European Heart Journal (2006) 27, 2573–2579
doi:10.1093/eurheartj/ehl207

EUROPEAN SOCIETY OF CARDIOLOGY®

Clinical research
Prevention and epidemiology

The relationship between coronary artery disease and abnormal glucose regulation in China: the China Heart Survey†

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Received 25 April 2006; revised 8 August 2006; accepted 10 August 2006; online publish-ahead-of-print 19 September 2006

See page 2491 for the editorial comment on this article (doi:10.1093/eurheartj/ehl300)

KEYWORDS
China Heart Survey;
Coronary artery disease;
Impaired glucose regulation;
Oral glucose tolerance test;
Type 2 diabetes

Aim The aim of this article is to characterize the glucometabolic state of patients with coronary artery disease (CAD) in China.
Methods and results This multicentre study recruited 3513 patients hospitalized for CAD, of whom 35.1% were admissions for acute CAD and 64.9% were elective admissions for CAD. At entry, 1153 patients had known type 2 diabetes and 97 had newly diagnosed diabetes [fasting plasma glucose level (FPG) $\geq$7.0 mmol/L]. Oral glucose tolerance tests (OGTTs) performed in the remaining patients revealed that 26.9% had diabetes and 37.3% had impaired glucose regulation (IGR). The prevalence of abnormal glucose regulation (AGR) was similar in the acute and elective admissions groups. Overall, the proportion of patients with diagnosed diabetes increased from 32.8% at baseline to 52.9% post-OGTT analysis. In total, 87.4% of patients with IGR and 80.5% of patients with diabetes would have remained undiagnosed if OGTTs had not been performed.
Conclusion AGR is common in patients with CAD. The prevalence of AGR is underestimated by FPG testing alone. OGTTs should be routinely used to assess the glucometabolic state of patients with CAD. Individuals identified with IGR or type 2 diabetes should receive treatment to reduce the progression of AGR and associated complications.

Introduction

People with type 2 diabetes have twice the annual mortality rate of non-diabetic individuals, and this increased rate is primarily owing to cardiovascular disease (CVD).[1] For example, a recent meta-analysis showed that the rate of fatal coronary artery disease (CAD) is higher in diabetic individuals than in non-diabetic individuals (5.4 vs. 1.6%).[2] Furthermore, the incidence and severity of CAD events are higher in diabetic individuals.[1] Results from large cohort studies indicate that individuals with pre-diabetes also have an increased risk of cardiovascular events[3] and mortality,[4] implying that hyperglycaemia is a continuous risk factor for CVD. As the numbers of individuals with type 2 diabetes and the pre-diabetic condition, impaired glucose tolerance (IGT), will account for 6 and 9% of the world's adult population, respectively, by 2025,[5] the number of patients requiring cardiovascular care will increase in the future.

The Glucose Tolerance in Patients with Acute MI (GAMI) Study showed that a substantial proportion of patients with acute MI have undiagnosed abnormal glucose regulation (AGR).[6] The Euro Heart Survey demonstrated that AGR is common, and usually undiagnosed, in patients with CAD.[7] Glucometabolic state at hospital admission for a cardiovascular event is an important indicator of long-term outcome in diabetic and pre-diabetic patients.[8–10] Moreover, strict glucometabolic control has been shown to improve survival in diabetic patients with acute MI.[8] Evidence, therefore, suggests that glucometabolic state should be assessed in patients with CAD before hospital discharge.

This study was prompted by interest in the relationship between AGR and CVD and in the high prevalence of undiagnosed AGR in patients with CAD demonstrated in the Euro Heart Survey. The main objectives of this China Heart Survey were to assess the prevalence of AGR in adult patients with CAD in China and to provide evidence to encourage an improvement in CAD management strategies in patients with CAD.

Methods

Patients and data collection

The study involved 52 centres in seven cities in China. Recruitment took place from 1 June to 31 August 2005. All patients admitted to hospital cardiovascular wards were screened for CAD. All patients

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†The institutions at which this study was carried out are listed in the Appendix.

were assessed, investigated, and treated at the discretion of their physician-in-charge according to the usual institutional practice. Individuals with type 1 diabetes were excluded from the study.

