Clin Invest Arterioscl. 2012;24(5):234–240

CLÍNICA E INVESTIGACIÓN EN ARTERIOSCLEROSIS

www.elsevier.es/arterio

ORIGINAL ARTICLE

Features of the risk profile of patients with type 2 diabetes and/or cardiovascular disease in a primary care centre in Barcelona (Spain)

Silvia Canivell[a,b,c,*], Jacinto Ortiz[c], Joan Mitjavila[c], Xavier Otero[c], Jose M. Sotoca[c], Ramon Gomis[a,b,d]

[a] *Diabetes and Obesity Laboratory, Endocrinology and Nutrition Unit, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Hospital Clinic de Barcelona, Spain*
[b] *Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain*
[c] *Primary Care Center Les Corts, Corporació Sanitaria Clinic, Barcelona, Spain*
[d] *University of Barcelona, Spain*

Received 12 April 2012; accepted 20 June 2012
Available online 4 August 2012

KEYWORDS
Diabetes mellitus, type 2;
Cardiovascular diseases;
General practice;
Epidemiology

Abstract
Background: We compared the clinical burden of patients with type 2 diabetes (DM), cardiovascular disease and type 2 diabetes (CVDM), and cardiovascular disease without type 2 diabetes (CVnoDM) who are currently attending a primary health care centre in Barcelona.
Methods: A cross-sectional study was performed on 2168 patients: 855 with CVnoDM, 301 with CVDM and 1012 with DM. Metabolic control, pharmacological therapy, comorbidity and death rate within one year were compared between groups.
Results: DM patients were younger, more obese and less sedentary than the others. Only 11% of all patients were smokers. Blood pressure (BP) readings were less than 135/75 mmHg in all groups. Total and LDL cholesterol were the lowest in CVDM. HbA1c levels were similar in CVDM and DM. DM received fewer flu vaccinations compared to the others. CVnoDM and CVDM had a higher proportion on antiplatelet therapy than DM. Comorbidity (assessed through the Charlson Index) reached its highest level in CVDM and its lowest level in CVnoDM. No significant differences in death rates were found.
Conclusions: In the Mediterranean area, everyday practice in primary care shows that, although there is similar metabolic control, there is no evidence of a lower clinical burden in patients with diabetes as compared to patients with cardiovascular disease.

Abbreviations: SD, standard deviation; CI, confidence interval; T2DM, type 2 diabetes mellitus; BMI, body mass index; CVnoDM, patients with established cardiovascular disease and without a diagnosis of T2DM; CVDM, patients with established cardiovascular disease and also T2DM; DM, patients with type 2 diabetes but without an established cardiovascular disease.

* Corresponding author.
E-mail addresses: canivell@clinic.ub.es (S. Canivell), jortiz@clinic.ub.es (J. Ortiz), jmitja@clinic.ub.es (J. Mitjavila), xotero@clinic.ub.es (X. Otero), jmsotoca@clinic.ub.es (J.M. Sotoca), rgomis@clinic.ub.es (R. Gomis).

0214-9168/$ – see front matter
http://dx.doi.org/10.1016/j.arteri.2012.06.001

PALABRAS CLAVE
Diabetes Mellitus tipo 2;
Enfermedad cardiovascular;
Atención primaria;
Epidemiología

Características del perfil de riesgo de los pacientes con diabetes tipo 2 y/o enfermedad cardiovascular en un centro de atención primaria del Sur de Europa

Resumen
Introducción: Comparar las características clínicas de los pacientes con diabetes tipo 2 (DM), enfermedad cardiovascular y diabetes tipo 2 (CVDM), y enfermedad cardiovascular sin diabetes tipo 2 (CVnoDM) de un centro de atención primaria de Barcelona.
Métodos: Estudio transversal reclutando 2.168 pacientes: 855 con CVnoDM, 301 con CVDM y 1012 con DM. El control metabólico, tratamiento farmacológico, comorbilidad y tasa de mortalidad durante un año se compararon entre los grupos.
Resultados: DM eran más jóvenes, más obesos y menos sedentarios que los demás. 11% de todos los pacientes eran fumadores. Los niveles de presión arterial eran menores a 135/75 mmHg en todos los grupos. El colesterol total y LDL fueron más bajos en CVDM. Los niveles de HbA1c fueron similares en CVDM y DM. DM recibieron un menor número de vacunas contra la gripe en comparación con los demás. CVnoDM y CVDM estaban más antiagregados que DM. La comorbilidad (evaluada a través del índice de Charlson) era mayor en CVDM y menor en CVnoDM. No se observaron diferencias significativas en las tasas de mortalidad durante el año analizado.
Conclusiones: La práctica habitual realizada en un centro de atención primaria del área mediterránea muestra que, a pesar de un control metabólico similar, no hay evidencia de una menor carga clínica en los pacientes con diabetes, en comparación con pacientes en prevención secundaria cardiovascular.

