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Research letter

High efficacy of screening for diabetes and prediabetes in cardiac rehabilitation after an acute coronary syndrome (ACS). The REHABDIAB study

The prevalence of glucose metabolism disorders in patients hospitalized for Acute coronary syndrome (ACS) is very high, observed in more than two thirds of the patients [1]. This is the reason why screening for glucose metabolism disorders with the oral glucose tolerance test (OGTT) is recommended in all patients after an ACS in several guidelines [2,3].

However, although it is recommended, we are concerned about the feasibility and the use of the OGTT in all patients after an ACS. We may wonder whether cardiac rehabilitation (CR) could be a good place to screen for glucose metabolism disorders. Because CR has been shown to significantly reduce cardiovascular morbidity and mortality, it is recognized as an integral part of the care strategy for patients with coronary heart disease and is a level A recommendation in these patients [4]. In addition, CR programs comprise care and education on cardiovascular risks including glucose metabolism disorders and diabetes.

The aim of this study was to evaluate the feasibility and the efficacy of the screening for glucose metabolism disorders in CR. In addition, we compared the uptake of OGTT screening in our CR center with its use in real-life in a representative sample of ACS patients from the whole French population.

Patients and methods

Patients

Among the 343 patients referred to our CR center from March 2013 to May 2015 following a recent ACS, 60 had previously known diabetes and 12 were diagnosed with diabetes because of HbA1c $\geq$ 6.5% at inclusion in the CR program. We prescribed the OGTT, as recommended [2,3], in the 271 remaining patients.

All of the patients were enrolled in an outpatient comprehensive CR program including 20 physical training sessions and educational programs on cardiovascular risks factors as previously reported [5].

Screening for glucose metabolism disorders with the OGTT

According to the guidelines, HbA1c was measured in each patient included in the study and patients with HbA1c $\geq$ 6.5% were considered to have diabetes [3]. The OGTT was prescribed in all patients with HbA1c $<$ 6.5%, as recommended [3]. In order to perform a "real-life" study, the OGTT was not performed in the CR center but was prescribed for each patient, who was asked to perform it in an external biology laboratory. The OGTT was performed in the morning after a 12-hour fast, with a 75-g oral glucose load. Plasma glucose was measured at baseline and 120 min after the oral glucose load. According to the WHO criteria, diabetes was defined as fasting plasma glucose (FPG) $\geq$ 7.0 mmol/L (126 mg/dL) or a glucose level 2 h (2hPG) after the OGTT $\geq$ 11.1 mmol/L (200 mg/dL). Impaired fasting glucose (IFG) was defined as FPG $\geq$ 6.1 mmol/L (110 mg/dL) and less than 7.0 mmol/L (126 mg/dL) and impaired glucose tolerance (IGT) was defined as a 2hPG $\geq$ 7.8 mmol/L (140 mg/dL) and less than 11.1 mmol/L (200 mg/dL).

Evaluation of the screening for glucose metabolism disorders with the OGTT after an ACS in the whole French population

Screening for glucose metabolism disorders with the OGTT was estimated at the national level from a representative sample of 1/97th of the French population recorded in the "National Health Insurance Inter-Regime Information System" (SNIIRAM), which collects individual hospital and non-hospital data for health care consumption.

The hospitalization for ACS was identified from the French hospital database by the codes I21, I22 and I23 [6] in the main diagnosis, according to the International classification of diseases (ICD-10). People with a history of diabetes mellitus were excluded. They were identified, by a long-duration disease classified as diabetes mellitus (ALD 8) before the onset of ACS, or reimbursements for diabetics medication identified by A10 codes in the ATC classification in the year prior to hospitalization for ACS, or codes for diabetes (E10-E14) in hospital discharge abstracts in the year immediately before and the year the ACS occurred (before the event). Screening for glucose metabolism disorders with an OGTT was explored using version 42 of the national table of biology (codes 0412 and 0413). The analysis was performed for the years 2013 and 2014.