Data were collected by means of a case record form, which recorded demographic data, medical history, CAD diagnosis, and treatment for glucometabolic abnormalities. Body measurements, blood pressure, blood glucose and lipid levels, urine albumin level, and smoking status were also recorded. Hypertension was defined as systolic blood pressure $\geq$140 mmHg, and/or diastolic blood pressure $\geq$90 mmHg, or current antihypertensive treatment. Hyperlipidaemia was defined as total cholesterol $\geq$5.20 mmol/L, and/or HDL-cholesterol $\leq$0.90 mmol/L, and/or LDL-cholesterol $\geq$3.12 mmol/L, and/or triglycerides $\geq$1.69 mmol/L, or undergoing current lipid-lowering treatment.

The study complies with the Declaration of Helsinki. The data collection protocol was approved by the Beijing University Research Ethics Committee. All participants signed informed consent statements that allowed access to their medical records.

Classification and diagnosis of CAD

'Acute' admissions were non-scheduled hospital admissions because of, or related to, acute coronary syndromes (ACSs), aggravated symptoms of heart failure or arrhythmias owing to CAD. 'Elective' admissions were scheduled hospital consultations for diagnostic procedures, treatment adjustments, or elective interventions related to CAD.

CAD was defined on clinical grounds, supported by at least one objective finding including ischaemic changes or previous MI in electrocardiography, abnormal stress tests (electrocardiography, scintigraphy, or echocardiography) indicating MI, a coronary angiogram revealing >50% stenosis of the lumen diameter in any major coronary artery, or history of revascularization procedures (percutaneous coronary intervention or coronary artery bypass grafting). CAD diagnosis was classified as stable angina pectoris, previous MI, and ACS. ACS included unstable angina pectoris, ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI).

Glucometabolic state measurements

Previously known type 2 diabetes was defined as a diagnosis based on the World Health Organization classifications[11] and established according to routines at the participating centres. Fasting plasma glucose (FPG) levels were recorded in all patients on enrolment or in the morning of the day following hospital admission. For patients admitted with acute CAD, FPG measurements were repeated in stable conditions prior to discharge from hospital.

All patients without previously known diabetes or newly diagnosed diabetes (FPG $\geq$7.0 mmol/L in two consecutive tests) underwent a standard oral glucose tolerance tests (OGTTs) (75 g anhydrous glucose in 250–300 mL water[11]) as soon as they were in a stable condition, prior to hospital discharge or within 2 months following the initial consultation. The safety of acute glucose exposure was considered before conducting the OGTT. Glucose concentrations in venous plasma were measured according to local routines.

Classification of glucometabolic state was based on FPG test result or OGTT results when performed. Plasma glucose levels were measured at the start of the OGTT (0 min) and at 2 h post-challenge (2 h). FPG test result classifications were normal fasting glucose (<6.1 mmol/L), impaired fasting glucose (IFG; 6.1–6.9 mmol/L), and type 2 diabetes ($\geq$7.0 mmol/L). OGTT result classifications, based on 0 min and 2 h values, respectively, were normal glucose tolerance (<6.1 and <7.8 mmol/L), isolated IFG (I-IFG; 6.1–6.9 and <7.8 mmol/L), IFG (6.1–6.9 and <11.1 mmol/L), isolated IGT (I-IGT; <6.10 and 7.8–11.0 mmol/L), IGT (<7.0 and 7.8–11.0 mmol/L), combined glucose intolerance (CGI; 6.1–6.9 and 7.8–11.0 mmol/L), isolated fasting hyperglycaemia (IFH; $\geq$7.0 and <11.1 mmol/L), isolated postchallenge hyperglycaemia (IPH; <7.0 and $\geq$11.1 mmol/L), combined hyperglycaemia (CH; $\geq$7.0 and $\geq$11.1 mmol/L), and type 2 diabetes ($\geq$7.0 or $\geq$11.1 mmol/L). As such, IFG = I-IFG + CGI, IGT = I-IGT + CGI, and type 2 diabetes = IFH + IPH + CH. Impaired glucose regulation (IGR) refers to the two pre-diabetic conditions, IFG and IGT, and AGR refers to type 2 diabetes and IGR.

Statistics

All case record form data were entered into two Epidata 3.02 databases by different people. The two databases were compared, and any necessary corrections made. The data were analysed using SPSS statistical software 12.0. The differences in continuous variables between groups were examined by the Wilcoxon (Mann–Whitney) rank sum test. The differences in discrete variables between groups were tested by the Pearson χ^2 test. The Jonchkeere–Terpstra test was used to evaluate ordered differences between groups.

