Severity of hypertension as a predictor of initiation of dialysis among study participants with and without diabetes mellitus

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ABSTRACT

To determine associations between severity of hypertension and risk of starting dialysis in the presence or absence of diabetes mellitus (DM). A nationwide database with claims data on 258 874 people with and without DM aged 19–72 years in Japan was used to elucidate the impact of severity of hypertension on starting dialysis. Initiation of dialysis was determined from claims using International Classification of Diseases-10 codes and medical procedures. Using multivariate Cox modeling, we investigated the severity of hypertension to predict the initiation of dialysis with and without DM. Hypertension was significantly associated with the initiation of dialysis regardless of DM. The incidence of starting dialysis in those with systolic blood pressure (SBP) ≤119 mm Hg and DM (DM+) was almost the same as in those with SBP ≥150 mm Hg and absence of DM (DM−). In comparison with SBP ≤119 mm Hg, SBP ≥150 mm Hg significantly increased the risk of the initiation of dialysis about 2.5 times regardless of DM+ or DM−. Compared with DM− and SBP ≤119 mm Hg, the HR for DM+ and SBP ≥150 mm Hg was 6.88 (95% CI 3.66 to 12.9). Although the risks of hypertension differed only slightly regardless of the presence or absence of DM, risks for starting dialysis with DM+ and SBP ≤119 mm Hg were equivalent to DM− and SBP ≥150 mm Hg, indicating more strict blood pressure interventions in DM+ are needed to avoid dialysis. Future studies are required to clarify the cut-off SBP level to avoid initiation of dialysis considering the risks of strict control of blood pressure.

Significance of this study

What is already known about this subject?

- Dialysis adversely affects the quality of life and is related to high rates of cardiovascular events and mortality.
- Avoiding the need for dialysis is clinically relevant.
- Both hyperglycemia and hypertension are highly predictive of kidney disease.

What are the new findings?

- Compared with diabetes mellitus (DM)− and systolic blood pressure (SBP) ≤119 mm Hg, the HR for DM+ and SBP ≥150 mm Hg was 6.88 (95% CI 3.66 to 12.9).
- Risks of hypertension were not very different between DM+ and DM−.
- Risks for the initiation of dialysis with DM+ and SBP ≤119 mm Hg were equivalent to DM− and SBP ≥150 mm Hg, indicating that stricter blood pressure interventions in DM+ are needed to avoid dialysis.

How might these results change the focus of research or clinical practice?

- Our findings are useful for targeting high-risk patients with diabetes in view of preventing initiation of dialysis.

INTRODUCTION

Since dialysis adversely affects the quality of life and is related to high rates of cardiovascular events and mortality, avoiding the need for dialysis is clinically relevant. Although both hyperglycemia and hypertension are highly predictive of kidney disease,[1] only a few studies have investigated the associations between the severity of hypertension and risk of end-stage renal disease (ESRD), especially the initiation of renal replacement therapy in the presence or absence of diabetes mellitus (DM) in the same cohort at the same time and under the same conditions.

More strict blood pressure targets were recently recommended in the guidelines for hypertension by the American College of Cardiology (ACC) and the American Heart Association (AHA).[2] In those guidelines, the definition of adult hypertension was reduced from the long-standing threshold of 140/90 mm Hg to 130/80 mm Hg. Although DM and hypertension defined as systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg or the use of antihypertensive treatment are well-known risk factors for ESRD

