

Prediabetes and incident heart failure in hypertensive patients: Results from the Swedish Primary Care Cardiovascular Database

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Abstract *Backgrounds and aims:* The cardiovascular risk conferred by concomitant prediabetes in hypertension is unclear. We aimed to examine the impact of prediabetes on incident heart failure (HF) and all-cause mortality, and to describe time in therapeutic blood pressure range (TTR) in a hypertensive real-world primary care population.

Methods and results: In this retrospective cohort study, 9628 hypertensive individuals with a fasting plasma glucose (FPG) in 2006–2010 but no diabetes, cardiovascular or renal disease were followed to 2016; median follow-up was 9 years. Prediabetes was defined as FPG 5.6–6.9 mmol/L, and in a secondary analysis as 6.1–6.9 mmol/L. Study outcomes were HF and all-cause mortality. Hazard ratios (HR) were compared for prediabetes with normoglycemia using Cox regression. All blood pressure values from 2001 to the index date (first FPG in 2006–2010) were used to calculate TTR. At baseline, 51.4% had prediabetes. The multivariable-adjusted HR (95% confidence intervals) was 0.86 (0.67–1.09) for HF and 1.06 (0.90–1.26) for all-cause mortality. For FPG defined as 6.1–6.9 mmol/L, the multivariable-adjusted HR were 1.05 (0.80–1.39) and 1.42 (1.19–1.70), respectively. The prediabetic group had a lower TTR ($p < 0.05$).

Conclusions: Prediabetes was not independently associated with incident HF in hypertensive patients without diabetes, cardiovascular or renal disease. However, prediabetes was associated with all-cause mortality when defined as FPG 6.1–6.9 mmol/L (but not as 5.6–6.9 mmol/L). TTR was lower in the prediabetic group, suggesting room for improved blood pressure to reduce incident heart failure in prediabetes.

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Abbreviations: ACE, angiotensin-converting enzyme; ADA, American Diabetes Association; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; ATC, anatomical therapeutic chemical; BB, beta adrenergic receptor blocker; BMI, body mass index; CI, confidence interval; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL, high density lipoprotein; HF, heart failure; HR, hazard ratio; ICD-10, 10th revision of the International Statistical Classification of Diseases and Related Health Problems; IQR, interquartile range; LDL, low density lipoprotein; SBP, systolic blood pressure; SPCCD-SKA, Swedish Primary Care Cardiovascular Database of Skaraborg; SPRINT, Systolic Blood Pressure Intervention Trial; TITRE, time at target; TTR, time in therapeutic range; WHO, World Health Organization.

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1. Introduction

Hypertension is highly prevalent and comprises an important risk factor for cardiovascular disease and mortality worldwide [1]. Furthermore, hypertension is a primary etiological cause for heart failure, and is the risk factor with the greatest attributable risk for incident heart failure [2]. Long term variability of blood pressure and the time of blood pressure spent in therapeutic range (TTR) may have an impact on heart failure risk and all-cause mortality [3–5]. However, these issues have not been well studied in a real-life primary health care setting, where these patients most often are treated.

Prediabetes has been suggested to be associated with an increased risk for cardiovascular disease [6], often coexists in heart failure and is a predictor of reduced survival in these patients [7,8]. Current definitions of prediabetes in the US (following the American Diabetes Association, ADA) are fasting plasma glucose (FPG) 5.6–6.9 mmol/L, postload plasma glucose 7.8–11.0 mmol/L or HbA1c 39–47 mmol/mol [9], and in Europe (following the World Health Organisation, WHO) FPG 6.1–6.9 mmol/L or the same postload plasma glucose as above [10]. Similar to hypertension the prevalence of prediabetes is high, with an estimated 6.2% of the global adult population having prediabetes when defined as impaired fasting glucose according to WHO [11]. In a recent meta-analysis, prediabetes defined by FPG was associated with a higher risk of cardiovascular disease and all-cause mortality when the WHO reference interval was used, compared with the ADA definition [6]. In populations with various prevalence of hypertension but no history of diabetes or heart failure, FPG in the prediabetic range according to the ADA was associated with a higher risk for incident heart failure, although results have not been unequivocal [12–14]. However, it was reported that concomitant prediabetes in hypertensive patients did not yield a higher cardiovascular risk, compared to hypertension alone, in studies where heart failure was not included as an outcome [15,16]. Of note, the Jackson Heart Study demonstrated similar results with heart failure included as an outcome, but the generalisability could be limited due to the inclusion of only black people in that study [17].

