Université de Bourgogne

UFR des Sciences de Santé

Circonscription Médecine

ANNEE 2016

N°

TITRE DE LA THESE

DETECTION OF GLUCOSE METABOLISM DISORDERS IN CARDIAC REHABILITATION: IS HbA1c USEFUL?

THESE

présentée

à l'UFR des Sciences de Santé de Dijon
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et soutenue publiquement le mercredi 7 septembre 2016

pour obtenir le grade de Docteur en Médecine

par Sopio TATULASHVILI

Née le 28/11/1982

à TÉLAVI, GÉORGIE

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Professeur d'Endocrinologie et Maladies Métaboliques

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SERMENT D'HIPPOCRATE

"Au moment d'être admise à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions.

J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité.

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J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences.

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Admise dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçue à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

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Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonorée et méprisée si j'y manque."

Abréviations

ACS: Acute coronary syndrome

ADA: American diabetes association

BMI: Body mass index

CABG: Coronary artery bypass grafting

CSTf: final cardiac stress test

CSTi: initial cardiac stress test

D: Diabetes

EASD: European association for the study of diabetes

ESC: European society of cardiology

FHC: Family history of coronaropathy

FPG: Fasting plasma glucose

IFG: Impaired fasting glucose

IGT: Impaired glucose tolerance

LVEF: Left ventricular ejection fraction

ND: New diabetes

NG: Normoglycemia

NPV: Negative predictive value

OGTT: Oral glucose tolerance test

PPV: Positive predictive value

PreD: Pre-diabetes

Tg: Triglycerides

WHO: World health organization

DETECTION OF GLUCOSE METABOLISM DISORDERS IN CARDIAC REHABILITATION: IS HbA1c USEFUL?

Abstract

Introduction: Diabetes and pre-diabetes are associated with increased cardiovascular morbidity and mortality. Especially in patients with a history of acute coronary syndrome (ACS). This is why screening for glucose metabolism disorders is recommended in patients following an ACS. The oral glucose tolerance test (OGTT) seems to be more sensitive to screen for glucose metabolism disorders, but some (American Diabetes Association) propose to use HbA1c alone for screening of diabetes and pre-diabetes. The aim of our study was to determine whether HbA1c alone compared with an OGTT could allow effective screening for glucose metabolism disorders in ACS patients undergoing cardiac rehabilitation.

Patients and Methods: Altogether, 347 patients with a recent history of ACS and treated at "Les Rosiers" cardiac rehabilitation center were recruited for this prospective study. An OGTT was prescribed in 277 patients without known diabetes and was performed in 267 of them (96.4%). We divided our patients into three groups: newly diagnosed diabetes mellitus, pre-diabetes (including impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT)) and normoglycemia according to the OGTT and HbA1c results. The results obtained with HbA1c were compared with those obtained with the OGTT, considered as the reference in our study.

Results: For the diagnosis of diabetes, HbA1c remained a good diagnostic test, with a sensitivity of 72% and a specificity of 100%. Positive and negative predictive values were high at 100 and 96%, respectively. However, for the diagnosis of pre-diabetes (IFG and IGT) the diagnostic sensitivity of HbA1c was low at 64% as was specificity (53%), with a positive

predictive value of only 37%. For the diagnosis of normoglycemia, the sensitivity of HbA1c was low (48%) with positive and negative predictive values of 71 and 50%, respectively.

Conclusion: According to our study, HbA1c has low sensitivity and specificity for the detection of pre-diabetes in patients with coronary disease enrolled in cardiac rehabilitation and HbA1c over diagnoses pre-diabetes in comparison with the OGTT.

Introduction

Diabetes is a frequent disease. Its incidence is increasing much faster than estimated. It was expected that 366 million people worldwide would be suffering from diabetes by 2030 but this number has already been reached (1,2).

Diabetes and pre-diabetes are associated with increased cardiovascular morbidity and mortality (3–6). Especially in patients with a history of acute coronary syndrome (ACS) (7,8).

Early screening and the treatment of glucose metabolism disorders in patients with a history of ACS could lower the risk of further complications. This is why screening for glucose metabolism disorders is recommended in patients following an ACS (9), and cardiac rehabilitation seems to be an optimal period to detect glucose metabolism disorders in such patients (10).

Recently, the American Diabetes Association (ADA) recommended using HbA1c alone for the diagnosis of diabetes (≥6.5%) and pre-diabetes (5.7 – 6.4%) (11). However, the oral glucose tolerance test (OGTT) seems to be more sensitive to screen for glucose metabolism disorders, but it is less frequently performed because it is more time-consuming (12).

The aim of our study was to determine whether HbA1c alone compared with an OGTT could allow effective screening for glucose metabolism disorders in ACS patients undergoing cardiac rehabilitation.

