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A 2-STEP PATHWAY IN ASSESSING LIVER FIBROSIS AMONG PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOSIS LIVER DISEASE (MASLD) IN A UNIVERSITY PRIMARY CARE SETTING

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ABSTRACT

Background: Metabolic dysfunction-associated steatosis liver disease (MASLD) is highly prevalent in primary care and it can progress to advanced fibrosis. FIB-4 is a recommended screening tool among patients with MASLD, before referral for liver stiffness measurement (LSM) to detect advanced fibrosis. However, implementation of this 2-step pathway is not well established in the Malaysian primary care setting.

Objectives: Therefore, this study aimed to demonstrate the implementation of the 2-step pathway in a university primary care setting. Specific objectives were to determine the proportion of patients with elevated FIB-4, compare the mean FIB-4 scores between those with and without advanced fibrosis, and determine the performance of FIB-4 in detecting advanced fibrosis against LSM as the reference standard.

Methods: A cross-sectional study was conducted at a university primary care clinic. Patients with MASLD were recruited according to the eligibility criteria. FIB-4 score was calculated, followed by LSM using vibration-controlled transient elastography to determine the fibrosis stages (F0–F4). F3 and F4 were defined as advanced fibrosis. The trend across F0–F4 was analysed using ANOVA, while the mean FIB-4 scores between the two groups were compared using independent t-test. The performance of FIB-4 against LSM was evaluated using sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and area under the curve (AUC).

Results: Among 200 participants, 27 (13.5%) had elevated FIB-4 and 28 (14%) had advanced fibrosis. The mean FIB-4 scores significantly increased across the fibrosis stages, from 0.99±0.38 (95%CI: 0.91–1.06) in F0 to 1.56±0.66 (95%CI: 0.74–2.37) in F4 (P=0.002). The mean FIB-4 score was significantly higher in the advanced fibrosis group (1.54±0.74) than those without (1.04±0.51). FIB-4 demonstrated a sensitivity of 50% (95%CI: 30.7–69.4), specificity of 92.4% (95%CI: 87.4–95.9), PPV of 51.9% (95%CI: 36.2–67.1), NPV of 91.9% (95%CI: 88.7–94.3), and AUC of 0.74 (95%CI: 0.60–0.84) for detecting advanced fibrosis.

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CHAPTER ONE: INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has undergone a terminology shift to better reflect its metabolic basis (1). In 2020, metabolic dysfunction-associated fatty liver disease (MAFLD) was introduced, incorporating metabolic dysfunction into its diagnostic criteria, which has been shown to better predict atherosclerotic cardiovascular disease (ASCVD) (1). MAFLD is defined by the accumulation of fat in the liver, diagnosed based on imaging, non-invasive score, or histology in individuals who are overweight or obese, have type 2 diabetes mellitus (T2DM), or have at least two metabolic risk abnormalities (2, 3). More recently, the European Association for the Study of the Liver (EASL) proposed another terminology - metabolic dysfunction-associated steatotic liver disease (MASLD), which is defined as steatotic liver disease (SLD) with at least one cardiometabolic risk factor, excluding excessive alcohol intake (2, 3). MASLD aims to unify disease classification while maintaining a strong metabolic emphasis (3).

Epidemiological studies suggest MASLD captures a larger patient population than MAFLD. A study conducted in the United States reported the prevalence of NAFLD, MAFLD, and MASLD as 18.5%, 19.3%, and 20.8%, respectively, with most individuals previously classified under NAFLD or MAFLD meeting MASLD criteria (4). Another study demonstrated a high degree of consistency among the three definitions, especially between NAFLD and MASLD, indicating that the adoption of MASLD does not substantially change the key clinical insights derived from previous NAFLD and MAFLD research (5). The study also emphasized the need to focus on individuals with multiple cardiometabolic risk factors, as they are at higher risk of liver disease progression (5). MASLD can progress to metabolic dysfunction - associated