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Cardiovascular Risk Assessment in People Affected with Diabetes in Primary Care

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Abstract

Several studies suggest that the cardiovascular disease (CVD) mortality rates of persons with type 2 diabetes are about two to four times higher than those of the general population. It is therefore considered necessary to develop specific tools to evaluate and reduce CVD risk in this population. In the present chapter, main CVD risk scores were explored: from the Framingham study developed in the 1960s to the last diabetes-specific models, passing through the concept of diabetes as a “CVD risk equivalent”. The scores developed in Italian population were specifically explored. The Italian experience, according to other countries, emphasizes that it may be appropriate for each country to validate existing models and eventually to adapt them to the different settings to improve targeted risk management.

Keywords: cardiovascular disease, diabetes mellitus, general practice, primary care, risk models, cardiovascular risk assessment

1. Introduction

Persons with type 2 diabetes are at increased risk for the development of cardiovascular events. Several studies suggest that cardiovascular disease (CVD) is the predominant source of morbidity and early mortality among these patients, with mortality rates about two to four times higher in persons affected with diabetes compared with the general population [1–3]. In particular, a recent study involving almost 1.2 million participants observed a hazard ratio (HR) for mortality of about 2 in patients who suffered from diabetes or myocardial infarction or stroke, while it almost doubles for a combination of CVDs and diabetes [4]. These results

emphasize the need to improve CVD preventive strategies specifically oriented to the diabetic population.

1.1. Rationale for CVD risk prediction in people with diabetes

Estimates of CVD risk can be useful for both clinicians and patients: for clinicians, it is a prognostic information that can support them in the choice of therapeutic and preventive strategies; and for patients, it can be a motivation tool to adopt healthy lifestyle measures and to observe prescribed risk-modifying treatments [5].

Considering that diabetes mellitus usually involves the coexistence of several cardiovascular risk factors, it was considered necessary to develop multifactorial approaches for CVD risk evaluation. The first studies aiming at developing reliable tools for evaluating CVD risk based on a combination of several risk factors were carried out in the United States by the Framingham investigators in the 1960s [6]. The Framingham risk score was first developed based on a long-term community cohort study, and it is applicable to general population. One of the main limitations of this model was that it did not consider diabetes status or any other indicator of chronic hyperglycaemia. In the following years, diabetes status was added to the model but only as categorical variable, and the tool was validated only in the general population [7, 8].

Three decades later, in the late 1990s, a study from Finland suggested for the first time that people suffering from diabetes, but without history of CVD, had a risk of CVD similar to that of people without diabetes who had survived a CVD event. Following this observation, several studies supported this concept of diabetes as a “CVD risk equivalent”: the presence of diabetes mellitus is considered to confer a 10-year CVD risk similar to individuals without diabetes with a prior history of CVD [9–12]. This approach has been confirmed by algorithms currently developed from both American and European cohorts, such as ATP-III guidelines [13], the European Systematic COronary Risk Evaluation (SCORE) algorithm [14] and the Prospective Cardiovascular Munster (PROCAM) model [15]. In these models, all patients with diabetes mellitus as those with existing CVD are considered as people at high risk and treated as if they required secondary prevention of CVD. In recent years, this approach has been called into question by several authors [16] considering more appropriate to develop diabetes-specific risk models. To date, some authors support the need to create models exclusively from cohorts of persons affected with diabetes, while others prefer to adapt existing risk models developed in the general population to diabetes [17].

2. Overview of diabetes-specific cardiovascular risk models

In contrast to the approach that every patient with diabetes has the same high risk for CVD events, some current guidelines include different treatment recommendations for diabetic patients without other CVD risk factors, who are considered to be at lower risk [18, 19]. In particular, a recent evidence showed a wide distribution of risk in diabetic population depending on, among others, glycated haemoglobin (HbA1c) level and numerous concomitant risk factors [20]. An accurate cardiovascular risk stratification is important in patients with

diabetes, as for general population, to determine the type and the intensity of treatment. In a recent systematic review [21], 45 cardiovascular prediction models applicable to patients with diabetes have been identified, of which 12 were specifically designed for patients with type 2 diabetes. Only few of these prediction models were evaluated in independent patient populations.