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defined according to the initiation of renal replacement therapy,[3] various SBP levels have not been investigated with regard to the avoidance of dialysis according to DM status. Such an investigation would have clinical relevance. The risk of chronic kidney disease (CKD) defined as the requirement for dialysis, transplantation or by the notation of kidney disease on the death certificate and confirmed by medical record review significantly increased from SBP ≥160 mm Hg compared with SBP <120 mm Hg with adjustment for DM.[4] Also, the risk of ESRD defined as receipt of renal transplant or maintenance dialysis increased in accordance with increases in SBP with adjustment for DM.[5] Although Hsu *et al*[5] investigated the impacts of the presence of DM and stratified SBP on ESRD defined as described above, glycated hemoglobin A1c (HbA1c) was not used in defining DM and only age was adjusted for as a covariate. Tozawa *et al*[6] showed that elevated SBP was a risk factor for the development of ESRD among Japanese with and without DM. Also, Iseki[7] showed that hyperglycemia defined as fasting blood glucose ≥126 mm Hg was a significant risk factor for the development of ESRD in a Japanese general population. However, these studies[6 7] did not use HbA1c to define DM and also did not evaluate the impact of combinations of various SBP cut-offs among people with and without DM on the requirement for dialysis. Thus, the impacts of blood pressure control and cut-off values on the administration of renal replacement therapy among people with and without DM are still unknown.

Moreover, although patients with renal disease or on dialysis tend to be prescribed antihypertensive medication more often than those without either[1 4], these studies[4 5] did not adjust for antihypertensive agents as a covariate. Thus, the effects of antihypertensive medication must be considered in evaluating the impact of various SBP levels on the initiation of dialysis.

We investigated the risk of various SBP values for the initiation of dialysis in the presence or absence of DM in addition to considering the risk of various levels of SBP with adjustments for the use of antihypertensive medications.

MATERIALS AND METHODS

Study participants

The present study analyzed data from a nationwide claims-based database that included information on 296 129 people enrolled with a health insurance provider for company employees and their dependents *in Japan*.[8] Details of the claims data and classifications were described elsewhere.[8–10] Patients aged 19–72 years who were followed for at least 3 years from 1 April 2008 to 31 March 2013 without a history of dialysis based on dialysis-related procedures performed in the 1 year before follow-up were included in this analysis and continued to be followed until 31 September 2016. For the present study, we examined data on 296 121 individuals. We then excluded 37 247 individuals who required dialysis within 1 month of enrollment and/or who had missing data. Finally, this study included 258 874 individuals who were outpatients at the time of baseline measurements (241 628 non-DM and 17 246 DM) (online supplemental figure S1).

Definitions

DM was defined according to the following information obtained from the claims database: fasting plasma glucose (FPG) ≥7.0 mmol/L or HbA1c ≥6.5% or both in individuals not taking an antidiabetic drug or who used antidiabetic medication(s) regardless of FPG or HbA1c.[9]

Blood pressure was measured at all participating facilities in accordance with the guidelines of the Japanese Society of Hypertension.[10] For medical checkups, these guidelines recommended measuring blood pressure twice by the oscillometric method and averaging the results.

The initiation of dialysis was determined according to claims showing medical procedures for the initiation of peritoneal dialysis or hemodialysis after 1 month of follow-up and that continued for >1 month.

Statistical analysis

Categorical variables were expressed as numerals and percentages and were compared with χ^2 tests. Continuous variables were expressed as mean±SD and were compared using the unpaired Student's t-test or the Mann-Whitney U test based on distribution.

Unadjusted overall time to initiation of dialysis was indicated by Kaplan-Meier analysis with log-rank testing. Cox proportional hazards regression model identified variables related to the initiation of dialysis. Covariates included traditional risk factors for dialysis in each model. Hypertension as a covariate was determined according to SBP diagnosed by seven different cut-offs (ie, ≥110 mm Hg, ≥115 mm Hg, ≥120 mm Hg, ≥125 mm Hg, ≥130 mm Hg, ≥140 mm Hg and ≥150 mm Hg). Data were compared among 10 groups of participants divided according to combinations of the presence or absence of DM and five stratified levels of SBP (ie, ≤119, 120–129, 130–139, 140–149 and ≥150 mm Hg). Cubic regression spline curves were obtained to examine the relationship between SBP and dialysis.

Analyses were performed using SPSS (V.19.0, IBM, Chicago, Illinois, USA) and STATA (V.14, STATA, College Station, Texas, USA). Statistical significance was considered for $p<0.05$. There was no risk of disclosure of the identity of any participant. Although we could not obtain signed informed consent for the use of data from all participants, an announcement describing the study was made through the internet, including the information that participants could opt out regarding use of their data.

RESULTS

Characteristics of individuals with and without dialysis in the presence or absence of DM are shown in table 1. The medium follow-up period was 5.2 years. Online supplemental table S1 shows the cumulative percentages of people with and without DM at each year of the follow-up period. During the follow-up, 113 individuals (0.047%) in *the without DM* group (DM−) and 76 individuals (0.44%) in *the with DM* group (DM+) developed the need for dialysis. The incidence of dialysis was 0.079 per 1000 person-years in the DM− group and 0.672 per 1000 person-years in the DM+ group. Online supplemental tables S2 and S3 show the number of patients in each grouping according to SBP mm Hg. As shown in table 1, among DM−, *baseline age*, per cent of men, body mass index (BMI), smoking rate,

Table 1 Characteristics of study participants according to presence or absence of diabetes and dialysis

		Diabetes mellitus (–)			Diabetes mellitus (+)		
		Dialysis			Dialysis		
	Total	(–)	(+)		(–)	(+)	
	(n=258 874)	(n=241 515)	(n=113)	P value	(n=17 170)	(n=76)	P value
Age (years)	45±9	**44±9**	**47±8**	**< 0.001**	50±8	50±8	0.947
Sex (male, %)	161 007 (62)	**146 602 (61)**	**91 (81)**	**< 0.001**	**14 243 (83)**	**71 (93)**	**0.015**
Body mass index (kg/m^2)	22.8±3.6	**22.6±3.4**	**23.6±4.0**	**0.003**	26.1±4.6	26.8±4.6	0.126
Smoking (%)	71 904 (28)	**65 365 (27)**	**44 (39)**	**0.005**	6462 (38)	33 (43)	0.299
Systolic blood pressure (mm Hg)	120±16	**119±15**	**129±21**	**<0.001**	**131±17**	**140±21**	**<0.001**
Diastolic blood pressure (mm Hg)	74±11	**73±11**	**79±15**	**<0.001**	80±11	83±11	0.078
HbA1c (%)	5.5±0.7	5.4±0.3	5.5±0.4	0.243	**7.2±1.4**	**7.8±2.1**	**0.015**
LDL cholesterol (mmol/L)	3.1±0.8	3.1±0.8	3.0±0.9	0.470	3.3±0.9	3.3±1.1	0.814
HDL cholesterol (mmol/L)	1.6±0.4	**1.7±0.4**	**1.4±0.4**	**<0.001**	**1.4±0.4**	**1.3±0.4**	**<0.001**
Medication for diabetes (%)	8136 (3)	–	–	–	**8080 (47)**	**56 (74)**	**<0.001**
Medication for hypertension (%)	21 103 (8)	**15 777 (7)**	**51 (45)**	**<0.001**	**5218 (30)**	**57 (75)**	**<0.001**
Prevalence of coronary artery disease (%)	13 055 (5)	**10 601 (4)**	**37 (33)**	**<0.001**	**2382 (14)**	**35 (46)**	**<0.001**

Data are presented as numbers, means±SD or percentages
Values in bold are of statistical significance (P<0.05)
HbA1c, glycated hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

SBP, DBP, per cent of users of medication for hypertension and prevalence of coronary artery disease were significantly higher in individuals with dialysis compared with those without dialysis. High-density lipoprotein cholesterol (HDL-C) was significantly lower in individuals with dialysis than without dialysis. Among DM+, baseline percentage of men, SBP, HbA1c, percentages of users of medication for DM and hypertension and prevalence of coronary artery disease *were* significantly higher in individuals with dialysis compared with those without dialysis. HDL-C was significantly lower in individuals with dialysis than without dialysis. The characteristics of study participants for whom FPG and triglycerides (TG) were added are shown in online supplemental table S4.

Table 2 shows Cox proportional hazard models for various risk factors for the initiation of dialysis in participants with and without DM. Each stratified SBP level includes the specified cut-off value and upward (eg, SBP ≥110 mm Hg and upward). SBP ≥140 mm Hg was an independent predictor for the initiation of dialysis in the DM− group whereas SBP ≥150 mm Hg was an independent predictor in the DM+ group. Online supplemental table S5 shows the results of the sensitivity analysis according to sex, age and BMI.

Table 2 Cox regression analysis of variables for the incidence of dialysis in participants with and without diabetes mellitus (DM)

	A	B	
	Total	DM (–)	DM (+)
Diabetes	**3.41 (2.45 to 4.76)**		
SBP mm Hg			
<110/≥110		0.98 (0.57 to 1.66)	1.31 (0.41 to 4.21)
<115/≥115		1.30 (0.81 to 2.11)	1.75 (0.70 to 4.38)
<120/≥120		1.14 (0.75 to 1.75)	1.47 (0.75 to 2.99)
<125/≥125		1.34 (0.89 to 2.01)	1.67 (0.94 to 2.97)
<130/≥130		1.35 (0.90 to 2.02)	1.42 (0.87 to 2.31)
<140/≥140		**2.01 (1.28to 3.16)**	1.44 (0.90to 2.30)
<150/≥150		**2.82 (1.67to 4.77)**	**1.81 (1.06to 3.07)**

Baseline variables for predictors of dialysis adjusted by age, sex, smoking, medication for hypertension, BMI, LDL-C and HDL-C.
(A) Adjusted for age, sex, smoking, medication for hypertension, BMI, LDL-C, HDL-C and DM. (B) Adjusted for age, sex, smoking, medication for hypertension, BMI, LDL-C, HDL-C and SBP (≥110 or ≥115 or ≥120 or ≥125 or ≥130 or ≥140 or ≥150 mm Hg).
Values in bold are of statistical significance (P<0.05)
BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Figure 1 shows the cumulative incidence of the initiation of dialysis according to five stratified SBP values (ie, ≤119, 120–129, 130–139, 140–149 and ≥150 mm Hg) and the presence or absence of DM. Hypertension was an independent predictor of the initiation of dialysis, and the incidence of starting dialysis in the DM+ group with SBP ≤119 mm Hg was almost the same as in the DM− group with SBP ≥150 mm Hg.

Table 3 shows Cox proportional hazard models for 10 groups divided according to combinations of DM+ and DM− and five stratified levels of systolic SBP (ie, ≤119, 120–129, 130–139, 140–149 and ≥150 mm Hg) for the initiation of dialysis. HRs for the initiation of dialysis among DM− and SBP ≥150 mm Hg, and DM+ and SBP ≥150 mm Hg were 2.87 (95% CI 1.55 to 5.32) and 2.28 (95% CI 1.03 to 5.01), respectively, values that were quite similar. Compared with DM− and SBP ≤119 mm Hg, HRs for the initiation of dialysis among DM− and SBP ≥150 mm Hg, and DM+ and SBP ≤119 mm Hg were about 3 times greater. Compared with DM− and SBP ≤119 mm Hg, the HR for the initiation of dialysis in DM+ and SBP ≥150 mm Hg was 6.88 (95% CI 3.66 to 12.9). No interaction was observed according to SBP levels and DM status.

Online supplemental table S6-1 and online supplemental table S7-1 show our model that included the addition of medication for DM as a covariate in DM+. Online supplemental table S6-2 and online supplemental table S7-2 show our model with the addition of FPG and TG as covariates in DM− and DM+ and also medication for DM as covariates in DM+. The HR weakened in the DM+ and SBP ≥150 mm Hg group in predicting the initiation of dialysis (online supplemental table S7-2).

