A new prognostic model for primary sclerosing cholangitis

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Primary sclerosing cholangitis (PSC) is a progressive liver disease characterized by destruction and inflammation of the intra-and/or extrahepatic biliary tract. Although the etiology is unknown, it is thought to be multifactorial. Recurrent cholangitis attacks and chronic cholestasis result in chronic liver injury, fibrosis and cirrhosis. The risk of malignancy, especially cholangiocarcinoma (CCC), is increased and the only curative treatment of the disease is liver transplantation (1-3). So, it is important to know the clinical course of disease at diagnosis and during follow up period. For that reason, several risk models have been developed to predict the outcome. However, their utility remains controversial.

To date, many risk models have been developed for the prognosis of PSC and those scoring systems have been compared to each other among them with Harrell's C statistic. It is generally considered a good prognostic model when C-statistic> 0.8.

Mayo clinic score (174 patients were studied and variables were age, bilirubin, histologic stage, hemoglobin level, presence of IBD) (1); King 's College, (126 patients were evaluated according to age, presence of hepatomegaly and splenomegaly , histologic stage, and ALP level) (2); Swedish, (305 patients assessed according to presence of IBD, bilirubin level and histologic stage) (3); Multicenter, (46 patients were analyzed according to age, bilirubin level, histologic stage and presence of splenomegaly) (4) are the models that have been used for the predicting of prognosis and clinical course of patients with PSC. However, most of those scoring systems need liver biopsy for histologic stage. On the other hand, revised Mayo clinic scoring was developed in 2000 and they studied the data of 405 patients with PSC to predict the prognosis by using non-invasive variables such as age, bilirubin, AST, history of variceal bleeding, albumin (5).

The Mayo risk score has been used more frequently to estimate short term survival for the end stage liver disease of patients with PSC, unfortunately, it was not able to predict LT requirement. Furthermore, it was not suitable to evaluate the patients with early stage of PSC since most of the data were collected from the patients with end stage liver disease due to PSC.

Recently the Amsterdam-Oxford model (AOM) was reported by of Vries. The main difference of the new model was being a population-based cohort and be able to predict both the short and the long-term consequences such as death and/or liver transplantation. The variables of the model also different from the other models since it was consisted of PSC subtype, age of diagnosis time, level of ALP and AST, bilirubin, albumin and thrombocyte. Although, it showed a high distinguishing features and adequate gauging in that study, further validation was needed to establish the usefulness of AOM in other cohorts and different centers and ethnic groups (7). Moreover, it should be noted that AOM does not have validation for use in children and it can only be used for those over the age of 18.

Recently, Goet et al. performed a multicenter study about a validation of AOM and to reveal the powerful of this model. In that study, they also investigated the usefulness of AOM for PSC and compared with the Mayo Risk Score (MRS). The study was retrospective and 534 patients with PSC (466-large duct, 52-features of AIH, 16-small duct PSC) were enrolled from three tertiary centers in Europe (PSC data between 1984-2016 at University of Padua, Italy; 1993-2018 at Ghent University Hospital, Belgium; 1977-2016 at Erasmus University

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Medical Center, Rotterdam, The Netherlands.). Patients, who were 18 years old or older, diagnosed with PSC according to EASL (European Association for the Study of the Liver) guideline were included in the study. Patients with/without any event a follow-up period of less than 6 months, with unknown date of diagnosis and concomitant liver disease were excluded from the study.

Biochemical findings (AST, ALT, PT, INR, ALP, GGT, Total Bilirubin, Albumin, PLT) and clinical data (sex, age, diagnosis date of PSC, liver histology, UDCA treatment, concomitant IBD, last follow-up or clinical outcome) were evaluated.

The AOM score was calculated annually from the initial diagnosis to the 5th year. (The formula of AOM score=0.323*PSC subtype (1=large duct PSC; 0=small duct PSC) +0.018*Age at diagnosis – 2.485*log(-albumin*lower limit of normal (LLN)) + 2.451* abs (log(platelets- 0.5)+ 0.347*log(aspartate aminotransferase(AST)*upper limit of normal (ULN)) + 0.393 * log(alkaline phosphatase (ALP)*ULN)) + 0.337*log(total bilirubin*ULN)).

Demographic features of 534 patients were as follows; mean age was 39.2±13.1 years, 66% were male, median follow-up was 7.8 (4-12.6) years and 93% were under UDCA treatment. There were 268 concomitant IBD (77% were UC and 20% were CD). Liver transplantation was performed in 167 of 534 patients and 65 patients died. Median LT-free survival was 13.2 (11.8-14.7) years. Liver transplant-free survival rates were 98.3%, 84.4% and 65.9% at 1, 5 and 10 years, respectively. The difference between expected and observed survival was -1.6% at 1st year and + 3.9% at 5th years. C-statistic for AOM 0.67 at diagnosis and 0.75 at 5th year of follow-up. They found that C statistic, for the overall discriminatory performance for death or liver transplantation of the AOM score at diagnosis, was 0.67 and ranged to 0.75 at 5 years following diagnosis. Moreover, AOM had a good fit at baseline and during follow-up with a hazard ratio for clinical events ranging from 2.18 (95% CI 1.77-2.68) at diagnosis to 2.94 (95% CI 2.42-3.57) at 5 years of follow-up which pointed that whose AOM score higher than 2.0 in the first 5-years has a remarkable risk of death or liver transplantation (time-dependent HR 4.09 95% CI 2.99-5.61).

In addition to that, the C-statistic of ALP alone was found as between 0.52 and 0.63 in the first 5 years for LT-free survival prediction.

de Vries et al. (7) study specified the 10-year LT-free survival rate was 75-80%, and the median survival rate was reported as 22 years, on the other hand, in the present study it was found as 66% and 13 years, respectively.

Furthermore, the authors also found that MRS was initially calculated in 498 patients; 311 patients were identified as low-risk group, 161 patients as intermediate risk group, 26 patients as high-risk group. LT-free survival rates were significantly different between those 3 groups. The 1-3-5-year survival rates were 99.4%, 95.5%, 91.5% for the low-risk group; 98.1%, 88.4%, 77.3% for the intermediate risk group and 92.3%, 65.4%, 47.4% for the high-risk group, respectively. MRS was found to be higher at the time of diagnosis and at the 5th year compared to C-statistic AOM (0.73 vs 0.68; 0.79 vs 0.75, respectively)

The present study has some advantages such as it can be used at the diagnosis and during follow-up and the data was collected from different centers which has complete follow up over 80% and evaluate liver transplantation and all cause of mortality. In addition to that, it may easily be used to perform repeated estimates for patients in different categories of risk in time in order to select optimal management for the patients.

In conclusion, we can say that AOM has sufficient discriminant value and adequate and good prediction accuracy for PSC prognosis at diagnosis and during the follow-up period. So, it can be useful for daily clinical practice. Further studies are needed to show its efficacy in other ethnic population from the worldwide. Finally, new scoring system should be developed in the future to predict more accurate clinical course and liver related events.

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