Background

There is an on-going debate regarding whether type 2 diabetes mellitus (T2DM) should be considered a cardiovascular risk factor equivalent to a previous cardiovascular event, such as coronary heart disease, stroke, or peripheral arterial disease. Indeed, evidence from large population-based studies supports this theory.[1–3] However, in other studies,[4–8] results are inconclusive. Possible explanations for this discrepancy may be that the different groups studied had substantial differences in the duration of diabetes or cardiovascular disease, in the treatment used, and finally, in the glycaemic and cardiovascular risk factors control. These differences limit comparability since duration of disease, therapy and cardiovascular risk factors control are key determinants of prognosis in both diabetes and cardiovascular diseases.[8–14] Another explanation is the role of different ethnicities and race in cardiovascular risk.[15,16] Cardiovascular risk factors vary by ethnic group, and it has been shown that differences in ethnic groups are important predictors of the burden of coronary heart disease[17] and of diabetic microvascular complications such as nephropathy.[18]

Since the prevalence of diabetes is reaching epidemic proportions worldwide[19] and incidence and diabetes deaths are predicted to increase in the next few years, it becomes crucial to apply the most efficient prevention and treatment strategies for tackling this disease. Very few studies have been conducted in Southern Europe, where the incidence of cardiovascular diseases is lower than in Northern Europe and the U.S.[20] Moreover, preliminary results from di@bet.es,[21] the latest population-based study performed in Spain on diabetes, indicate that around 30% of the Spanish population suffer from some carbohydrate metabolism-related.[21]

Primary health care centres are the principal settings where the majority of patients suffering from T2DM and/or cardiovascular disease goes and receives the preventive programs to prevent complications of their diseases. Therefore, a study focussed in the daily clinical management of these patients is needed in order to perform enhanced preventive programs of T2DM and cardiovascular disease in primary care.

The present study was set out to describe the real situation of clinical management and complications of patients with established cardiovascular disease (distinguishing patients who also have T2DM from non-diabetic patients) and patients with T2DM but without cardiovascular disease, who are currently attending a primary health care centre in Barcelona, Spain.

Methods

Setting

A cross-sectional study was designed that included patients currently attending a primary health care centre in Barcelona. The primary care clinic Les Corts is a general clinic focussed in both adult and pediatric medicine. The population registered at the clinic totaled 32,318 at the time of recruitment (May 2007), representing 2% of the population living in the city. The study was approved by the Ethics Committee of the reference hospital for the primary health care centre (Hospital Clinic, Barcelona), complying with all laws and international ethics guidelines outlined in the Declaration of Helsinki.

Inclusive and exclusive criteria for recruitment

All the patients who had received a diagnosis, according to database information, of type 2 diabetes mellitus and/or a cardiovascular disease were included in the study. Patients were recruited by performing a search of the clinic's database for diagnoses of type 2 diabetes mellitus and/or a cardiovascular disease according to the ICD-10 international codes. Cardiovascular disease was defined as evidence

of a previous episode of coronary heart disease, stroke or peripheral arterial disease. The clinic's database was highly accurate for that purpose. The total population recruited was defined as the total number of patients who had at least one visit to the clinic during the period between May 1, 2006, and May 10, 2007. Inclusion criteria for patients included previous diagnosis of type 2 diabetes mellitus and/or cardiovascular disease, and age of at least 18 years. Patients who were included in a palliative care program were excluded.

