



## Trend for Clinical Use of Metabolic Associated Fatty Liver Disease (MAFLD)

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**Received date:** 24 February 2021; **Accepted date:** 21 April 2021; **Published date:** 30 April 2021

**Citation:** Bando H. Trend for Clinical Use of Metabolic Associated Fatty Liver Disease (MAFLD). *Asp Biomed Clin Case Rep.* 2021 Apr 30;4(2):99-102.

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### Abstract

The problems among obesity, diabetes mellitus (DM), fatty liver, metabolic dysfunction have been prevalent, and diagnostic criteria as non-alcoholic fatty liver disease (NAFLD) has been used in practice. When diagnosing NAFLD, to exclude other related liver diseases was necessary, including excessive alcohol intake. The international experts proposed the proper term from NAFLD to metabolic associated fatty liver disease (MAFLD). MAFLD criteria include the evidence of the presence of hepatic steatosis associated with three situations. They are obesity/overweight, presence of Type 2 DM (T2DM), or metabolic impaired function, which were studied in the light of pathophysiology, epidemiology, diagnosis and pharmacotherapy.

### Keywords

Fatty Liver, Non-Alcoholic Fatty Liver Disease, Metabolic Associated Fatty Liver Disease, Non-Alcoholic Steatohepatitis

### Abbreviations

NAFLD: Non-Alcoholic Fatty Liver Disease; MAFLD: Metabolic Associated Fatty Liver Disease; NASH: Non-Alcoholic Steatohepatitis

As the prevalence of obesity and type 2 diabetes mellitus (T2DM) has been increasing worldwide, fatty liver disease from metabolic dysfunction has been a global medical and health problem [1]. Especially, it was observed in early stages preceding the T2DM development. The problems among fatty liver, T2DM, metabolic syndrome have been important. Further, diagnostic criteria of non-alcoholic fatty liver disease (NAFLD) was common for usual practice of medicine [2].

NAFLD has affected approximately one quarter of adult population across the world, and brought medical, health and economic burden to many societies [2,3]. The effective pharmacotherapy for NAFLD has not been approved until now [4]. Higher NAFLD prevalence would be from several elements, such as excess carbohydrate intake, elevated calorie energy intake, decreased physical activity, habit of sedentary behavior, imbalance of diet and exercise, and so on [5]. Along with this tendency, health situation of adult has

been not satisfactory, even if the adult shows normal BMI in the affluent country [6,7].

NAFLD has recently shown higher ratio of the cause for chronic liver disease [2]. Regarding NAFLD in most guidelines, it is defined for the evidence of steatosis in 5%<sup><</sup> of existing hepatocytes by medical imaging and/or histological examination [8]. Furthermore, it is important to show the situation of the absence in several causes including alcohol, B or C type of viral hepatitis, some kinds of hereditary liver diseases, or steatogenic medication for long term [9].

This diagnostic way has been adopted as an exclusive method, and for which liver biopsy would be the golden standard. It covers a spectrum for progressive liver diseases including steatosis to fibrosis, cirrhosis, nonalcoholic steatohepatitis (NASH) and hepatocellular carcinoma (HCC) [10]. It was well-known that it is clearly associated with metabolic dysfunction, where several components co-exist for abdominal obesity, hypertension, dyslipidemia and hyperglycemia [11]. As the existing ratio of NAFLD grows dramatically, there are urgent clinical problems [12]. They include i) the absence of clear nomenclature of the fatty liver due to non-alcohol use, ii) the lack of positive diagnosis with proper definition, iii) no approved medical agents for this disease, etc.

From statistic point of view, NAFLD has been found about 25% of the population worldwide [2,3]. According to the previous data, diabetics have chronic liver disease associated with about three-fold higher risk, which is mainly from non-alcohol or non-virus etiology leading to NAFLD [13]. NAFLD prevalence in T2DM shows up to 55.5%, which is more than twice than general people [14]. A recent meta-analysis data showed the prevalence of NAFLD as follows: general people 29.8%, T2DM 51.8%, non-diabetic 30.7%, obesity 66.2% and lean 11.7% [15]. As obesity shows rising trend from 2%-7% in 2000-2014, NAFLD showed increase in parallel [16]. Further, obesity and T2DM showed the elevated risk of progression for NASH, cirrhosis and HCC [17,18]. Consequently, growing epidemic situation of obesity and T2DM will bring increasing prevalence for NAFLD across the world [19].

Related to NAFLD, a panel of international experts was gathered from 22 countries [3]. The experts have proposed a changing medical term from NAFLD to new medical term, which is metabolic associated fatty liver disease (MAFLD). They reached a consensus that the term NAFLD would not reflect proper knowledge and that MAFLD would be more appropriate from terminological point of view. The new definition of MAFLD puts emphasis on the important function from metabolic aspect. In comparison with former NAFLD, newly summarized definition of MAFLD is supposed to include wider perspective. MAFLD criteria showed the evidence of hepatic steatosis found with the following three situations. They are obesity/overweight, T2DM presence, and/or the evidence of metabolic dysfunction (dysregulation) [20]. There are some differences of shared features between the words of NAFLD and MAFLD, in the light of pathophysiology, epidemiology, diagnosis and pharmacotherapy.

Similar to previous medical term NAFLD, MAFLD has represents hepatic manifestation for multisystem disorder. It shows heterogeneous factors in underlying cause, symptom and signs, clinical outcomes and progress course [13]. However, due to the complex pathophysiological aspects, a single diagnostic test is not likely to be available. Metabolic syndrome contains some definitions, and it seems necessary to develop the new criteria for diagnosing MAFLD in this way [21,22].

When diagnosing MAFLD, to exclude the other chronic liver diseases is necessary, including excessive alcohol intake [23]. With the elucidation of the pathophysiological processes causing to MAFLD, it would be increasingly understood that the existence of generalized metabolic syndrome seems to exist at the fundamental level. As a result, MAFLD is recognized for an independent disease that guarantees a positive diagnostic process, rather than excluding other diseases. Furthermore, the prevalence of MAFLD has been elevated, which makes it possible to exist in combination of other chronic liver diseases. Therefore, the method of excluding comorbidities becomes inappropriate. From the above, MAFLD definition will be made not according to the exclusion criteria but from the set of additional positive criteria [3].

Regarding the proposal from the experts, the disease assessment and stratification of MAFLD severity should cover the wider area, which are beyond a simple dichotomous classification of non-steatohepatitis and steatohepatitis [20]. There are other proposals including a set of criteria for the definition of MAFLD associated liver cirrhosis, and a conceptual perspective for other possible causes for fatty liver. Consequently, the distinction would be clarified for the distinction of diagnostic criteria and also the inclusion criteria for research and clinical trials. To reaching a certain consensus on MAFLD criteria will contribute the unification of the medical terms including the International Classification of Diseases (ICD)-coding, Disease-Related Groups (DRG), verification of clinical trials, development of liver research and the improvement of clinical care [20].

In summary, current topics concerning the changing term from NAFLD to MAFLD were described in this article. Some clinical trials are found concerning the inclusion criteria and endpoints [24]. Such studies will bring various initiatives evolving for clinical application of new nomenclature MAFLD definition.

### Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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