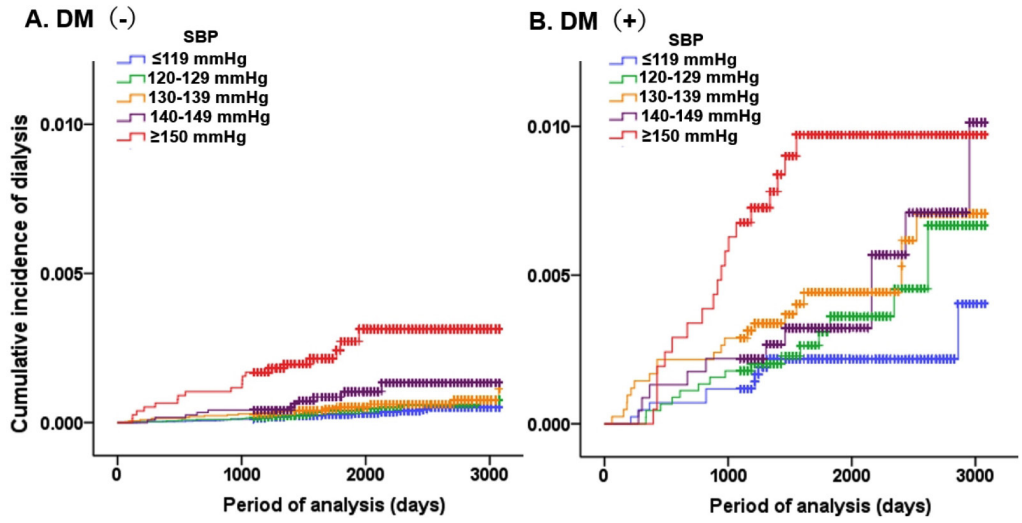

Figure 1 Kaplan-Meier analysis of unadjusted overall time to initiation of dialysis. (A) Kaplan-Meier analysis of unadjusted overall time to initiation of dialysis for five groups without DM according to SBP (≤119 or 120–129 or 130–139 or 140–149 or ≥150 mm Hg). (B) Kaplan-Meier analysis of unadjusted overall time to initiation of dialysis for five groups with DM according to SBP (≤119 or 120–129 or 130–139 or 140–149 or ≥150 mm Hg). DM, diabetes mellitus; SBP, systolic blood pressure.

Online supplemental figure S2 shows cubic regression spline curves. The risk of the initiation of dialysis for DM+ increased on a continuum, whereas the risk for DM− drastically increased at around SBP 100–130 mm Hg showing J-shaped curves.

DISCUSSION

This is the first study to elucidate the impact of the severity of hypertension on the initiation of dialysis in people with and without DM in a large-scale longitudinal setting. The risks for the initiation of dialysis in those with DM+ and SBP ≤119 mm Hg were equivalent to those with DM− and SBP ≥150 mm Hg, showing that the presence of DM could indicate the need for more strict blood pressure interventions to avoid dialysis. Also, the risks of hypertension were not very different between those with and without DM. The risk of the initiation of dialysis was almost seven times greater in those with both DM+ and hypertension compared with DM− and non-hypertension. However, we could not use renal function as a covariate, and SBP was measured at only one point in time. Further studies are needed to confirm our findings considering those important risk factors for the initiation of dialysis.

