Cardiovascular Risk Reduction in Diabetes in Sub-Saharan Africa: What should the Priorities be in the Absence of Global Risk Evaluation Tools?

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Abstract

Background: The growing burden of type 2 diabetes in Sub-Saharan Africa (SSA) and related cardiovascular complications call for vigorous actions into prevention. Comprehensive cardiovascular risk evaluation is important for the success of such actions.

Methods: We have reviewed 3 currently existing sets of recommendations for cardiovascular prevention in diabetes in SSA. Distribution of major risk factors and patterns of reported cardiovascular outcomes are used to suggest orientations for cardiovascular prevention in diabetes in this region. Papers and reports published over the period 1990 to 2007 were used.

Results: Existing guidelines share some similarities, but also have areas of inconsistencies. They are generally adaptations of existing guidelines, focused more on individual risk factors, and are not usually backed-up by local evidence. They all have a projection on blood pressure lowering. This focus is supported by the high prevalence of hypertension among people with diabetes in SSA. Blood pressure and tobacco smoking are the modifiable risk factors accessible to evaluation and interventions on a wide scale in SSA. Appropriate blood pressure control will have a major impact on stroke (the commonest cardiovascular disease) through a reduction of the cerebrovascular risk, and to a lesser extent on coronary heart disease and total deaths in diabetes in this region.

Conclusions: In the absence of global risk evaluation tools, the use of blood pressure lowering as a primary focus of cardiovascular prevention strategies is relevant for SSA. However, there is a need to set-up diabetes and stroke registers to monitor outcomes and generate tools for accurate risk prediction and management in diabetes in this region.

Keywords: diabetes mellitus, cardiovascular disease, risk factors, prevention, Sub-Saharan Africa

Introduction

Diabetes mellitus is becoming increasingly important on a global scale. According to the third edition of the International Diabetes Federation (IDF) Atlas, there are currently 10.4 million individuals with diabetes in Sub-Saharan Africa (SSA), representing 4.2% of the global population with diabetes. By 2025, these figures will increase by 80% to reach 18.7 millions in this region. By then, 75.8% of individuals with diabetes in Africa will be found in urban area (International Diabetes Federation 2006). This highlights the rapid epidemiologic transition operating in this part of the world. Diabetes is associated with increased risk of cardiovascular disease (CVD). Indeed, compared to their non-diabetic mates, people with diabetes have a 2- to 4-fold greater risk of coronary heart disease (CHD), ischemic and hemorrhagic strokes, and peripheral vascular diseases (Asia Pacific Cohort Studies Collaboration 2003). In major ways, determinants of cardiovascular risk in individuals with diabetes are similar to those among individuals without diabetes (Kannel and McGee, 1979). Furthermore, successful actions on the determinants amenable to modification are associated with at least a similar beneficial impact on cardiovascular outcomes in diabetes (Blood Pressure Lowering Treatment Triaslists' Collaboration 2005; Costa et al. 2006).

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Traditional approaches to cardiovascular risk evaluation and reduction in general and in people with diabetes have most often been focused on individual risk factors. However, no single risk factor has been found to accurately discriminate individuals who will go on to develop a cardiovascular event. Neither has any been shown to erase the risk of CVD when appropriately controlled. Risk models have therefore been derived from cohort studies and clinical trials that integrate the effect of major risk factors in a single equation to predict the individual risk of future cardiac or vascular events. These models therefore reliably select those likely to benefit more from preventive measures (Wilson et al. 1998). These tools in general perform well in the population from which they are derived, but tend to perform poorly when applied to other populations without recalibration (Chambless et al. 1990). For example, risk tools derived in the general population tend to underestimate the risk of people with diabetes (Brindle et al. 2006). Risk assessment tools specific to diabetic populations have also been developed and at times (Stevens et al. 2001), it has been proposed that individuals with diabetes should just be considered and treated as high risk without further risk stratification.