2.1. The UK Prospective Diabetes Study (UKPDS) risk engine

The oldest and most commonly used prediction model is the UK Prospective Diabetes Study (UKPDS) risk engine. The score was initially designed to estimate coronary heart disease (CHD) risk and stroke risk separately. It was developed on a cohort of 5102 patients with type 2 diabetes followed for a median of 10.7 years [22]. On the contrary, the Framingham calculator that tended to underestimate risks for people with diabetes included relatively few diabetic subjects; it was created using data from 5573 individuals followed for 12 years, but only 337 were known to have diabetes. Moreover, this and the other models for CVD risk evaluation in general population used dichotomous variables for glycaemia, such as the presence or absence of diabetes. The UKPDS diabetes-specific approach included HbA1c as a continuous variable for the first time; it also replaced age as a risk factor by two diabetes-specific variables: age at diagnosis of diabetes and time since the diagnosis of diabetes. Risk factors included in the first UKPDS model and the main limitations of this equation are shown in Table 1.

| Indicators | Main limitations of the score |
|---|---|
| Age at diagnosis of diabetes | It was implemented only in newly diagnosed diabetic patients |
| Sex | - In may be invalid in specific patient group: - People outside baseline ranges (25–65 years) - People diagnosed when <25 years - People of ethnic background other than Anglo-Celt, Afro-Caribbean or Indian-Asian - People with prior CVD |
| Ethnic group | |
| Smoke: current smoking of tobacco in any form, at diagnosis of diabetes | |
| HbA1c (%) mean values | |
| Systolic blood pressure (mmHg), mean values | |
| Total cholesterol/HDL cholesterol ratio, mean values | It does not consider renal function and diabetic therapy |

Table 1. Risk factors included in the first UKPDS and related limitations

In 2007, a new model was published [23] that estimates CVD risk directly (defined as first occurrence of fatal or non-fatal myocardial infarction, sudden cardiac death, other ischaemic heart disease, fatal or non-fatal stroke, or fatal peripheral vascular disease). The underlying risk equation was first validated in the Collaborative Atorvastatin Diabetes Study (CARDS) cohort, a primary prevention trial including 2838 patients with diabetes [24], and then in the European Prospective Investigation of Cancer (EPIC)-Norfolk Cohort, a prospective cohort study in which patients aged 40–79 years were recruited from general practitioners in the Norfolk region of the United Kingdom [25]. A sample of 10,137 patients, of which 272 diag-

nosed with diabetes, was extracted from this cohort to evaluate the performance of the UKPDS risk engine compared to the Framingham risk equations in both general and diabetic population. Both these equations performed reasonably well for identifying patients with high CVD risk. UKPDS performed better in diabetic population than the Framingham score, even if both equations overestimated the risk in this group of patients. Considering that in previous studies the Framingham score used in diabetic population underestimated CVD risk [26–29], these tools appear to be very useful to support clinicians in treatment management, but not entirely adequate to communicate risk information to patients.

2.2. Diabetes Audit and Research in Tayside, Scotland (DARTS)

In Tayside, Scotland, a population cohort with type 2 diabetes (4569 men and women of any age) without previous cardiovascular events was constructed from Diabetes Audit and Research in Tayside, Scotland (DARTS) and followed up for a maximum of 9.5 years. Ten risk factors were considered to develop a CVD risk equation, and the main outcome measure for its validation was the first major CHD event (fatal or non-fatal acute myocardial infarction or CHD death) [30].

Compared to UKPDS, the Scottish model has no age restrictions; it includes body mass index (BMI), height, triglycerides and antihypertensive treatment (dichotomous variables: yes/no); and it does not take into account the racial/ethnic background.

2.3. The Action in Diabetes and Vascular disease: preterAx and diamicroN-MR Controlled Evaluation (ADVANCE) risk engine

The Framingham and UKPDS CVD risk models have been validated on a large ethnically different sample of patients with diabetes from the “Action in Diabetes and Vascular disease: preterAx and diamicroN-MR Controlled Evaluation (ADVANCE)” cohort study [31]. The cohort was composed of 7168 persons with diabetes without previous CVD. This validation study revealed that the 4-year absolute risk of CVD events was overestimated by both these models. A new model for risk prediction was consequently assessed to improve performance in a multiethnic cohort of patients. Ten risk factors were included in the ADVANCE risk model: age at diagnosis, gender, duration of diabetes, pulse pressure, retinopathy, atrial fibrillation, HbA1c, log of urinary albumin/creatinine ratio, cholesterol and treated hypertension. The new elements introduced in this model were the attention to comorbidities (retinopathy and atrial fibrillation) and the publication of both a risk-scoring chart [32] and an online calculator [33] to facilitate the uptake of the model in clinical practice.