Table 3 HRs for initiation of dialysis according to combinations of DM and SBP

	DM (–)	DM (+)
SBP mm Hg	HR (95% CI)	
≤119	1.00 (ref.)	1.00 (ref.)
120–129	0.98 (0.58 to 1.64)	1.22 (0.55 to 2.70)
130–139	0.94 (0.52 to 1.67)	1.41 (0.65 to 3.04)
140–149	1.28 (0.63 to 2.61)	1.31 (0.55 to 3.14)
≥150	**2.87 (1.55 to 5.32)**	**2.28 (1.03 to 5.01)**
≤119	1.00 (ref.)	**3.01 (1.45 to 6.25)**
120–129	0.97 (0.58 to 1.62)	**3.70 (1.96 to 7.00)**
130–139	0.95 (0.54 to 1.68)	**4.26 (2.32 to 7.81)**
140–149	1.31 (0.65 to 2.65)	**3.94 (1.89 to 8.19)**
≥150	**3.00 (1.65 to 5.44)**	**6.88 (3.66 to 12.9)**

HR for the initiation of dialysis compared with the combination of DM (–) and SBP ≤119 mm Hg/DM (+) and SBP ≤119 mm Hg as a reference group. Baseline variables as predictors for dialysis adjusted by age, sex, smoking, medication for hypertension, BMI, LDL-C and HDL-C.
**Values in bold are statistical significance (P <0.05).
**
DM, diabetes mellitus; SBP, systolic blood pressure; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Recently, more strict blood pressure targets were recommended in accordance with the change in the definition of hypertension from ≥140/90 to ≥130/80 mm Hg in the ACC/AHA guidelines. However, the target value for hypertensive individuals to avoid dialysis is still unknown. Although DM and hypertension defined as SBP ≥140 mm Hg, DBP ≥90 mm Hg or antihypertensive treatment are well-known risk factors for ESRD defined according to the initiation of renal replacement therapy,[3] no evidence was established for the prevention of dialysis according to DM status. Our findings demonstrated that SBP ≥140 mm Hg was a significant independent predictor for the initiation of dialysis in people without DM, whereas this level increased to SBP ≥150 mm Hg in people with DM. However, the risk of the initiation of dialysis for DM+ and, especially, SBP ≤119 mm Hg was almost the same as that for DM− and hypertension, especially with SBP ≥150 mm Hg. This indicates that patients with could require more severe blood pressure interventions to prevent dialysis. However, we could not use estimated glomerular filtration rate (eGFR) as a covariate since serum creatinine is not always measured as part of medical health checkups in Japan. Moreover, changes in targets for SBP and antihypertensive treatments should be considered. Further studies are needed to confirm our findings concerning those important risk factors for the initiation of dialysis with an adequate number of patients and over a long-term period.

Generally, hypertension is a well-known risk factor for renal dysfunction.[1] However, little is known about whether the associations also apply to ESRD, and especially whether such associations also apply to renal replacement therapy, not only ESRD, among people with and without DM. The risk of CKD defined as the requirement for dialysis or transplantation or by the notation of kidney disease on the death certificate and confirmed by a medical record review significantly increased from SBP ≥160 mm Hg, compared with SBP <120 mm Hg with adjustment for DM.[4] Also, the risk of ESRD defined as the receipt of renal transplantation or maintenance dialysis increased along with the SBP level after adjustment for DM.[5] Hypertension is a well-known risk factor for renal dysfunction in patients with DM,[11–13] and SBP ≥120 mm Hg could be associated with the development of nephropathy in patients with DM.[14] SBP reportedly predicts early onset of doubling of serum creatinine concentration or ESRD as indicated by dialysis or renal transplantation in patients with diabetes with nephropathy.[15] Higher SBP increases the risk of ESRD among Japanese people with and without DM.[6] Hyperglycemia defined as fasting blood glucose ≥126 mg/dL (7.0 mmol/L) was shown to be a risk factor for the development of ESRD in a Japanese general population.[7] However, that study did not evaluate the impact of the combination of the SBP cut-offs and the presence or absence of DM on starting dialysis. Hsu *et al*[5] showed that all of the stratified SBP values in DM+ had higher impacts on ESRD defined as the receipt of renal transplantation or maintenance dialysis than in DM−. These findings are consistent with our results suggesting that elevated SBP is a useful marker to predict the initiation of dialysis as well as DM. However, adjustments were not made for antihypertensive medications as a covariate.[4 5] Moreover, although HbA1c is the gold standard for reflecting hyperglycemia[16] in clinical settings to evaluate the risk of initiation of dialysis and development of nephropathy,[17–19] the above study[5] did not use HbA1c to define DM and adjusted only for age. Also, we showed that the risk of initiation of dialysis with DM+, even at SBP ≤119 mm Hg, was almost the same as that according to DM− and SBP ≥150 mm Hg.