Results

Patient group

Case record forms were collected for 3687 patients. A group of 174 patients were excluded owing to protocol violations (*Figure 1*). Analysis was carried out for 3513 patients, of whom 1234 (35.1%) were acute admissions and 2279 (64.9%) were elective admissions.

Most of the patients (66.6%) enrolled were male (*Table 1*). The average age was 69 years; the female patients were on average older than the male patients ($P < 0.01$). Weight, highest previous weight, waist circumference, and smoking status were significantly higher in male than in female patients ($P < 0.05$). Systolic blood pressure was significantly

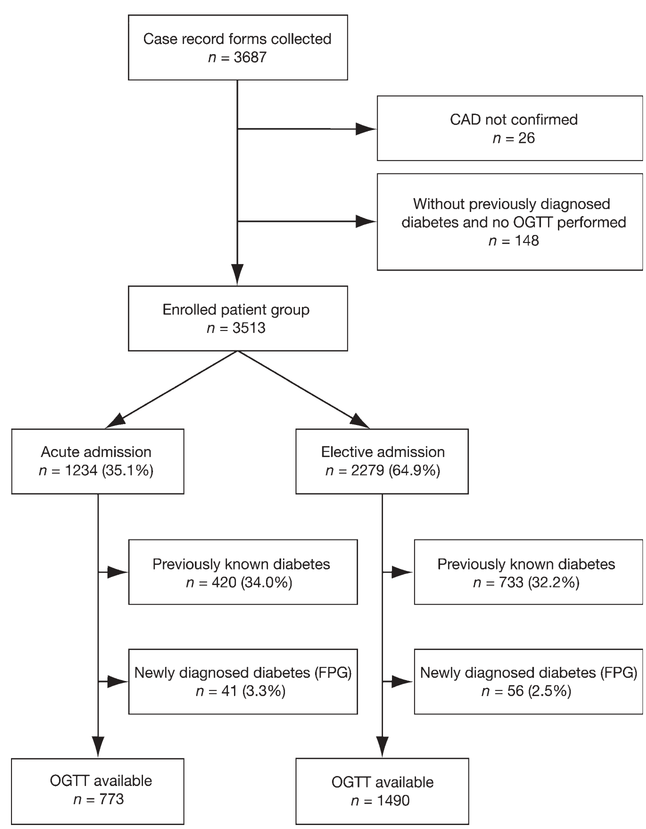

Figure 1 China Heart Survey patients.

Table 1 Patient baseline demographics

	Male (n =2341)	Female (n =1172)	Total (n =3513)	P-value
Age (years)	68 (56–75)	71 (65–77)	69 (59–76)	<0.01
Weight (kg)	70 (64–77)	60 (53–66)	67 (60–75)	<0.05
Highest previous weight (kg)	75 (68–80)	65 (58–70)	71 (64–80)	<0.05
Body mass index (kg/m^2)	24.4 (22.3–26.3)	24.1 (21.7–26.7)	24.2 (22.1–26.4)	0.083
Waist circumference (cm)	90 (85–98)	88 (80–94)	90 (83–97)	<0.05
Systolic blood pressure (mmHg)	130 (120–145)	138 (120–150)	130 (120–150)	<0.001
Diastolic blood pressure (mmHg)	80 (70–85)	80 (70–85)	80 (70–85)	0.607
Smoking status (%) (never/former/current)	30/42/28	91/6/3	50/30/20	<0.05

Data are median (lower–upper quartiles) unless otherwise stated.