2.4. The Fremantle Australian risk score

In 2009, a study was published that was conducted on a cohort of CVD-free type 2 diabetes from the Fremantle Diabetes Study (FDS) in Australia, assessing the performance of UKPDS and Framingham scores in the prediction of 5-year CVD [34]. Both these algorithms did not perform satisfactorily in this Australian population. The investigators decided to develop and validate a multivariate risk function for 5-year cardiovascular risk prediction in these patients [35]. A total of 1240 patients with type 2 diabetes were followed from baseline (1993–1996) for

5 years or until they experienced a cardiovascular event or died. CVD during follow-up was defined as hospitalization for myocardial infarction or stroke and death from cardiac or cerebrovascular causes or sudden death. The model includes several variables routinely available in primary care: age, sex, racial/ethnic background (in particular, Aboriginal or Southern-European) prior CVD, diabetes treatment (diet, oral hypoglycaemic agents, insulin), serum high-density lipoprotein cholesterol (HDL), HbA1c, urinary albumin (creatinine ratio, mg/mmol) and estimated glomerular filtration rate. Compared to UKPDS, the Australian model includes people with diabetes with prior CVD, it takes into account the racial/ethnic background, it does not consider age at diagnosis and diabetic duration but only current age, and it excludes systolic blood pressure or antihypertensive treatment.

2.5. The New Zealand Diabetes Cohort Study

The New Zealand model for CVD risk assessment in people with diabetes was implemented from the Diabetes Cohort Study (DCS), a prospective open cohort created from a national primary care annual review programme. A total of 36,127 patients with type 2 diabetes without previous CVD was considered to derive a CVD equation. Risk factors taken into account were as follows: age at diagnosis, diabetes duration, sex, systolic blood pressure, smoking status, total cholesterol-to-HDL ratio, ethnicity, HbA1c and urine albumin-to-creatinine ratio. One of the most important characteristics of this model is that was assessed on a very large cohort of patients with diabetes available, thanks to the use of routinely collected data. The authors highlighted the importance of taking into account the ethnicity as a risk factor, which is considered a critical point to reduce health inequalities [36].

2.6. The Swedish National Diabetes Register

The Swedish National Diabetes Register was used to produce a prediction equation for five-year CVD risk in the Swedish diabetic population. The study was based on 11,646 female and male patients, aged 18–70 years. Risk factors considered in this longitudinal study were as follows: age at onset of diabetes, duration of diabetes, HbA1c, BMI, systolic blood pressure, sex, antihypertensive and lipid-lowering drugs and smoking habit [37]. An interesting indicator used in this score is treatment with lipid-lowering drugs, and the main limitation is that it did not include renal function. As for the New Zealand model, the use of routinely collected data, in this case a Disease Register, allowed to include a very large number of patients with diabetes.

3. European Guidelines on Cardiovascular Disease Prevention in Clinical Practice

The latest Guidelines of the European Society of Cardiology (ESC) on CVD Prevention in Clinical Practice [38] recommend total risk estimation using multiple risk factors, such as the SCORE [39], a validated system of risk estimation adopted since the 2003 edition of the above-mentioned guidelines, for asymptomatic adults without evidence of CVD [40]. Moreover,

other recommendations are that high-risk individuals can be detected based on established CVD, diabetes mellitus, moderate to severe renal disease, very high levels of individual risk factors or a high SCORE risk, and they are a high priority for intensive advice about all risk factors. However, always in the European context, the recent updates of the guidelines on lipid modification and cardiovascular risk assessment of the National Institute for Health and Care Excellence (NICE) in the United Kingdom [41] recommend the use of a new tool for assessing CVD risk in primary prevention until the age of 84 years and also for persons with type 2 diabetes: the QRISK2 [42].

