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Coronary artery disease screening in diabetic patients: how good is guideline adherence?

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Summary

Introduction: Diabetic patients are at high risk for coronary artery disease (CAD), which is the leading cause of death in this population. The Swiss Society of Endocrinology-Diabetology (SSED) recommends CAD screening for diabetic patients with ≥2 additional cardiovascular risk factors (CVRF), by stress echocardiography (SE) or myocardial perfusion imaging (MPI). The aim of this study was to assess the application of these guidelines and the treatment of CVRF in the diabetes outpatient clinics of the five Swiss University Hospitals.

Methods: The study was initiated in Lausanne and the study questionnaires were circulated to the endocrinologists of the five Swiss University Hospitals. Practitioners were asked to include consecutive patients attending the diabetes outpatient clinics over one month. Prevalence of CAD, screening methods for CAD, prevalence of CVRF, biological analyses over the last 6 months and medical therapy were recorded.

Results: A total of 302 subjects were included. The mean age was 53 ± 14 years, 68% had type 2 diabetes, 27% type 1 and 5% other types. Among T2DM with ≥2 CVRF, 45% were screened for CAD according to SSED guidelines. In T2DM 25% had blood pressure ≤130/80 mm Hg, 15% a lipid profile within target, 23% HbA_{1c} ≤7.0%. Overall, 2% achieved all 3 targets.

Conclusions: Only 45% of T2DM with ≥2 CVRF were screened for CAD according to SSED guidelines and 2% of T2DM had proper control over all CVRF. Efforts are still necessary to improve CAD prevention and screening of diabetic patients in Swiss University Hospitals.

Key words: diabetes mellitus; coronary artery disease; screening; cardiovascular risk factors

Introduction

The prevalence of coronary artery disease (CAD) in diabetic patients is 2–4 times that in the general population [1], and CAD is the leading cause of death in those patients. Furthermore, type 2 diabetic patients (T2DM) with no history of myocardial infarction are at the same risk as non-diabetic patients with a previous myocardial infarction [2], a view which, however, is not unanimous [3]. In addition, CAD more often has a silent course in diabetic patients (20–30% compared to 10–20% in the general population [4, 5]). These findings suggest that diabetes is a major cardiovascular risk factor (CVRF) and that screening of asymptomatic diabetic patients for CAD may be useful. Systematic screening guidelines were first proposed by the French Diabetes Association (ALFEDIAM) in 1995 [6], which recommended screening of T2DM with at least one additional CVRF. In 1998, the American Diabetes Association (ADA) also recommended the screening of T2DM with at least two additional CVRF [7]. In 2000, the Swiss Society of Endocrinology-Diabetology (SSED) proposed the same screening

Abbreviations

ADA	American Diabetes Association
ACE	Angiotensin-converting enzyme
AT2 receptor antagonist	Angiotensin II receptor antagonist
ALFEDIAM	French Diabetes Association
CAD	Coronary artery disease
CVRF	Cardiovascular risk factor
SE	Stress echocardiography
SPECT-MPI	Myocardial perfusion imaging
SSED	Swiss Society of Endocrinology-Diabetology
T1DM	Type 1 diabetic patients
T2DM	Type 2 diabetic patients

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pattern as ADA, viz. by stress echocardiography (SE) or myocardial perfusion imaging (SPECT-MPI) [8]. On the other hand, many pharmacological treatments for CVRF have proved to be highly cost effective in this high risk population [9]. In this context, the present survey sets out to assess the application of systematic screening guidelines for CAD and the form assumed by treatment of CVRF in the five Swiss University Hospitals.

Methods

Study design

A retrospective and observational survey was drawn up to evaluate the management of CVRF, follow-up of CAD and the application of CAD screening guidelines in diabetic patients in Switzerland. The main investigating centre was the diabetes unit of Lausanne University Hospital.

