

## 新陳代謝異常與肝臟疾病

### Metabolic derangement and liver diseases

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Non-alcoholic fatty liver disease (NAFLD) has been recognized as the most prevalent liver disorder globally, which affects more than quarter of the global population. The relative lower BMI in Asians is not protective from metabolic insults. Moreover, Asian people are more prone to metabolic syndrome (MetS), type 2 DM (T2DM) and NAFLD than other races. Previous studies from Taiwan clearly demonstrated that the prevalence of NAFLD has been increasing for more than 2 folds within less than 20 years. Therefore, there is a pressing need for elucidation of the clinical characteristics of NAFLD and its management in a practical fashion since the increasing trend of NAFLD epidemic can't be overlooked in recent decade.

Non-alcoholic steatohepatitis (NASH) was defined by histopathologic evidence as an extreme form of NAFLD. NASH has been a histologically defined disease, characterized by hepatic steatosis, ballooning, and lobular inflammation with variable fibrosis. The metabolic liver disorder carries the risk of development of fibrosis, cirrhosis and liver-related deaths. It's commonly associated with related metabolic diseases, leading to cardiovascular events as its leading cause of death. Metabolic dysfunction, mainly insulin resistance (IR), plays a major role in the pathogenic mechanisms underlying fatty liver disease and its disease progression. The metabolic disorders include abdominal obesity, hypertension, dyslipidemia and insulin resistance (IR) and further increase the risk of cardiovascular disease (CVD), T2DM and chronic kidney disease (CKD). The scenario of a higher overall mortality due to CVD as compared with controls has made it a critical global issue.

Lifestyle modification consisting of diet, exercise, and weight loss has been advocated to be the initial step for management of NASH patients. The strategies have been widely adopted into the major current guidelines. Among them, weight loss has been reported as the most effective one in improving the histology features and regression of NASH. Several studies have evaluated lifestyle changes, particularly diet and exercise in managing NASH. However, the adherence of lifestyle modification remains problematic in a large proportion of NASH patients. It is difficult for patients with morbid obesity and musculoskeletal disorders to do sufficient exercise. Besides, the efficacy of lifestyle modification could not be applied to those lean NASH patients.

Therefore, pharmacological treatment may be required in some patients. Currently, there is no effective drug approved for therapeutic indication for NAFLD/NASH. With multiple agents and/or compounds currently recruited into phase 2 to 3 clinical trials, it is important to consider how the eventual approval of a pharmacologic agent for NASH will impact ongoing and future clinical trials in this aspect.