Equivalent Prevalence and Progression of Chronic Kidney Disease in NAFLD and MASLD

Running title: CKD prevalence and progression in NAFLD and MASLD

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To the editor,

The consensus group, composed of multiple societies, resolved in June 2023 to change the term nonalcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated steatotic liver disease (MASLD) to diminish the potential for stigmatization and more accurately capture its underlying pathophysiology. MASLD should fulfill a new inclusion criterion of “the presence of at least one or more cardiometabolic risk factors,” which emphasizes the significance of chronic inflammatory diseases (e.g., extrahepatic) in the management of steatotic liver disease (SLD). Patients with SLD, associated with cardiometabolic dysregulation, have a higher incidence of extrahepatic diseases, such as chronic kidney disease (CKD). Several reports including systematic reviews and meta-analyses have demonstrated a significant relationship between NAFLD/MASLD and incident CKD (hazard ratio 1.12–1.43). It is essential to extend research on NAFLD to MASLD to ensure that valuable resources are effectively utilized and contribute to advancing knowledge in this field. Although there have already been some reports on the impact of NAFLD changing to MASLD in cardiovascular risk, the evidence on the development of chronic kidney disease is not sufficient. Therefore, our study aimed to compare the prevalence and progression of CKD risk in patients with NAFLD and MASLD.

The present study included 7,286 consecutive health check examinees who underwent ultrasonography and were monitored at the Saga Health and Clinical Examination Center (Saga, Japan) from January 2010 to March 2020. Of these, 895 were excluded because of insufficient data on alcohol consumption habits (n = 541), alcohol consumption ≥60 g/day (n = 161), hepatitis C virus infection (n = 112), and hepatitis B virus infection (n = 81). The final sample of this study comprised 2,306 individuals of Asian origin, all diagnosed with SLD based on ultrasonography. NAFLD was identified in 63.4% (1,462/2,306) of the patients, including those who...
did not meet the cardiometabolic criteria for MASLD. These cases were classified as cryptogenic SLD, and a substantial portion (93.3%) of the patients with NAFLD were also diagnosed with MASLD. Our results are consistent with previous studies that reported that nearly all NAFLD patients fulfilled the MASLD criteria.\textsuperscript{10-12} CKD was defined as an estimated glomerular filtration rate (eGFR) of \textless 60 mL/min/1.73 m\textsuperscript{2} and defined an event as a patient whose renal function was "normal" at the initial visit, but who developed CKD (whose renal function became and persistently abnormal, eGFR <60 mL/min/1.73 m\textsuperscript{2}) during follow-up.

There were no significant differences in age, sex, and baseline estimated glomerular filtration rate [median eGFR (range); 79.8 (36.1–149.8) vs. 79.6 (36.1–149.8)] between the NAFLD and MASLD groups (\textbf{Supplementary Table 1}). The prevalence of CKD in the NAFLD and MASLD groups was 5.34\% (78/1,462) and 5.43\% (74/1,364), respectively. This data aligns well with a recent study using UK Biobank, which showed a CKD prevalence of 5.42\% (410/7,560) in the MASLD group.\textsuperscript{13} In the present study, we excluded 12.3\% (895/7,286) of individuals, including heavy drinkers and patients with viral hepatitis. These patients may have had an influence on the prevalence of CKD. Therefore, it is important to note that this exclusion may have affected the overall prevalence of CKD in patients with SLD. To compare the development of CKD between the groups, we constructed Kaplan-Meier curves (\textbf{Figure 1}). The rate of five-year/ten-year cumulative incidence of CKD were 0.054\%/0.262\% in patients with NAFLD and 0.057\%/0.261\% in patients with MASLD, respectively. There were no significant differences in the development of CKD between patients with NAFLD and MASLD (\textbf{Figure 1}). These results indicate that the prevalence and progression of CKD are similar in patients with MASLD and those with NAFLD. However, since this study included only Asians, further research should be conducted to investigate whether these findings are applicable to other ethnic or regional groups (e.g., Western populations).

In conclusion, data on CKD obtained using the term NAFLD can be extrapolated to MASLD. Furthermore, MASLD has clarified the complications of metabolic dysfunction, it is
expected to develop therapeutic strategies through new monitoring and multifaceted interventions for CKD.

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**Authors' contributions**

Hiroyuki Suzuki and Tsubasa Tsutsumi: study concept, design, and drafting; Machiko Kawaguchi: interpretation of data, statistical analysis, and interpretation of data and critical revision of the manuscript; Keisuke Amano: data extraction, interpretation of data, and critical revision of the manuscript; Takumi Kawaguchi: study concept, interpretation of data and critical revision of the manuscript.

**Conflict of interest**

Takumi Kawaguchi received lecture fees from Janssen Pharmaceutical K.K., Taisho Pharmaceutical Co., Ltd., Kowa Company, Ltd., Otsuka Pharmaceutical Co., Ltd., Eisai Co., Ltd., ASKA Pharmaceutical Co., Ltd., AbbVie GK., and EA Pharma Co., Ltd. The other authors have no conflicts of interest to declare.
References


**Figure Legends**

**Figure 1.** Differences in CKD development between the NAFLD and MASLD groups.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; CKD, chronic kidney disease.
### Supplementary Table 1. Baseline patient characteristics between NAFLD and MASLD.

<table>
<thead>
<tr>
<th>Value</th>
<th>NAFLD (n = 1,462)</th>
<th>MASLD (n = 1,364)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53 [21–83]</td>
<td>50 [21–83]</td>
<td>0.33</td>
</tr>
<tr>
<td>Sex, female/male</td>
<td>583/879</td>
<td>537/827</td>
<td>0.78</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.8 [14.3–59.8]</td>
<td>24.8 [15.6–59.8]</td>
<td>0.19</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>21 [9–102]</td>
<td>22 [9–102]</td>
<td>0.43</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>24 [5–278]</td>
<td>25 [5-278]</td>
<td>0.35</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>79.8 [36.1–149.8]</td>
<td>79.6 [36.1–149.8]</td>
<td>0.61</td>
</tr>
<tr>
<td>FIB-4 index</td>
<td>0.95 [0.26–5.74]</td>
<td>0.94 [0.26–5.74]</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Data are presented as medians [range].

Abbreviations: NAFLD, non-alcoholic fatty liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; AST, aspartate aminotransferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate.