Brief Report
Complications

Diabetes Metab J 2021;45:120-124
https://doi.org/10.4093/dmj.2020.0175
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

Trends in Cardiovascular Complications and Mortality among Patients with Diabetes in South Korea

Jung Hwan Park[1,*], Kyoung Hwa Ha[2,3,*], Bo Yeon Kim[4], Jae Hyuk Lee[5], Dae Jung Kim[2,3]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Hanyang University College of Medicine, Seoul,
[2]Department of Endocrinology and Metabolism, [3]Cardiovascular and Metabolic Disease Etiology Research Center, Ajou University School of Medicine, Suwon,
[4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon,
[5]Division of Endocrinology and Metabolism, Department of Internal Medicine, Myongji Hospital, Goyang, Korea

We investigated the cardiovascular complications and mortality rates of patients with diabetes in South Korea. The rates of hospitalization due to cardiovascular complications and mortality were analyzed using the Korean National Health Insurance Service-National Sample Cohort. From 2006 to 2015, the rates of hospitalization due to major cardiovascular complications decreased, while those due to heart failure (from 72 to 146 and 124 to 161 per 10,000 men and women, respectively) and peripheral artery disease (from 39 to 55 and 19 to 35 per 10,000 men and women, respectively) increased. In the period 2007 to 2015, the mortality rates for cancer, cerebrovascular disease, diabetes, heart disease, and hypertensive disease all decreased. However, the mortality rate for pneumonia increased. We observed a continuous reduction in cardiovascular complications and mortality in adults with diabetes. However, with the increase in some diabetes complications, more efforts are needed to prevent diabetes complications.

Keywords: Diabetes mellitus; Cardiovascular disease; Epidemiology; Mortality

INTRODUCTION

Diabetes is known to be associated with cardiovascular disease (CVD) morbidity and mortality [1]. Unlike the increased prevalence of diabetes itself, the incidence of CVD and CVD-related mortality among patients with diabetes have decreased significantly over the past two decades [2].

This study was aimed to investigate the rates of cardiovascular complications and mortality among Korean adults (aged ≥30 years) with diabetes by analyzing the data of the National Health Insurance Service-National Sample Cohort (NHIS-NSC).

METHODS

Data source and study design

The NHIS-NSC enrolled 1,021,208 individuals (2.2% of the total eligible Korean population in 2006) using a systematic sampling method. Detailed information on the NHIS-NSC can be found elsewhere [3]. The protocol of this study was approved by the Institutional Review Board of Ajou University Hospital, Suwon, Korea (approval No. AJIRB-MED-EXP-19-347) and the requirement for informed consent was waived.

For each calendar year, we identified individuals with diabetes aged 30 years or older. Diabetes was defined as diagnosed with E10–E14 codes of the 10th edition of the International Classification of Diseases (ICD-10) more than twice, or when a patient had a prescription for oral glucose-lowering medications (Anatomical Therapeutic Chemical [ATC] code A10B) for more than 30 days, or (in outpatients) a prescription for insulin (ATC code A10A).

Definitions of cardiovascular complications and mortality

We identified patients hospitalized due to six diabetes-related cardiovascular complications, namely ischemic heart disease, myocardial infarction, heart failure, hemorrhagic stroke, isch-

Corresponding author: Dae Jung Kim http://orcid.org/0000-0003-1025-2044
Department of Endocrinology and Metabolism, Ajou University School of Medicine, 164 World cup-ro, Yeongtong-gu, Suwon 16499, Korea
E-mail: djkim@ajou.ac.kr

*Jung Hwan Park and Kyoung Hwa Ha contributed equally to this study as first authors.

Received: Jul. 21, 2020; Accepted: Sep. 6, 2020

emic stroke, and peripheral artery disease (PAD), based on ICD-10 and procedure codes that contributes to clinically hospitalizations regardless of the principal reason for hospitalization (Supplementary Table 1). Information on the date and underlying cause of death was obtained from the National Death Registry using unique resident registration numbers. Causes of death were identified based on ICD-10 codes. There were six mutually exclusive cause of death categories (Supplementary Table 1).

Statistical analysis

We calculated the rates of hospitalization due to cardiovascular complications separately for each year by dividing the number of patients hospitalized for cardiovascular complications by the corresponding number of patients with diabetes for that year. For each calendar year, hospitalization rates were expressed as age-standardized rates per 10,000 individuals; mortality rates were expressed as age-standardized rates per 100,000 individuals, separately for men and women. The rates were age-standardized according to the weighted distribution of the 2011 population, across sexes and 5-year age groups from 30 to 34 years up to 85 years and above. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Hospitalization rate for cardiovascular complications

In the period 2006 to 2015, the hospitalization rates due to major cardiovascular complications (ischemic heart disease, ischemic stroke, and myocardial infarction) all decreased. There was a decreasing trend in ischemic heart disease rates (from 438 to 461 and 419 to 397 per 10,000 men and women with diabetes, respectively), ischemic stroke rates (from 257 to 205 and 257 to 204 per 10,000 men and women with diabetes, respectively), and myocardial infarction rates (from 111 to 81 and 97 to 60 per 10,000 men and women with diabetes, respectively). There was a slight increase in the hemorrhagic stroke rates (from 38 to 46 and 44 to 51 per 10,000 men and women with diabetes, respectively) (Fig. 1, Supplementary Table 2).

However, increasing rates of heart failure (from 72 to 146 and 124 to 161 per 10,000 men and women with diabetes, respectively) and PAD (from 39 to 55 and 19 to 35 per 10,000 men and women with diabetes, respectively) were seen (Fig. 1, Supplementary Table 2). The hospitalization rates for revascularization slightly decreased or remained the same (percutaneous coronary intervention, from 97 to 95 and 56 to 50 per 10,000 men and women with diabetes, respectively; coronary artery bypass surgery from 11 to 7 and 4 to 4 per 10,000 men and women with diabetes, respectively) (Supplementary Table 2).

Mortality rate and cause of death in patients with diabetes

In 2007 to 2015, the mortality rate decreased in both men and women (from 2,599 to 2,010 and 1,939 to 1,662 per 100,000 adults with diabetes, respectively) (Supplementary Table 3). The mortality rates for cancer, cerebrovascular disease, diabetes, heart disease, and hypertensive disease decreased in both

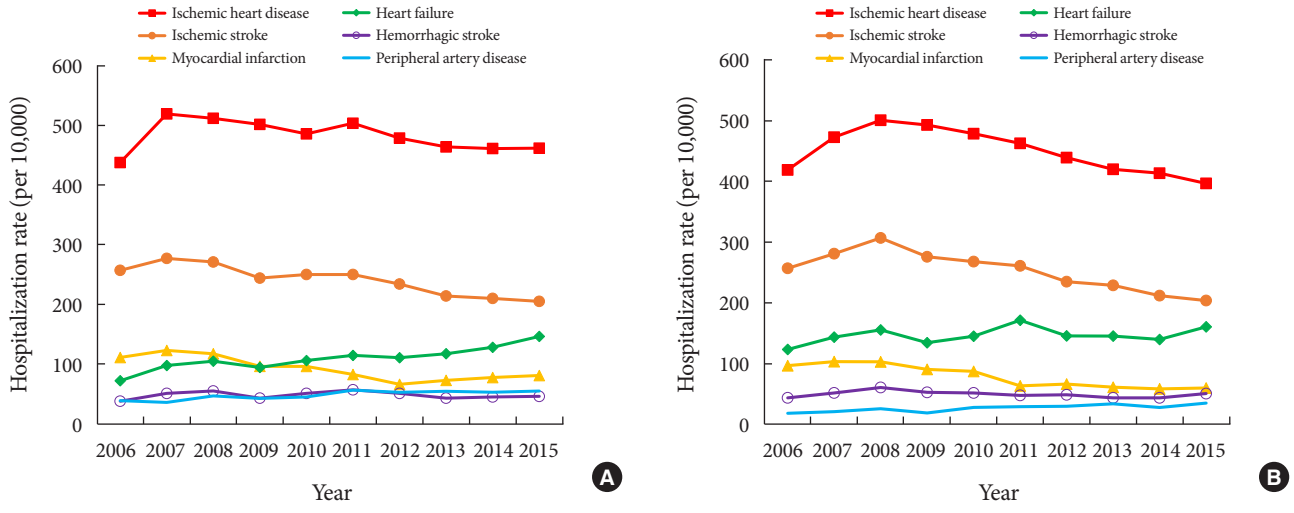


Fig. 1. Rates of hospitalization due to cardiovascular complications among men (A) and women (B) with diabetes in South Korea (2006 to 2015).

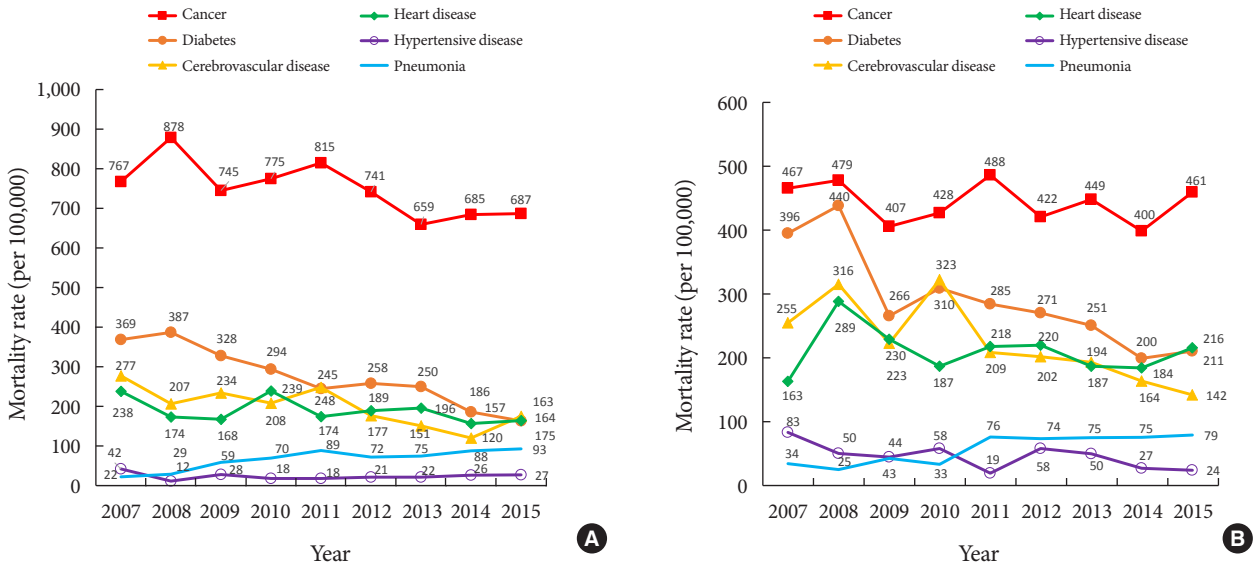


Fig. 2. Mortality rates among men (A) and women (B) with diabetes in South Korea (2007 to 2015).

men and women. However, the mortality rates due to pneumonia increased in both men and women (from 22 to 93 and 34 to 79 per 100,000 adults with diabetes, respectively) (Fig. 2, Supplementary Table 3).

In 2015, the six leading causes of death accounted for 66.7% of all deaths in Korean adults with diabetes (cancer, 30.3%; diabetes, 10.5%; heart disease, 10.5%; cerebrovascular disease, 8.9%; pneumonia, 5.0%; and hypertensive disease, 1.5%) (Supplementary Fig. 1). The five most common causes of cancer deaths were lung, liver, colorectal, pancreas, and stomach cancer (Supplementary Table 4).

DISCUSSION

The rates of hospitalization due to major cardiovascular complications and deaths caused by vascular disease and cancer decreased among adult (aged ≥30 years) with diabetes in Korea. These findings are consistent with previous study in Korea [4]. In patients with diabetes, the proportion of patients with good glycemic control remains less than half of them, while the proportion of patients with extremely poor glycemic control is dramatically decreasing [5]. In addition, the overall improvement of cardiovascular risk factors management such as blood pressure, smoking, and lipid level and proper treatment of cardiovascular events and the regular national cancer screening program in Korea is related with the decrease in mortality in patients with diabetes [6-9].