Thus, given the poor prognosis of heart failure [18], high prevalence of the two cardiovascular risk factors hypertension and prediabetes and their common coexistence, the question if prediabetes adds risk for incident heart failure in hypertensive patients warrants further investigation. Accordingly, the primary aim of this study was to assess how prediabetes adds to the risk of incident heart failure in patients attending primary health care for hypertension with no previous cardiovascular or renal disease.

2. Methods

2.1. Study population

The current observational retrospective cohort study used data obtained from the Swedish Primary Care

Cardiovascular Database of Skaraborg (SPCCD-SKA). SPCCD-SKA is similar to SPCCD in methodology [19], but has a longer follow-up, wider population and smaller geographical coverage, as described previously [20]. SPCCD-SKA (73 835 individuals) comprises all patients ≥ 18 years old with a registered diagnosis of hypertension or related to hypertension who visited any of 20 (out of 30) primary health care centres in the rural area of Skaraborg during a period from 2001 to 2016. The prevailing definition of hypertension in Sweden during the time of the study was a brachial office blood pressure of ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic pressure, measured in a supine or seated position on three different occasions. The participants have at least one of the following diagnoses (according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems; ICD-10): hypertension (I10–I15), diabetes mellitus (E10–E11), heart failure (I50), ischemic heart disease (I20–I25), cerebrovascular disease (I60–I69), atrial fibrillation and atrial flutter (I48), peripheral artery disease (I70–I74) and chronic kidney disease (N18). In addition to diagnostic codes, blood biochemistry including creatinine, total cholesterol, low-density and high-density lipoproteins (LDL, HDL), triglycerides, fasting glucose, and blood pressure measurements were extracted from the medical records. First registered FPG within the study period was considered index date. Drug classes assessed according to ATC-codes prescribed in the electronic medical records within 18 months prior to index date were acetylsalicylic acid (B01AC06), thiazide diuretics (C03A), beta adrenergic receptor blockers (C07), calcium channel blockers (C08), angiotensin-converting enzyme inhibitors (C09A and C09B), angiotensin receptor blockers (C09C and C09D) and statins (C10AA).

The unique personal identity number was used to interconnect data from electronic medical records, the National Patient Register (provided registered diagnoses from both inpatient and outpatient hospital care), Cause of Death Register (provided data on all deaths of people registered in Sweden), Prescribed Drug Register (provided data on all dispensed prescribed drugs at pharmacies in Sweden since 2005), and Statistics Sweden (provided data on country of birth, income and level of education).

2.2. Design

All individuals with a diagnosis of hypertension (I10–I15) and a registered FPG from January 1, 2006 to December 31, 2010 were included (20 116 of all 73 835 patients in the database). Subjects with registered hypertensive blood pressure values but no diagnosis were not included since these measurements not necessarily mean that the diagnostic criteria for hypertension were fulfilled. Prediabetes was defined as a FPG value of 5.6–6.9 mmol/L (according to the ADA definition), and as 6.1–6.9 mmol/L (according to the WHO definition) in a secondary analysis. All participants with a diagnosis of diabetes mellitus (E10–E11), heart failure (I50), chronic kidney disease (N18), stroke (I60–I69 and G459), ischemic heart disease (I20–I25),

peripheral artery disease (I70 and I74), or atrial fibrillation (I48) in the electronic medical record at primary care or the National Patient Register, or antidiabetic drug therapy (ATC classification A10), prior to the index date were excluded (Fig. 1). Participants without a registered blood pressure measurement within two years prior to and 30 days after date of inclusion were excluded as well as 817 participants with FPG ≥ 7.0 mmol/L and 19 participants with FPG < 3.9 mmol/L. There were 54 lost to follow-up due to emigration. The study population was followed from inclusion until occurrence of the primary endpoint, death, or end of study December 31, 2016.