Intensive lowering of SBP increased the risk of eGFR loss with and without DM, although the risk was greater in those with DM.[20] At the same time, strict control of blood pressure increased renal dysfunction due to decreased renal blood flow in patients with DM, especially with progressive atherosclerosis.[21] On the other hand, patients with DM might benefit from intensive lowering of blood pressure regarding cardiovascular disease risk.[22] We showed by cubic curve analysis that the impact of SBP to avoid dialysis differed in people with and without DM. Interventional studies are needed to conclude the optimal cut-off level of SBP for the initiation of dialysis.

Our present study's strengths were its large sample size and accurate definitions of DM, hypertension and dialysis based on data from health examinations and a claims database that included information on medical practice, which allowed for the certainty that study participants actually had diabetes and to identify almost all patients who began dialysis during the follow-up.

Our study also had some limitations. First, we could not use either the eGFR or proteinuria as a covariate. Unfortunately, the serum creatinine level is not always included in medical health checkups in Japan, and there were much missing data on proteinuria. Therefore, further studies are needed to confirm our findings considering those important risk factors for the initiation of dialysis. Second, it was also not possible to ascertain the duration of diabetes and hypertension and to distinguish between type 1 and type 2 diabetes in this cohort. However, type 2 diabetes is more common than type 1 diabetes and accounts for 95% of diabetes in Japan. Although renal anemia according to the progression of renal failure could affect the HbA1c level, HbA1c was widely used as the glycemic index in clinical practice even among patients with chronic renal failure.[23] Third, we used claims data to confirm that there were no dialysis-related procedures in the 1 year before follow-up to exclude a history of dialysis. However, we could not completely exclude patients with CKD4/5. Also, we did not include renal transplantation as an end point in this study. The influence of excluding renal transplantation from the analysis would be minimal because the incidence of renal transplantation is very low in Japan. We defined the initiation of dialysis as that which required dialysis treatment for >1 month according to actual procedure codes for dialysis. However, we might not have been able to exclude cases who had undergone long-term dialysis for acute kidney injury and who subsequently could withdraw from dialysis. Although our incidence rate was similar to the incidence of newly initiated dialysis in 'National Health and Nutrition Survey in 2012'[24] and 'An overview of regular dialysis treatment in Japan as of December 31, 2012'[25] in Japan, the number of initiations of dialysis was relatively small as was that for the sensitivity analysis (online supplemental table S5). Therefore, no conclusions can be drawn on the impact of SBP on the initiation of dialysis, especially according to the sensitivity analysis. Further studies are necessary to clarify the influence of SBP on the initiation of dialysis with an adequate number of patients. Fourth, since all data, including those for HbA1c and SBP, were obtained at only one point in time it was impossible to identify participants whose glucose control and blood pressure control had either improved or deteriorated or participants who crossed over from DM− to DM+ during the follow-up period. We also could not identify participants who started dialysis based on accelerated vascular disease during the follow-up period.

In conclusion, although the risks of hypertension did not differ greatly between DM+ and DM−, the risks for the initiation of dialysis in those with DM+ and SBP ≤119 mm Hg were equivalent to those with DM− and SBP ≥150 mm Hg, indicating that individuals with DM would require more strict blood pressure interventions to avoid dialysis. Future studies are needed to conclude the cut-off level of SBP for the initiation of dialysis under the consideration of the risk of strict control of blood pressure.

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