

Documents

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Development and validation of a REcurrent Liver cAnceR Prediction ScorE (RELAPSE) following liver transplantation in patients with hepatocellular carcinoma: Analysis of the US Multicenter HCC Transplant Consortium

(2023) *Liver Transplantation*, 29 (7), pp. 683-697. Cited 6 times.

DOI: 10.1097/LVT.0000000000000145

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Abstract

HCC recurrence following liver transplantation (LT) is highly morbid and occurs despite strict patient selection criteria. Individualized prediction of post-LT HCC recurrence risk remains an important need. Clinico-radiologic and pathologic data of 4981 patients with HCC undergoing LT from the US Multicenter HCC Transplant Consortium (UMHTC) were analyzed to develop a REcurrent Liver cAnceR Prediction ScorE (RELAPSE). Multivariable Fine and Gray competing risk analysis and machine learning algorithms (Random Survival Forest and Classification and Regression Tree models) identified variables to model HCC recurrence. RELAPSE was externally validated in 1160 HCC LT recipients from the European Hepatocellular

Cancer Liver Transplant study group. Of 4981 UMHTC patients with HCC undergoing LT, 71.9% were within Milan criteria, 16.1% were initially beyond Milan criteria with 9.4% downstaged before LT, and 12.0% had incidental HCC on explant pathology. Overall and recurrence-free survival at 1, 3, and 5 years was 89.7%, 78.6%, and 69.8% and 86.8%, 74.9%, and 66.7%, respectively, with a 5-year incidence of HCC recurrence of 12.5% (median 16 months) and non-HCC mortality of 20.8%. A multivariable model identified maximum alpha-fetoprotein (HR = 1.35 per-log SD, 95% CI, 1.22-1.50, $p < 0.001$), neutrophil-lymphocyte ratio (HR = 1.16 per-log SD, 95% CI, 1.04-1.28, $p < 0.006$), pathologic maximum tumor diameter (HR = 1.53 per-log SD, 95% CI, 1.35-1.73, $p < 0.001$), microvascular (HR = 2.37, 95%-CI, 1.87-2.99, $p < 0.001$) and macrovascular (HR = 3.38, 95% CI, 2.41-4.75, $p < 0.001$) invasion, and tumor differentiation (moderate HR = 1.75, 95% CI, 1.29-2.37, $p < 0.001$; poor HR = 2.62, 95% CI, 1.54-3.32, $p < 0.001$) as independent variables predicting post-LT HCC recurrence (C-statistic = 0.78). Machine learning algorithms incorporating additional covariates improved prediction of recurrence (Random Survival Forest C-statistic = 0.81). Despite significant differences in European Hepatocellular Cancer Liver Transplant recipient radiologic, treatment, and pathologic characteristics, external validation of RELAPSE demonstrated consistent 2-and 5-year recurrence risk discrimination (AUCs 0.77 and 0.75, respectively). We developed and externally validated a RELAPSE score that accurately discriminates post-LT HCC recurrence risk and may allow for individualized post-LT surveillance, immunosuppression modification, and selection of high-risk patients for adjuvant therapies. © 2023 John Wiley and Sons Ltd. All rights reserved.

Index Keywords

alpha fetoprotein; adjuvant chemotherapy, adult, Article, cancer recurrence, cancer size, cancer survival, controlled study, explant, female, high risk patient, human, human tissue, immunosuppressive treatment, independent variable, liver cell carcinoma, liver graft, liver transplantation, machine learning, major clinical study, male, microvasculature, multicenter study, neutrophil lymphocyte ratio, patient selection, recurrence free survival, recurrence risk, tumor differentiation, clinical trial, liver tumor, pathology, recurrent disease, retrospective study, risk factor, tumor recurrence; Carcinoma, Hepatocellular, Humans, Liver Neoplasms, Liver Transplantation, Neoplasm Recurrence, Local, Recurrence, Retrospective Studies, Risk Factors

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Publisher: Wolters Kluwer Medknow Publications

ISSN: 15276465

CODEN: LITRF

PubMed ID: 37029083

Language of Original Document: English

Abbreviated Source Title: Liver Transplant.

2-s2.0-85160310874

Document Type: Article

Publication Stage: Final

Source: Scopus

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