Patients and Methods

1. Population and study description

Altogether, 347 patients with a recent history of ACS and treated at "Les Rosiers" cardiac rehabilitation center were recruited for this prospective study. We excluded 60 patients with known diabetes mellitus and 10 patients who stopped cardiac rehabilitation early. An OGTT was prescribed in the remaining 277 patients and was performed in 267 of them (96.4%).

We divided our patients into three groups: newly diagnosed diabetes mellitus, pre-diabetes (including impaired fasting glucose and/or impaired glucose tolerance) and normoglycemia according to the OGTT and HbA1c results. The results obtained with HbA1c were compared with those obtained with the OGTT, considered as the reference in our study.

The OGTT results were classified according to the HAS (Haute Autorité de Santé, National Health Authority) recommendations, which are based on the recommendations of the World Health Organization (WHO)(13,14). The OGTT was performed in the morning after a 12 hour fast and with a 75g glucose load. Diabetes is defined as fasting plasma glucose (FPG) greater or equal to 7.0mmol/L (126 mg/dL) or a glucose level 2h (2hPG) after an OGTT greater or equal to 11.1mmol/L (200mg/dL). Impaired fasting glucose (IFG) was defined as FPG greater or equal to 6.1 mmol/L (110mg/dL) and less than 7.0 mmol/L and impaired glucose tolerance (IGT) was defined as 2hPG greater or equal to 7.8 mmol/L (140 mg/dL) and less than 11.1mmol/L.

HbA1c results were classified according to ADA recommendations. HbA1c < 5.7% was considered normal. Pre-diabetes was defined as HbA1c between 5.7 and 6.4% and diabetes was diagnosed if HbA1c level is ≥ 6.5%(11).

2. Statistical analysis

Data are reported as mean ± SD. The SPSS software package (Chicago, Illinois, USA) was used for the statistical analyses. Percentages between groups were compared using the Chi-square test. Means between groups were compared using Student's t-test. A two-tailed probability level of 0.05 was accepted as statistically significant. Sensitivity was calculated as the ratio of number of true positives divided by the number of true positives + the number of false negatives. Specificity was calculated as the ratio of the number of true negatives divided by the number of true negatives + the number of false positives. The positive predictive value was defined as the ratio of the number of true positives divided by the number of true positives + the number of false positives. The negative predictive value was defined as the ratio of the number of true negatives divided by the number of true negatives + the number of false negatives.

Results

1. Baseline characteristics

This study included 267 patients, mainly men (81%) with a mean age of 59 years. More than half of them presented an ACS with ST-segment elevation (n=153; 57.1%) and most had single-vessel coronary artery disease on the coronarography (n=156; 58%). Sixty and 47 patients had two and three-vessel coronary artery disease, respectively (22.4% and 17.5%). Overall, half of the patients had a family history of coronary disease. The baseline characteristics of our population are presented in Table 1.

2. Glycemic state according to OGTT and HbA1c

All 267 patients underwent OGTT and plasma HbA1c measurement. We divided patients into groups according to the results for each test. For the OGTT, we constituted five groups: patients with normoglycemia, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), both IFG+IGT and newly diagnosed diabetes. As shown in Figure 1, the OGTT revealed normoglycemia in 156 patients (58%), pre-diabetes in 80 patients (30%), among whom 24 patients (9%) had IFG, IGT in 42 patients (16%) and IFG + IGT in 14 patients (5%). New diabetes was revealed in 32 patients (12%) (Figure 1).

We constituted three groups according to results of HbA1c: patients with normoglycemia, pre-diabetes and newly diagnosed diabetes. Pre-diabetes was revealed in 140 patients, more than half of our study population (52%). Twenty-three patients (9%) had newly diagnosed diabetes and 104 patients (39%) had normoglycemia (Figure 2).

When we compared these results, pre-diabetes was over-diagnosed with HbA1c as compared to OGTT (52% vs. 30%, $p<0.0001$). There was no significant difference between the two methods for the diagnosis of diabetes (Table 2).

3. Description of the subgroups of glucose metabolism disorders diagnosed with OGTT and with HbA1c

As compared with normoglycemic patients, diabetic and pre-diabetic patients diagnosed with both methods (OGTT, HbA1c) were older and had a higher incidence of cardio-vascular risk factors, including HTA, a family history of coronary disease and dyslipidemia. Initial and final cardiac stress test results were worse in patients with diabetes mellitus (already known or newly diagnosed) than in normoglycemic patients, while initial and final cardiac stress test results in patients with pre-diabetes were between those observed in diabetic patients and those observed in normoglycemic patients. Coronary disease affecting three arteries was more

frequent in pre-diabetic and diabetic patients than in normogylcemic patients, among whom almost two third had coronary artery disease limited to one artery. (Tables 3 and 4)

4. **Comparison of the subgroups of glucose metabolism disorders diagnosed with OGTT and with HbA1c**

We recorded each characteristic for each subgroup according to results of the OGTT and HbA1c and then compared the different subgroups for age, BMI, HbA1c, LVEF, initial and final cardiac stress test results and lipids.

