Silent myocardial ischaemia. To screen or not to screen? That is...☆

Ischémie myocardique silencieuse. Dépister ou ne pas dépister? Telle est la question

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Coronary artery disease occurs more frequently and is more severe in diabetic patients. Some studies suggest that the cardiovascular prognosis of diabetic patients without known coronary disease is as poor as that for non-diabetic patients with known coronary disease, which has led to the suggestion that diabetes should be considered a 'coronary heart disease equivalent' [1]. In fact, many diabetic patients live with significant coronary lesions without experiencing the signs or symptoms of coronary artery disease. As a consequence, it appears logical to detect coronary artery disease at the silent stage to enable the prevention of cardiac events. A number of studies have shown clearly that silent myocardial ischaemia (SMI) — as evidenced by non-invasive tests such as the electrocardiogram stress test, myocardial scintiscan or stress echocardiography — affects 20—50% of diabetic patients with additional risk factors, and that 40—90% of patients with SMI have significant coronary stenoses on angiography [2]. Moreover, the predictive value of SMI for coronary events is well established, particularly if SMI is associated with coronary stenoses [3,4].

Recently, a controversy has emerged about the usefulness of screening diabetic patients for SMI [5—7]. This controversy is based on several arguments. The first concerns feasibility, as the number of diabetic patients with other risk factors is huge and screening tests cannot be performed in them all. The cost-effectiveness ratio has also been questioned;
coronary revascularization is performed in very few patients screened for SMI and the benefit of revascularization is not established clearly. Another line of argument has been generated by the marked improvement in cardiovascular prognosis due to the intensification of preventive medical treatments. Indeed, the rates of coronary events in the placebo arms of major randomized studies that included diabetic patients have decreased by over 50% since the 1990’s [8–10]. Moreover, a multifactorial approach targeting several risk factors is more effective than unifactorial treatment, as shown in the Steno-2 study [11]. Compared with conventional management, an intensified approach applied to high-risk type 2 diabetic patients reduced the rate of cardiovascular and microangiopathic complications by 50%, and the benefit remained significant 10 years after the end of the randomized period [11]. Based on these data, the current guidelines have defined lower targets for blood glucose, blood pressure and blood lipid concentrations and stand strongly in favour of intensification of preventive treatments.

While it may be attractive to consider that the accurate treatment of all risk factors will render screening for coronary disease unnecessary, there are several limitations to this theory. The multifactorial intensive strategy requires training of doctors and healthcare providers, and patient education and coaching. In addition, when using this approach, the targets—in particular those for blood glucose and blood pressure—are achieved in very few patients [11]. Furthermore, changes in clinical practice are slow to materialize in real life, as shown by the European Action on Secondary and Primary prevention through Intervention to Reduce Events (EUROASPIRE) studies [12], and patient compliance with multiple treatments is difficult to obtain. Finally, in the Steno-2 study, the residual cardiovascular risk remained high, which could be due to late treatment intensification, insufficient intensification or possibly unknown risk factors. More potent intensification could be dangerous due to the risk of severe hypoglycaemic events, as suggested recently by the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, this risk being higher in elderly patients [13].

In the future, in line with recent guidelines, treatment intensification should be started earlier, at the onset of diabetes or even in prediabetic stages, to increase the potential for controlling blood pressure more efficiently and to prevent diabetic complications more effectively.

In the current issue of this journal, Barthélémy et al. [13] report their results on SMI screening in a series of 122 patients who were treated intensively before inclusion. The control of blood glucose, lipids and blood pressure at inclusion was rather good, albeit not at the targets for greater than 50% of the patients, which confirms the difficulty in reaching all of these goals. Most of the patients were receiving blockers of the renin-angiotensin system and around 50% were receiving antplatelet therapy (no data were reported on statin treatment). The authors considered these patients to be at high risk. In fact, the major risk factors were present in a low proportion of these patients: 32% had microalbuminuria and 12% had evidence of peripheral artery disease, whereas obesity and retinopathy were taken as risk factors, which is not consensual. As expected, the prevalence of SMI was low (16%) and only seven patients had significant coronary stenoses. The rate of cardiac events after a mean follow-up duration of 2 years was very low (0.8% per year).

The prevalence of SMI was lower than in many previous studies that included higher-risk patients [2], and was also lower than in the authors’ previous report [13]; they suggest that the most likely reason for the difference is treatment intensification before inclusion. In fact, it may also result from the inclusion criteria and assessment methods, as SMI was detected by two functional tests in their previous work compared with only one in the present paper. The authors also suggest that the low cardiac event rate, particularly the lack of events in the patients with SMI, may result from previous intensive treatment and coronary revascularization. The latter factor was probably the most important one, in addition to more intensive medical treatments in the patients with SMI (which could not be documented).

We reported recently some data obtained from a population of 781 diabetic patients whom we have screened for SMI since 1992, always using stress myocardial scintigraphy [16]. When we compared the results in those screened before and after 2000, it appeared that the patients screened since 2000 had a higher-risk profile (more patients with microalbuminuria and more hypertensives). SMI prevalence was similar before and after 2000 but the percentage of patients with coronary stenoses on angiography was lower after 2000, possibly due to the recent medical treatment intensification recommended in practice guidelines. Interestingly, in the group of patients included after 2000, no cardiovascular event occurred after a mean 3-year follow-up period in the patients free of SMI, whereas in the patients with SMI, the prognosis was as severe as in the group included before 2000. This suggests that SMI still warrants specific management and coronary revascularization when appropriate, in addition to risk factor correction. Similarly, a recent randomized study that included 141 asymptomatic patients with type 2 diabetes has shown that the rate of cardiac events was significantly lower in patients screened for SMI and revascularized when necessary than in patients who were not screened [17]. This observation needs to be confirmed in other randomized studies involving larger numbers of patients.

In conclusion, it is not yet time to stop screening diabetic patients for SMI. Such a scenario can be foreseen at a stage when all risk factors are treated very early, intensively and long term. In the meantime, screening should be continued but the strategy needs to be improved. The current French guidelines [18] recommend the screening of high-risk patients. In order to reduce the number of patients that have to be screened, increase the positive predictive value of non-invasive tests and detect the highest number of patients with silent coronary stenoses who need to be revascularized, non-invasive tests should be performed in a subset of patients with the greatest a priori probability of having coronary stenoses. The selection criteria ought to be changed as the traditional risk factors are poor determinants of SMI and silent stenoses, and more and more patients are treated with statins even if they don’t have lipid disorders, and by blockers of the renin-angiotensin system without being hypertensive. The new criteria might be based on ‘new’ risk factors or risk integrators such as coronary artery calcifications, artery stiffness or endothelial
dysfunction, or biomarkers may be used [2]. Some of these explorations could be used as a first step before carrying out the functional test for ischaemia. Whether this strategy will improve the risk:benefit ratio of SMI screening needs to be evaluated in further research.

References