The hospitalization rate for heart failure increased. Better preventive treatments of cardiovascular risk factors may also have contributed to the reduced risk of developing heart failure [10]. However, paradoxically, due to ageing and the development of treatments that allow increased survival after acute heart insults or with chronic cardiac abnormalities, number of patients with heart failure increased [11]. In Korea, appropriate treatment by the certification system for cardiovascular intervention institute/specialist since 2011, efforts to improve awareness of early symptoms, decreasing of the proportion of ST-elevation myocardial infarction led to a decrease in the case-fatality in hospitalized acute myocardial infarction patients from 2007 to 2016 [12]. Also, according to the Korean hospitalized heart failure registry, the development of cardiovascular treatment has increased the survival rate of acute coronary syndrome, as a result, ischemic heart disease is a major cause of hospitalized for heart failure [13]. In addition, the prevalence of heart failure increased with age, and the proportion of patients with diabetes has increased [13,14].

PAD also increased slightly. Recent meta-analysis reported that the prevalence of PAD increased from 2000 to 2010 in high-income countries due to an ageing population [15]. However, in this study, the outcome events were ascertained from health insurance claims data, and diagnoses were not adjudicated by medical records. In addition, using diagnoses code will tend to result in higher observed incidence and prevalence. Thus, to increase accuracy of diagnoses in claim database, we re-

stricted patients undergoing PAD-related procedures and surgery. Recently, the advance of new technology of peripheral angiography has led to an increase of PAD-related procedures and surgery. Thus, the increase of PAD is partly due to the diagnosis of hidden patients with PAD. In Korea, using the database of the NHIS, amputation involving diabetic foot based on vascular interventions for PAD steadily increased from 2011 to 2016, particularly in minor amputations [16]. During the study period from 2004 to 2013, endovascular revascularization including balloon angioplasty, stent placement, and percutaneous atherectomy increased, while open revascularization such as bypass with artificial graft and autologous vein decreased. This study suggested that the endovascular revascularization for PAD treatment expanded by ageing, increasing number of patients with diabetes and chronic kidney disease on hemodialysis—risk factors for the development of PAD, and repeated interventions for maintaining reasonable clinical outcomes [17].

Deaths from pneumonia also increased. The increased risk of intensive care unit hospitalization and death due to pneumonia in diabetes patients have been reported [18]. In diabetes, impaired immune response is associated with hyperglycemia, and hospitalization for hyperglycemia has been shown to increase the risk of pneumonia-related mortality [19,20].

In conclusion, the present study revealed a decrease in the rates of cardiovascular complications and mortality, among Korean adults with diabetes, which may reflect advances in diabetes care. However, the hospitalization rates for heart failure and PAD and the mortality rates for pneumonia increased. Thus, more efforts are needed to prevent diabetes complications.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at https://doi.org/10.4093/dmj.2020.0175.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conception or design: B.Y.K., J.H.L., D.J.K.
Acquisition, analysis, or interpretation of data: J.H.P., K.H.H., D.J.K.
Drafting the work or revising: J.H.P., K.H.H., B.Y.K., J.H.L., D.J.K.
Final approval of the manuscript: J.H.P., K.H.H., D.J.K.

ORCID

Jung Hwan Park *https://orcid.org/0000-0003-3941-4836*
Kyoung Hwa Ha *https://orcid.org/0000-0002-3408-7568*
Dae Jung Kim *https://orcid.org/0000-0003-1025-2044*

FUNDING

None

ACKNOWLEDGMENTS

This study used NHIS data (NHIS-2020-2-110) made by National Health Insurance Service (NHIS). The authors declare no conflict of interest with NHIS. The authors declare no conflict of interest with NHIS.

Some of the data was released in October 2019 in the form of 'Diabetes & Complications in Korea' from the Korean Diabetes Association. We would like to thank the Committee of Public Relation, Korean Diabetes Association for helping with the work.