The characteristics of pre-diabetic patients of the two subgroups diagnosed with the OGTT and HbA1c were comparable for each characteristic except for HbA1c, which was significantly higher in the subgroup diagnosed with HbA1c (Table 5) .

Characteristics of diabetic patients of the two subgroups diagnosed with the OGTT and HbA1c were comparable for each characteristic. (Table 6)

Characteristics of normoglycemic patients of the two subgroups diagnosed with the OGTT and HbA1c were comparable for each characteristic except for HbA1c, which was significantly higher in the subgroup diagnosed with the OGTT (Table 7).

5. **Sensitivity and specificity of HbA1C for the diagnosis of glycemic metabolism disturbances**

We also evaluated the sensitivity, specificity and positive and negative predictive values of HbA1c compared with the OGTT.

For the diagnosis of diabetes, HbA1c remained a good diagnostic test, with a sensitivity of 72% and a specificity of 100%. Positive and negative predictive values were high at 100 and 96%, respectively. However, for the diagnosis of pre-diabetes (IFG and IGT) the diagnostic sensitivity of HbA1c was low at 64% as was specificity (53%), with a positive predictive

value of only 37%. For the diagnosis of normoglycemia, the sensitivity of HbA1c was low (48%) with positive and negative predictive values of 71 and 50%, respectively. (Table 8)

6. Agreement between the OGTT and HbA1c test for the diagnosis of diabetes and pre-diabetes

We tested the agreement between OGTT and HbA1c for the diagnosis of diabetes and pre-diabetes. Twenty-three patients were diagnosed with diabetes with both tests and nine patients with the OGTT only. As for pre-diabetes, 53 patients were diagnosed with both tests, 27 with the OGTT alone and 87 with HbA1c alone. As expected, the agreement rate between the two tests was higher for the diagnosis of diabetes than for the diagnosis of pre-diabetes, 72% vs 32%. We can also mention that 32% of the patients were misclassified as pre-diabetic, but no patients were misclassified as diabetic (Figures 3 and 4).

Discussion

Our results clearly show that HbA1c has low sensitivity and specificity for the detection of pre-diabetes in patients with coronary disease enrolled in cardiac rehabilitation. We showed that the HbA1c test over-diagnoses pre-diabetes in comparison with the OGTT. In addition, the positive predictive value of HbA1c was very low for the diagnosis of pre-diabetes. The agreement rate between the OGTT and HbA1c was higher for the diagnosis of diabetes than for the diagnosis of pre-diabetes.

This is the first study to evaluate the use of HbA1c in screening for glucose metabolism disorders in cardiac rehabilitation after ACS. It is known that the prevalence of glucose metabolism disorders is higher in patients with a history of ACS (15–18). It is also known that the incidence of mortality and morbidity is elevated in patients with glucose metabolism disorders and coronary artery disease (19,20) and that correcting glucose metabolism

disorders can reduce the incidence of further complications in these patients (21). Moreover, abnormal glucose tolerance is known to be associated with lower functional recovery and reduced exercise capacity at the end of cardiac rehabilitation (22,23). It has also been shown in a prospective study that good glycemic control during cardiac rehabilitation improves significantly exercise capacity (24). Furthermore, glucose metabolism disorders worsen short- and long-term outcomes after ACS (25–29). It is therefore important to identify the most sensitive screening test for glycemic metabolism disorders in such populations so as to reduce incidence of further complications and to choose appropriate cardiac rehabilitation programs to obtain a greater benefit.

The ADA recommends using HbA1c alone to screen for glucose metabolism disorders (11), but these recommendations do not seem to be appropriate for patients such as ours, who have a high risk of glucose metabolism disorders. It must be noted that in the European Society of Cardiology (ESC) and European Association for the Study of Diabetes (EASD) guidelines on diabetes, pre-diabetes and cardiovascular disease (30), patients without known diabetes but with established cardiovascular disease should undergo an OGTT if HbA1c and fasting plasma glucose are inconclusive (normal). The OGTT, however, is still not recommended by the ADA for use in routine practice (11).

Several studies have investigated screening for glucose metabolism disorders during hospitalization for ACS. The objective of these studies was to determine whether OGTT results at discharge from hospital can be representative of the future glycemic state. The results, however, have been contradictory. Knudsen and al. investigated whether an OGTT performed after an acute STEMI could predict the presence of glucose metabolism disorders at three months (31). In 200 patients, they showed that the prevalence of GMD at three months was much lower than at discharge, 24% versus 46%, respectively. Interestingly,

another study of 122 patients after ACS showed different results. In this study, the OGTT was performed at discharge and at 3 and 12 months after discharge from hospital. More than 90% of patients remained in the same subgroup of glycemic status at 12 months (32).

