UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

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TITLE: THE PREDICTION OF POST-LIVER TRANSPLANT ANASTOMOTIC BILIARY STRICTURE USING BIOMARKER-DEPENDENT PROGNOSTIC MODELS: A BOOTSTRAPPING-ENHANCED ANALYSIS

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Background and Aims

In patients who undergo liver transplants (LT), the development of post-LT anastomotic biliary strictures (ABS) can undermine the prognosis of grafts/recipients. Given the implications, it is important that the probabilistic risk of such development is predicted early in the post-LT stage using noninvasive prediction models.

Methods

This was a single-center retrospective study that collected patients who underwent LT from 2016-2018. The endpoint was the development of (ABS) within a year from LT, diagnosed by ERCP. Relevant biomarkers were collected at serial time points (7, 14, 30d) and were compared to the endpoint using iterations of cox regression analysis. The logarithmic outcomes of the iterations were incorporated into regression-based and bootstrapping-enhanced (100 iterations) prediction models; their performance was evaluated via the area-under-receiver-operating-characteristics curves (AUROC).

Results

There were total 163 LT patients in the study, from which there were 15.3% with strictures identified in ERCP. The median follow-up period was 36 days. Comparing those with ABS to the ABS-absent controls, there was no difference in age (57.1 vs 55.5y p=0.67), gender (female 0.32 vs 0.36 p=0.91), race category (non-white [opposed to White] 28 vs 24.6% p=0.92), or in underlying etiology (HCV: 24 vs 28.3 alcoholic liver disease: 28 vs 30.4, NASH: 24 vs 13, other: 24 vs 28.3% p=0.56); however, those with ABS had higher usage of living donors (living 20 vs 4.35% p=0.02). Selecting the variables identified from the univariate, multivariate cox showed the following core biomarkers to be associated with ABS: total bilirubin at 14d (p<0.001) and alkaline phosphatase (AP) at 30d (p=0.048). Using the core biomarkers and an escalating number of variable categories, following model iterations were constructed (in the order of cutoff, AUROC, specificity/PPV/NPV at approximately 0.9 TPR); model 1 (core only - equation: 0.087 x total bilirubin at 14d + 0.001 x AP at 30d - 2.52): 0.091, 0.747 95%CI 0.634-0.747, 0.24, 0.17, 0.92; model 2 (prior model + demographic variables): 0.103, 0.767 95%CI 0.667-0.767, 0.43, 0.22, 0.95; model 3 (prior model + liver etiologies): 0.098, 0.781 95%CI 0.691-0.781, 0.47, 0.23, 0.96; model 4 (prior model + donor type): 0.088, 0.797 95%CI 0.707-0.797, 0.45, 0.22,0.95. Bootstrapping-enhanced models also showed the following AUROC; model 1: 0.09, 0.747 95%CI 0.631-0.842, 0.24, 0.17, 0.92; model 2: 0.104, 0.767 95%CI 0.673-0.850, 0.43, 0.22, 0.95; model 3: 0.098, 0.781 95%CI 0.690-0.872, 0.47, 0.23, 0.96; model 4: 0.088, 0.797 95%CI 0.705-0.868, 0.45, 0.22, 0.95.

Conclusion

Both the regression-based and bootstrapping-enhanced models show the bilirubin at 14 days and AP at 30 days to be prognostically-relevant biomarkers that are able to predict the risk of post-LT ABS.

Standard Models

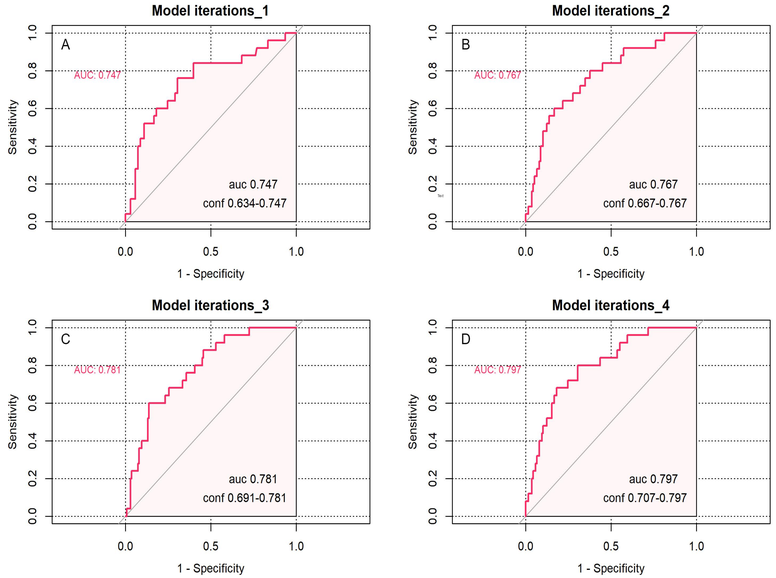

Figure 1a. These figure represent the regression-based models that characterize the probability of anastomotic biliary stenosis in liver transplant patients. A) represents Model 1: core variables only (bilirubin at 14 days and AP at 30 days), B) represents Model 2: core + demographics, 3) represents Model 3: core + demographics + liver etiologies, D) represents Model 4: core + demographics + liver etiology + donor type.

Prognostic Models

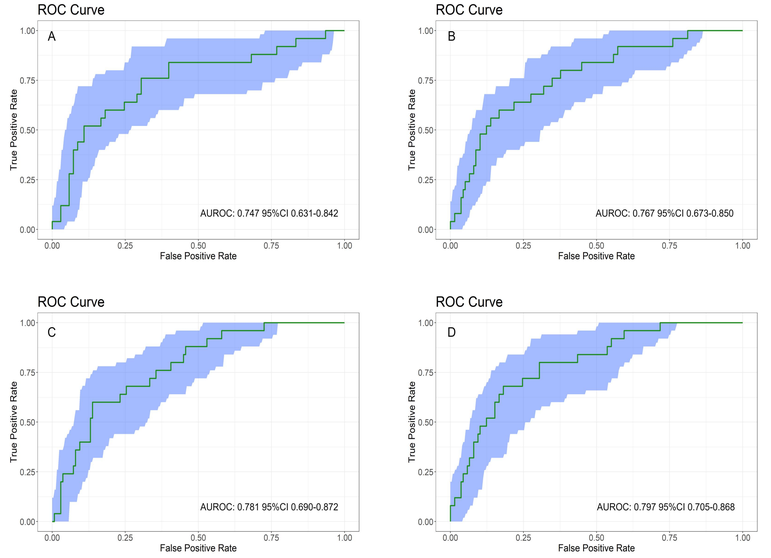

Figure 1b. These figures represent the bootstrapping-enhanced models that characterize the probability of anastomotic biliary stenosis in liver transplant patients. A) represents Model 1: core variables only (bilirubin at 14 days and AP at 30 days), B) represents Model 2: core + demographics, 3) represents Model 3: core + demographics + liver etiologies, D) represents Model 4: core + demographics + liver etiology + donor type.

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