Blood biochemistry values were used if registered within two years prior to and 30 days after the index date. Estimated glomerular filtration rate (eGFR, mL/min/1.73 m²) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [21]. Height, weight, smoking status, and body-mass index (BMI) were used if registered at any point in the database.

2.3. Blood pressure time in therapeutic range

TTR was defined as the proportion of time with blood pressure levels $\leq 140/90$ mmHg, calculated as described previously [22], for all patients with ≥ 2 measurements registered from January 1, 2001 to 30 days after index date.

From the first measurement and onwards, the subject was considered in or out of range 50% of days until next measurement. Likewise, up to the last measurement, the subject was considered in or out of range 50% of days since the previous measurement. With > 2 blood pressure measurements, for each intermediary measurement the subject was considered in or out of range from 50% of days to previous measurement to 50% of days to next measurement.

2.4. Outcome definitions

The primary endpoint was the occurrence of a registered diagnosis of heart failure (I50). All-cause mortality and incident diabetes (E10-E11) were examined as secondary endpoints. Registered diagnoses were obtained from the National Patient Register and used both when registered as a main diagnosis or as a secondary diagnosis. Diagnoses in the register were documented by clinicians in inpatient and outpatient hospital care.

3. Statistics

Data are presented as mean values \pm standard deviation, or as frequencies and percentages, as appropriate. Differences between groups were tested with Chi-square test,