Questionnaires were circulated to endocrinologists in the diabetes outpatient clinics of the five Swiss University Hospitals (Basel, Bern, Geneva, Lausanne and Zürich). Each of these centres received 150 questionnaires in English (Appendix 1), and were requested to return them after one month (between September and December 2003). The number of completed questionnaires for each hospital was 72 in Basel, 15 in Bern, 71 in Geneva, 102 in Lausanne and 42 in Zürich. Recruitment comprised consecutive patients over one month. The questionnaires were completed with regard to current treatment and CAD screening.

The questions focused on the presence of CAD, micro- and macrovascular complications of diabetes and CVRF. If systematic screening for CAD was performed, we requested information on strategy and reference. Data on treatments before and after CAD screening were collected. A qualitative question on the patient's presumed compliance was asked (yes or no). The rate of incomplete replies was also recorded.

Definitions

The usual definition of diabetes was used: fast plasma glucose >7 mmol/l and plasma glucose >11 mmol/l. Obesity was defined as a body mass index (BMI) ≥30 kg/m^2, sedentarity as physical activity <2 hours 30 minutes of walking per week, and family history of premature CAD as the occurrence of an event in parents or relatives aged <55 years in men and <65 years in women.

Patients

Any diabetic patient who attended one of the diabetes outpatient clinics was included in the study. There was no exclusion criterion.

Analysis

CVRF were evaluated, and a CAD screening score was worked out on the basis of the CAD screening criteria in the ADA and SSED guidelines [7, 8]. CVRF were hypertension, obesity, family history of premature CAD, sedentarity, current or former smoking and age >45 years. Two cardiovascular risk markers were also included, viz. lower limb arteriopathy and nephropathy. These guidelines suggest screening for CAD by non-invasive tests when the "screening score" is equal to or higher than 2 points: 2 points are given for lower limb arteriopathy and 1 point for nephropathy, hypertension, obesity, family history of premature CAD, sedentarity, current or former smoking and age ≥45 years.

The targets for CVRF, diabetes control and treatment of microalbuminuria were defined according to the Swiss guidelines and to the Steno-2 study: systolic blood pressure ≤130 mm Hg, diastolic blood pressure ≤80 mm Hg, total cholesterol ≤5.0 mmol/l, HDL-cholesterol ≥1.0 mmol/l, LDL-cholesterol ≤2.6 mmol/l, triglycerides ≤1.7 mmol/l, HbA_{1c} ≤7.0% or 6.5%, urine albumin/creatinine ratio: ≤3.5 mg/mmol in women and ≤2.5 mg/mmol in men, albuminuria/24 hours <30 mg/24 h) [8–10].

Statistical analysis

Descriptive statistical and univariate analyses were performed. Categorical variables were expressed with frequency and differences between groups were based on chi-square test when appropriate. Continuous variables, normally distributed, were expressed in means and standard deviation. Non-normally distributed continuous variables were expressed by the median, 25th–75th percentiles, and analysed by non-parametric statistics: Mann-Whitney rank sum test and Wilcoxon signed-rank test. Statistical significance was defined by $p < 0.05$. Data analysis was done with JMP 5.0 software (SAS Institute, Cary, USA).

Sponsorship

This survey was sponsored by MSD; the authors formulated the study design and results on a fully independent basis.

Results

Baseline characteristics

The main patient characteristics are shown in table 1. Between September and December 2003, 302 surveys were received out of a total of 750 questionnaires distributed (40% response rate). Mean age was 53 ± 14 years for the total study population. T1DM were aged 43 ± 16 years and T2DM 57 ± 11 years. A positive history of CAD was found in 5% (n = 4) of T1DM and in 20% (n = 41) of T2DM.

Incomplete answer rates varied between 1% for diabetes type and 14% for systematic screening rate.

CAD screening was performed by SE, SPECT-MPI or stress ergometry in 42% (n = 127) of the whole study population, in 52% (n = 106) of T2DM and 20% (n = 16) of T1DM. The strategy of CAD screening in T2DM with ≥2 CVRF is shown in table 2. Screening rate increased with the screening risk score (data not shown).

