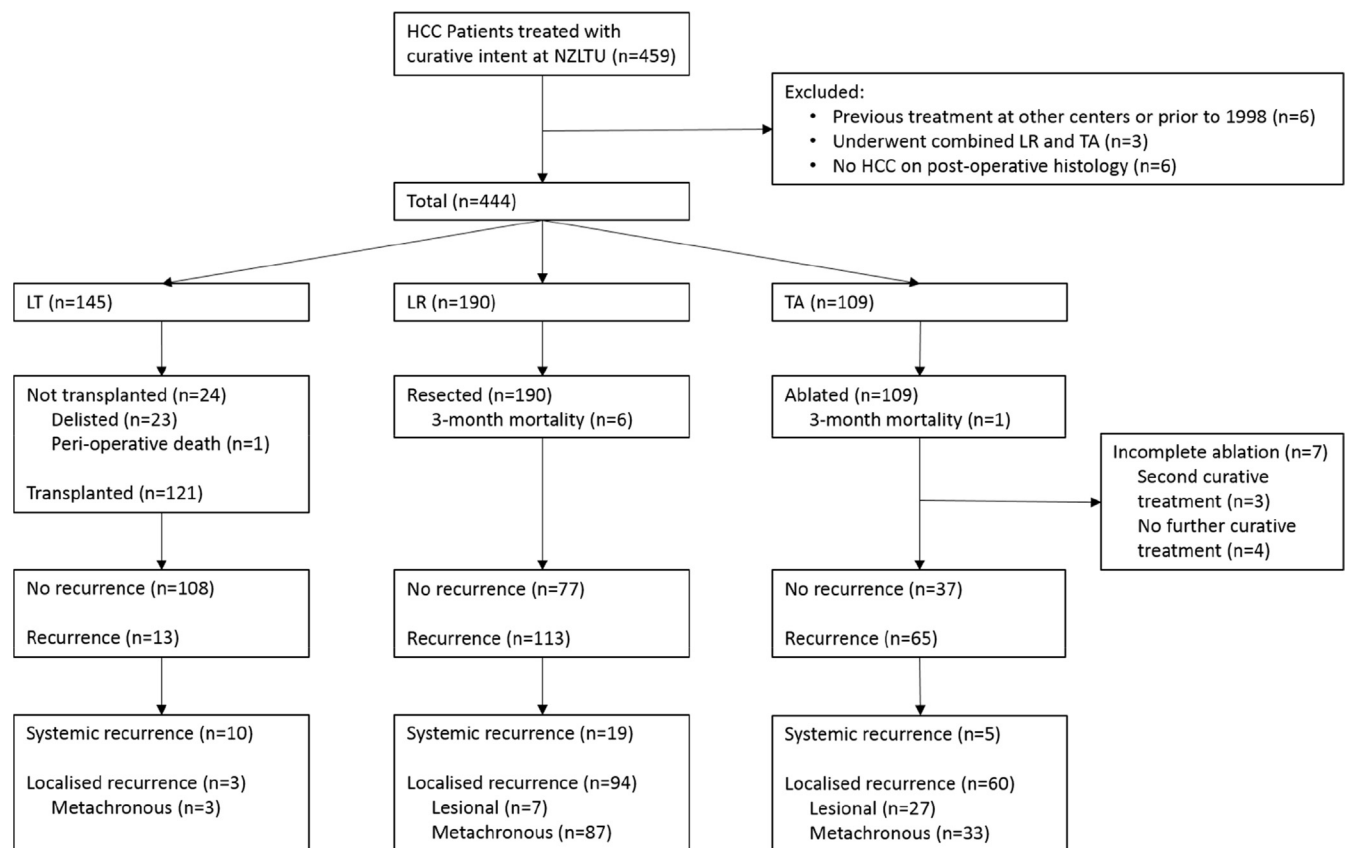


Figure 1 Overview of treatment and recurrence for all patients undergoing LT, LR or TA for HCC included in the study

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