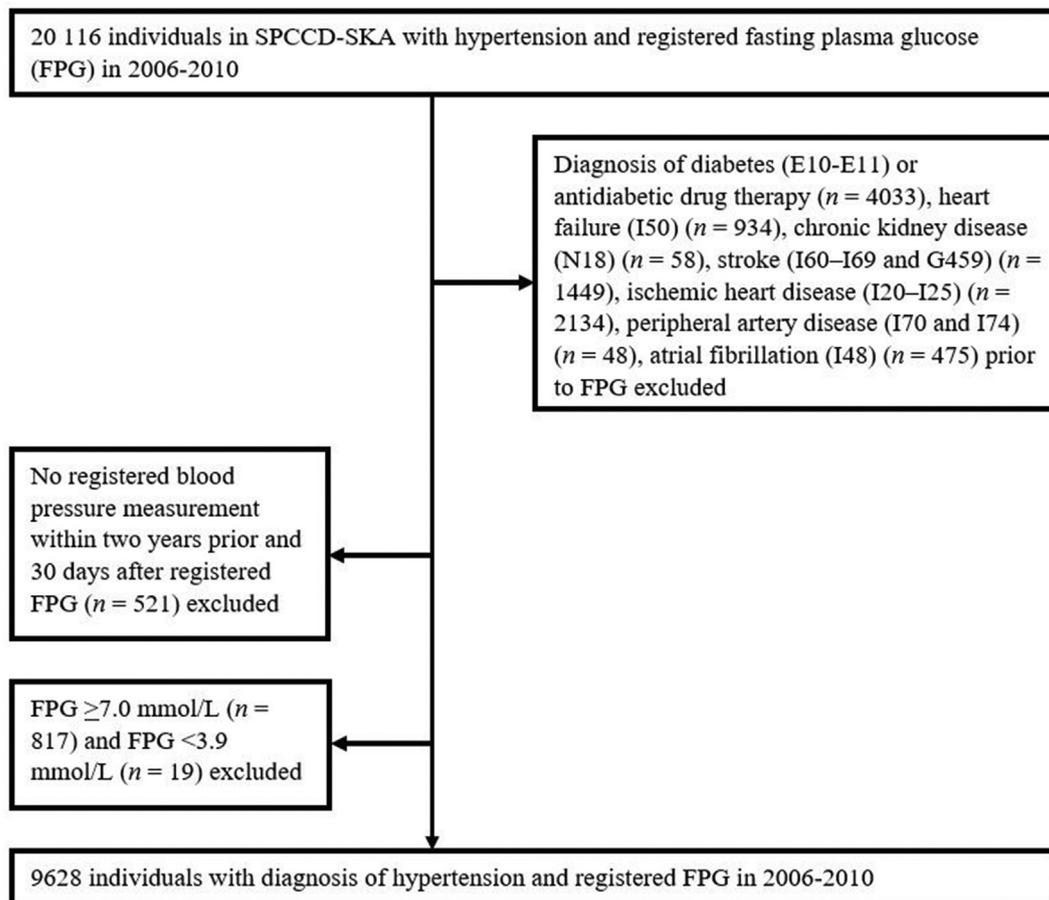


Figure 1 Flowchart of patient selection.

independent *t*-test or Wilcoxon rank-sum test as appropriate. Hazard ratios for incident heart failure and all-cause mortality were calculated using Cox proportional hazards models with age as the timescale. FPG was modelled in two categories, normoglycemia (FPG <5.6 mmol/L) and prediabetes (FPG 5.6–6.9 mmol/L, i.e. the ADA definition). In a secondary analysis, normoglycemia and prediabetes were modelled as FPG <6.1 mmol/L and FPG 6.1–6.9 mmol/L, respectively (i.e. the WHO definition). Because of missing data for some variables, not all participants were included in the Cox proportional hazards models. In a first model, age, sex, BMI and smoking were adjusted for and 7485 individuals included. In a second model, the following covariates were added: estimated glomerular filtration rate and baseline prescription rates of diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and beta adrenergic receptor blockers, for which 7278 individuals were included. In a third model, the following covariates were added: systolic blood pressure at index, duration of a hypertension diagnosis and time in therapeutic range, for which 5900 individuals were included. In a separate analysis, subjects with missing TTR were excluded in model 2. The proportionality of hazards was investigated using plots of weighted Schoenfeld residuals. Based on the plots, the baseline hazards were stratified on smoking and sex. The proportional hazards assumption was found reasonable for the remaining variables. A two-tailed probability (*p*) < 0.05 was considered significant. Due to fewer than two blood pressure measurements, the TTR analysis was restricted to 7651 individuals. All data management and statistical

analyses were performed with SAS version 9.4 TS1M6 (SAS Institute, Cary, North Carolina, USA).

The study was approved by the Regional Ethical Review Board in Gothenburg (#577-17). The need for individual consent was waived, as all data were coded.

4. Results

4.1. General

Of the 9628 participants included, 48.5% had a registered FPG of <5.6 mmol/L and 51.5% a value within the prediabetic range (5.6–6.9 mmol/L). In the total population, mean age was 63.7 years and 41.9% were men. The baseline characteristics and frequency of prescribed drugs within 18 months prior to index date are presented in greater detail in Table 1. The median number of blood pressure measurements for patients available for TTR analysis was 3 (interquartile range (IQR) 2–5). A low TTR (<25%) was more common in the prediabetic group, while a high TTR (>75%) was more frequent in the normoglycemic group (Fig. 2).

4.2. Unadjusted outcomes

There were 456 heart failure events during 82 783 person years and a median follow-up of 9 years (IQR 7–10). There were 1246 deaths during 83 871 person years and a median follow-up of 9 years (IQR 8–10). A total of 966 diabetes events occurred during 80 051 person years and a

Table 1 Baseline characteristics and frequencies of prescribed drugs according to ATC-codes within 18 months prior to index date according to glycaemic status.