In light of the articles cited above, OGTT results in the acute phase of coronary disease cannot be used as a reference for the diagnosis of glucose metabolism disorders, as the evolution of the glycemic state may vary after several weeks. This difference might be explained by the constraints of hospitalization (stress, hospital diet…). As mentioned above, cardiac rehabilitation following an ACS therefore seems to be an optimal period to detect glucose metabolism disorders (10).

The small number of patients, even patients with known diabetes mellitus, referred for cardiac rehabilitation after an ACS is still an issue. In different studies, the percentage of diabetic patients referred for cardiac rehabilitation after an ACS ranges from 15 to 26% (33–38).

If we take into account HbA1c screening alone to determine the glycemic state during hospitalization for an ACS, our results are in agreement with a study of Bhuvnesh et al. (15), in which 7% of patients were diagnosed with new diabetes mellitus and almost 40% with pre-diabetes compared with 8% of patients diagnosed with new diabetes mellitus and nearly 50% with pre-diabetes in our study. These results contrast with those from another study, which, in similar circumstances, diagnosed new diabetes mellitus in 18% and pre-diabetes in only 31% of patients (39). In light of these results, which are different in each study, we suggest that HbA1c needs to be used with caution.

As noted above, this is the first study to evaluate the use of HbA1c to screen for glucose metabolism disorders during cardiac rehabilitation after ACS and we cannot compare our results with others, but it would be interesting to continue our study by performing the same

screening tests (HbA1c and OGTT) over several months or a year to see whether patients remain in same glycemic state groups.

Concerning agreement between HbA1c and OGTT criteria for the diagnosis of glucose metabolism disorders, our results show a low agreement between the two screening methods in patients with coronary disease enrolled in cardiac rehabilitation. This low agreement has also been observed in studies performed in other patient populations (40–43). Our study showed 72% of agreement between the two tests for the diagnosis of diabetes and only 32% for that of pre-diabetes. Other studies showed lower agreement rates for the diagnosis of diabetes. In the study of Kim et al.(40), for example, the agreement rate was 45%. In the same study (40), the percentage of patients misclassified as diabetic was 27% if the HbA1c test without the OGTT was used. In our study, no patients were misclassified as diabetic. In contrast, for pre-diabetes, 32% of patients were misclassified as pre-diabetic. These differences might stem from the different study populations. The study population of previously cited article (40) consisted of patients with an abnormal fasting glucose test but without known diabetes and without known coronary artery disease. We can suggest that in the general population with abnormal fasting plasma glucose, the OGTT should be proposed directly, while in patients with coronary artery disease, HbA1c can be used for the diagnosis of diabetes, but in such cases if the HbA1c is normal, an OGTT should be performed. These suggestions match the ESC and EASC guidelines.

Our study has some limitations. The number of patients is small and the data were collected in one cardiac rehabilitation center. Therefore, further studies should be undertaken to confirm our results.

In conclusion, according to our study, HbA1c has low sensitivity and specificity for the detection of pre-diabetes in patients with coronary disease enrolled in cardiac rehabilitation and HbA1c over diagnoses pre-diabetes in comparison with the OGTT.

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Tables and Figures

Table 1. Main baseline characteristics of the studied population

n	267
Age, years	59,7 +/- 11,1
Sex male, %	81
BMI, kg/m²	26,9 +/- 4,7
HTA , %	43,7
Cigarette smoking,%	73,4
Dyslipidemia,%	64,2
LDLc (g/l)	1,24 +/-0,43
HDLc (g/l)	0,46 +/- 0,13
Tg (g/l)	1,43 +/- 0,79
1VCAD,%	58,0
2VCAD,%	22,4
3VCAD,%	17,5
STEMI,%	57,1
CSTi watts	92,3 +/- 31
CSTf watts	125,3 +/- 41
HbA1c,%	5,82+/-0,5
FHC,%	49,1

FHC, family history of coronaropathy; 1VCAD, 1 vessel coronary artery disease; 2VCAD, 2 vessel coronary artery disease; 3VCAD, 3 vessel coronary artery disease; CSTi, initial cardiac stress test; CSTf, final cardiac stress test;

Table 2. Comparison of OGTT and HbA1c results in 267 patients

	OGTT	HbA1c	p
NG	**58%**	**39%**	**<0.0001**
PreD	**30%**	**52%**	**<0.0001**
ND	**12%**	**9%**	**NS (p=0.20)**