Clinical data collected

Data from all participants were recorded regarding sex, age, smoking habit, level of physical activity reported, body mass index (BMI), flu vaccination in the previous winter period, duration of type 2 diabetes or cardiovascular disease since original diagnosis appearing in the database (in years), morbidity (calculated using the Charlson Index, see supplementary table) and treatment (use of lipid lowering drugs, antihypertensive drugs, antiplatelet drugs and anticoagulation therapy). In addition, the most recent values within the previous year of BP, total cholesterol, LDL-cholesterol and HbA1c concentration (in diabetic patients) were taken. Levels of physical activity reported were defined as a categorical variable with 3 categories: 1 for optimum level, 2 for moderate exercise and 3 for a sedentary person. During current nursery care, each patient answers a physical activity questionnaire and then nurses assign a score (1, 2 or 3) depending on their answers. Sedentary patients were defined as the percentage of score 3 among the total. BMI was defined as the individual's body weight (in kg) divided by the square of his or her height (in m). Duration of T2DM or cardiovascular disease was registered as from the year when the condition really began (rather than the data entry of the condition into the database) until the year when the cross analysis was done. The Charlson Index is a continuous measure of comorbidity. It contains 19 categories of comorbidity, which are primarily defined using ICD-9-CM diagnoses codes. Each category has an associated weight, taken from the original Charlson paper,[22] which is based on the adjusted risk of one-year mortality. The overall comorbidity score reflects the cumulative increased likelihood of one-year mortality; the higher the score, the more severe the burden of comorbidity.

Lost patients were defined as patients having no open clinical history in the clinic's database when the cross-analysis was done. Manual inspection of the clinical histories corresponding to all *lost* patients within the previous year was then performed to try to elucidate the cause of the loss (whether due to death, move or other reasons). Dead patients were defined as such only when the investigator saw the death certificate in the database. The cause of death was sought as well in the death certificate. Patients who changed addresses were defined as so if in the clinical history there was a clear statement saying the change of address. All other reasons were classified as ''other reasons''.

Data extraction

Diabetes and cardiovascular disease durations were recorded through manual inspection of each individual's clinical history. In the present study, the Charlson Index was calculated creating a model that gave each ICD-9-CM diagnosis from the Charlson Index its corresponding weight (see supplementary table). Then, for each patient, all weights were added up to get the total score of the Index per patient. Means of the Charlson Index score for each group of patients (DM, CVDM, and CVnoDM) were compared. Losses within the year of the cross-sectional analysis (with its cause specified, including mortality data) were assessed through manual inspection of the clinical history of each *lost* patient. The rest of variables included were taken automatically from the clinic's database using the last value registered in the database within the previous year.

Primary and secondary outcomes

The primary outcome had two endpoints. First, the aim was to compare the cardiovascular risk factors control (BP, cholesterol serum levels, smoking status, levels of physical activity, and obesity), nursery care interventions (flu vaccinations in the previous winter period), glycaemic control in diabetic patients, and pharmacological therapy between DM, CVDM and CVnoDM patients. Secondly, we aimed to compare the clinical burden of these patients which was assessed through the Charlson Index. The secondary outcome was the comparison of the proportion of dead patients (with their cause specified where possible) within the year of the cross analysis between the different groups.

Data analysis

Software STATA.11 was used for the statistical analyses of this study. Results are expressed as means $\pm$ SD, confidence interval (CI) for continuous variables or as % for categorical variables. Chi-squared tests were performed for categorical variables and ANOVA tests for comparisons between continuous variables. Adjustments for age and sex have been done as necessary. The significance level was set up at $p < 0.05$ (two-sided). Proportion of deaths was calculated as the number of dead patients divided by the total of *lost* patients in each group (CVnoDM, CVDM and DM) within the year of the cross analysis.

Results

Baseline characteristics and cardiovascular risk factors of the study population

855 patients had established cardiovascular disease and had not been diagnosed with T2DM (CVnoDM), 301 suffered from a cardiovascular disease and also had T2DM (CVDM) and 1012 patients had type 2 diabetes (DM) but had not an established cardiovascular disease. Baseline characteristics and cardiovascular risk factors of these patients are shown in Table 1. The control group was defined as the group of patients with a history of cardiovascular disease but no previous diagnosis of T2DM.

In all three groups, the majority of patients were men, however the proportion of men to women was lower in the DM group (54% as compared to 65% and 71% in CVnoDM and

Table 1 Clinical characteristics of patients included in the study.