	All (n = 9628)	Normoglycemia (ADA) (n = 4674)	Prediabetes (ADA) (n = 4954)	Normoglycemia (WHO) (n = 7441)	Prediabetes (WHO) (n = 2187)	Missing values, n
Male sex, n (%)	4033 (41.9)	1795 (38.4)*	2238 (45.2)*	3040 (40.9)*	993 (45.4)*	0
Age at study entry, years	63.7 ± 11.3	62.7 ± 11.5*	64.7 ± 11.0*	63.3 ± 11.4*	65.3 ± 10.5*	0
Height, cm	169 ± 9	169 ± 9*	169 ± 9*	169 ± 9	169 ± 9	1490
Weight, kg	81.8 ± 17.2	79.6 ± 16.8*	83.9 ± 17.3*	80.6 ± 16.9*	85.7 ± 17.9*	859
BMI, kg/m ²	28.7 ± 5.4	28.0 ± 5.4*	29.3 ± 5.4*	28.3 ± 5.4*	29.9 ± 5.3*	1491
Smoking	3379 (41.9)	1583 (40.3)*	1799 (43.3)*	2520 (40.4)*	862 (46.6)*	1560
SBP, mmHg	147 ± 19	146 ± 19*	148 ± 19*	147 ± 19*	149 ± 19*	0
DBP, mmHg	83 ± 11	83 ± 11	83 ± 11	83 ± 11	83 ± 11	0
FPG, mmol/L	5.6 ± 0.6	5.1 ± 0.3*	6.1 ± 0.4*	5.4 ± 0.4*	6.4 ± 0.2*	0
eGFR, mL/min/1.73 m ²	82 ± 16	82 ± 16	82 ± 16	82 ± 16	82 ± 16	286
Total cholesterol, mmol/L	5.7 ± 1.0	5.8 ± 1.0*	5.6 ± 1.0*	5.7 ± 1.0*	5.6 ± 1.0*	820
HDL, mmol/L	1.5 ± 0.4	1.5 ± 0.4*	1.5 ± 0.4*	1.5 ± 0.4*	1.5 ± 0.4*	943
LDL, mmol/L	3.4 ± 0.9	3.5 ± 0.9*	3.4 ± 0.9*	3.5 ± 0.9*	3.3 ± 0.9*	1051
Triglycerides, mmol/L	1.5 ± 0.9	1.5 ± 0.9*	1.5 ± 0.9*	1.5 ± 0.9*	1.5 ± 0.9*	915
ASA, n (%)	843 (8.7)	376 (8.0)*	467 (9.4)*	633 (8.5)	210 (9.6)	0
Thiazide diuretics, n (%)	2471 (25.7)	1204 (25.7)	1267 (25.6)	1888 (25.4)	583 (26.7)	0
BB, n (%)	3849 (40.0)	1746 (37.3)*	2103 (42.5)*	2891 (38.9)*	958 (43.8)*	0
Ca channel blocker, n (%)	2203 (22.9)	1005 (21.5)*	1198 (24.2)*	1658 (22.3)*	545 (24.9)*	0
ACE inhibitor, n (%)	2731 (28.3)	1307 (27.9)	1424 (28.7)	2107 (28.3)	624 (28.5)	0
ARB, n (%)	1537 (16.0)	736 (15.7)	800 (16.1)	1174 (15.8)	362 (16.6)	0
Statin, n (%)	1578 (16.4)	731 (15.6)	847 (17.1)	1208 (16.2)	370 (16.9)	0

Abbreviations: ADA, American Diabetes Association; WHO, World Health Organization; BMI, body mass index; SBP, systolic blood pressure at index; DBP, diastolic blood pressure at index; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ASA, acetylsalicylic acid; BB, beta adrenergic receptor blocker; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker. An asterisk indicates *p* < 0.05. Values are presented as means ± standard deviation or frequencies (%) as appropriate.

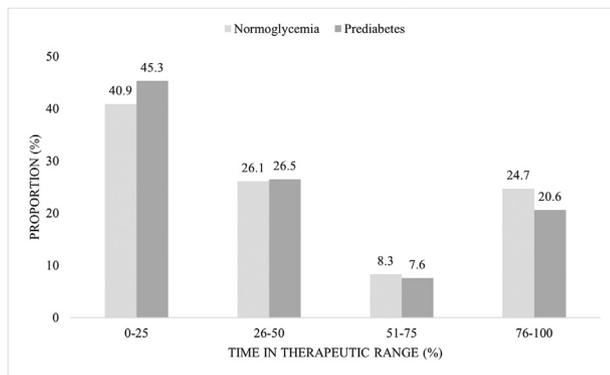


Figure 2 Proportion of time in therapeutic range according to glyce-mic status, $p < 0.01$ for no differences between groups.

median follow up of 9 years (IQR 7–10). Numbers and incidence rates for all endpoints according to prediabetic status are presented in Table 2.