Results

Uptake of screening for glucose metabolism disorders with the OGTT after an ACS in our cardiac rehabilitation center

Among the 343 patients referred to our CR center, 60 had previously known diabetes and 12 were diagnosed with diabetes, because of and HbA1c $\geq$ 6.5%. The OGTT was prescribed in the 271 remaining patients.

Among the 271 patients in whom the OGTT was prescribed, only nine did not perform it. Thus, the OGTT was performed in 262 patients representing a very high uptake (97%).

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Use of the OGTT for screening for glucose metabolism disorders after an ACS in the general French population

In the hospital data (2013–2014), we identified 1149 patients who were hospitalized for ACS from a representative sample of 1/97st French population. We excluded 218 patients with a history of diabetes. The screening rate estimation for glucose metabolism disorders with the OGTT after an ACS, was very low: only 0.54% of patients were screened in the first year after hospitalization for ACS.

Data for screening for glucose metabolism disorders after an ACS in our cardiac rehabilitation center

Considering the 262 patients who were screened with the OGTT, the OGTT was normal in 158 patients and abnormal in 104 patients (39.7%) including 22 patients (8.4%) with diabetes, and 82 patients (31.3%) with prediabetes: 25 patients (9.6%) with IFG alone, 43 patients (16.4%) with IGT alone and 14 patients (5.3%) with both IFG and IGT. If we include the 12 patients in whom diabetes was directly diagnosed because of HbA1c $\geq$ 6.5%, 116 patients (42.3%) showed glucose metabolism disorders including 34 patients (12.4%) with diabetes, 25 patients (9.1%) with IFG alone, 43 patients (15.7%) with IGT alone and 14 patients (5.1%) with both IFG and IGT (Fig. 1A).

When we combine the 274 patients screened for glucose metabolism disorders with the OGTT/HbA1c and the 60 patients with previously known diabetes, the proportion of patients with normal glucose metabolism enrolled in CR was only 47.3% while 17.9% had known diabetes, 10.2% showed newly diagnosed diabetes with the OGTT, 7.5% showed IFG alone, 12.9% showed IGT alone and 4.2% showed both IFG + IGT (Fig. 1B).

Characteristics of the patients according to their glucose metabolism profile

Because the clinical, biological and cardiovascular characteristics were not different between the 12 patients in whom diabetes was diagnosed with the HbA1c and the 22 patients in whom diabetes was diagnosed with the OGTT, data from both groups were combined in a group identified as "newly diagnosed diabetes".

The characteristics of the patients with normal glucose tolerance, IFG, IGT, both IFG + IGT, newly diagnosed diabetes and previously known diabetes are shown in Table 1. Compared with the patients with normal glucose metabolism, patients with newly diagnosed diabetes and patients with previously known diabetes were older. Mean BMI was not different between groups except for patients with IFG who showed higher values. Patients with IGT, newly diagnosed diabetes or previously known diabetes had significantly higher plasma triglyceride levels. Baseline peak workload, end-CR peak workload as gain in peak workload during CR was significantly lower in patients with newly diagnosed or previously known diabetes.

Discussion

The OGTT is recommended in all non-diabetic patients after an ACS [2,3]. However, its feasibility and uptake is a matter of concern. We showed for the first time, in the present study that CR is an optimal place to screen for glucose metabolism disorders on a regular basis as uptake and efficacy are very high.

We showed that during an evaluation period of 26 months, the OGTT was performed in 97% of patients, indicating very high uptake. In contrast, during the same period, screening for glucose metabolism disorders with the OGTT after an ACS in the French population was very low (0.54%). This indicates that screening for glucose metabolism disorders after an ACS is probably not a priority among General Practitioners and many cardiologists. In the present study, cardiologists specialized in CR were able to motivate patients to perform the OGTT by explaining the importance of screening for possible glucose metabolism disorders. Because cardiologists specialized in CR are highly motivated and involved in cardiac prevention and because CR increases motivation and the commitment of coronary patients to changing their lifestyle in order to reduce cardiovascular risk, CR appears to be, as shown here, an ideal place to screen for glucose metabolism disorders.