Patient' characteristics	Patients with previous CV[a] disease non diabetics ($n = 855$) CVnoDM	Patients with previous CV disease and T2DM ($n = 301$) CVDM	Patients with T2DM and no previous CV disease ($n = 1012$) DM	p-Value[†] from Chi squared or ANOVA	N, missing values (%) (total $N = 2168$)
Male gender, %	65	71	54	**<0.0001**	2168 (0%)
Age, mean and CI,	74.4 (SD 11.6)	74.7 (SD 9.3)	70.7 (SD 12.7)	1.0/**<0.0001**	2168 (0%)
years	95%CI [73.7–75.2]	95%CI [73.6–75.7]	95%CI [69.9–71.5]	**<0.0001**	
Smokers, %	12	11	12	0.9	2168 (0%)
Sedentary, %	34	39	27	**<0.0001**	2124 (2%)
BMI, mean and CI,	27.6 (SD 4.00)	28.7 (SD 5.00)	29.0 (SD 5.03)	**0.002**/**<0.0001**	2063 (5%)
kg/m^2	95%CI [27.3–27.9]	95%CI [28.1–29.3]	95%CI [28.7–29.3]	1.00	
Systolic BP,[a] mean	130.1 (SD 17.5)	133.2 (SD 18.1)	131.8 (SD 17.6)	**0.03**/0.1	2140 (1%)
and CI, mmHg	95%CI [128.9–131.3]	95%CI [131.2–135.2]	95%CI [130.7–132.8]	0.6	
Diastolic BP, mean	74.2 (SD 12.1)	73.1 (SD 14.2)	74.3 (SD 9.7)	0.5/1.0	2139 (1%)
and CI, mmHg	95%CI [73.4–75.1]	95%CI [71.5-74.8]	95%CI [73.7–74.9]	0.4	
Total chol, mean	184.4 (SD 39.2)	166.3 (SD 30.3)	178.5 (SD 34.0)	**<0.0001**/0.057	1001 (54%)
and CI, mg/dL	95%CI [180.1–188.6]	95%CI [161.5–171.1]	95%CI [175.6–181.5]	**<0.0001**	
LDL chol, mean	113.1 (SD 32.7)	92.7 (SD 22.1)	102.4 (SD 27.9)	**<0.0001**/**<0.0001**	1020 (53%)
and CI, mg/dL	95%CI [109.6–116.6]	95%CI [89.2–96.1]	95%CI [100.0–104.8]	**0.001**	
Flu vaccine, %	63	74	12	**0.004**	2168 (0%)
Hb1c if T2DM,		6.7 (SD 1.20)	6.6 (SD 1.25)	0.6	1273
mean and CI		95%CI [6.52–6.80]	95%CI [6.54–6.70]		(41%)

p-value in bold corresponds to p-value lower than 0.05.

[a] CV: cardiovascular; BP: blood pressure.

[†] The first p-value refers to the comparison between CVnoDM and CVDM, the second to the comparison between CVnoDM and DM, and in the second line, to the comparison between CVDM and DM.

Table 2 Therapy used in the study populations.

Pharmacological therapy (%)	Patients with CV[a] disease non diabetics (CVnoDM) ($n = 855$)	Patients with CV[a] disease and T2DM (CVDM) ($n = 301$)	Patients with T2DM and no previous CV[a] disease (DM) ($n = 1012$)	p-Value[†]
Lipid lowering drugs	58	68	57	0.1/0.9
Antihypertensive drugs	61	75	58	**0.03**/0.7
ACE inhibitors/ARA II	43	64	52	**0.003**/0.2
Beta blockers	28	31	13	0.6/**0.009**
Antiplatelet/anticoagulation therapy	67	77	47	0.1/**0.004** **<0.0001**

[a] CV: cardiovascular.
[†] The first p-value refers to the comparison between CVnoDM and CVDM, the second to the comparison between CVnoDM and DM, and in the second line, to the comparison between CVDM and DM.

CVDM, respectively). The DM group was significantly younger than the other two groups (70.7 mean age in years as compared to 74.4 mean years in CVnoDM and 74.7 mean years in CVDM). Overall, 11% of patients were currently smoking. The proportion of patients leading a sedentary lifestyle differed among the groups, with a maximum in CVDM (39%), 34% in CVnoDM, and a minimum in DM (27%, $p < 0.0001$). Patients with T2DM had a higher BMI as compared with those with cardiovascular disease but without T2DM ($p < 0.01$). Levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were similar in the three groups and followed ADA recommendations (<135/85 mmHg in average). Lipid profile (total cholesterol serum levels and LDL cholesterol serum levels) was significantly lower in CVDM as compared with CVnoDM and with DM. Glycaemic control was similar between the two groups with T2DM (CVDM and DM), with HbA1c mean levels less than 7%. There was a significant lower proportion of flu vaccinations in the diabetic patients (12%) as compared with the other groups (65% and 71%, $p = 0.004$).