REFERENCES

1. Matheus AS, Tannus LR, Cobas RA, Palma CC, Negrato CA, Gomes MB. Impact of diabetes on cardiovascular disease: an update. Int J Hypertens 2013;2013:653789.
2. Rawshani A, Rawshani A, Franzen S, Eliasson B, Svensson AM, Miftaraj M, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. N Engl J Med 2017;376:1407-18.
3. Lee J, Lee JS, Park SH, Shin SA, Kim K. Cohort profile: the National Health Insurance Service-National Sample Cohort (NHIS-NSC), South Korea. Int J Epidemiol 2017;46:e15.
4. Jung CH, Chung JO, Han K, Ko SH, Ko KS, Park JY, et al. Improved trends in cardiovascular complications among subjects with type 2 diabetes in Korea: a nationwide study (2006-2013). Cardiovasc Diabetol 2017;16:1.
5. Ha KH, Kim DJ. Current status of managing diabetes mellitus in Korea. Korean J Intern Med 2016;31:845-50.
6. OECD: Cardiovascular disease and diabetes: policies for better health and quality of care. Available from: https://www.oecd.

org/publications/cardiovascular-disease-and-diabetes-policies-for-better-health-and-quality-of-care-9789264233010-en.htm (cited 2020 Oct 26).
7. Chang Y, Kang HY, Lim D, Cho HJ, Khang YH. Long-term trends in smoking prevalence and its socioeconomic inequalities in Korea, 1992-2016. Int J Equity Health 2019;18:148.
8. Kang SH, Kim SH, Cho JH, Yoon CH, Hwang SS, Lee HY, et al. Prevalence, awareness, treatment, and control of hypertension in Korea. Sci Rep 2019;9:10970.
9. Son M, Yun JW. Cancer mortality projections in Korea up to 2032. J Korean Med Sci 2016;31:892-901.
10. Canto JG, Kiefe CI, Rogers WJ, Peterson ED, Frederick PD, French WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. JAMA 2011;306:2120-7.
11. Chen J, Normand SL, Wang Y, Krumholz HM. National and regional trends in heart failure hospitalization and mortality rates for Medicare beneficiaries, 1998-2008. JAMA 2011;306:1669-78.
12. Kim RB, Kim HS, Kang DR, Choi JY, Choi NC, Hwang S, et al. The trend in incidence and case-fatality of hospitalized acute myocardial infarction patients in Korea, 2007 to 2016. J Korean Med Sci 2019;34:e322.
13. Youn JC, Han S, Ryu KH. Temporal trends of hospitalized patients with heart failure in Korea. Korean Circ J 2017;47:16-24.
14. Lee JH, Lim NK, Cho MC, Park HY. Epidemiology of heart failure in Korea: present and future. Korean Circ J 2016;46:658-64.
15. Song P, Rudan D, Zhu Y, Fowkes FJI, Rahimi K, Fowkes FGR, et al. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. Lancet Glob Health 2019;7:e1020-30.
16. Kim J, Chun DI, Kim S, Yang HJ, Kim JH, Cho JH, et al. Trends in lower limb amputation in patients with diabetic foot based on vascular intervention of peripheral arterial disease in Korea: a population-based nationwide study. J Korean Med Sci 2019;34:e178.
17. Park YY, Joh JH, Han SA, Kim SH, Cho S, Park HC, et al. National trends for the treatment of peripheral arterial disease in Korea between 2004 and 2013. Ann Surg Treat Res 2015;89:319-24.
18. Kim EJ, Ha KH, Kim DJ, Choi YH. Diabetes and the risk of infection: a national cohort study. Diabetes Metab J 2019;43:804-14.
19. Koh GC, Peacock SJ, van der Poll T, Wiersinga WJ. The impact of diabetes on the pathogenesis of sepsis. Eur J Clin Microbiol Infect Dis 2012;31:379-88.
20. van Vught LA, Wiewel MA, Klein Klouwenberg PM, Hoogendijk AJ, Scicluna BP, Ong DS, et al. Admission hyperglycemia in critically ill sepsis patients: association with outcome and host response. Crit Care Med 2016;44:1338-46.