Table 2 CAD diagnosis and baseline medical history

	Acute admission (n =1234)	Elective admission (n =2279)	Total (n =3513)	P-value
Diagnosis of CAD				
Stable angina pectoris	132 (10.7)	759 (33.3)	891 (25.4)	
Previous MI	205 (16.6)	555 (24.4)	760 (21.6)	
ACS	1026 (83.1)	1219 (53.5)	2245 (63.9)	
Unstable angina pectoris	378 (36.8)	1048 (86.0)	1426 (63.5)	
STEMI	485 (47.3)	118 (9.7)	603 (26.9)	
NSTEMI	163 (15.9)	53 (4.3)	216 (9.6)	
Medical history				
Heart failure	380 (30.8)	629 (27.6)	1009 (28.7)	0.046
Stroke	173 (14.0)	208 (9.1)	381 (10.8)	<0.001
Type 2 diabetes	420 (34.0)	733 (32.2)	1153 (32.8)	0.259
Hypertension	861 (69.8)	1614 (70.8)	2475 (70.5)	0.516
Hyperlipidaemia	278 (22.5)	679 (29.8)	957 (27.2)	<0.001
Family history of type 2 diabetes	82 (6.6)	136 (6.0)	218 (6.2)	0.427
Family history of hypertension	233 (18.9)	489 (21.5)	722 (20.6)	0.071

Data are number of patients (%).

higher in female patients than in male patients. The numbers of male and female patients were similar in the acute and elective admission groups and in the different glucometabolic groups.

ACS was the most common diagnosis at admission for CAD (*Table 2*). There was a significant difference between the proportions of ACS in the acute and elective admission groups (χ^2 =581.89, $P < 0.001$). STEMI (47.3%) was the most common diagnosis in the acute admission group, and unstable angina pectoris (86.0%) was the most frequent diagnosis in the elective admission group. There was no significant difference in the proportion of patients with known diabetes between the acute and elective admission groups (χ^2 =1.27, $P = 0.2592$). Hypertension was common in both patient groups.

Glucometabolic state

Patients with previously known type 2 diabetes (n =1153) and those with newly diagnosed diabetes (n =97; FPG ≥7.0 mmol/L in two consecutive tests) did not undergo an OGTT. The remaining 2263 patients underwent OGTTs (OGTT cohort) to assess their glucometabolic state.

The majority (91.3%) of the patients with previously known diabetes were receiving antidiabetes therapy. The median (lower–upper quartile) FPG level in this patient group was 7.0 mmol/L (5.7–8.7 mmol/L).

A further 609 (26.9%) patients in the OGTT cohort were found to have type 2 diabetes (*Table 3*). The overall proportion of patients diagnosed with diabetes therefore increased from 32.8% (n=1153) at baseline to 52.9% (n =1859) following the OGTT analysis. IGR was detected in 844 (37.3%) patients in the OGTT cohort (*Table 3*).

Analysis of glucometabolic state

The glucometabolic state of the OGTT cohort determined using both 0 min and 2 h plasma glucose values was compared with that determined using only the 0 min value. The proportion of patients with AGR was substantially higher in the analysis that included both plasma glucose values (*Figure 2*). Without the post-challenge data provided by the OGTTs, most patients with AGR in the acute (437/517; 84.5%) and elective (791/936; 84.5%) admission groups would have remained undiagnosed. In total, 87.4% (738/844) of patients with IGR and 80.5% (490/609) of patients with diabetes in the OGTT cohort would not have been diagnosed.

In the OGTT cohort, the prevalences of IGR (χ^2 =1.58, $P = 0.2090$) and newly diagnosed diabetes (χ^2 =0.4862, $P = 0.4856$) were similar in the acute and elective admission

Table 3 Glucometabolic state of the OGTT cohort

Glucometabolic state	Acute admission (n =773)	Elective admission (n =1490)	Total (n =2263)
Normal glucose regulation	256 (33.1)	554 (37.2)	810 (35.8)
IGR	302 (39.1)	542 (36.4)	844 (37.3)
I-IFG	13 (1.7)	18 (1.2)	31 (1.4)
IFG	35 (4.5)	71 (4.8)	106 (4.7)
I-IGT	267 (34.5)	471 (31.6)	738 (32.6)
IGT	289 (37.4)	524 (35.2)	813 (35.9)
CGI	22 (2.8)	53 (3.6)	75 (3.3)
Type 2 diabetes	215 (27.8)	394 (26.4)	609 (26.9)
IFH	10 (1.3)	9 (0.6)	19 (0.8)
IPH	170 (22.0)	320 (21.5)	490 (21.7)
CH	35 (4.5)	65 (4.4)	100 (4.4)

Data are number of patients (%).