Therapy used in the study populations

Data about pharmacological drugs used by the patients are presented in Table 2. In summary, the most important result in Table 2 revealed that patients with established cardiovascular disease were more frequently on antiplatelet or anticoagulation therapy (67% in CVnoDM and 77% in CVDM) as compared with type 2 diabetes but with no history of cardiovascular disease (47%, $p < 0.01$). There was a higher use of ACE inhibitors or ARA II drugs found in patients with diabetes and established cardiovascular disease (64% versus 43%, $p = 0.003$) as compared with patients with cardiovascular disease but without diabetes. No significant differences were observed in the use of lipid lowering drugs among the three groups, with an average use of 61% in total. Patients with both diabetes and cardiovascular disease had a higher use of antihypertensive drugs as compared with non-diabetic patients with cardiovascular disease (control group) (75% versus 61%, $p = 0.03$). There was more than twice the use of beta blockers in the control group as compared with diabetics (28% versus 13%, $p = 0.009$). No differences in the treatment of T2DM were found between CVDM and DM groups (data not shown).

Comorbidity and ten-year mortality prediction (Charlson Index)

General morbidity (assessed using the Charlson Index, see supplementary table) reached its maximum when both cardiovascular disease and diabetes were present (mean of 3.24, 95%CI 3.03–3.44), then diminished to 2.09 (95%CI 2.00–2.18) if only diabetes was present, whereas the group with less associated morbidity was the one with only cardiovascular disease (mean index 1.83, 95%CI 1.72–1.93, $p < 0.0001$). Results did not change after adjustments for age and sex (results not shown). The Charlson Index was created initially to provide physicians with a rough idea of the general comorbidity facing patients and to give an approximation of ten-year survival predictions (the higher the score, the lower the survival rate).[22] According to this statement, in our study, patients with T2DM would have a worse 10-year survival rate as compared to patients with cardiovascular disease but without T2DM, with the poorest 10-year survival rate found in those with both cardiovascular disease and T2DM.

Losses and deaths during the last year

There was on average a 10% of losses in the three groups. The proportion of deaths within the last year in each group did not differ significantly among them (2.2% in the control group, 3.2% in the diabetic, cardiovascular disease group and 1.1% in the diabetic group). Results did not change after adjustments for age and sex (data not shown). 70% of deaths were men in all three groups, with an average age of 79 years in the diabetic group, 83 years in the control group and 84 years in the diabetic group with established cardiovascular disease.

There was almost double the number of cardiovascular deaths in patients with diabetes and established cardiovascular disease as compared with non-diabetics with cardiovascular disease (27.3% versus 14.4%, $p = 0.02$). Cardiovascular deaths were higher in the group with both diabetes and cardiovascular disease (27.3%) as compared with the group with only diabetes (16.7%), but this difference did not reach statistical significance. A similar proportion of deaths due to cancer was found in the three

groups (18% on average). These results did not change after controlling for sex and age (data not shown).

Discussion

Summary of main findings

Present results show that overall patients with T2DM are younger, and in a larger proportion women and more obese than patients with established cardiovascular disease. Lipid control is more efficiently achieved in patients with both T2DM and cardiovascular disease as compared with patients with only T2DM and patients with cardiovascular disease but without T2DM. This result reflects the fact that physicians make a special effort to reduce lipid profile when both diseases (cardiovascular disease and diabetes) are present. Lipid lowering drugs are used in a similar proportion in all 3 groups. Consequently, the use of statins is now generally widespread in all diabetic patients. Flu vaccinations are given less frequently to patients with T2DM as compared with those with cardiovascular disease. Glycaemic control is similar in diabetic patients regardless of the presence of cardiovascular disease. It must be noted that the three groups shared similar periods of evolution since the time of diagnosis of diabetes or the cardiovascular event (7 years on average) registered in the database. Comorbidity data showed that patients with established cardiovascular disease but without diabetes had a lower comorbidity than patients with T2DM but without cardiovascular disease. Mortality data revealed that there is a similar mortality in patients with diabetes and no history of cardiovascular disease, patients with diabetes and cardiovascular disease, and in non-diabetic patients with established cardiovascular disease. There is a trend towards an increased risk of death if the patient is both diabetic and has established cardiovascular disease. Cardiovascular mortality is almost double in patients with diabetes and cardiovascular disease as compared with non-diabetic patients in secondary cardiovascular prevention. Cancer mortality was similar in the three groups of patients.