The uptake of currently existing recommendations for cardiovascular risk reduction is very poor, particularly in developing countries of Sub-Saharan Africa. Yet, the growing burden of cardiovascular complications in this region calls for more action into prevention. This paper is a critical review and our opinion of the existing recommendations for cardiovascular risk reduction in people with diabetes in Africa. The distribution of classical risk factors in diabetes and the pattern of cardiovascular disease are also reviewed for evidence to prioritize cardiovascular prevention approaches in this region.

Methods

Three guidelines were reviewed: the global guideline for type 2 diabetes of the International Diabetes Federation (IDF) (IDF Clinical Guidelines Task Force 2005), the type 2 diabetes clinical practice guidelines for sub-Saharan Africa (International Diabetes Federation Africa Region 2006) and the guideline for diagnosis and management of type 2 diabetes at primary health care level in South Africa (SEMDA 2002). South Africa was chosen on the preamble that up-to-date management guidelines were not available for most African countries as acknowledged by the IDF (International Diabetes Federation Africa Region 2006); and where available, they will not always be accessible online. Guidelines' review was complemented by a Medline search in July 2007 using the key words diabetes and Africa, and restricted to papers published in the last 17 years from sub-Saharan Africa. Abstracts and reference lists where available were reviewed for information relating to cardiovascular risk factors and complications. Literature from elsewhere was used where relevant.

Global Cardiovascular Risk Evaluation in Diabetes

Global cardiovascular risk evaluation refers to the process of integrating information from several risk factors to define or predict the chances of experiencing a cardiovascular outcome. Many models of risk prediction tools have been developed. They vary in their baseline risk prediction function, the number of risk factors included in the model and the ways those risk factors are handled in each model. The International Diabetes Federation global guideline for type 2 diabetes recommends the diabetes-specific risk engine for comprehensive risk evaluation in people with diabetes (IDF Clinical Guidelines Task Force 2005). The current diabetes specific risk models derived from the UKPDS tool (Stevens et al. 2001; Kothari et al. 2002; Donnan et al. 2006; Yang et al. 2007). Variables used in the UKPDS tool include age, sex, ethnicity, smoking, duration of the known diabetes, systolic blood pressure, lipid ratio (total cholesterol/HDL cholesterol ratio) and HbA_{1c}. The risk engine uses these variables to estimate the future risk of fatal CHD, non Fatal CHD, fatal and non-fatal strokes. The availability of the model in software version free of charge makes it easily accessible on a wide scale (UKPDS Group). However, apart from limitations inherent to risk prediction models in general, some variables required for computing the risk using the UKPDS risk engine will not always be available in routine practice in Sub-Saharan Africa. While patients in major urban settings can have access to HbA1c and lipid profile assessment, these parameters are unlikely to be available in the rural settings and sub-urban cities. The UKDPS and other risk engines that use information from many variables will therefore be of limited use in SSA. The few studies that have attempted to use global risk evaluation tools in Africa have rather used the Framingham-based tools (Steyn et al. 2004; Adedoyin et al. 2006; Badr et al. 2007; Kengne et al. 2007). These studies were all

cross-sectional and have therefore not provided information about the accuracy of these tools when applied in Africa and particularly in people with diabetes (Kengne et al. 2007). Although global cardiovascular risk is the most logical and sound approach cardiovascular risk evaluation and reduction, it is of note that this approach has not yet been validated by outcome trials.