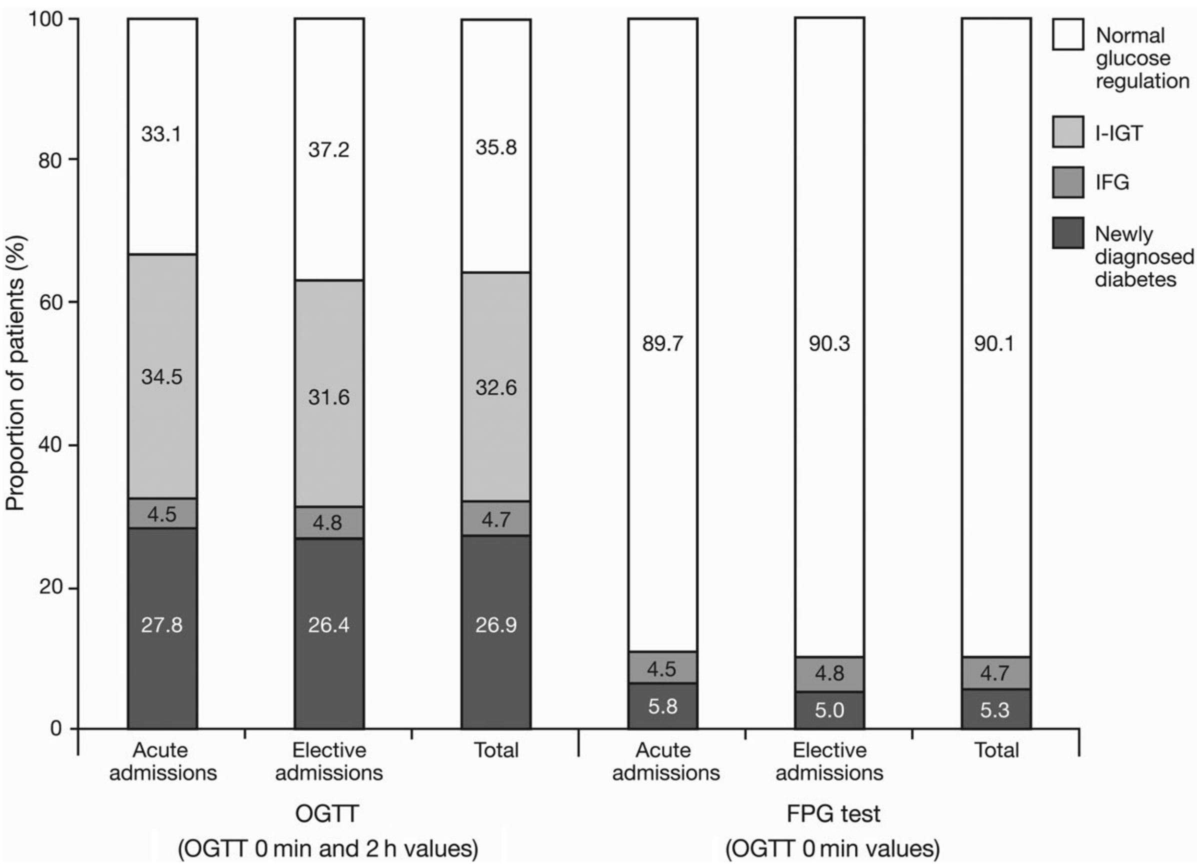

Figure 2 Comparison of glucometabolic state determined by OGTT (OGTT 0 min and 2 h values) and FPG test (OGTT 0 min values only).

groups (*Table 3*). Overall, there was no significant difference in glucometabolic state (normal glucose regulation, IGR, diabetes) between the acute and elective admission groups (χ^2 =3.6927, $P = 0.158$). There were also no significant differences in glucometabolic state between the three types of CAD diagnosis (χ^2 =8.361, $P = 0.079$) and between the three types of ACS diagnosis (χ^2 =0.987, $P = 0.913$). Overall, there was no significant difference in glucometabolic classification (normal glucose regulation, IGR, known diabetes, new FPG diabetes, new OGTT diabetes) between the three types of CAD diagnosis ($\chi^2 = 15.648$, $P = 0.048$) or between the three types of ACS diagnosis (χ^2 =8.902, $P = 0.351$).

Worsening glucometabolic state was associated with significant increases in systolic blood pressure, and serum creatinine, glycosylated haemoglobin A1c (HbA1c), and triglyceride levels, and a significant decrease in HDL-cholesterol level (*Table 4*).