Supplementary Table 1. Codes of diagnoses and procedures

	Code
Cardiovascular complications	
Ischemic heart disease	ICD-10 codes, I20-I25
Myocardial infarction	I21, I22
Heart failure	I50
Stroke	I60-I64
Hemorrhagic	I60-I62
Ischemic	I63
Peripheral artery disease	Procedure codes, HA633, HA651, HA652, M6597, M6605, M6612, M6613, M6620, M6632, M6633, N0571, N0572, N0573, N0574, N0575, O0161, O0162, O0163, O0164, O0165, O0166, O0167, O0168, O0169. O0170, O171, O1643, O1644, O1645, O1646
Percutaneous coronary intervention	M6551, M6552, M6561, M6562, M6563, M6564, M6565, M6566, M6567, M6571, M6572
Coronary artery bypass surgery	O1640, O1641, O1642, O1647, O1648, O1649
Mortality	
Cancer	ICD-10 codes, C00-C97
Diabetes	E10-E14
Cerebrovascular disease	I60-I69
Heart disease	I20-I51
Hypertensive disease	I10-I13
Pneumonia	J12-J18

ICD-10, 10th edition of the International Classification of Diseases.

Supplementary Table 2. Rates of hospitalization due to cardiovascular complications per 10,000 adults with diabetes

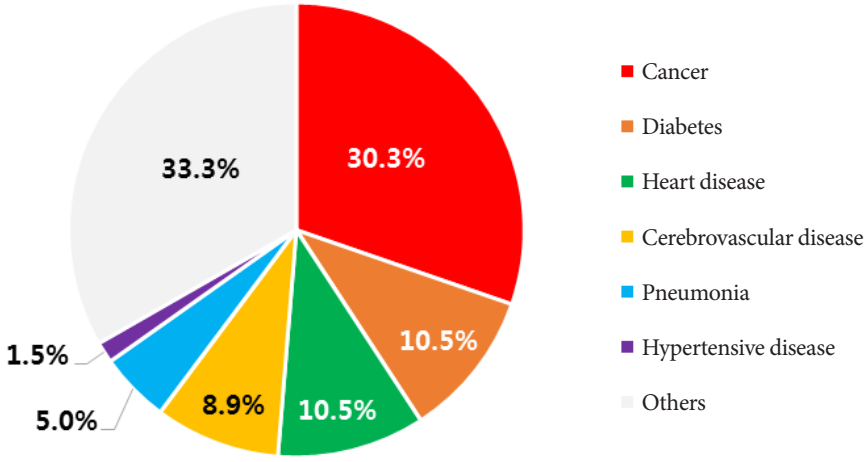
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Total										
Ischemic heart disease	426	494	505	496	481	484	460	444	440	433
Myocardial infarction	103	113	110	93	92	73	67	68	69	71
Heart failure	98	120	130	114	125	142	128	131	135	154
Stroke	297	330	339	302	306	305	283	266	260	257
Ischemic	255	278	287	259	258	255	235	222	212	206
Hemorrhagic	41	51	58	48	51	53	50	44	45	49
Peripheral artery disease	28	28	36	31	37	43	42	45	42	46
Percutaneous coronary intervention	76	73	83	75	76	86	79	75	80	74
Coronary artery bypass surgery	7	8	6	6	6	6	6	5	6	6
Men										
Ischemic heart disease	438	519	512	501	485	503	478	464	461	461
Myocardial infarction	111	123	117	96	96	83	66	73	78	81
Heart failure	72	98	105	94	106	115	111	117	128	146
Stroke	291	323	322	281	297	305	283	257	254	254
Ischemic	257	277	271	244	250	250	234	214	210	205
Hemorrhagic	38	51	55	43	51	57	51	43	45	46
Peripheral artery disease	39	36	47	43	45	56	53	55	53	55
Percutaneous coronary intervention	97	93	97	96	98	113	98	97	99	95
Coronary artery bypass surgery	11	9	10	7	8	8	9	8	8	7
Women										
Ischemic heart disease	419	473	501	493	478	463	439	420	413	397
Myocardial infarction	97	104	103	91	88	64	67	61	59	60
Heart failure	124	144	156	135	145	172	146	146	140	161
Stroke	308	340	360	326	316	305	283	274	264	258
Ischemic	257	281	307	276	268	261	235	229	212	204
Hemorrhagic	44	52	61	53	52	48	49	44	44	51
Peripheral artery disease	19	21	26	19	28	29	30	34	28	35
Percutaneous coronary intervention	56	54	69	53	53	56	59	50	59	50
Coronary artery bypass surgery	4	6	2	4	4	3	4	2	4	4