4.3. Adjusted outcomes

Adjusted hazard ratios for heart failure and for all-cause mortality from the Cox proportional hazards models are presented in Fig. 3. There were no differences in outcomes according to prediabetic status when defined according to ADA (i.e. FPG 5.6–6.9 mmol/L). TTR was not associated with the outcomes. Hazard ratios for model 2 with subjects with missing TTR excluded are presented in the electronic supplementary material.

4.4. Secondary analysis: prediabetes defined by WHO

Tables 1 and 2 and Fig. 3 show baseline characteristics and outcomes of the study population when the WHO definition of prediabetes (i.e. FPG 6.1–6.9 mmol/L) was applied. With this definition, the hazard ratio for the association between prediabetes and incident heart failure was significantly increased but not when adjusted for covariates. It was significantly increased for all-cause mortality in all adjusted models. In model 3, prediabetes was associated with a 42% higher risk of all-cause mortality.

5. Discussion

There are two main findings from this large real-world retrospective cohort study of 9628 hypertensive patients without previous diabetes or cardiovascular disease attending primary health care. First, prediabetic hypertensive patients were not at increased risk of new onset heart failure or all-cause mortality, as compared to normoglycemic hypertensive patients. However, using the WHO definition of prediabetes demonstrated an increased risk for all-cause mortality. Second, the blood pressure TTR was lower in the prediabetic group. Additionally, the analysis demonstrated that the entire study population had a low TTR, with less than one quarter of the population with TTR >75% at baseline.

5.1. Incident heart failure

The overall incidence rate of heart failure in this real-world hypertensive population without previous diabetes, or other cardiovascular disease was 5.5 cases per 1000 years of follow-up. This finding can be compared with the incidence rate of congestive heart failure in the total Swedish population in 2010 in the age group 60–69 years, 3.7 per 1000 years of follow-up [18]. Hypertension was the most common comorbidity in congestive heart failure (73% in women, 69% in men), but other cardiovascular diseases were also frequent [18]. Our finding is somewhat higher than these national results, possibly owing to a higher prevalence of hypertension. Additionally, since the national results include considerable cardiovascular comorbidity that also accounts for many cases of heart failure, it is likely that the difference in incidence rate would be larger if these were excluded in the comparison with our results.

The observed similar hazard ratio for incident heart failure for hypertensive patients with and without prediabetes suggests that prediabetes itself does not add to the risk for heart failure in hypertensive patients. Our findings extend previous findings in a black hypertensive population [17], in older mostly hypertensive people [14], and a study on prediabetes and risk for myocardial infarction by hypertension status in a Chinese population

Table 2 Unadjusted incidence rates according to glyce-mic status for heart failure, diabetes and all-cause mortality per 1000 years of follow-up.

	All	Normoglycemia (ADA)	Prediabetes (ADA)	Normoglycemia (WHO)	Prediabetes (WHO)
Heart failure					
Events, <i>n</i>	456	194	262	322	134
Incidence rate (CI)	5.5 (5.0–6.0)	4.7 (4.1–5.4)	6.2 (5.5–7.0)	5.0 (4.5–5.6)	7.3 (6.2–8.6)
Diabetes					
Events, <i>n</i>	966	181	785	417	549
Incidence rate (CI)	12.1 (11.3–12.8)	4.5 (3.8–5.2)	19.9 (18.5–21.4)	6.5 (5.9–7.2)	33.8 (31.1–36.7)
All-cause mortality					
Events, <i>n</i>	1246	545	701	884	362
Incidence rate (CI)	14.8 (14.0–15.7)	13.2 (12.1–14.4)	16.4 (15.3–17.7)	13.5 (12.7–14.5)	19.4 (17.5–21.5)

Abbreviation: ADA, American Diabetes Association; WHO, World Health Organization; CI, 95% confidence intervals.