Table 1
Baseline characteristics (n = 302).

All patients	Prevalence mean or median value
Age (years) *	53 (± 14)
Males	67%
Type 1 diabetes	27%
Type 2 diabetes	68%
Other types of diabetes	5%
Diabetes duration (years)‡	8 (3–15)
CAD+	16%
Weight	84 (± 20)
BMI	29 (± 7)
Waist	107 (± 14)
Number of questionnaires/centre‡	71 (15–102)
Type 1 diabetic patients	
HbA_{1c} (%)‡	7.7 (7.0–8.4)
SBP (mm Hg)*	124 (± 7)
DBP (mm Hg)*	75 (± 12)
Total cholesterol (mmol/l)*	4.8 (± 1.1)
LDL cholesterol (mmol/l)*	2.7 (± 1.0)
HDL cholesterol (mmol/l)*	1.6 (± 0.6)
Triglycerides (mmol/l)‡	1.0 (0.7–1.4)
Type 2 diabetic patients	
HbA_{1c} (%)‡	7.7 (7.0–8.6)
SBP (mm Hg)*	134 (± 17)
DBP (mm Hg)*	79 (± 9)
Total cholesterol (mmol/l)*	4.7 (± 1.1)
LDL cholesterol (mmol/l)*	2.6 (± 1.0)
HDL cholesterol (mmol/l)*	1.2 (± 0.3)
Triglycerides (mmol/l)‡	1.9 (1.2–2.9)

* Mean (+ SD) ‡ Median (p10-p90)
SBP: systolic blood pressure
DBP: diastolic blood pressure

The prevalence of CVRF in T1DM and T2DM is reported in table 3. The incomplete answer rate was 24% in T1DM and 2% in T2DM.

The median CAD screening score yielded 4 points (1–7) in the whole study population, 1 point (0–5) in T1DM and 4 points (1–7) in T2DM. In T2DM 87% had ≥2 points.

The absolute cardiovascular risk in our total population was 18.4% to 10 years according to the UPKDS risk engine (available data for 196/302 patients).

Therapy

Medication of T1DM and T2DM is reported in figure 1. The prescription rate of aspirin was 73% (n = 30) in T2DM for tertiary prevention (post CAD) and 41% (n = 79) for secondary prevention, if the patient had ≥2 CAD risk points.

In figure 2 we evaluated the rate of T2DM who reached the objectives of the Steno-2 study intervention group [9]. 13% had an HbA_{1c} value ≤6.5% and 23% ≤7.0%. 24% had blood pressure <130/80 mm Hg. The percentage with lipids meeting the recommendations (total cholesterol <5 mmol/l and LDL-cholesterol <2.6 mmol/l) was 49%. Taken together, all the targets of this study were achieved in 1% of patients (n = 1) if HbA_{1c} ≤6.5% and 2% (n = 5) if HbA_{1c} ≤7%.

Discussion

Many guidelines for CAD screening in diabetic subjects have been published. However, no study has yet evaluated adherence to these new recommendations in tertiary centres. This survey aims to assess the application of screening guidelines and treatment of CVRF in the outpatient diabetes clinics of the five Swiss University Hospitals.

CAD screening

In our survey, the screening rate in T2DM with ≥2 CVRF was 54% by SE, SPECT-MPI or exercise stress testing and only 26% in T1DM with ≥2 CVRF. Methods used and screening rates in the 5 University Hospitals were heterogeneous. In T2DM with ≥2 CVRF, Basel screened only 21% of its patients according to recent guidelines (by SE, SPECT-MI or exercise stress testing), and the majority (14%) by SPECT-MPI. In Zürich, these

Table 2
CAD screening in T2DM with ≥2 CVRF.