3.1. QRISK and QRISK2 score

QRISK2 is the development of a previous score, QRISK [43]; the QRISK study, built based on collected from general practice in the United Kingdom, aimed to develop a new algorithm to estimate 10-year risk of CVD (cardiac or cerebrovascular) and to validate its performance against the Framingham and Scottish Score (ASSIGN) algorithms. The derivation cohort of QRISK consisted of persons free of diabetes and existing CVDs. QRISK2, instead, was based on an open cohort of 2.29 million patients (sum of derivation and validation cohort) from UK practices and belonging to different ethnic groups. The cohort was enrolled between 1993 and 2008 with a mean follow-up of 7.3 years for women and 6.9 for men; the considered subjects were aged 32–74 years, without previous recorded diagnosis of CVD and not taking statins at baseline. Many risk factors, such as diabetes, ethnicity and deprivation, are incorporated in the score, which is annually updated and refined (Table 2). A 2011 study for independent and external validation of an updated version of QRISK2 [44] extended the age for risk evaluation and demonstrates good discriminative and calibration properties when compared with the Framingham equation.

| QRISK2 Risk factors | |
|--|--------------------------------------|
| Self-assessed ethnicity | Chronic kidney disease |
| Age (25–84 years) | Atrial fibrillation |
| Sex | Systolic blood pressure |
| UK postcode | Blood pressure treatment |
| Smoking status | Rheumatoid arthritis |
| Diabetes status (type 1, type 2 or none) | Ratio of total serum cholesterol/HDL |
| Family history of coronary heart disease in first-degree relative under 60 years | Body mass index |

Table 2. Risk factors: QRISK2 variables included in the web calculator, version 2014 (www.qrisk.org)

Differently from previous editions, the above-mentioned NICE guidelines recommend the use of QRISK2 score also for persons with type 2 diabetes, but not for persons with type 1 diabetes.

The authors validated the QRISK2-2014 version, which collected also the type of diabetes, on a cohort of patients with diabetes (both type 1 and type 2) for the next release of the score in patients with diabetes [45]. In this study, there was no significant improvement for a model that included HbA1c and duration of diabetes, and QRISK-2014 demonstrates to be appropriate for both patients with type 1 and type 2 diabetes. The latest version of QRISK2 (2015) is available at website www.qrisk.org.

3.2. SCORE charts

The SCORE Project assembled a pool of datasets from 12 European cohort studies (205,178 persons), and absolute risk charts (available from website www.escardio.org) were developed separately for high-risk and low-risk regions of Europe. In addition, relative risk charts were developed, helpful for young person with a low absolute but high relative risk, to convey the message of the need for lifestyle change.

An electronic, interactive and improved version of SCORE (available from www.heart-score.org) was also implemented, which is used to accommodate the results of new SCORE analyses, such as those relating to HDL cholesterol, that proved to contribute substantially to risk estimation if entered as an independent variable.

These tools are applicable in primary prevention, and they estimate the 10-year risk of fatal cardiovascular event; the variables used in the model are listed in Table 3, comparing SCORE charts and CUORE project. CVD mortality charts have also been recalibrated for some European countries. According to the European guidelines, the intensity of advice should increase with increasing risk. In general, persons with a CVD risk of $\geq 5\%$ qualify for intensive advice and may benefit from drug treatment. At risk levels $>10\%$, drug treatment is more frequently required. In subjects older than 60 years, however, these thresholds should be interpreted less strictly, because their age-specific risk is normally around these levels even in the absence of diabetes.

| SCORE | CUORE |
|--|--|
| SCORE model estimates the 10-year risk of fatal cardiovascular event in primary prevention | CUORE model estimates the 10-year risk of fatal and non-fatal cardiovascular event in primary prevention |
| Age (more detailed in 50–65 age range. Charts provided for 40–65 years) | Age (40–69 years for charts, 35–69 years for individual score) |
| Sex | Sex |
| Systolic blood pressure | Systolic blood pressure |
| – | Antihypertensive treatment (only for individual score) |
| Total cholesterol | Total cholesterol |
| HDL cholesterol | HDL cholesterol (only for individual score) |
| Smoking habits | Smoking habits |
| – | Diabetes |

