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Non-invasive and accurate diagnostic system for biliary atresia

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Biliary atresia (BA) is the most common cause of obstructive jaundice in infancy [1]. Early diagnosis is essential for the successful management of BA. The accurate diagnosis of BA using the existing diagnostic approaches is not easy due to the overlapping features between BA and the other cause of neonatal cholestasis. The current diagnostic methods such as a liver biopsy and intraoperative cholangiography are invasive, and the radiological investigations (magnetic resonance imaging (MRI) etc.) are time-consuming and costly [2]. Many institutions use gamma-glutamyl transpeptidase (GGT) as a serum marker for differentiating BA from neonatal hepatitis. However, the reliability and reproducibility of GGT alone is not sufficient for the accurate diagnosis of BA.

In *EBioMedicine*, Dong et al. [3] investigated the development of a novel nomogram using GGT, in combination with other BA-associated risk factors. The authors retrospectively analyzed data from 1728 newborn infants with neonatal obstructive jaundice including 1512 patients with BA from a single large center in China during a six year period from 2012 to 2017 [3]. They found following main findings: [1] the levels of direct bilirubin (DB), alkaline phosphatase (ALP), and GGT were significantly higher in BA patients; [2] the area under curve (AUC) value for the multivariate logistic regression-based nomogram was greater than that for the levels of GGT, ALP, or DB alone in the prediction of BA [3]; the discriminatory ability was significantly improved when GGT was combined with additional risk predictors, including weight, gender, DB, and ALP. Although, the authors acknowledge the limitations of their study that it is a retrospective study based on a single-center cohort, they concluded that their nomogram using GGT in combination with other BA-related factors is superior to the GGT alone in the preoperative diagnosis of BA [3].

Currently, machine learning is a hot topic. Machine learning is a part of a computer science and a field in which systems can be designed to learn concepts from data to make predictions. Machine learning is used for pattern recognition based on models for classification and prediction of novel unseen data. Sowa et al. [4] reported that machine learning techniques (logistic regression, decision trees, support-vector machines and random forest) relying on some biomarkers to distinguish non-alcoholic fatty liver disease from alcoholic liver disease. Similarly, Dong et al. [3] used machine learning (logistic regression, decision tree and random forest) to differentiate between BA and other non-BA neonatal cholestasis. Machine learning techniques can provide a robust multivariate approach with multiple features taken into account simultaneously, without the need for variable selection [4].

Ultrasonography (US) and hepatobiliary scintigraphy are helpful investigations, however, they still require liver biopsy and/or intraoperative cholangiography for the definitive diagnosis of BA. Abdominal US in BA shows an enlarged liver, absence of biliary dilation, and an absent or contracted gallbladder after 4 h fasting. A triangular cord sign considered as a specific finding in BA has been reported with its sensitivities varying from 49% and 73% [2,5].Hepatobiliary scintigraphy is useful for excluding BA. Its sensitivity is high (98.7%), however its specificity for a differentiate diagnosis BA is relatively low (33%–80%) [6,7].Dong et al. [3] did not include US and hepatobiliary scintigraphy in their study. Recently, it was reported that phenobarbital-enhanced hepatobiliary scintigraphy in the diagnosis of BA with high accuracy (sensitivity, 100%; specificity, 93%; accuracy 94.6%) [8].More recently, Kim et al. [9] reported that a new scoring system combining clinical, US findings and hepatobiliary scintigraphy can help to arrive at an accurate diagnosis for BA in patients with neonatal cholestasis. This scoring system was able to differentiate biliary atresia in the derivation cohort (C statistic, 0.981; 95% confidence interval [CI]: 0.970, 0.992) and the validation cohort (C statistic, 0.995; 95% CI: 0.987, 1.000) [9]. Recently, it was reported that MRI-based decision tree model for diagnosis of BA improved the accuracy of a differential diagnosis between BA and other cases of infant cholestasis, with a sensitivity of 97.3%, specificity of 94.8%, and accuracy of 96.2% [10]. However, for a precise MRI examination, infants usually require procedural sedation or a general anesthesia.

The development of an early, non-invasive and accurate diagnosis system for BA is required for the better management of BA. The novel nomogram developed by Dong et al. [3] using GGT in combination with BA-related factor holds promise for future clinical application.

Disclosure

The authors declared no conflicts of interest.

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