Table 3. Characteristics of patients according to glucose metabolism disorder subgroups diagnosed with OGTT

characteristic	NG	IFG	IGT	IFG+IGT	ND	D
Number	156	24	42	14	32	60
Age, years	58,4+/-11,3	59,5+/-9,1	61,3+/-10,3	61,6+/-11,4	63,3+/-11,2	63,3+/-12,6
Male sex, %	80,1	91,7	85,4	71,4	78,1	80,0
BMI, kg/m²	26,0+/-4,3	29,0+/-5,8	27,4+/-4,3	29,5+/-5,4	27,4+/-5,0	28,1+/-4,8
Cigarette S, %	71,1	95,8	65,9	71,5	78,2	60,0
HTA	39,7	37,5	48,8	57,1	56,3	76,7
HbA1c, %	5,66+/-0,31	5,79+/-0,39	5,71+/-0,32	6,03+/-0,24	6,68+/-0,72	7,22+/-1,23
FHC, %	47,4	41,7	53,7	50,0	56,3	55,0
LVEF, %	56,7+/-10,2	58,1+/-10,3	56,7+/-7,6	54,1+/-11,4	57,5+/-11,6	53,7+/-10,9
1VCAD, %	63,5	45,8	53,7	57,1	50	33,3
2VCAD, %	24,4	20,8	22,0	7,1	21,9	23,3
3VCAD, %	10,9	33,3	24,4	35,7	21,9	40,0
STEMI, %	57,1	37,5	70,0	78,6	50	35,0
CABG, %	9	16,7	9,8	7,1	21,9	20,0
Dyslipidemia,%	58,3	75,0	80,5	57,1	68,8	78,3
LDLc, g/l	1,22+/-0,4	1,25+/-0,49	1,3+/-0,5	1,28+/-0,44	1,22+/-0,39	0,99+/-0,51
HDLc g/l	0,47+/-0,1	0,52+/-0,17	0,46+/-0,14	0,44+/-0,09	0,41+/-0,10	0,43+/-0,15
Tg g/l	1,25+/-0,6	1,31+/-0,57	1,63+/-0,79	1,51+/-0,55	2,05+/-1,14	1,71+/-1,45
CSTi, watts	97,8+/-33,3	99,5+/-23,0	84,5+/-28,9	74,6+/-28,3	77,8+/-23,7	74,0+/-28,0
CSTf, watts	131,9+/-43,5	134+/-27,4	116,0+/-35,6	111,4+/-46,8	103,7+/-28,7	99,2+/-33,1

NG, normoglycemia; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ND, new diabetes; D, diabetes; FHC, family history of coronaropathy; Cigarette S, cigarette smoking; 1VCAD, 1 vessel coronary artery disease; 2VCAD, 2 vessel coronary artery disease; 3VCAD, 3 vessel coronary artery disease; CABG, coronary artery bypass grafting; CSTi, initial cardiac stress test; CSTf, final cardiac stress test;

Table 4. Characteristics of patients according to glucose metabolism disorder subgroups diagnosed with HbA1c

Characteristic	NG	PreD	ND	D
Number	104	140	23	60
Age, years	58,2+/-11,4	60,2+/-10,4	63,7+/-12,4	63,3+/-12,6
Male sex, %	84,5	80,0	73,9	80,0
BMI, kg/m²	26,0+/-4,0	27,4+/-5,0	27,6+/-5,6	28,1+/-4,8
Cigarette S, %	68,9	76,4	78,3	60,0
HTA	41,7	43,6	52,2	76,7
HbA1c, %	5,4+/-0,20	5,94+/-0,20	6,97+/-0,63	7,22+/-1,23
FHC, %	52,4	45,0	60,9	55,0
LVEF, %	56,6+/-10,6	57,0+/-9,4	55,7+/-11,5	53,7+/-10,9
1VCAD, %	57,3	61,4	43,5	33,3
2VCAD, %	22,3	21,4	30,4	23,3
3VCAD, %	18,4	17,1	17,4	40,0
STEMI, %	59,8	57,1	52,2	35,0
CABG, %	11,7	9,3	21,7	20,0
Dyslipidemia,%	63,1	64,3	69,6	78,3
LDLc, g/l	1,23+/-0,42	1,24+/-0,45	1,21+/-0,40	0,99+/-0,51
HDLc g/l	0,45+/-0,14	0,47+/-0,13	0,42+/-0,10	0,43+/-0,15
Tg g/l	1,33+/-0,71	1,42+/-0,77	1,91+/-1,05	1,71+/-1,45
CSTi, watts	100,1+/-33,5	89,1+/-30,0	75,2+/-20,4	74,0+/-28,0
CSTf, watts	134,3+/-43,9	121,8+/-37,8	100,9+/-26,6	99,2+/-33,1

NG, normoglycemia; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ND, new diabetes; D, diabetes; FHC, family history of coronaropathy; Cigarette S, cigarette smoking; 1VCAD, 1 vessel coronary artery disease; 2VCAD, 2 vessel coronary artery disease; 3VCAD, 3 vessel coronary artery disease; CABG, coronary artery bypass grafting; CSTi, initial cardiac stress test; CSTf, final cardiac stress test;

Table 5. Comparison of the main characteristics of patients diagnosed with pre-diabetes according to the OGTT and HbA1c.