Discussion

High prevalence of AGR in patients with CAD

The estimated prevalences of diabetes and IGT in the Western Pacific Region in 2003 were 3.1 and 5.7%, respectively.[5] In contrast, the prevalences of type 2 diabetes and

Table 4 Baseline patient characteristics by glucometabolic state (*n* =3513)

Clinical characteristic	Normal glucose regulation	IGR	Type 2 diabetes	*P*-value
Systolic blood pressure (mmHg)	130 (120–140)	130 (120–150)	135 (120–150)	<0.001
Diastolic blood pressure (mmHg)	80 (70–83)	80 (70–86)	80 (70–85)	0.082
Serum creatinine (μmmol/L)	86 (72–100)	86 (74–104)	88 (73–107)	<0.001
HbA1c (%)	5.5 (5.1–5.9)	5.7 (5.3–6.1)	6.6 (7.0–7.6)	<0.001
Total cholesterol (mmol/L)	4.37 (3.72–5.12)	4.46 (3.73–5.20)	4.47 (3.76–5.20)	0.683
LDL-cholesterol (mmol/L)	2.55 (2.09–3.15)	2.64 (2.06–3.20)	2.59 (2.07–3.09)	0.700
HDL-cholesterol (mmol/L)	1.10 (0.91–1.31)	1.07 (0.91–1.28)	1.04 (0.86–1.24)	<0.001
Triglyceride (mmol/L)	1.36 (0.96–1.92)	1.43 (1.03–2.10)	1.58 (1.08–2.29)	<0.001

Data are median values (lower–upper quartiles). *P*-values are for glucometabolic trend and are from age- and sex-adjusted analyses.

IGR in the China Heart Survey were 52.9 and 24.0%, respectively. Most (2703/3513; 76.9%) patients in this study had AGR. In addition to the 32.8% of patients with previously known diabetes, a further 20.1% of the study population had newly diagnosed diabetes. These proportions are markedly higher than those reported in a Chinese population-based survey that assessed the prevalence of type 2 diabetes in middle-aged and elderly individuals (4.6% previously known diabetes, 10.3% newly diagnosed diabetes).[12] A recent Austrian study, which enrolled patients undergoing elective coronary angiography for suspected CAD, reported that 85% of the study population had AGR.[13] After analysis, the prevalence of AGR was found to be significantly higher in the patients with confirmed CAD than in those without a confirmed diagnosis. Collectively, these data suggest that AGR is considerably more common in patients with CAD than in the general population.

Most cases of AGR (1550/2703; 57.3%) were undiagnosed at the start of the China Heart Survey. In the OGTT cohort, 66.9% of patients admitted for acute CAD were shown to have undiagnosed AGR. This finding is similar to that reported by the GAMI Study, which enrolled patients with acute MI and without previously known diabetes. OGTTs showed that 66% of the GAMI population had undiagnosed AGR at discharge from hospital and that a similar proportion still had AGR 3 months later.[6] The prevalence of AGR was significantly higher than that reported in an age- and sex-matched control group (35%),[14] and long-term follow-up showed that AGR was significantly associated with an increased risk of future cardiovascular events.[10]

The proportion of patients known to have type 2 diabetes at baseline in the China Heart Survey (32.8%) is similar to that reported in the Euro Heart Survey (31%)[7] and the Austrian study (32%).[13] However, the proportions of patients with newly diagnosed diabetes or IGR, as diagnosed by OGTT, were generally higher in the China Heart Survey. This suggests that AGR is more common in patients with CAD in China than in Europe and that glucometabolic testing is less frequently conducted in such patients in China.

The mean body mass index was lower in the China Heart Survey population (24.2 kg/m^2) than in the Euro Heart Survey population (27.4 kg/m^2),[7] despite AGR being more common in the former group. There is growing evidence that metabolic and cardiovascular risk profiles are different in Asian and Caucasian individuals and the thresholds for diagnosing obesity are lower in Asian individuals.[15] Data from this study therefore imply that, after metabolic considerations, AGR is distinctly more common in patients with CAD in China than in Europe.

OGTT as a diagnostic tool in patients with CAD

In this study, the prevalence of AGR identified by FPG tests only was 9.9%, whereas the actual prevalence of AGR was 64.2% in the OGTT cohort alone. Using only FPG tests to assess glucometabolic state would therefore have resulted in most patients (84.5%) with AGR remaining undiagnosed.