Centres	Basel (n = 42)	Bern (n = 11)	Geneva (n = 42)	Lausanne (n = 79)	Zürich (n = 19)	Total (n = 193)
SE	2%	9%	0%	46%	5%	20%
SPECT-MPI	14%	0%	36%	33%	5%	24%
Exercise stress testing	5%	45%	17%	4%	11%	10%
ECG at rest	22%	0%	42%	1%	21%	17%
Presence of symptoms	40%	9%	0%	4%	0%	11%
No screening	17%	37%	5%	12%	58%	17%

Table 3

Prevalence of CVRF in T1DM and T2DM.

Diabetes type	T1DM	T2DM
Hypertension	32%	72%
Dyslipidaemia	32%	72%
Obesity	5%	53%
Family history of premature CAD	6%	10%
Sedentarity	17%	46%
Current / former smoking	16%/10%	22%/21%

subjects were screened predominantly by exercise stress testing (11% of patients). Bern preferred stress ergometry (45%) and SE (9%). Geneva screened essentially by SPECT-MPI (36%) and exercise stress testing (17%) and Lausanne by SE (46%) and SPECT-MPI (33%). Moreover, 28% of all type 2 diabetic patients with ≥2 CVRF were screened for CAD by an ECG at rest or by symptoms alone, and 17% were not screened at all.

If we compare the screening rates in French- and German-speaking Switzerland, we observe that 85% of T2DM patients in Geneva and Lausanne were screened by SE, SPECT-MI and exercise stress testing versus only 31% in Basel, Bern and Zürich ($p < 0.005$). A plausible explanation is that the ALFEDIAM CAD screening report was published in French in 1995, the implementation of CAD screening being of longer standing in French-speaking than in German-speaking Switzerland despite the high absolute risk for CAD (18.4% at 10 years). The Swiss CAD screening guidelines were published five years later in 2000.

We observed that the screening rate was proportional to the number of CVRF (data not shown). However, the recently published DIAD study demonstrated that the traditional CVRF were not significantly predictive of abnormal tests [11].

Several hypotheses may explain the low rate of CAD screening in these university centres. First, the efficiency of these guidelines in patients with asymptomatic CAD is low. In a previous study done in Lausanne we analysed the rate of positive screening tests when systematic CAD screening was performed in T2DM with ≥2 CVRF, according to SSED guidelines. In our study population of 154 patients, only 20% presented a positive non-invasive screening test (SE or SPECT-MPI) [12]; thus, 5 patients need to be screened to detect one with ischaemia. In the DIAD study, the prevalence of positive SPECT-MPI was 22% in a population of 522 T2DM with ≥2 CVRF [11]. These findings suggest that new strategies are needed to increase the efficiency of these guidelines, and to select patients at higher risk of CAD in order to decrease the number needed to screen. The second hypothesis for the low screening rate is that thus far there has been no study evaluating the capacity of systematic CAD screening to reduce cardiovascular mortality in these subjects. Indeed, some experts consider diabetes as an equivalent of CAD, and that diabetic patients should be treated aggressively for CVRF, independently of the presence of CAD [9]. Finally, it appears that in Switzerland the network between endocrinologists and cardiologists is not well developed. This suggests that we should develop the same strategy as in France, where there is a consensus between the cardiologists and endocrinologists who have published recommendations for CAD screening [13].

Figure 1

Treatment of diabetes and CVRF.
1. Oral anti-diabetic drugs
2. Insulin
3. ACE inhibitors
4. AT2 receptor antagonists
5. Beta-blockers
6. Ca^{2+} antagonists
7. Diuretics
8. Aspirin
9. Anticoagulation
10. Lipid lowering agents