	OGTT	HbA1c	p
n	80	140	
Age, years	60,8+/-10,1	60,2+/-10,4	NS
BMI, kg/m²	28,3+/-5	27,4+/-5	NS
HbA1c, %	5,7+/-0,3	5,9+/-0,2	<0,0001
FEVG, %	56,7+/-9,2	57+/-9,4	NS
CST I, %	87,2+/-28,3	89,1+/-30	NS
CST f, %	120,6+/-36,5	121+/-37	NS
Tg, g/l	1,5+/-0,7	1,4+/-0,7	NS
LDLc, g/l	1,28+/-0,4	1,2+/-0,4	NS
HDLc, g/l	0,47+/-0,1	0,47+/-0,1	NS

CSTi, initial cardiac stress testing; CSTf, final cardiac stress testing; NS, not significant

Table 6. Comparison of the main characteristics of patients diagnosed with diabetes with the OGTT and HbA1c

	OGTT	HbA1c	p
n	32	23	
Age, years	63,3+/-11,2	63,7+/-12,4	NS
BMI, kg/m²	27,4+/-5,0	27,6+/-5,6	NS
HbA1c, %	6,6+/-0,7	6,9+/-0,6	NS
FEVG, %	57,5+/-11,6	57+/-9,4	NS
CST I, %	77,8+/-23,7	75,2+/-20,4	NS
CST f, %	103,7+/-28,7	100,9+/-26,6	NS
Tg, g/l	2,0+/-1,1	1,9+/-1,0	NS
LDLc, g/l	1,22+/-0,3	1,2+/-0,4	NS
HDLc, g/l	0,45+/-0,1	0,42+/-0,1	NS

CSTi, initial cardiac stress test; CSTf, final cardiac stress test; NS, not significant

Table 7. Comparison of the main characteristics of patients diagnosed as normoglycemic with the OGTT and HbA1c

	OGTT	HbA1c	p
n	156	104	
Age, years	58,4+/-11,3	58,2+/-11,4	NS
BMI, kg/m²	26,0+/-4,3	26,0+/-4,0	NS
HbA1c, %	5,6+/-0,3	5,4+/-0,2	<0,0001
LVEF,%	56,7+/-10,2	56,6+/-10,6	NS
CST I,%	97,8+/-33,3	100,1+/-33,5	NS
CST f,%	131,9+/-43,5	134,3+/-43,9	NS
Tg, g/l	1,25+/-0,6	1,3+/-0,7	NS
LDLc, g/l	1,22+/-0,4	1,2+/-0,4	NS
HDLc, g/l	0,47+/-0,1	0,45+/-0,1	NS

CSTi, initial cardiac stress testing; CSTf, final cardiac stress test; NS, not significant

Table 8. Sensitivity and specificity of HbA1c for the diagnosis of glucose metabolism disturbances

HbA1c	**Normoglycaemia**	**Pre-diabetes**	**Diabetes**
Sensitivity	**48%**	**65%**	**72%**
Specificity	**73%**	**53%**	**100%**
PPV	**71%**	**37%**	**100%**
NPV	**50%**	**79%**	**96%**

