Electronic Frailty index and hazard of with MACE event in patients with Type 2 diabetes melitus

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Background

The prolonged presence of type 2 diabetes meliltus (T2DM) significantly elevates the risk of cardiovascular diseases (CVD), affecting approximately 30% of individuals with T2DM [1]. This is attributed to the association between T2DM and aging-related processes, such as frailty and multimorbidity, which worsens the adverse effects of T2DM [2-3]. Understanding the independent effect of frailty on CVD in patients with T2DM could help identify at risk for CVD earlier and reduce mortality in the context of novel therapies [3]. However, the association of frailty with incidence of CVD patients with T2DM has not been thoroughly studied [4-8]. Frailty index is a tool to assess the overall health and vulnerability of older individuals. However, the most commonly used frailty index, the Fried frailty index, requires additional tests such as gait speed and grip strength for its calculation. There is a need to quantify frailty using only electronic medical record (EMR) and expand the use of the Frailty index [8]. Therefore, this study aims to explore the association between frailty index obtained from EMR and major adverse cardiovascular events (MACE) in patients with T2DM.

Methods

This study was conducted using the observational medical outcomes partnership common data model (OMOP-CDM) database at Ajou University School of Medicine (AUSOM). Study population inclusion criteria were patients with T2DM over 40 years of age who had never experienced MACE. The observation period is the previous one year as of the index date. The index date was defined as the first date of diagnosis of T2DM.

The electronic frailty index (eFI) is similar to the frailty index, but uses EMR data to quantify frailty severity without testing for the index alone. The eFI employed in this study comprised 40 variables collected before the index date. All variables were binarized based on its presence or absence, and the frailty index was calculated as the sum of the relevant items (range, 0-40 with a higher score indicating increased frailty) [8]. The 99th percentile score less than 0.7 is typical of all sample types [9]. Following this suggestions, we categorized the patient groups into normal (0 ~ 8), pre-frail (9 ~ 16), and frail (17~40) groups. The outcomes of interest was defined as MACE, which includes myocardial infarction, cardiovascular disorders, acute ischemic heart disease, chronic ischemic heart disease and acute myocardial infarction. Hazard ratios (HR) were estimated using the Cox proportional hazards regression model, and Kaplan-Meier plots were generated to visually depict the temporal occurrence of outcomes across groups. The log-rank test was used to compare the survival distribution of the three groups.

To assess the robustness of age's effect, sensitivity analyses were conducted by dividing the participants into two age groups: those 65 years and younger, and those 66 years and older.

Results

The study cohort comprised 32,966 individuals. The risk of MACE was significantly high in the frail group compared to the normal group (HR, 2.0 [95% CI, 1.21-3.30]; P=.005), but there was no significant

result in the pre-frail group compared to the normal group (HR, 1.1 [95% CI, 0.88-1.4]; P=.400) (Figure 1).

In a subgroup analysis, among individuals under 65 years of age, there were 12,793 (60%) in the pre-frail group, and 491 (2.3%) in the frail group; for those over 65 years of age, the counts were 8,309 (70%) in the pre-frail group, and 346 (2.9%) in the frail group. For patients under 65 years of age, the risk of MACE showed a trend towards increased risk, but it was not statistically significant in the frail group compared to the normal group (HR, 2.0 [95% CI, 0.97-4.20]; P=.058). For patients over 65 years of age, there was no significant difference in MACE between the frail and the normal group (HR, 1.61 [95% CI, 0.82-3.15]; P=.167) or the pre-frail and normal group (HR, 0.99 [95% CI, 0.93-1.35]; P=.948) (Table 1).

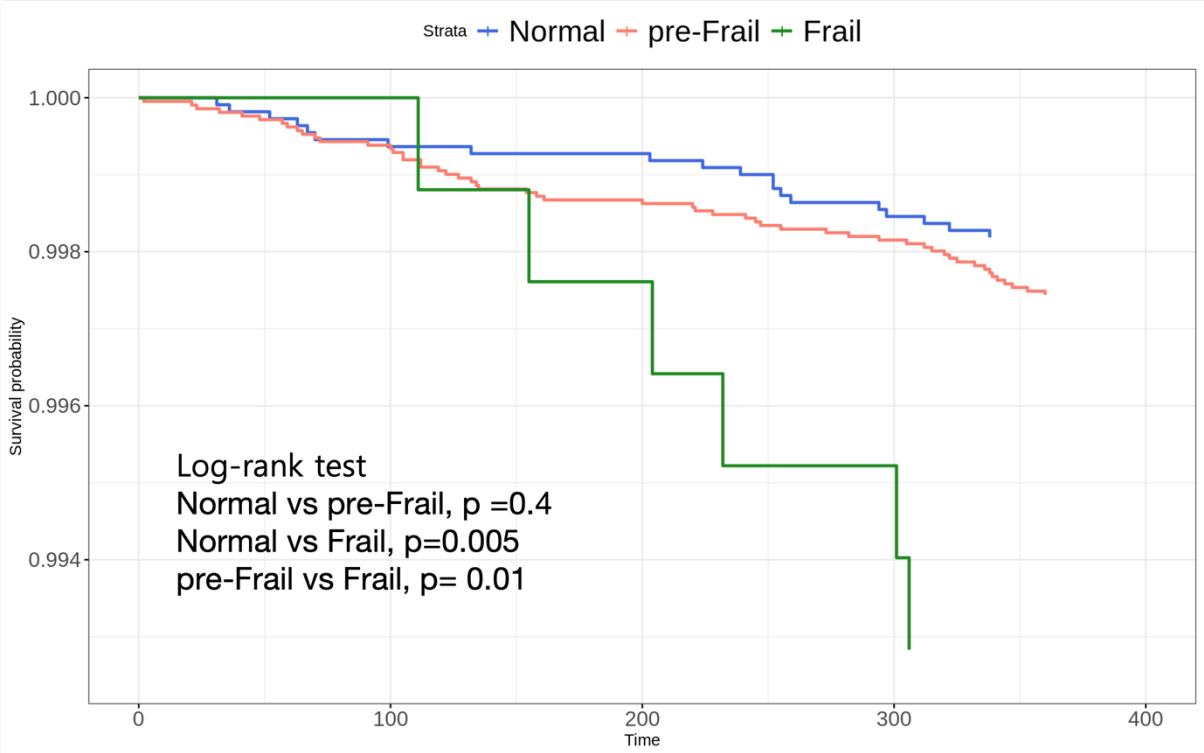

Figure 1. Survival probability curve for normal, pre-frail, and frail groups

Table1. Hazard ratio for MACE in Subgroup

Age	Frailty category	N	Hazard ratio (95% CI)
Below 65	Normal	7,938	1.0 (ref)
	Pre-Frail	12,793	1.0 (0.73 – 1.4)
	Frail	491	2.0 (0.97 – 4.2)
Over 65	Normal	3,089	1.0 (ref)
	Pre-Frail	8,309	0.99 (0.73 – 1.3)
	Frail	346	1.61 (0.82– 3.1)

Conclusion

This study shows an association between increasing eFI scores and the occurrence of MACE in patients with T2DM aged 40 years or older. The eFI used in this study has the advantage of not requiring separate frailty testing, and it showed the feasibility of using eFI in OMOP-CDM to screen for CVD risk groups in patients with T2DM. Further research is needed to develop more accurate frailty index using information such as gait and grip strength.

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