Strengths and limitations of the study

The strength of this study lies in its depiction of the real situation of clinical health care practice in patients with T2DM, with and without cardiovascular disease, who attend a primary health care centre in Barcelona. Since this study does not belong to any large epidemiological study in primary care, the present results reflect accurately the clinical management and complications of the patients suffering from T2DM and/or cardiovascular disease in a day-to-day practice. The most important limitation is the study design, a cross sectional study at one year. In order to compare survival rates among these groups of patients, a cohort design with an appropriate follow-up time is needed. Other limitations exist such as that there were not enough cardiovascular events and corresponding data of *lost* patients may not have been registered correctly in the clinic's database. Indeed, the inclusion of death certificates within the clinic's database was not hundred percent complete, so it remains possible that more deaths occurred but that they were accounted for as ''other causes'' (misclassification). Therefore interpretation of mortality data must be performed carefully.

Comparison with existing literature

Present results are in concordance with the preliminary results of the di@bet.es study,[21] a national cross-sectional study about the prevalence of diabetes in Spain and associated cardiovascular risk factors.[21] Physicians seem not to treat T2DM as a cardiovascular event equivalent given the lower use of antiplatelet drugs in patients in primary cardiovascular prevention suffering from T2DM. This finding is in accordance with the latest recommendations from the ADA about the use of antiplatelet treatment in primary prevention in people with diabetes.[23,24]

Implications for future research or clinical practice

Regarding clinical practice, it was shown that diabetic patients received lower flu vaccinations. Taking into account that infections in diabetic patients can have a worse prognosis, intervention should be done at primary health care centres aimed at increasing flu vaccinations in patients with T2DM. On the other hand, given the theory that inflammatory status underlies the cause of arteriosclerosis, vascular damage and diabetes,[25] flu vaccinations could have an additional benefit in patients with diabetes,[26] which future research would need to confirm. In addition, BMI should be reduced in T2DM patients and physical activity promoted in order to ameliorate cardiovascular outcomes.

Future research should focus on performing cohort studies to compare survival rates of CVnoDM, CVDM and DM patients in a primary health care setting since these results show that T2DM confers a higher comorbidity burden than cardiovascular disease without diabetes.

Likewise, preventive programs involving both nursery and medical interventions focussing in an improvement of a healthy lifestyle (diet, exercise, loss of weight, stop smoking, flu vaccinations) in patients with T2DM or in secondary cardiovascular prevention need to be revised and ameliorated in primary care centres.

In summary, special attention to clinical management in patients with T2DM (and without cardiovascular disease) must be made because results show that, even though a similar metabolic control, there is no evidence of a lower clinical burden in patients with diabetes as compared to those in secondary cardiovascular prevention without diabetes in the Mediterranean area.

Authors' contributions

SC conceived of the study, participated in data collection, performed the statistical analysis and wrote the manuscript. JO, JM, XO, and JS participated in the data collection and critically revised the draft. RG conceived of the study, coordinated and supervised the study and manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

Acknowledgements

The authors thank Dr. Angels Montroig, Dr. Susanna Bermudez, Dr. Berta Forné, Dr. Guillem Fluxà and Dr. Montse Pinyol for their contribution in collecting data.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.arteri.2012.06.001.