PPV, positive predictive value; NPV, negative predictive value

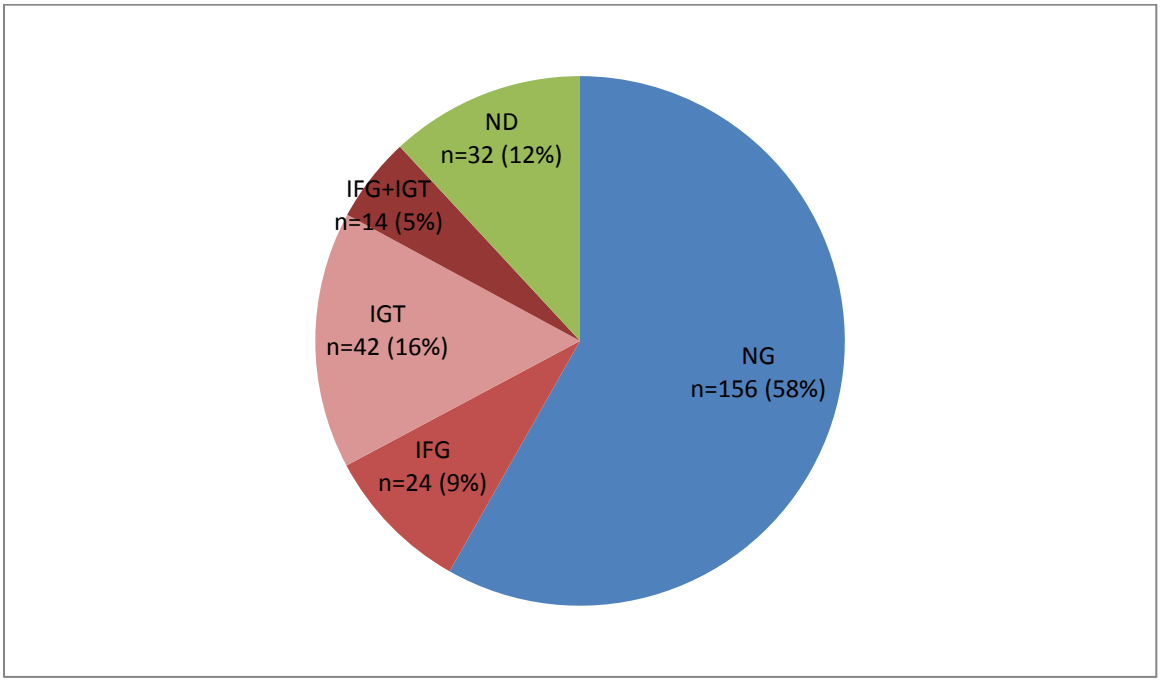


Figure 1. Glycemic state according to the OGTT. NG, Normoglycemia; ND, new diabetes.

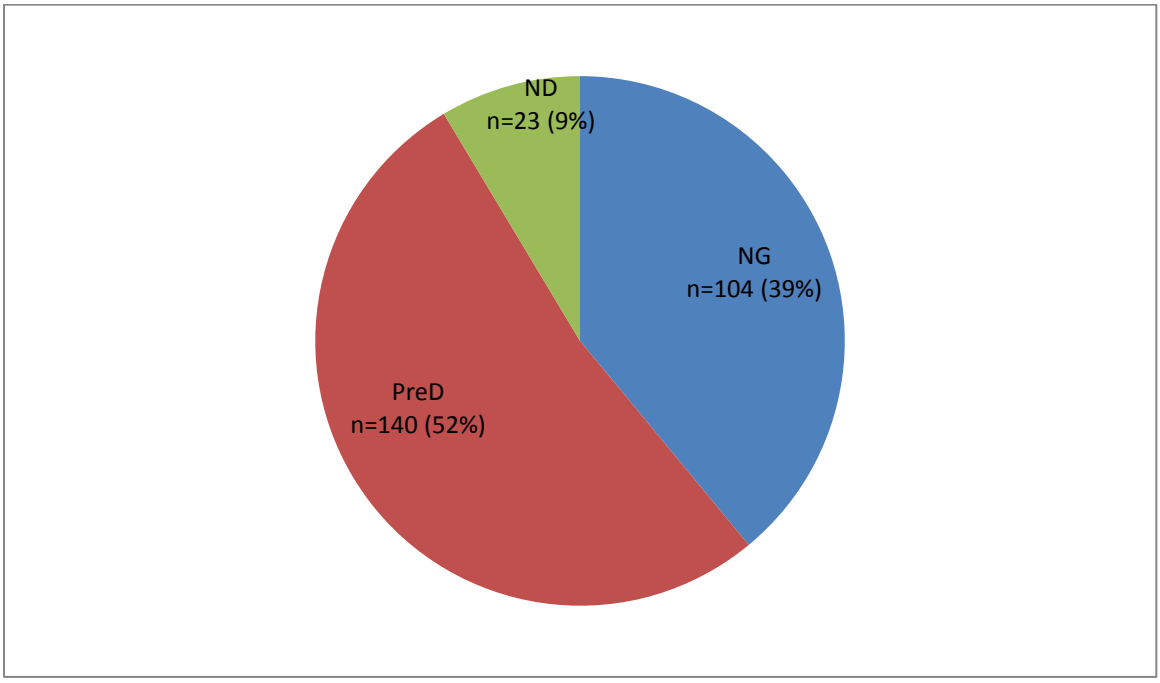


Figure 2. Glycemic state according to HbA1c. NG, Normoglycemia; ND, new diabetes; PreD, pre-diabetes.

Figure 3. Agreement between the OGTT and HbA1c for the diagnosis of diabetes

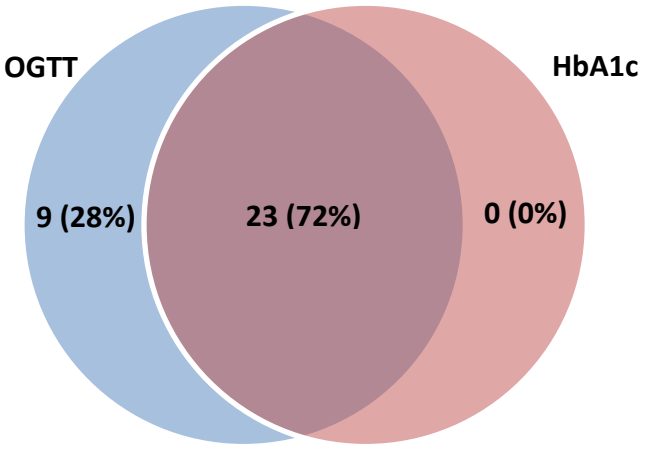
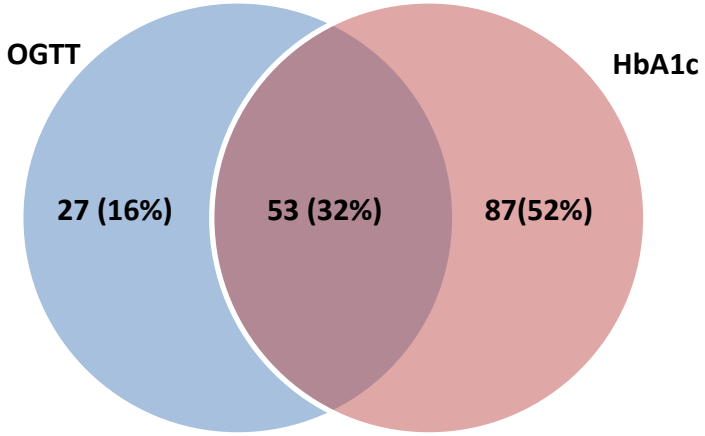