The Euro Heart Survey reported that approximately two-thirds of patients with AGR would have been undiagnosed if FPG tests only had been performed.[7] In the Austrian study, 59% of patients with newly diagnosed AGR had fasting blood glucose levels below 5.5 mmol/L and so would have remained undiagnosed without the performance of OGTTs.[13] The investigators of these studies recommend performing OGTTs in the comprehensive management of patients with CAD and those scheduled for elective coronary angiography, respectively. Furthermore, the GAMI Study demonstrated that it is possible to determine the glucometabolic state of patients with acute MI by an OGTT performed as early as within a few days of the event and before hospital discharge.[16] Given the association between AGR and poor patient outcome,[3,10,17,18] and the suggestion that diabetes itself contributes to the severity of CAD,[19] it is essential that OGTTs be performed to fully disclose the glucometabolic state of high-risk patients.

Several studies in a range of patient populations have shown that post-challenge hyperglycaemia measures are better predictors of cardiovascular morbidity and mortality than fasting hyperglycaemia measures.[20–22] The inclusion of OGTT data in a model based on FPG test data has been shown to significantly improve the prediction of coronary heart disease (CHD) and cardiovascular mortality, whereas the inclusion of FPG test data in a model based on OGTT data had no significant effect.[23] In another study, individuals with I-IGT and CGI had a higher prevalence of CHD risk factors than those with I-IFG.[24] This association remained when the lower threshold for the FPG test was reduced to 5.6 mmol/L. These studies add credibility to the use of the OGTT for the assessment of glucometabolic state of patients with CAD. Even after considering the limitations of the OGTT,[25] this test remains the most valuable tool for the early identification of individuals with AGR and those at increased risk for both worsening glucometabolic state and future cardiovascular events.[25]

Although this and the other studies described earlier indicate that OGTTs can be safely performed in patients with CAD and no known diabetes, the safety of these high-risk individuals must be considered when administering an acute glucose load. Given that AGR is common in patients with CVD, the presence of CVD should alert physicians to perform an OGTT when the patient is stable and initiate antihyperglycaemia therapy if indicated.

Patient selection

The question of whether the patient sample is an accurate representation of the actual patient population can be raised when a survey is conducted. The opportunity to monitor the inclusion process may be reduced in a survey compared with a clinical trial. The patients in this study were recruited in a hospital-based setting. In general, hospitalized patients represent more severe cases than non-hospitalized individuals, and selection bias may therefore exist in hospital-based surveys. In epidemiological studies, new incidence cases are the best representation of the general patient population. Therefore, acute admission patients, especially those who are new incidence cases, are representative of the general population of patients with CAD. In this study, there was no statistical difference in glucometabolic state between acute and elective admission groups or between different CAD diagnoses. This indicates that patient selection was not a factor in determining the outcomes of this study. In addition, the size and design of the study make it reasonable to assume that the patterns revealed accurately represent the actual clinical situation in China.

This survey is a cross-sectional study. A prospective study is required to assess the mortality rates in patients with newly diagnosed AGR. Clinical trials are warranted to investigate the effects of lifestyle modification and pharmacological intervention in this patient population.

Conclusions

AGR is common in patients admitted to hospital with CAD in both acute and elective conditions and is undiagnosed in the majority of these patients. As AGR is a strong risk factor for cardiovascular events, earlier detection will allow clinicians to institute more rigorous control of patients' hyperglycaemia and therefore improve outcomes. In particular, early identification and treatment of individuals with IGR will reduce the risks of progression of AGR and associated complications. An OGTT should be added to standard risk-evaluation procedures in the hospital setting and is an important tool in the planning of secondary prevention treatment strategies in high-risk individuals.

Acknowledgements

The involvement of the study coordinators and their hospitals is acknowledged (see Appendix). The principal writer of the manuscript was J.-M.Y. Editorial assistance was provided by Gardiner-Caldwell London. The study was supported by an unrestricted research grant from Bayer HealthCare Company Ltd.

Conflict of interest: none declared.