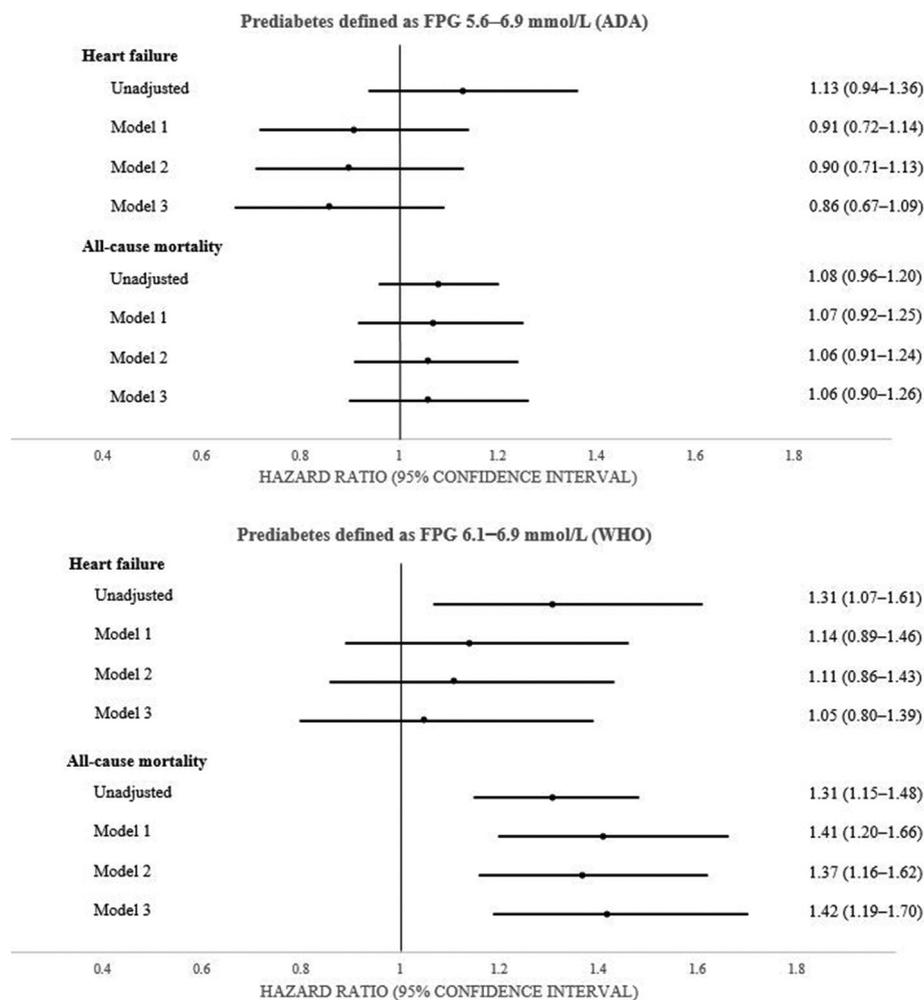


Figure 3 Adjusted hazard ratios (95% confidence intervals) for the association of prediabetes status with incident heart failure and all-cause mortality. Model 1: adjusted for age, sex, BMI and smoking. Model 2: adjusted for estimated glomerular filtration rate, baseline prescription of diuretics, beta adrenergic receptor blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and the factors included in model 1. Model 3: adjusted for systolic blood pressure at index, duration of hypertension diagnosis, time in therapeutic blood pressure range and the factors in model 2. Abbreviations: ADA, American Diabetes Association; WHO, World Health Organization.

[23], to a large European contemporary hypertensive cohort attending primary health care. Whereas prediabetes has been shown to be associated with coronary heart disease and heart failure [6,12], it may be that the inclusion of hypertension negates the risk for incident heart failure conferred by prediabetes per se.

5.2. Secondary outcomes: all-cause mortality and incident diabetes

Similar to incident heart failure, we found that hypertension with concomitant prediabetes was not associated with increased all-cause mortality than hypertension alone. All-cause mortality was similarly examined in the Jackson Heart Study and the results were consistent with those of the present study [17].

The incidence rate ratio for diabetes was 4.5 in the prediabetic group in this study. This number is in agreement with previous findings from a European study [24].

