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Additive Effects of Diabetes and NAFLD on Liver Disease Severity and Clinical Outcomes in the General Population (NASH-CO Study)

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ABSTRACT

BACKGROUND AND AIMS - Relationships between diabetes and NAFLD have been mainly investigated at the hospital setting, with the risk of an overestimation of the true burden of liver disease. From a general population-based cohort, this study aimed to assess the severity of NAFLD and clinical outcomes among type 2 diabetic subjects in a community setting. **METHOD** - The study population consisted of 199, 341 participants from the nationwide CONSTANCES cohort. After exclusion of subjects with excessive alcohol consumption, viral hepatitis or other causes of liver diseases, 164, 285 were analyzed. Among them, 8386 (5.3%) had type 2 diabetes. Non-invasive diagnosis of NAFLD and advanced fibrosis was performed using the combination of Fatty Liver Index and Forns Index. Outcomes analyzed were liver-related events, cardiovascular disease, extrahepatic cancer, chronic kidney disease, liver transplantation and overall mortality. Median follow-up was 2.5 years. **RESULTS** - The prevalence of NAFLD and NAFLD with advanced fibrosis among diabetic versus non-diabetic subjects was 61.1% (95% CI 60–62.2) vs 15.2% (95% CI 15–15.3) ($p < 0.0001$) and 4.8% (95% CI 4.2–5.4) vs 1.2% (95% CI 1–3) ($p < 0.0001$), respectively. Rate of advanced fibrosis raised to 10% (95% CI 8–12) in case of additional metabolic disorders and to 13.9% (95% CI 7.2–20.6) in diabetic requiring insulin therapy. When adjusted for other risk factors, diabetes remained associated with both NAFLD and advanced fibrosis (OR = 1.36, 95% CI 1.24–1.51 and OR = 1.95, 95% CI 1.36–2.8, respectively). When adjustment for usual risk factors, presence of diabetes in NAFLD subjects was associated with increased risk of liver-related events (aHR = 4.26, 95% CI 2.46–7.38), while presence of NAFLD in diabetic subjects was associated with increased risk of cardiovascular-related events or extra-hepatic malignancy (aHR = 1.99, 95% CI 1.16–4.22, and aHR = 4.63, 95% CI 1.18–15.1, respectively). Risk of death was significantly increased by both the presence of diabetes among NAFLD subjects (aHR = 1.32, 95% CI 1.02–2.31) and the presence of NAFLD among diabetic subjects (aHR = 1.25, 95% CI 1.03–2.51). **CONCLUSION** - From a large community-based cohort with no excessive alcohol consumption, this study confirms the additive effect of diabetes and NAFLD on liver disease progression, diabetes-related complications and overall mortality, regardless of usual risk factors. Advanced fibrosis, which was less frequent in this unselected population than previously reported, should be screened in subjects with additional metabolic disorders or advanced diabetes.

KEYWORDS: -

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