Cardiovascular Risk Evaluation and Prevention: Current Approaches for SSA

Recommendations exist at the international, regional and sometimes at the country levels to guide aspects or overall cardiovascular risk approaches in people with diabetes in Africa. However, these recommendations are not supported by local evidence and their influence on local practice is still obscure. In the absence of online access to resources from most countries, we have used South Africa as model country. Guidelines exist in this country for the evaluation and management of individual risk factors including diabetes (SEMDA 2002). The current diabetes guidelines refer to major modifiable cardiovascular risk factors and recommendations target individual risk factors with no reference to global risk evaluation. The most authoritative support for diabetes management at the regional level is the type 2 diabetes Clinical Practice Guidelines for Sub-Saharan Africa, a publication of the Regional office of the International Diabetes Federation (International Diabetes Federation Africa Region 2006). This guidelines approaches cardiovascular risk evaluation and prevention in a way similar to that of the South African guidelines, with no reference to global risk evaluation. While the SSA guidelines recognizes the need for further risk stratification when evaluating patients with hypertension, it does not make any suggestion as to which risk stratification tool should be used. At the global level, the International Diabetes Federation Global Guidelines for type 2 diabetes elaborates more on cardiovascular risk protection, recommends the use of the UKPDS risk engine if possible for risk assessment (IDF Clinical Guidelines Task Force 2005). Variations in aspects of these three guidelines (Table 1) reflect their reliance on external sources, but also the complexity of cardiovascular risk reduction and diabetes management in general. However, they all acknowledge in some ways the importance of blood pressure as major risk factor in people with diabetes, and consequently a major focus for intervention. Nevertheless, the major focus on blood pressure needs to be supported by the profile of individuals with diabetes for this risk factor in SSA.

Risk Factors for Cardiovascular Diseases in Diabetes in SSA

Nature and strength of the association

Determinants of cardiovascular disease are well known and consistent across populations and regions. These include the classical risk factors and the emerging or novel risk factors. Apart from few exceptions and unresolved issues, these risk factors predict on a relative scale, the risk of major cardiovascular outcomes in a similar way in individual with and without diabetes (Asia Pacific Cohort Studies Collaboration 2007a; Asia Pacific Cohort Studies Collaboration 2007b). The few exceptions relate to sex and age. Among individuals without diabetes, men are more at risk of experiencing cardiovascular disease at most age strata. This has been termed the "female advantage". The onset of diabetes at least attenuates this advantage in major ways, to such an extent that compared with their non-diabetic mates, women with diabetes are more at risk of cardiovascular disease than men (Huxley et al. 2006). The onset of diabetes is also associated with early accelerated cardiovascular disease. On average compared to the general population, people with diabetes develop CVD 10 to 15 years earlier (Booth et al. 2006). Uncertainty relates to novel risk factors and particularly diabetes-related risk factors including glucose exposure and duration of the known diabetes (Coutinho et al. 1999; Selvin et al. 2004). Although there exists a significant association between these predictors and the risk of vascular diseases, causality has not yet been established. In the rest of this development, we will focus more on the established risk factors.

Distribution among individuals with diabetes in Africa

The classical approach of dichotomizing individuals based on arbitrary cut-offs for most continuous risk factors makes it difficult to have accurate comparative data. In addition, reports on lipid studies among those with diabetes in Africa are scanty. In

Table 1. Available guidelines for cardiovascular risk reduction in diabetes in Sub-Saharan Africa.

Variables	SEMDA[1](SEMDA 2002)	IDF[2](IDF Clinical Guidelines Task Force 2005)	IDF Afro[3](International Diabetes Federation Africa Region 2006)
Year published	2002	2005	2006
Risk evaluation	Single factor	Single factor and Global risk (UKPDS risk engine)	Single factor
Blood pressure targets	130/80 mmHg	130/80 mmHg	130/80 mmHg
Fist line BP lowering medications	ACE inhibitors	Any except alpha-adrenergic blockers	ACEI or diuretics
Lipid modifying therapy	Based on lipid levels	>40 years, CVD, high risk	Based on lipid levels
Lipid targets (mmol/l)	LDL ≤ 3; TC < 5 Triglycerides < 1.5; HDL > 1.2	LDL < 2.5; Triglycerides < 2.3; HDL > 1.0	LDL ≤ 2.6; TC < 5.2 Triglycerides < 1.7; HDL > 1.1
Aspirin prescription	Secondary prevention	High risk individual or CVD	Secondary prevention, >40y + other risk factor
Aspirin dosage	150–300 mg/day	75–100 mg/day	75–162 mg/day
Smoking cessation	Complete cessation	Complete cessation	Complete cessation
Optimal glucose	HbA1c < 7%	HbA1c < 6.5%	HbA1c < 7%
	FBS:4–6 mmol/l	FBS < 6.0 mmol/l	FBS:4–6 mmol/l
	2h-glucose 4–8	2h-glucose < 8 mmol/l	2h-glucose 4–8
Optimal BMI	<25 kg/m^2	Not defined	<25 kg/m^2
Optimal waist circumference	<94 cm (men) <82 cm (women)	Not defined	<102 cm (men) <88 cm (women)