Supplementary Table 3. Mortality rates per 100,000 adults with diabetes

	2007	2008	2009	2010	2011	2012	2013	2014	2015
Total									
All-cause mortality	2,255	2,353	2,036	2,156	2,200	2,089	1,977	1,792	1,865
Cancer	614	678	575	603	657	591	562	555	587
Diabetes mellitus	379	412	296	301	264	266	252	194	188
Cerebrovascular disease	264	259	227	264	229	189	172	142	161
Heart disease	200	231	197	213	196	205	193	171	190
Hypertensive disease	63	30	36	37	18	39	35	27	26
Pneumonia	27	27	50	51	83	73	75	83	88
Men									
All-cause mortality	2,599	2,563	2,330	2,345	2,481	2,248	2,116	1,966	2,010
Cancer	767	878	745	775	815	741	659	685	687
Diabetes mellitus	369	387	328	294	245	258	250	186	163
Cerebrovascular disease	277	207	234	208	248	177	151	120	175
Heart disease	238	174	168	239	174	189	196	157	164
Hypertensive disease	42	12	28	18	18	21	22	26	27
Pneumonia	22	29	59	70	89	72	75	88	93
Women									
All-cause mortality	1,939	2,156	1,754	1,975	1,900	1,902	1,809	1,567	1,662
Cancer	467	479	407	428	488	422	449	400	461
Diabetes mellitus	396	440	266	310	285	271	251	200	211
Cerebrovascular disease	255	316	223	323	209	202	194	164	142
Heart disease	163	289	230	187	218	220	187	184	216
Hypertensive disease	83	50	44	58	19	58	50	27	24
Pneumonia	34	25	43	33	76	74	75	75	79

Supplementary Table 4. Most common causes of death as a proportion of all deaths among patients with diabetes in 2015

	%
Cancer	30.3
Malignant neoplasms of lip, oral cavity and pharynx x (C00-C14)	0.3
Malignant neoplasm of esophagus (C15)	0.2
Malignant neoplasm of stomach (C16)	2.5
Malignant neoplasms of colon, rectum and anus (C18-C21)	3.6
Malignant neoplasms of liver and intrahepatic bile ducts (C22)	5.0
Malignant neoplasm of pancreas (C25)	3.3
Malignant neoplasm of larynx (C32)	0.1
Malignant neoplasms of trachea, bronchus and lung (C33-C34)	6.7
Malignant melanoma of skin (C43)	0.2
Malignant neoplasm of breast (C50)	0.7
Malignant neoplasm of cervix uteri (C53)	0.3
Malignant neoplasms of corpus uteri and uterus, part unspecified (C54-C55)	0.2
Malignant neoplasm of ovary (C56)	0.6
Malignant neoplasm of prostate (C61)	0.8
Malignant neoplasms of kidney and renal pelvis (C64-C65)	0.6
Malignant neoplasm of bladder (C67)	0.5
Malignant neoplasms of meninges, brain and other parts of central nervous system (C70-C72)	0.4
Malignant neoplasms of lymphoid, hematopoietic and related tissue (C81-C96)	2.1
Others malignant	2.3
Diabetes mellitus	10.5
Heart disease	10.5
Cerebrovascular disease	8.9
Pneumonia	5.0
Hypertensive disease	1.5
Others	33.3



Supplementary Fig. 1. Most common causes of death as a proportion of all deaths among patients with diabetes in 2015.