Abstracts

Genetic testing in a national cohort of adults with chronic kidney disease of unknown origin

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Background: Chronic kidney disease (CKD) remains unexplained in at least 20% of patients. Massively parallel sequencing (MPS) can be a valuable diagnostic tool in patients with unexplained CKD, but prospective data from routine clinical practice are limited. We aimed to determine the diagnostic yield and relevance of MPS-based gene panel testing in patients with unexplained CKD in a real-world context. We additionally examined barriers to implementation of genetic testing.

Methods: In this prospective cohort study, we recruited patients with unexplained CKD (estimated glomerular filtration rate <60 ml/min/1.73 m^2 without underlying clinical diagnosis) with onset at <50 years of age who underwent MPS-based multigene panel testing from 11 academic and non-academic hospitals across the Netherlands. In patients with a (likely) pathogenic variant, we verified that the variant likely explained the clinical phenotype. A nationwide online survey was sent to all Dutch nephrologists and residents to investigate potential barriers for gene panel testing.

Results: A diagnostic variant was identified in 59/340 participants (17%). Most common diagnostic variants were in *NPHP1* (13 patients), *COL4A3* (12 patients), *COL4A4* (5 patients), *COL4A5* (6 patients) and *PAX2* (5 patients). A genetic diagnosis led to at least one clinical consequence in 73% of patients. Main barriers reported by Dutch nephrologists (N = 71) included genetic illiteracy (53%), difficulties with test selection (51%) and a lack of time (43%).

Conclusions: MPS-based multigene panel testing yielded a genetic diagnosis in 17% of patients with unexplained CKD. Our findings support the relevance of MPS in the diagnostic workup of adults with unexplained CKD with onset at <50 years of age. Additionally, our results underline the need to improve genetic education among nephrologists to better the implementation of MPS-based diagnostic testing in clinical practice.

Keywords: chronic kidney disease, diagnostic yield, exome sequencing, genetics, massively parallel sequencing

Reference: de Bernardi A, Nedara K, Dupain C, Mc Leer A, Alberti L, Cockenpot V, Neviere ZM, Guillou I, Blons H, Selves J, Patrikidou A. 698P Clinical, pathological and molecular characteristics of brain metastases from cancer of unknown primary (BM-CUP): A multicenter French retrospective cohort. Annals of Oncology. 2025;36:S497.

Comparison of NAFLD, MAFLD, and MASLD Prevalence and Clinical Characteristics in Asia Adults

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Background/Aims: The principal limitations of the term non-alcoholic fatty liver disease (NAFLD) are the reliance on exclusionary confounder terms and the use of potentially stigmatizing language. Within three years, NAFLD went through two name changes, from NAFLD to metabolic-dysfunction-associated fatty liver disease (MAFLD) to metabolic dysfunction-associated steatotic liver disease (MASLD). However, there is no Asian consensus statement on the renaming of MASLD, and evidence on the epidemiology and characteristics in the Asia population under different diagnostic criteria remain limited. This study aimed to fill these gaps by analyzing the prevalence and characteristics of MASLD, NAFLD, and MAFLD in an Asian population.

Methods: A retrospective, cross-sectional study was conducted in regional China with participants from the health management database in 2017–2022. Demographic and laboratory metabolic profile and body composition data were obtained. Hepatic steatosis were diagnosed by ultrasound. The likelihood of having fibrosis was assessed using the NAFLD fibrosis score (NFS). Recently proposed criteria for metabolic dysfunction-associated steatotic liver disease (MASLD) were applied.

Results: A total of 20,226 subjects were included for final analysis. 7465 (36.91%) participants were categorized as MASLD patients, 10,726 (53.03%) participants were MAFLD, and 7333 (36.26%) participants were NAFLD. Compared with MAFLD, body composition of MASLD and NAFLD patients were obviously different. MASLD patients were older, had a higher body mass index and percentage of male gender, and had a higher ALT, diastolic blood pressure, triglyceride, and waist circumference but lower High-Density Lipoprotein Cholesterol (HDL-C) than non-MASLD patients. Using binary regression analysis, we found for the first time that putative bone mass (OR = 4.62, 95CI% 3.12–6.83) is associated with the risk of developing MASLD. The area under the receiver operating curve (AUC) for predicting cardiovascular outcomes (CV) was 0.644 for MAFLD and 0.701 for MASLD.

Conclusion: MASLD (36.91%) prevalence was closed to NAFLD (36.26%) and lower than MAFLD (53.03%). Presumed bone mass might be the predictor of disease progression in MASLD patients. MASLD better identifies patients likely to have a higher risk of metabolic disorders or CV events.

Reference: Huang X, Yu R, Tan X, Guo M, Xia Y, Zou H, Liu X, Qin C. Comparison of NAFLD, MAFLD, and MASLD prevalence and clinical characteristics in Asia adults. Journal of clinical and experimental hepatology. 2025; 15(1):102420.