Notes: [1]Guidelines for the Management of Type 2 Diabetes Mellitus at Primary Healthcare Level in South Africa.
[2]Global guidelines for type 2 diabetes.
[3]Type 2 diabetes clinical practice guidelines for Sub-Saharan Africa.

general, as summarized in Table 2, 10 to 67% of individuals with diabetes in Africa have hypertension, while smoking prevalence ranges from 6 to 28%. Dyslipidemia has been reported in 2 to 20% of them while obesity is as prevalent as hypertension. One of the major goals of global cardiovascular risk evaluation is to select individuals who are more likely to benefit from cardiovascular prevention and particularly lipid modification therapies. Indeed, benefits of lipid lowering extend beyond the traditional thresholds for defining dyslipidemia. The limited number of reports on lipid variables among individuals with diabetes in Africa indicates that lipid profile is either not accessible in routine practice in most settings, or that based on existing cut-offs, most patients would fall in the so-called "normal range" of lipid parameters. Indeed, there has been this false believe that lipid disorders were not common in this region (Nyarko et al. 1997; Okesina et al. 1999).

Association with individual CVD and expectations from intervention

Major cardiovascular risk factors do not predict the risk of major outcomes in a similar way. While they are nearly all associated with the risk of each outcome, the strength and nature (for some) of this association might differ. Indeed, non optimal lipid levels are more associated with the risk of CHD while blood pressure predicts more the risk of stroke. In addition, while total or LDL cholesterol is always positively associated with the risk of CHD, the association is different for stroke subtypes, being positive for ischemic stroke and a negative for hemorrhagic stroke. Smoking conveys a similar risk of CHD and stroke and a somewhat higher risk of

Table 2. Prevalence of hypertension, obesity, smoking and dyslipidemia in people with diabetes in selected African countries*

Study country	Year	Sample	Hypertension	Obesity	Smoking	Dyslipidemia
Nigeria (Akanji and Adetuyidi 1990)	1990	50	42.0%	-	-	-
Tanzania (Swai et al. 1990)	1990	1250	26.7%	14.6%	-	-
Sudan (Elmahdi et al. 1991)	1991	413	-	46.2%	-	-
Ethiopia (Lester 1993)	1993	1386	24%	-	-	-
Zanzibar (Makame and Tull 1993)	1993	323	11.29%	16.2%	-	-
Sudan (Bani and Anokute 1994)	1994	523	38%	-	-	-
South Africa (Gill et al. 1995)	1995	64	22%	-	28%	19%
Burkina Faso (Drabo et al. 1996a)	1996	260	29%	59%	15%	2.3%
Burkina Faso (Drabo et al. 1996b)	1996	400	20%	28%	20%	-
Cameroon (Ducorps et al. 1996)	1996	550	42.2%	-	-	-
Uganda (Nambuya et al. 1996)	1996	252	27.3%	53%	-	-
Ethiopia (Seyoum et al. 1999)	1999	302	21.2%	22.8%	6.6%	20.2%
South Africa (Rotchford and Rotchford 2002)	2002	253	65.4%	36.5%	-	-
Ethiopia (Seyoum et al. 2003)	2003	160	-	-	-	18.5%
Cameroon (Kengne et al. 2007)	2007	210	67.7%	-	-	-