Table 3. Risk factors included in SCORE and CUORE projects

4. Cardiovascular risk assessment models in Italy: from individual's global risk evaluation to diabetes-specific models

4.1. The CUORE Project

The Italian version of CVD Prevention Guidelines [18] stated that for Italy it is preferable to use the tools of CUORE Project of the National Institute of Health to estimate CVD risk in the general population. Several studies on Italian cohorts have compared SCORE and CUORE tools: a study published in 2010 [46] highlighted that the first one reflects quite well the Italian cardiovascular mortality, and, correspondingly, Italian cohorts of CUORE Project are quite representative of European countries with a low risk of cardiovascular mortality, at least as regards male subjects. It was not possible to make the same evaluation for women, because the number of fatal cardiovascular events was not enough to allow a reliable estimate of the risk functions. Other studies found moderate level of agreement between the two tools, in particular in discriminating high-risk subjects. The reasons may be attributed in one case to the use of a smaller and different sample of cases than the previous study [47] and in the other case to the “threshold issue” in the score [48]; in this last study, in fact, using risk scores as continuous variables, the concordance between SCORE and CUORE tools resulted higher.

Since 1998, the year of its birth, the CUORE Project aimed at the following objectives [49]:

- to implement a population-based register of cardiovascular events;
- to realize a survey to assess risk factors distribution, prevalence of high-risk conditions and CVD;
- to assess cardiovascular risk of the Italian population and make tools for risk assessment easily applicable;
- to implement a training plan on cardiovascular risk assessment for General Practitioners;
- to explain the declining trend of mortality for CHDs; and
- to update the Italian tools for risk prediction.

The global cardiovascular risk score of CUORE Project was developed using data from different cohorts enrolled in the north, centre and south of Italy between the 1980s and the 1990s, whose risk factors had been collected using standardized procedures. It was validated on 20,647 persons, with a median follow-up duration of 9.5 years for men and 8.0 years for women [50]. The individual score (available from website www.cuore.iss.it) can be calculated in subjects aged 35–69 years and predicts 10-year risk of a first fatal and non-fatal cardiovascular event based on risk factors listed in Table 3. In addition to the individual score, are also available risk charts, which differ for the number of risk factors used and for the age group in which they are applied (Table 3) and moreover for accuracy of information (charts are less accurate, offering classes of absolute global risk calculated for categories of risk factors). According to this tool, individuals are considered at high risk if their 10-year CVD risk is 20% or more; instead, they are at low risk if it is <5%; risk categories were stratified in six levels.

As shown in Table 3, differently from CUORE Project, SCORE risk charts do not include a dichotomous diabetes variable into the risk function, because there was a lack of uniformity in the ascertainment of diabetes. Furthermore, the instruction for the use of these charts argues that they underestimate the risk in patients with diabetes and should be used only in patients with type 1 diabetes without any target organ damage. It must be emphasized that, as mentioned above, ESC Guidelines on CVD Prevention, also in its versions for diabetes, pre-diabetes and CVDs [51], ranks subjects with diabetes mellitus (both type 1 and type 2), respectively, at high or very high risk, depending on whether they have one or more cardiovascular risk factors and/or target organ damage.

As concluded by the World Health Organization Multinational Study Group on Vascular Disease in Diabetes, developments in the assessment of CVD risk in diabetes must include diabetes-related variables as well as the conventional risk factors [52].

The Italian “National Prevention Plan” 2005–2007 and 2010–2012 included 10-year cardiovascular risk assessment using the CUORE Project’s tools [53], and this allowed the realization of a national training programme for general practitioners. Preliminary results underline the importance of its evaluation in clinical practice and demonstrate the feasibility to implement a risk factor surveillance system involving trained general practitioners [49, 54].

Moreover, guidelines and studies on these issues emphasize the need for updating charts and scores for risk assessment, since population’s risk profile and mortality for CVD change over time. It is therefore necessary to enrol new cohorts or to update existing ones. In this perspective, CUORE Project has expanded database of cardiovascular risk factors by adding the cohort of the Osservatorio Epidemiologico Cardiovascolare (OEC), enlisted in the late 1990s and was followed until December 2004. Preliminary analyses have confirmed for both men and women the predictive role of the main risk factors is already included in the algorithm, but additional studies should be conducted to assess the inclusion of new risk factors, primarily glycaemia [55].

4.1.1. Use of cardiovascular risk score for lipid-lowering reimbursement

In the recent past, cardiovascular risk assessment obtained through CUORE Project’s tools was scarcely applied, despite recommendations of their use from the Ministry of Health to assess cardiovascular risk for statins reimbursement in primary prevention, laid down in the past version of the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA) Note 13. Also data from PASSI Study 2009–2012 [56] found that risk chart is still rarely used: only 7% of interviewed aged 35–69 years, without CVD, said that their CVD risk was measured, with significant differences at regional level. It is, however, likely this is an underestimation, being based on patient’s interviews and not on medical records data. Recent updates on Note 13 provide, however, for the use of SCORE charts for lipid-lowering reimbursement by National Health System.

