Performance of Noninvasive Tests in Identifying Appropriate Patients for Resmetirom Treatment: Real World Data from Four Tertiary Care Centers.

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Background: Resmetirom was recently approved as the first medication for patients with metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis stages F2-F3. There is an urgent need for noninvasive tests (NITs) to identify eligible patients accurately without the need for invasive liver biopsies. Recently, the following combination of NITs was proposed for the identification of eligible patients: controlled attenuation parameter (CAP)≥280 dB/m, liver stiffness measurement (LSM) 10-20 kPa, and platelet count≥150x10^3/ µL. We aimed to test this strategy for the correct classification of patients using liver biopsy data derived from four tertiary care centers as the gold standard.

Methods: Data of consecutive patients with biopsy-proven MASLD derived from two tertiary care centers were collected between 2017 and 2023. Histological classification of biopsies was performed according to the Steatosis, Activity, Fibrosis/Fatty Liver Inhibition of Progression (SAF/FLIP) algorithm and the NASH-Clinical Research Network (NASH-CRN) scoring system. Eligible patients based on histological criteria were those with MASH (NAS ≥ 4) and F2-F3. Cohen's Kappa statistic was used as a measure of agreement between the diagnostic tests and the liver biopsy.

Results: Prospectively collected data from 1006 biopsy-proven MASLD patients were included in the analysis and retrospectively analyzed (Age: 55 [19-84] years, 374 males (37.3%)). A total of 346 patients (34.4%) met the histological criteria for resmetirom use and 349 patients (34.7%) the NIT criteria. The combination of the NIT criteria was able to identify the patients with accurate histological features with a sensitivity of 39.3% and specificity of 67.7% (positive predictive value: 0.390, negative predictive value: 0.680). Cohen´s Kappa indicated a poor agreement between the reference standard and non-invasive diagnostic algorithm (Kappa: 0.070, P=0.026). In patients that met the NIT criteria, the following reasons were exclusionary from treatment with resmetirom based on the histological findings: 31 (9.0%) had cirrhosis on biopsy (F4), 115 (33.0%) had F0-F1, and 67 (19.2%) had F2-F3 but NAS < 4. Similarly, the NIT criteria had poor performance in predicting the presence of F2-F3 on biopsy regardless of the presence of MASH or the NAS (Kappa: 0.071, P=0.016, Sensitivity 38.1%, specificity 69.1%, PPV 0.582, and NPV 0.498).

Conclusion: The proposed non-invasive diagnostic criteria for selecting patients eligible for resmetirom use showed a poor performance in comparison to the histological criteria. Further studies and modification of the cut-offs are needed.