As suspected, we found a very high rate of glucose metabolism disorders in patients referred for CR after an ACS (52.7%) and the systematic screening allowed detecting abnormal glucose metabolism in 42.3% of the patients. So far, the prevalence of glucose metabolism disorders in CR has been assessed in very few studies and in unselected patients [7–9]. The present study is, to our knowledge, the first in which a homogeneous population of patients referred to CR following an ACS was screened for glucose metabolism disorders. The high frequency of glucose metabolism disorders detected by systematic screening was not very different

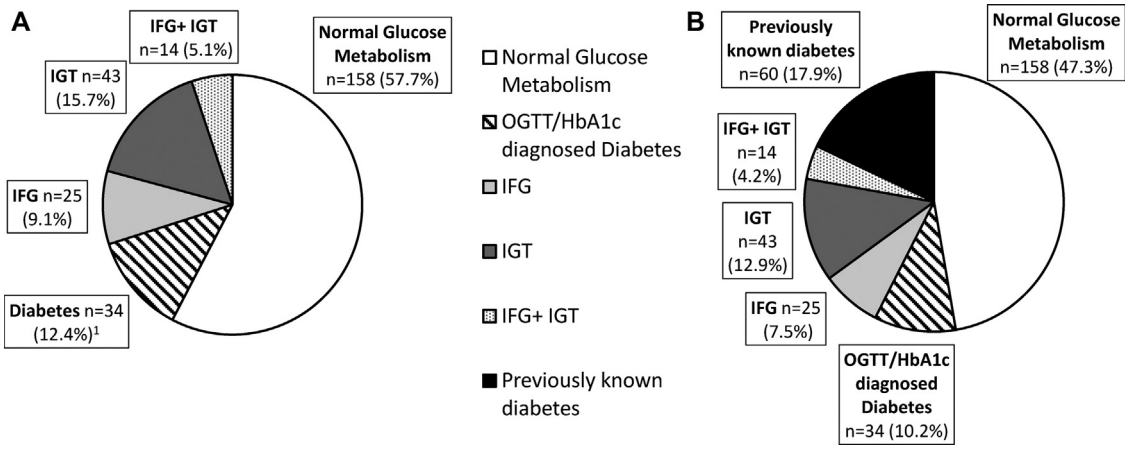

Fig. 1. A. Glucose metabolism disorders in the 274 patients enrolled in cardiac rehabilitation and tested with the OGTT/HbA1c. IFG: impaired fasting glucose; IGT: impaired glucose tolerance. 1: Among these 34 patients, diabetes was diagnosed with HbA1c $\geq$ 6.5% in 12 patients and with the OGTT in 22 patients. B. Glucose metabolism disorders in the 334 patients enrolled in cardiac rehabilitation combining those tested with the OGTT/HbA1c and those with previously known diabetes.

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Table 1
Main characteristics of the patients with normal glucose tolerance, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), both IFG + IGT, newly diagnosed diabetes and previously known diabetes.