Italian cohorts of the CUORE project are quite representative of the European countries at low risk for cardiovascular mortality, and the > 5% risk of fatal CV events in SCORE charts corresponds to a >20% risk of fatal CV events in CUORE Project. Furthermore, the Italian

contribution to the cohort used to define SCORE charts was 6% of the subjects evaluated for men and 8% for women, and the duration of follow-up was higher in CUORE Project. On this basis, about the definition of risk levels, the Multidisciplinary Working Group of the Emilia-Romagna Region Drug Commission reaffirmed the validity of CUORE charts and the possibility to continue using them in clinical practice, with the established conversion between CUORE and SCORE risks [57]. Moreover, the estimation of fatal and non-fatal CV events that characterizes CUORE algorithm also allows a better transfer of clinical trial results.

4.2. The Riskard score

Another tool for cardiovascular risk assessment was developed in Italy. The Research Group for Assessment of Cardiovascular Risk in Italy developed a risk chart [58, 59] and then a software named Riskard 2002 [60]. The study enrolled a cohort of over 9000 individuals from three Italian studies, aged 35–74 years and followed up from 5 to 15 years. In subsequent years, the chart and the software were further updated (Riskard 2005), with the purpose to offer tools based on larger and more diversified populations, larger numbers of individuals exposed to risk and events, longer follow-up periods and some other innovative concepts. The chart, by its nature, can incorporate only a limited number of risk factors, while many more can be included in the software [61]. Data were collected from nine population studies in eight Italian regions, for a total of 17,153 subjects. The new chart that allows an estimate of the 10-year risk of undergoing a first cardiovascular event was produced for men and women aged 45–74 years, free from CVDs. Estimates were produced for absolute risk and for relative risk for CVD, the latter against levels expected in the general population.

The software, instead, was produced to predict risk of major coronary, cerebrovascular and cardiovascular events for follow-up at 5, 10 or 15 years, in men and women aged 35–74 years at entry and free from CVDs. Risk factors taken into consideration in the Riskard 2005 software were sex, age, BMI, mean physiological blood pressure, HDL cholesterol, non-HDL cholesterol, cigarette smoking, diabetes and heart rate. The output yielded several indicators, such as absolute risk, relative risk (as defined above), ideal risk (for a very favourable risk profile) and biological age of risk.

4.3. Cardiovascular risk assessment in cohorts of Italian patients with type 2 diabetes

In a recent systematic review that compared performance of CVD risk models developed exclusively from people with diabetes and those developed in the general population [62], a study conducted in Italy in three diabetes clinics of Modena was also included [63]. The study involved 1532 patients and aimed to evaluate the prognostic accuracy of four algorithms used to estimate cardiovascular risk: the UKPDS (constructed on a population of persons with type 2 diabetes), the Framingham and two Italian algorithms, the Riskard and the CUORE.

The Framingham model shows a risk overestimation in the Italian population; also, the function proposed by the UKPDS study, when applied for Italian diabetic population, tends to overestimate cardiovascular risk, without differences between sexes.

Taking into account the Italian situation, the most widely adopted function, the CUORE Project algorithm, underestimates cardiovascular risk, particularly in females. The Riskard algorithm appears more coherent on the evaluation of cardiovascular risk in the cohort examined; however, dividing population according to sex, an overestimation of events in males and large underestimation in females emerge. So, these algorithms agree in overestimating risk in males and underestimating risk in females.

The conclusions are that estimation of cardiovascular risk is dependent on the algorithm used and on the baseline risk of the reference cohort, and functions designed for a specific population, including risk variables peculiar for diabetes, should be adopted to increase the performance of such functions.