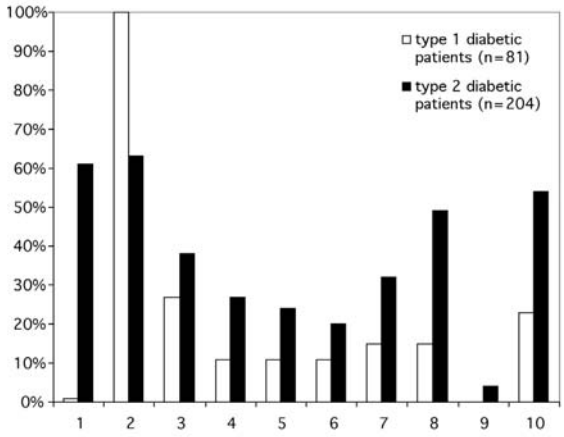
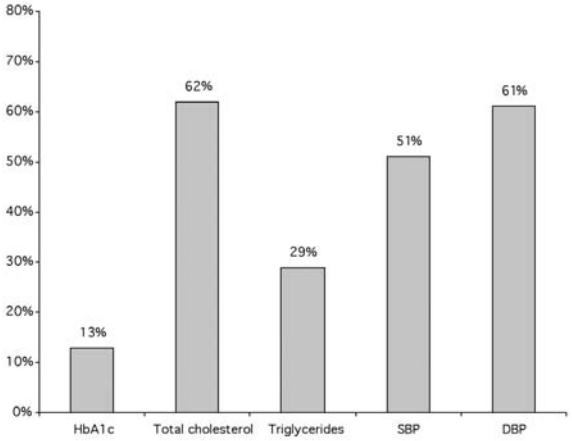


Figure 2

Percentage of T2DM reaching the targets according to the Steno-2 study objectives. Objectives: HbA_{1c} ≤6.5%; total cholesterol ≤5.0 mmol/l; triglycerides ≤1.7 mmol/l; SBP ≤130 mm Hg; DBP ≤80 mm Hg.



Management of cardiovascular risk factors

Another important issue in T2DM is prevention of cardiovascular complications by treating CVRF. Management of hyperglycaemia has shown a reduction in microvascular complications in T2DM [14] and treatment of hypercholesterolaemia with a statin has been shown to reduce mortality in patients with CAD [15, 16]. The Steno-2 study demonstrated that intensive treatment of all CVRF reduced the risk of cardiovascular complications by more than 50% in T2DM after 8 years of follow-up (number needed to treat = 5) [9]. If we compare our data with the Steno-2 study, we observe that 13% of our T2DM had an HbA_{1c} ≤6.5% versus 15% in the Steno-2 study population. The lipid pattern and blood pressure control were also better in the Steno-2 study. Nevertheless, these 2 studies cannot be compared directly because the Steno-2 study was an interventional monocentric study whereas ours was an observational multicentric study. In the EUROASPIRE survey [17], the aim was to evaluate the control of CVRF in a population of 5556 patients with CAD in 15 European countries. In this study, which was also observational and multicentric, the prevalence of CVRF was high and the therapeutic goals hard

to achieve, and only 62% of T2DM had a total cholesterol ≤5.0 mmol/l.

Finally, these results illustrate the physicians' difficulty in applying evidence-based medicine from well structured clinical trials in tertiary diabetes reference centres. Many elements may influence the decision to screen or to treat. Freeman et al. [18] reported that practioners are influenced by previous experience and feelings (about the patient, about the evidence itself or where the evidence has come from), and by the physician-patient relationship.

Study limitations

It could be argued that a survey of 302 diabetic patients may not reflect the follow-up of the diabetic population in Switzerland. However, the St Vincent Declaration showed that a survey of this kind is globally reproducible in time [19]. The wide disparity in the number of questionnaires completed at each University Hospital is more disturbing, because the proportion of completed questionnaires at each centre affects global results. Out of the 150 questionnaires sent to every diabetology outpatient clinic the median rate of completed questionnaires was 40%. This survey did not investigate the reasons for weak guideline adherence, nor the control efficiency of CVRF.