Figure 4. Agreement between the OGTT and HbA1c for the diagnosis of pre-diabetes



UNIVERSITE DE BOURGOGNE

THESE SOUTENUE PAR Mme TATULASHVILI Sopio

CONCLUSIONS

Le dépistage des troubles du métabolisme glucidique est important dans la population à haut risque CV. Nous avons souhaité étudier si l'HbA1c permettait un dépistage efficace des troubles du métabolisme glucidique en rééducation cardio-vasculaire, au décours d'un syndrome coronaire aigu (SCA). 347 patients ayant présenté un SCA récent et en réadaptation cardiaque au centre « Les Rosiers » de Dijon ont été inclus dans l'étude. Les données obtenues par HGPO, examen de référence, ont été comparées à celles obtenues par l'HbA1c. Pour un diagnostic de pré-diabète (hyperglycémie à jeun et/ou intolérance au glucose) la sensibilité diagnostique de HbA1c est faible à 65% ainsi que la spécificité (53%), avec une valeur prédictive positive de seulement 37%. Nous avons ainsi démontré que HGPO est un meilleur examen de dépistage des troubles du métabolisme glucidique après syndrome coronaire aigu en réadaptation cardiaque.

Le Président du jury,

Pr. B. VERGÈS

Vu et permis d'imprimer

Dijon, le 18 juillet 2016

Le Doyen

Pr. F. HUET

TITRE DE LA THESE:

DEPISTAGE DES TROUBLES DU METABOLISME GLUCIDIQUE EN READAPTATION CARDIAQUE: L'HbA1c A-T-ELLE UN INTERET ?

AUTEUR: SOPIO TATULASHVILI

RESUME:

Introduction : Diabète et pré-diabète sont des pathologies associées à une augmentation importante du risque cardiovasculaire (CV). Ainsi le dépistage des troubles du métabolisme glucidique est important dans la population à haut risque CV, notamment après un syndrome coronaire aigu. L'hyperglycémie provoquée per os (HGPO) est l'examen de référence du dépistage des troubles du métabolisme glucidique, mais certains (ADA) proposent d'utiliser l'HbA1c seul pour le dépistage du diabète et du pré-diabète. Nous avons souhaité étudier si l'HbA1c permettait un dépistage efficace des troubles du métabolisme glucidique en rééducation cardio-vasculaire, au décours d'un syndrome coronaire aigu (SCA).

Patients et Méthodes : 347 patients ayant présenté un SCA récent et suivis en réadaptation cardiaque au centre « Les Rosiers » de Dijon ont été inclus dans l'étude. Une HGPO a été prescrite chez les 277 patients non diabétiques connus et réalisée chez 267 patients (96,3%). Les données obtenues par HGPO, examen de référence, ont été comparées à celles obtenues par l'HbA1c. Les patients ont été classés en 3 catégories : diabète, pré-diabète ou normoglycémie.

Résultats : Pour un diagnostic de diabète, l'HbA1c reste un examen bien adapté, avec une sensibilité de 72% et une spécificité de 100%. Les valeurs prédictives positive et négative sont élevées respectivement à 100 et 96%. Par contre, pour un diagnostic de pré-diabète (hyperglycémie à jeun et/ou intolérance au glucose) la sensibilité diagnostique de l'HbA1c est faible à 65% ainsi que la spécificité (53%), avec une valeur prédictive positive de seulement 37%. Pour le diagnostic de normoglycémie, la sensibilité de l'HbA1c est faible (48%) avec des valeurs prédictives positive et négative respectivement de 71% et 50%.

Conclusion : Nous avons démontré dans cette étude que la sensibilité et la spécificité de l'HbA1c pour dépister des troubles du métabolisme glucidique après syndrome coronaire aigu en réadaptation cardiaque sont basses et que l'HbA1c surdiagnostique le pré-diabète comparé a l'HGPO.

MOTS-CLES: Diabète, trouble du métabolisme glucidique, dépistage, rééducation cardiaque, HGPO, HbA1c