4.4. An Italian score for quality of diabetes care evaluation and its association with cardiovascular event risk

In recent years, the pressure on Health Care Systems to deliver high-quality care while controlling costs progressively increased. In this context, the Qualità ed Esito in Diabetologia (QuED) study was developed [64], whose main aim was to develop a score for evaluating quality of diabetes care. In this study, the close relation between a score of quality of diabetes care and long-term outcomes was documented. The QuED study was conducted in Italy by the Consorzio Mario Negri Sud—Department of Clinical Pharmacology and Epidemiology, in collaboration with the Center for Health Policy Research—University of California, Irvine. Overall, 101 diabetes outpatient clinics and 103 general practitioners from all regions of Italy participated in the study, enrolling, respectively, 2448 and 785 patients with type 2 diabetes irrespective of age, diabetes duration or treatment. These patients, representative of all settings of diabetes care, were recruited from March 1998 and December 1999 and followed up for a median of 5 years. The score was calculated using process and intermediate outcome indicators readily available (HbA1c, blood pressure, low-density lipoprotein cholesterol, microalbuminuria) and consistent with those adopted for other initiatives such as the Diabetes Quality Improvement Project (DQIP) [65], started in 1997 in the United States to implement a comprehensive set of national measures for quality improvement. The only difference was the use of a lower threshold for HbA1c (8%) and the addition of a process indicator, referring to the use of ACE inhibitors in the presence of microalbuminuria, based on evidence that linked it to cardiovascular risk [66]. In the tool construction, a discrete score was given to each variable as follows: 0 points if the patient was not treated for the specific condition despite elevated values, or the patient showed unsatisfactory values despite the treatment; 5 points if the measurement of a parameter was not performed in the latest 12 months; 10 points if the desired goals were attained. The indicators and cut-off used are shown in Table 4. This score ranged from 0 to 40, with a higher score reflecting better quality of care. This score was defined in the following studies also as Q-Score.

The study shows that the risk to develop a cardiovascular event was 89% greater in patients with a score of ≤ 10 and 43% higher in those with a score between 10 and 20, when compared to patients with a score of >20 . It is also important to emphasize that a linear relation between

| Indicators | Cut-off |
|------------------|--|
| HbA1c | <8% |
| Blood pressure | <140–90 |
| LDL cholesterol | <3.37 mmol/L (130 mg/dl) |
| Microalbuminuria | <30 mg/die or ≥30 mg/die with ACEinhibitors or ARB treatment |

Note: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

Table 4. Quality-of-care scoring system (QUED and QUASAR studies)

QuED score and incidence of cardiovascular events was documented both in patients with and without previous cardiovascular events, and this was true for different outcomes, such as CHD, cerebrovascular accidents, peripheral vascular disease and cardiovascular mortality. The authors stated that QuED score is not intended to replace other risk models utilized to predict the individual risk of cardiovascular events, but rather an indicator of the average quality of the diabetes care provided by a specific setting in health care system.

On this basis, subsequently, the Italian Associazione Medici Diabetologi (AMD), a scientific society, realized the QUASAR study (Quality Assessment Score and Cardiovascular Outcomes in Italian Diabetes Patients) [67]. The score developed and validated in QuED study was applied to the QUASAR population (5181 patients enrolled in 67 Italian diabetes clinics and followed up for a median of 28 months) and was confirmed the strong correlation between this quality of care score and cardiovascular events, both in patient with and without previous cardiovascular events. In QUASAR study, the risk to develop a new cardiovascular event was 84% higher in patients with a score of <15 and 17% higher in those with a score between 15 and 25, when compared with those with a score of >25. This simple score began to be widely used to monitor quality of care and compare the performance of different diabetes clinics [68]. A further article published by the same working group analysed the trends over 8 years in quality of diabetes care, evaluating process and outcome indicators, indicators of treatment intensity or appropriateness and the score developed in QuED and QUASAR [69]. The studies showed a relevant improvement in quality of care for diabetes in Italy from 2004 to 2011, while the economic resources available did not increase. The authors hypothesized that systematic control of quality of care through regular collection of data improved adherence to standards of care and that longitudinal improvements in Q score can be translated in less cardiovascular events. Along years, an increasing numbers of diabetes clinics participated in the AMD initiatives.

4.4.1. *Q-home: the application of Q score to a cohort of people with type 2 diabetes in general practice*

In the contest of type 2 diabetes integrated care of Local Health Authority (ASL) of Modena in Italy, Q score has been adopted and transposed by the more special setting to that of general practice and it formed the cornerstone for creating an individual and collective report and for developing audit (Q-home). The involvement of general practitioners by returning data

analysis on patients with diabetes through dedicated annual reports and digitization of data collection on individual patients has led, over 3 years, to the involvement of a growing cohort of patients (from about 12.000 to 18.000) and of almost all general practitioner of the Modena AUSL. The rate of missing data was analysed and showed a marked decrease, as shown in Table 5.

| Indicators | Missing rate (%) | |
|------------------|------------------|------|
| | 2011 | 2013 |
| HbA1c | 9 | 5 |
| Blood pressure | 11 | 6 |
| LDL cholesterol | 12 | 9 |
| Microalbuminuria | 16 | 12 |

Table 5. Missing rate of collected data in Q-home project through 3 years.