Conclusion

Despite a high cardiovascular risk in the diabetic population, the rates of systematic CAD screening and CVRF control are not optimal. This survey illustrates the difficulty for diabetes specialists of transferring guidelines into everyday clinical practice. Moreover, the issues on screening efficiency and the expected benefit of systematic application of guidelines have not yet been resolved on the individual level for the asymptomatic diabetic patient. A recent study suggested that systematic CAD screening in diabetic patients may reduce cardiovascular mortality [20]. The 140 patients of this study were either systematically screened for CAD or had follow-up visits for 4 years. Mortality was lower in the patients screened for CAD. However, it remains unresolved whether the best strategy is to treat every CVRF aggressively (Steno-2 study [10]) or to screen diabetic patients with ≥2 CVRF systematically for CAD .

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Appendix 1
Questionnaire.

Patient # _____ **University** _____

Gender ☐ ♂ male ☐ ♀female Current date ____/____/ 2003

Date of birth ____/____/_____ Patient considered compliant: ☐ yes ☐ no

Diagnoses

Type of diabetes ☐ 2 ☐ 1 ☐ other _____ **Year of diagnosis** _____

Coronary artery disease ☐ yes ☐ no

☐ Asymptomatic

☐ Typical angina pectoris Date _____

☐ Atypical angina pectoris Date _____

☐ Myocardial infarction Date _____

Interventions

☐ Coronary artery bypass Date _____

☐ PTCA / Stent Date _____

Coronary artery disease screening mode

☐ Resting ECG ☐ Symptoms + ☐ Ergometry

☐ Stress echocardiography ☐ Scintigraphy

Systematic screening for CAD ☐ Yes ☐ No

Screening guidelines ☐ ADA ☐ Swiss ☐ Other

Lower limb arteriopathy

☐ No ☐ Yes ☐ Unknown Date _____

Cerebrovascular disease

☐ No ☐ Yes ☐ Unknown Date _____

Cardiovascular risk factors

☐ Hypertension

☐ Hyperlipidaemia

☐ Currently smoking Former Never

☐ Obesity (BMI >30 kg/m^2)

☐ Family history of premature coronary artery

☐ (♂<55 years / ♀<65 years)

☐ Sedentarity (<2h30 of walk / week)

Complications of diabetes

Nephropathy ☐ No ☐ Microalbuminuria ☐ Macroalbuminuria ☐ Renal insufficiency ☐ Unknown

Retinopathy ☐ No ☐ Background ☐ Pre-prolif. ☐ Proliferative ☐ Blind

Neuropathy ☐ No ☐ Sensitive ☐ autonomous ☐ Impotence ☐ Unknown

Lower limb amputation ☐ No ☐ Yes

Biological analyses of the last 6 months

Plasma creatinine	_____ µmol/l	Microalbuminuria	_____ mg/24h or
Total cholesterol	_____ mmol/l	Microalb/creatininuria	_____ mg/mmol
LDL-C	_____ mmol/l	Weight	_____ kg
HDL-C	_____ mmol/l	Height	_____ cm
Triglycerides	_____ mmol/l	Waist	_____ cm
Blood pressure	____/____ mm Hg	Hip	_____ cm
HbA_{1c}	_____ %		

Treatments	Before screening Drug / Dosage	After screening Drug / Dosage
☐ Oral antidiabetic 1	_____/_____	_____/_____
☐ Oral antidiabetic 2	_____/_____	_____/_____
☐ Oral antidiabetic 3	_____/_____	_____/_____
☐ Insulin Nb injections/j _____	_____/_____	_____/_____
☐ Insulin 2 Nb injections/j _____	_____/_____	_____/_____
☐ ACE inhibitor	_____/_____	_____/_____
☐ AII receptor antagonist	_____/_____	_____/_____
☐ Beta blocker	_____/_____	_____/_____
☐ Calcium antagonist	_____/_____	_____/_____
☐ Diuretic	_____/_____	_____/_____
☐ Aspirin	_____/_____	_____/_____
☐ Anticoagulant	_____/_____	_____/_____
☐ Lipid lowering	_____/_____	_____/_____

Reason why no lipid lowering drug was prescribed _____

Reason why no antihypertensive drug was prescribed _____

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