	Normal glucose metabolism $n = 158$	IFG $n = 25$	IGT $n = 43$	IFG + IGT $n = 14$	Newly diagnosed diabetes $n = 34$	Previously known diabetes $n = 60$
Age (years)	58 ± 11	60 ± 9	61 ± 10	62 ± 11	63 ± 11*	63 ± 13**
Gender (M/F)	127/31	22/3	35/8	10/4	27/7	48/12
BMI (kg/m^2)	26.1 ± 4.3	29.1 ± 5.8*	27.4 ± 4.3	29.6 ± 5.5**	27.4 ± 5.0	28.2 ± 4.9**
Smoking, *n* (%)	64 (40.5%)	12 (48%)	17 (39.5%)	6 (42.9%)	15 (44.1%)	16 (26.6%)
Hypertension, *n* (%)	63 (39.9%)	9 (37.5%)	21 (48.8%)	8 (57.1%)	19 (55.9%)	46 (76.6%)
LDL-C (mg/dL)	122 ± 42	125 ± 49	130 ± 50	128 ± 44	121 ± 39	100 ± 51**
HDL-C (mg/dL)	47 ± 13	52 ± 17	47 ± 15	44 ± 9	42 ± 10*	43 ± 15
Triglycerides (mg/dL)	126 ± 66	131 ± 57	163 ± 80**	152 ± 56	204 ± 112***	171 ± 145**
STEMI, *n* (%)	90 (57.0%)	10 (40.0%)	30 (69.7%)	11 (78.6%)	17 (50%)	21 (35.0%)
OGTT fasting glycaemia (mg/dL)	93 ± 10	116 ± 5***	98 ± 6	118 ± 10***	121 ± 25***	
OGTT post load glycaemia (mg/dL)	94 ± 21	103 ± 20	161 ± 17***	168 ± 18***	208 ± 45***	
LVEF (%)	56.8 ± 10.2	58.1 ± 10.3	56.7 ± 7.6**	54.1 ± 11	57.2 ± 11.7	53.7 ± 10.9
Baseline peak workload (watt)	97 ± 33	100 ± 23	84 ± 29*	75 ± 28*	77 ± 23***	74 ± 28***
End-CR peak workload (watt)	132 ± 43	135 ± 27	116 ± 35*	111 ± 47	104 ± 29***	99 ± 33***
Gain in peak workload (watt)	34 ± 21	35 ± 12	31 ± 16	37 ± 25	26 ± 25*	25 ± 13**

For patients with IFG, IGT, IFG + IGT, newly diagnosed diabetes and previously known diabetes, comparisons were made with patients from the Normal glucose metabolism group. BMI: body mass index; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; STEMI: ST-segment elevation myocardial infarction; OGTT: Oral Glucose Tolerance Test; LEVF: left ventricular ejection fraction; CR: cardiac rehabilitation.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

from the rates reported in previous studies (ranging from 51 to 63%) [7–9].

As previously reported, we found that patients with known diabetes had a significantly lower gain in peak workload during CR [5]. Interestingly, we showed here that this also applied to patients with newly diagnosed diabetes. Detection of diabetes in CR seems important in order to initiate optimal treatment to obtain good glycaemic control which has been shown to improve the effectiveness of CR [10].

In addition, screening for glucose metabolism disorders during CR is totally in keeping with this global approach to coronary patients in which they are encouraged to embrace lifestyle modifications. Patients with newly diagnosed abnormal glucose disorders during CR can take advantage of counseling on diet and physical exercise. If good glycaemic control is not obtained with lifestyle modifications alone in newly diagnosed diabetic patients, an antidiabetic treatment may be introduced and, when needed, patients may be referred to a diabetologist/endocrinologist.

Conclusion

We showed that screening for glucose metabolism disorders with the OGTT during CR after an ACS was extremely feasible (in 97% of the patients) when its use in the whole post-ACS population was very low (in 0.54% of the patients). This screening strategy was very effective as it detected diabetes/prediabetes in nearly 40% of the patients. CR seems to be an optimal place for such screening because it offers to these patients with diabetes/prediabetes appropriate care including education on diet and physical activity.

Author contributions

B.V. and B.P.V. contributed to the conception of the work. B.P.V., A.M. and M.C.B. contributed to the acquisition of the data in CR patients. K.G., J.C. and C.Q. contributed to the acquisition and analysis of the data for the epidemiological study performed in the whole French population. B.V., B.P.V. and A.M. performed the analysis and interpretation of the data. B.V. and B.P.V. wrote the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Disclosure of interest

The authors declare that they have no competing interest.

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