In the period of 2011–2013, in parallel, the number of all parameters in range grew. Consequently, the percentual of the population with Q score between 30 and 40 points increased. In 2013, all Health Districts were homogenized with each other and exceeded the threshold of 30 points of mean Q score. The next step of the study group will be to associate individual Q score with annual cardiovascular events, hospitalizations, revascularization, access to the emergency department and deaths from all causes. Five years of observation will be considered (from 2011 to 2015), to validate the Q score in general practice, obtaining percentages of risk specific for this setting.

5. Patient–doctor communication on cardiovascular risk

If, on the one hand, giving cardiovascular risk communication to the patient is not simple, on the other hand, it is not clear what and how much the patient understands about the message received.

To date, few studies have been conducted on this topic, and most of these count few patients surveyed. A low awareness of the disease is highlighted. In particular, patients remain anchored to a conception of diabetes as a glycaemic problem, rather than as a pathology at high cardiovascular risk [70–73]. Among the studies that investigated the perception of risk, in Italy, the PRICAD Study (Percezione del Rischio Cardiovascolare nella popolazione Diabetica), promoted by the Associazione Italiana Medici di Famiglia (AIMEF), is designed for the purpose of trying to measure how the patient perceives the diabetes in the context of cardiovascular risk [73]. More than 11,000 persons were actively encouraged to meet the questionnaire, but only 4600 (41%) answered. The majority of them (60%) said that diabetes is only an excess of glucose in the blood and that it is possible to get old in good health despite

diabetes. More than half of the subjects fail to recognize the importance of controlling cardiovascular risk factors and believe to have the same blood pressure, cholesterol and BMI target of a peer without diabetes. Only 9% of respondents, less than a fifth the people asked, expressed a serious concern for the greater complication of diabetes.

Analysing the frequencies of concerns considered higher by persons with diabetes, losing the driving licence emerges as an element of utmost concern, while only 9.3% consider the fear for cardiovascular complications a factor of maximum concern. Only 30% of people with diabetes are aware of the close relation between diabetes and cardiovascular risk. Almost two-thirds of the persons with diabetes believe that their blood pressure and cholesterol goals are similar to those of other hypertensive patients. The same lack of awareness is also common in people without diabetes but having other cardiovascular risk factors [74]. Where available, visual tools of communication were of help for the patient in the understanding of the risk [75–77]. Unfortunately, even among patients who receive a clear illustration of their cardiovascular risk, it is not observed a clear memory of what perceived, neither there is a significant nor lasting permanence in their lifestyle change [78].

6. Conclusions

In the present chapter, the main CVD risk scores for patients with diabetes are explored, starting from the first one developed in the 1960s, the Framingham study, to the latest diabetes-specific models. In recent years, diabetic disease is included in most models, even if only the absence or presence of the disease is considered in most of them. The level of HbA1c or blood glucose seems to be an important indicator for the evaluation of CVD risk in both diabetic and general population, and in particular diabetes-specific scores should take into account these variables. It could be useful also to detect impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) conditions in persons without diabetes and to assess the metabolic balance in persons with diabetes. In general, the most recent studies agree on the importance of using diabetic-specific cohorts to adequately assess CVD risk models in this population. Furthermore, the diabetes care settings and the ethnic group need to be taken into account in the development and evaluation of CVD risk in patients with diabetes. Literature data highlight that cardiovascular risk prediction models perform non-optimally in people with diabetes of different ethnic groups. Thus, it may be appropriate for each country to validate the existing models on their populations and eventually to adapt them to the different setting, to improve targeted risk management.

Risk modelling and stratification are important tools for clinicians, because these models represent a useful guide for therapeutic decisions and for patients monitoring. Furthermore, they can be used to communicate with patients and to improve their compliance. In this regard, new strategies are needed to optimize patient's understanding and the internalization of its own level of risk.

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