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## **Biosketch**

Dr. Patrick Kamath is a Professor of Medicine at the Mayo Clinic. His major research area has been in identifying patients at risk for mortality in cirrhosis and other liver diseases. He played a key role in developing the Model for End-stage Liver Disease (MELD), which is currently used in the United States and in much of the western world for organ allocations for liver transplantation, and to determine prognosis in patients with cirrhosis. He has also been instrumental in identifying risk factors in mortality in patients with cirrhosis following non-liver transplant surgery, validating MELD scores in patients with acute liver failure and with alcohol hepatitis, as well as helping develop a new score to differentiate alcoholic from nonalcoholic steatohepatitis. His team has demonstrated that even asymptomatic outpatients with cirrhotic ascites may have spontaneous bacterial peritonitis. I have been a principal investigator in an international study comparing TIPS versus large volume paracentesis for refractory ascites, and another study of lanreotide in the control of variceal hemorrhage. He was Chair of the AASLD Special Interest Group (SIG) on Acute on Chronic Liver Failure (ACLF), and has been given the task of putting together a consortium to develop treatment modalities for patients hospitalized with complications of cirrhosis. He was a course director of the Single Topic Conference (STC) cosponsored by AASLD/EASL on “Intensive Care of the Patient with Acute on Chronic Liver Failure” held in Atlanta, March 2010. The aims of the conference included organization of a consortium of investigators to develop an international network such that specific treatments can be studied in hospitalized cirrhotic patients. He gave the State of the Art lecture on “Acute on Chronic Liver Failure (ACLF)” at the Digestive Diseases Week held in New Orleans in 2010. ACLF is a condition where patients with cirrhosis develop multiple organ dysfunctions, usually as a result of infection or superimposed drug induced liver injury (DILI).

## **Abstract: Best use of MELD/CTP scores for baseline and treatment assessment**

The Model for End-stage Liver Disease (MELD) is a generic model whose components include prothrombin time expressed as the International Normalized Ratio (INR), serum creatinine, and serum bilirubin. MELD is mainly used to determine short-term mortality in patients with cirrhosis of the liver. The model was created initially in patients undergoing transjugular intrahepatic portosystemic shunts (TIPS) but has been validated widely in patients with cirrhosis of varying etiology and severity, as also in patients with alcoholic hepatitis and fulminant liver failure. MELD has been shown to be comparable with the Child-Pugh score in some studies, and superior to the Child-Pugh score in determining risk for mortality in most studies. The MELD score has replaced the Child-Pugh score in the United States as the tool to prioritize organs for liver transplantation.

The MELD score is an excellent predictor of 3-month survival in all patient populations with a concordance (c statistic) generally >0.8. (A c statistic >0.7 is accepted as a clinically useful test, whereas a c statistic >0.8 indicates excellent accuracy.) Thus, a c statistic for a MELD score of 0.8 indicates that 8 out of 10 times a patient with a higher MELD score is more likely to die within 3 months compared to a patient with a lower MELD score.

## **Comparison of Child-Turcotte-Pugh (CTP) and MELD Scores**

The Child-Turcotte classification modified by Pugh is now commonly referred to as the Child-Pugh score but, should more accurately be referred to as the Child-Turcotte-Pugh score (CTP). Although the CTP score was derived empirically, it has proven to be an excellent predictor of outcome in patients with complications of portal hypertension. However,

the CTP classification has several shortcomings. It has subjective parameters such as ascites and encephalopathy, which are dependent on the observer, and may be altered substantially by medical intervention. Among the objective variables, that is, albumin, prothrombin time and bilirubin, there is both a “ceiling” and a “floor” effect. For example, a patient with a serum bilirubin of 4 mg/dL would be assigned the same score as a patient with a bilirubin of 40 mg/dL. Similarly, a serum albumin of 2.8 g/dL and 1.8 g/dL are assigned the same score. In essence, there are only three classes (A, B or C) and the CTP cannot distinguish between patients within a single class.

Even among the objective variables, such as prothrombin time and albumin, there are laboratory variables that change values. The normal values for serum albumin differ markedly across medical centers within the United States. Moreover, the sensitivity of thromboplastin can cause variation in the prothrombin time. These variations are sufficient that there may be a significant difference in Child score based on variations in laboratory variability alone.

The Model for End-stage Liver Disease, or MELD, uses only objective parameters, that is, INR, bilirubin and creatinine, which are readily available. The laboratory values for bilirubin and creatinine are standardized worldwide, and the prothrombin time as expressed by the INR is standardized worldwide, at least as far as it relates to patients on anticoagulation. However, some variability does exist in INR reporting and can impact the MELD score as well.

#### Use of MELD Scores for Baseline and Treatment Assessment

MELD score and Lille score in combination have been used to determine outcome of treatment in patients with alcoholic hepatitis. In patients with drug-induced liver injury, multivariate analysis showed that the MELD score (OR 1.21, 95% CI: 1.12–1.30) and decrease in hemoglobin (OR 0.77, 95% CI: 0.61–0.98) are independent predictors of poor outcome. For 30-day mortality, the c-statistics for MELD alone and for combination of MELD and hemoglobin were 0.93 (95% CI: 0.89–0.97) and 0.94 (95% CI: 0.90–0.97), respectively. This suggests that the MELD score can be used to assess outcome in patients with DILI.

#### Future Directions

It is not clear how the MELD score or the CTP score can be used to diagnose DILI in patients with underlying liver disease. Adjudication by experts is required to differentiate worsening of underlying liver disease from DILI superimposed on underlying liver disease. Within these populations, analysis of carefully collected data will be required to determine whether change MELD or CTP score can be used to diagnose DILI and determine prognosis.