*Figures are as provided by the investigators with no reference to the diagnostic criteria. Since these studies were conducted over a long period, diagnostic criteria for hypertension, obesity and dyslipidemia are likely to vary. Most studies were hospital-based studies in major cities.

peripheral vascular disease (PVD). Among those presenting with CHD in SSA, hypertension and dyslipidemia are reported at almost equal frequencies (Kengne et al. 2005). However, among those presenting with stroke, hypertension is by far the dominant risk factor (Kengne and Anderson, 2006). No study has assessed the joint effects of diabetes and other major risk factors on the risk of cardiovascular events in SSA. Prevalence studies indicate that diabetes may be found in 26% and 30% of patients with CHD and stroke respectively (Kengne et al. 2005). Assuming that findings in the general population compare to those in people with diabetes, actions on blood pressure will have a tremendous effect not only on the risk of stroke in people with diabetes in SSA, but also a significant effect on the risk of CHD. Moreover, it has recently been shown that lowering blood pressure regardless of blood pressure status could reduce overall deaths in people with diabetes (Patel et al. 2007).

Rationale for Targeting Preferentially Stroke as CVD in SSA

The monitoring of cardiovascular outcomes and the trajectory of risk factors over time is a good approach to generate the information required for making projections about the future trends and guide preventive measures. In the absence of reliable data on the trends of cardiovascular disease in SSA, lessons from other regions of the world are alternatives for making such projections. The experience that is being gained in other populations, and especially in Asia, informs us that stroke is by far the dominant manifestation of CVD, resulting to a large extent from population-wide elevations in blood pressure levels during the early and middle stages of the epidemiological transition (Yusuf et al. 2001a). Although SSA is going though a rapid epidemiological transition, in general this part of the world lags behind Asia by one of two stages (Yusuf et al. 2001a). Already, stroke appears to be the dominant CVD in Africa now and will maintain the lead over CHD in at least the next ten to fifteen years (Yusuf et al. 2001a; Kengne and Anderson, 2006). It was estimated that in 1990 stroke killed twice more men and women than CHD in sub-Saharan Africa. This ratio will most likely remain the same by the year 2020. By then, the proportion of deaths occurring through each of these conditions would have increased by more than a hundred percent (Yusuf et al. 2001a; Yusuf et al. 2001b).

Conclusions

Global risk evaluation is relevant for cardiovascular risk prevention strategies in the general population and in people with diabetes. However, the prevailing circumstances in most African countries largely limit the availability of information required to compute global risk using existing tools such as the UKPDS risk engine. In addition, there are still some uncertainties regarding the performances of such tools if applied to the African population. The approaches suggested by existing guidelines that focus on blood pressure reduction while attempting at the same time to target other cardiovascular risk factors hold for most African countries. Indeed, blood pressure is the most assessable risk factor in every setting in SSA. Blood pressure lowering medications are likely to be locally available in their generic forms and would therefore be cheaper. Non-optimal blood pressure levels are the likely prevalent CVD risk factor in SSA, and optimizing blood pressure will have a tremendous effect on the incidence of stroke, the most frequent CVD in Africa at this stage, by reducing the high cerebrovascular risk, and also on the emerging CHD as well as microvascular complications of diabetes. However, the focus on blood pressure lowering should not detract clinicians from targeting other risk factors. For example, it is well known that treatment with a statin, regardless of lipid level achieved significantly reduces the risk of cardiovascular outcomes in people with diabetes (Costa et al. 2006). Where feasible in SSA, routine treatment of individuals with diabetes with such medications should be considered. This must go along way with efforts to generate evidence required to assist global cardiovascular risk evaluation and reduction in diabetes in this region. To this end, a simple approach could consist of setting-up multicenter diabetes and stroke registers where patients are screened for risk factors and monitored for outcomes in view of global risk management/reduction.

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