References

1. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339:229–34.
2. Juutilainen A, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Type 2 diabetes as a ''coronary heart disease equivalent'': an 18-year prospective population-based study in Finnish subjects. Diabetes Care. 2005;28:2901–7.
3. Schramm TK, Gislason GH, Kober L, Rasmussen S, Rasmussen JN, Abildstrom SZ, et al. Diabetes patients requiring glucose-lowering therapy and nondiabetics with a prior myocardial infarction carry the same cardiovascular risk: a population study of 3.3 million people. Circulation. 2008;117:1945–54.
4. Evans JM, Wang J, Morris AD. Comparison of cardiovascular risk between patients with type 2 diabetes and those who had had a myocardial infarction: cross sectional and cohort studies. BMJ. 2002;324:939–42.
5. Lee CD, Folsom AR, Pankow JS, Brancati FL. Cardiovascular events in diabetic and nondiabetic adults with or without history of myocardial infarction. Circulation. 2004;109:855–60.
6. Pajunen P, Koukkunen H, Ketonen M, Jerkkola T, Immonen-Raiha P, Karja-Koskenkari P, et al. Myocardial infarction in diabetic and non-diabetic persons with and without prior myocardial infarction: the FINAMI Study. Diabetologia. 2005;48:2519–24.
7. Natarajan S, Liao Y, Sinha D, Cao G, McGee DL, Lipsitz SR. Sex differences in the effect of diabetes duration on coronary heart disease mortality. Arch Intern Med. 2005;165:430–5.
8. Natarajan S, Liao Y, Cao G, Lipsitz SR, McGee DL. Sex differences in risk for coronary heart disease mortality associated with diabetes and established coronary heart disease. Arch Intern Med. 2003;163:1735–40.
9. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837–53.
10. Cho E, Rimm EB, Stampfer MJ, Willett WC, Hu FB. The impact of diabetes mellitus and prior myocardial infarction on mortality from all causes and from coronary heart disease in men. J Am Coll Cardiol. 2002;40:954–60.
11. Donnan PT, Donnelly L, New JP, Morris AD. Derivation and validation of a prediction score for major coronary heart disease events in a U.K. type 2 diabetic population. Diabetes Care. 2006;29:1231–6.
12. Fox CS, Sullivan L, D'Agostino Sr RB, Wilson PW. The significant effect of diabetes duration on coronary heart disease mortality: the Framingham Heart Study. Diabetes Care. 2004;27:704–8.
13. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359:1577–89.
14. Vaccaro O, Eberly LE, Neaton JD, Yang L, Riccardi G, Stamler J. Impact of diabetes and previous myocardial infarction on long-term survival: 25-year mortality follow-up of primary screenees of the Multiple Risk Factor Intervention Trial. Arch Intern Med. 2004;164:1438–43.
15. Kurian AK, Cardarelli KM. Racial and ethnic differences in cardiovascular disease risk factors: a systematic review. Ethn Dis. 2007;17:143–52.
16. Liu R, So L, Mohan S, Khan N, King K, Quan H. Cardiovascular risk factors in ethnic populations within Canada: results from national cross-sectional surveys. Open Med. 2010;4:e143–53.
17. Beohar N, Davidson CJ, Massaro EM, Srinivas VS, Sansing VV, Zonszein J, et al. The impact of race/ethnicity on baseline characteristics and the burden of coronary atherosclerosis in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. Am Heart J. 2011;161:755–63.
18. Zitouni K, Nourooz-Zadeh J, Harry D, Kerry SM, Betteridge DJ, Cappuccio FP, et al. Race-specific differences in antioxidant enzyme activity in patients with type 2 diabetes: a potential association with the risk of developing nephropathy. Diabetes Care. 2005;28:1698–703.
19. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27:1047–53.
20. Grau M, Subirana I, Elosua R, Solanas P, Ramos R, Masia R, et al. Trends in cardiovascular risk factor prevalence (1995–2000–2005) in northeastern Spain. Eur J Cardiovasc Prev Rehabil. 2007;14:653–9.
21. Rojo-Martínez G, Goday A, Boch A, Bordiú E, Calle A, Carmena R, et al. Prevalencia de diabetes y otras alteraciones del metabolismo hidrocarbonado en España. Estudio di@bet.es. Av Diabetol. 2011;27 (Espec Congr):32–107.
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
23. Buse JB, Ginsberg HN, Bakris GL, Clark NG, Costa F, Eckel R, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation. 2007;115:114–26.
24. Pignone M, Alberts MJ, Colwell JA, Cushman M, Inzucchi SE, Mukherjee D, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: a position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. Diabetes Care. 2010;33:1395–402.
25. Herder C, Baumert J, Zierer A, Roden M, Meisinger C, Karakas M, et al. Immunological and cardiometabolic risk factors in the prediction of type 2 diabetes and coronary events: MONICA/KORA Augsburg Case-Cohort Study. PLoS One. 2011;6:e19852.
26. Bongartz T, Kudva Y. Can treatment of chronic inflammatory diseases reduce the risk of diabetes mellitus? JAMA. 2011;305:2573–4.