In studies from populations with lower prevalence of hypertension, it has been suggested that an apparent association between prediabetes and cardiovascular mortality can be explained by development of type 2 diabetes during follow-up rather than prediabetes itself [25]. There are, however, conflicting results regarding this [12,26]. We found, in a hypertensive population, that the adjusted hazard ratios for the association of prediabetic status with incident heart failure and all-cause mortality were not significant (Fig. 3), which may be taken to suggest that an apparent association between prediabetes and incident heart failure and all-cause mortality may be related to other components associated with the metabolic syndrome.

5.3. Prediabetes defined according to WHO

In a secondary analysis, we found that when prediabetes was defined as FPG 6.1–6.9 mmol/L, there was an

association between prediabetes in hypertensive patients and all-cause mortality, but not with heart failure. A meta-analysis has previously reported that this higher cut-off point for prediabetes is associated with a higher risk for all-cause mortality in general populations [6], and more recently, a prospective study in a Swedish population without cardiovascular disease at baseline found that prediabetic levels of FPG as defined by WHO resulted in an increasing risk of incident heart failure [27]. However, that study contained no information on hypertension [27], and thus our findings add new knowledge on the association between prediabetes and incident heart failure in hypertensive patients, since the increased hazard ratio for heart failure was not retained upon multivariate adjustment in this population. All-cause mortality has previously been shown to be higher in patients with moderate systolic hypertension (systolic blood pressure 140–160 mmHg) with prediabetic levels of FPG (defined according to WHO) compared to normoglycemia [28], and in hypertensive patients with normal renal function [29], and our results support this.

5.4. Blood pressure control and TTR

The concept of TTR as a measure of hypertension management has been proposed in recent years [4,30]. TTR was defined as the time spent within the range of systolic blood pressure 120–140 mmHg, and the authors reported a gradual inverse association between TTR and all-cause mortality in hypertensive patients [4]. Similarly, time spent at blood pressure target (TITRE, defined as <140/90 mmHg, and <150/90 mmHg for patients aged 60 years or above without diabetes or kidney disease) was shown to be related to lower risk for cardiovascular complications, with consistent findings for heart failure and any cardiovascular disease and death [30]. Similarly, a post-hoc analysis of the SPRINT study observed that increased TTR was associated with a decreased risk of a first heart failure hospitalisation in fully adjusted models [5]. The present study, based on real-world data, shows that almost half of the study population had a TTR of ≤25%. Additionally, we found that TTR was lower ($p < 0.01$) in the prediabetic than in the normoglycemic group. Given the importance of blood pressure control to prevent incident heart failure, these findings collectively indicate considerable room for improvement in the control of blood pressure in patients with known hypertension, which is likely to reduce the risk for future cardiovascular complications.

6. Limitations

Retrospective cohort studies have inherent limitations, including missing data. We used a registered diagnosis of hypertension for inclusion, and patients with registered hypertensive blood pressure values but no diagnosis were thus not included. However, we have previously shown a high sensitivity for a diagnosis of hypertension in SPCCD [31]. Selection bias for measuring risk markers such as FPG in patients considered to be at higher risk is possible,

which could be sources of residual unknown confounding. Likewise, selection bias could also underlie the missing data for descriptive variables. Additionally, some confounding factors adjusted for, e.g. eGFR, could possibly be both mediators and confounders. Changes in drug prescription during follow-up were not adjusted for in this study. Since the prescription rates at baseline was higher for some medications in the prediabetic groups, these differences could during follow-up potentially reduce the hazard ratio for HF and mortality. Lastly, information on left ventricular ejection fraction to describe type of heart failure was not available in this study.

7. Conclusion

Prediabetes is not independently associated with incident heart failure in treated hypertensive patients attending primary health care without diabetes or cardiovascular disease. There is an association between prediabetes and all-cause mortality when prediabetes is defined according to WHO, but not according to ADA. Finally, there is room for improved blood pressure control, which is likely to reduce the overall incidence of heart failure in these patients.

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Declaration of competing interest

The authors have no competing interests to report.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.numecd.2022.09.007>.

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