氏　　　　　　名　　TRAN NGOC HOANG PHAP

学 位 の 種 類　　博士（医学）

学 位 記 番 号　　博士第 968 号

学 位 授 与 の 要 件　　学位規則第４条第１項

学 位 授 与 年 月 日　　令和５年３月１０日

学 位 論 文 題 目　　Effect of diabetes and prediabetes on the development
　　　　　　　　　　of disability and mortality among middle-aged Japanese
　　　　　　　　　　adults: A 22-year follow up of NIPPON DATA90
　　　　　　　　　　（中壮年期の糖尿病および前等糖尿病状態が ADL に及ぼす影
　　　　　　　　　　響 NIPPON DATA90 22 年追跡）

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論　文　内　容　要　旨

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博士論文題目			Effect of diabetes and prediabetes on the development of disability and mortality among middle‐aged Japanese adults: A 22‐year follow up of NIPPON DATA90 （中壮年期の糖尿病および前等糖尿病状態がADLに及ぼす影響NIPPON DATA90 22年追跡）

Background and purpose

Disability is considered a long-term effect of diabetes. Among older population, people with diabetes have higher risk of disability and mortality than people with normal glucose tolerance, most of studies used cross-sectional design and focus on diabetes and comorbidities among older population, these studies has some limitations in diagnosis of diabetes, using cross-sectional design which report some limitations in establish cause-related outcome in epidemiology study. In addition, there are less studies examine the association between middle-aged population with prediabetes and disability, and all-cause mortality. Therefore, we conduct the study to examine the association between pre-diabetes, diabetes and development of disability and mortality in later among middle-aged adults Japanese, using representative data, NIPPON DATA90, which has long time follow-up up to 22 years.

Research methods

We used longitudinal data from National Integrated Project for Prospective Observation of Non-communicable Disease and its Trends in the Aged 1990 (NIPPON DATA90), a cohort study, which was carried out in 1990 as the National Survey on Circulatory Disorders. A total of 8,383 community residents from 300 randomly selected areas participated in the survey. There were 1771 participants aged 45 to 64 were eligible for the analysis. Diabetes status at baseline in1990 was classified as normal, prediabetes and diabetes based on comprehensive methods using fasting plasma glucose, plasma glucose, HbA1c certified by NGSP, self-reported medication for Diabetes. We used the modified Katz questionnaire for measuring activities of daily living (ADL) with demonstrated reliability and validity. Over a 22-years follow up, participants who had reached age 65 years and over at four time points (1995, 2000, 2006, 2012) were eligible for the ADL survey. In pooled survey, each participant has at least 1 survey of ADL and 4 survey in max. According to their living status for the period of study, the participants who were still alive at the end of the study without observation of ADL decline were considered as "normal", and participants without observation of ADL decline who died before the next ADL survey were considered as "death without an observation of ADL decline" (death without disability). The participants who died after having observation of ADL decline were also considered as having disability (death with disability).

（備考）　１．論文内容要旨は，研究の目的・方法・結果・考察・結論の順に記載し，
　　　　　　　２千字程度でタイプ等で印字すること。
　　　　　２．※印の欄には記入しないこと。

In aim to deal with competing risk, considered the happening of concurrence event of disability and mortality, we used multinomial logistic regression model to examine the effect of prediabetes, diabetes on development of ADL disability and all-cause mortality. The multinomial logit models were adjusted as follows: model 1: age, sex, smoking status and alcohol drinking status; model 2: model 1 and cardiovascular risk factors (hypertension, hypercholesterolemia, triglycerides, low serum high-density lipoprotein); model 3: model 1 and BMI only; and model 4, the final fully adjusted model including all previous variables. ORs and 95% CIs were used, P values <0.05 were considered as significant results. We also carried out the analysis stratified by sex, because the association might differ by sex.

Results

In the present study, 334 participants (18.7%) reported at least one disability, and 350 (19.6%) were reported dead without observation of disability during follow-up. Adjusting sex and other risk factors, participants with diabetes and prediabetes had a higher risk for disability (Model 4, OR 1.43, 95% confidence interval [CI] 1.07-1.91 and OR 1.66, 95% CI 1.10-2.50, respectively) and for mortality (Model 4, OR 1.56, 95% CI 1.16-2.08 and OR 1.77, 95% CI 1.18-2.65, respectively) than individuals with normal glucose tolerance.

Discussion

The present longitudinal cohort study was the first study to be carried out in Asia that used longitudinal analysis and repeated measurements in middle-aged adults, with a focus on the relative association between prediabetes in middle-aged population with disability and mortality in later life. Our findings support the conceptual framework that middle-aged adults with prediabetes have higher risks of disability and death without disability than individuals with normal glucose tolerance. Middle-aged women with blood glucose tolerance disorder were more likely to be associated with disability and mortality at 22-year follow up than others. Furthermore, the present results support the hypothesis that middle-aged participants with diabetes have higher risk of disability and mortality than people with normal glucose tolerance.

Conclusion

In summary, prediabetes in middle-aged adults is a predictor for disability and increases the risk of mortality in later life, especially in women. Early screening and intervention might decrease the progression of diabetes and its complications. Other prominent factors need to be considered to explore the causal relationship between prediabetes and disability in further studies.

別紙様式８（課程博士・論文博士共用）

学位論文審査の結果の要旨

整理番号	977	氏　名	Tran Ngoc Hoang Phap
論文審査委員			

（学位論文審査の結果の要旨）※明朝体１１ポイント、６００字以内で作成のこと

　　中年期における、糖尿病及び前糖尿病状態が、日常生活動作（ADL）の低下や死亡率にどのように影響するかを調査した。NIPPON DATA 1990 を用い、22 年間の追跡が可能であった 45 歳～64 歳の 1788 人（男 766 人、女 1022 人）を対象とした。65 歳を超えた時点で質問紙によって ADL の低下があったか確認され、観察終了時に生存して ADL の低下がない群（正常群）、ADL の低下がないが死亡した群（死亡群）、生存及び死亡を含めて ADL の低下があった群（障害群）に大別し、多項ロジットモデルにより解析された。

　　解析対象者の 18.7％で何らかの障害を認め、19.6％は障害がなく死亡していた。年齢、性、喫煙及び飲酒状況、高血圧、脂質異常症の項目を補正して解析を行ったところ、中年期の糖尿病及び前糖尿病状態では正常な耐糖能に比べて有意に障害を有する可能性が高くなること（オッズ比と 95％信頼区間、1.43 [1.07-1.91] 及び 1.66 [1.11-2.50]）、死亡率が高くなること（1.56 [1.16-2.08] 及び 1.77 [1.18-2.65]）が分かった。

　　本研究は、中年期の糖尿病及び前糖尿病状態が、ADL 低下及び死亡率増加に有意に影響を及ぼすことを明らかにした。中年期の耐糖能障害患者に対して、障害や死亡の予防に向けた介入の必要性を明確にし、その社会的意義は高いと考えられた。

　　申請者は外国語試験に合格し、英文論文を執筆して著名な当該雑誌に英文論文が掲載された。さらに、最終試験として論文内容に関連した試問および学力確認の試問にも合格したので、博士（医学）の学位授与に十分値する。

（総字数　594 字）

（令和 5 年 1 月 25 日）