Appendix

Beijing Tong Ren Hospital: Yushen Xu; Beijing He Ping Li Hospital: HaiYan Li, Liping E; Beijing General Hospital of Beijing Military Area Command of PLA: Lili Niu, Xian Wang; Beijing Shi Ji Tan Hospital: Shuixiang Yang, Kaiying Jia; Beijing Chui Yang Liu Hospital: Li Li, Xiaomin Zheng; The People's Hospital of Beijing University: Ningling Sun, Mingzhu Yan, Hongyi Wang; Chinese PLA General Hospital: Li Fan; Hua Cui; Beijing Ji Shui Tan Hospital: Huayi Sun; Liwen Fan; Beijing Hospital: Qing He; Fu Liu; Third Hospital of Beijing University: Fuchun Zhang, Hui Zeng; Peking Union Medical College Hospital: Xiaowei Yan, Ling Li; Xuanwu Hospital of the Capital University of Medical Sciences: Jiaping Wei; Fuxing of the Capital University of Medical Sciences: Xiaoming Zhuang; China–Japan Friendship Hospital: Yuannan Ke, Xiaoli Wang; Beijing Friendship Hospital Affiliate of Capital University of Medical Sciences: Luhua Shen, Hongwei Li; Peking University First Hospital: Yong Huo, Baowei Zhang; Beijing An'zhen Hospital of the Capital University of Medical Sciences: Yundai Chen, Hua Chen; Shanghai First People's Hospital: Qiuyan Dai, Ying Wu; Tongji Hospital of Tongji Medical Lollege: Mingzhong Zhao, Yan Xing; East Hospital of Shanghai Tongji University: Shifu Zhang, Lan Ma; Xinhua Hospital of Shanghai Second Medical University: Yigang Li, Yuehua Li; East Hospital of Shanghai: Mingcheng Zhou, Hongman Huang; Shanghai Shuguang Hospital: Hongjun Fang, Meiguang Jiang; Shanghai Huadong Hospital: Minde Yin, Zhongru Tan; Changhai Hospital of Shanghai Second Military Medical University: Rongliang Xu, Xing Zheng; Changzheng Hospital of Shanghai Second Military Medical University: Jiguang Wu, Yusheng Ren; Shanghai Tenth People's Hospital: Yawei Xu, Yongqi Wang, Ji Zhang; The Ninth People's Hospital of Shanghai Sencond Medical University: Tuyao Wu, Jian Wang; Ruijin Hospital of Shanghai Jiaotong University Health Science Center: Xiaoying Luo, Hongzhen Wang; Huashan Hospital of Fudan University: Weihu Fan, Yuewen Xi; Renji Hospital of Shanghai Second Medical University: Ben He, Hongbo Li, Yongping Du; Shanghai Jiaotong University Affiliated Sixth People's Hospital: Meng Wei, Zhigang Lu; Nanjing Drum Tower Hospital: Biao Xu, Xiaohong Li; Jiangsu Province People's Hospital: Kejiang Cao, Chunjian Li; Shao Yi Fu Hospital of The Zhejiang University: Jian'an Wang, Youqi Fan; The First People's Hospital of Hangzhou: Ningfu Wang, Zhong Yu; The Third Hangzhou Hospital of Zhejiang University of Traditional Chinese Medicine: Ling Lin, Liping Ma; First Hospital of Zhejiang University: Junzhu Chen, Xiaogang Guo; The Second Hospital of Zhejiang University: Jing Xu, Shan Chen; Zhejiang Province People's Hospital: Baiming Qu, Naiji Shen; Zhejiang Hospital: Farong Shen; The First Affiliated Hospital of Zhongshan University: Qunying Zeng, Xiuren Gao; Guangzhou First Municipal People's Hospital: Guanglian Li, Yi Luo; The First Affiliated Hospital of Guangzhou Medical College: Zhaochu He, Biru Ou; The First Affiliated Hospital of Guangzhou College of Traditional Chinese Medicine: Wei Wu; The Second Affiliated Hospital of Guangzhou Medical College: Shiming Liu, Minsong Xiong; Guangzhou Province People's Hospital: Luyuan Chen; The First Center Hospital of Tianjin: Qun Dang, Dasheng Xia; Tianjin Chest Hospital: Genyi Sun, Gang Chen, Bingrang Zhao, Qin Qin; The General Hospital of Tianjin Medical University: Zheng Wan, Yuemin Sun; Tongji Hospital of Tongji Medical College: Hesong Zeng, Qinggang Xie; People's Hospital of Wuhan University: Xuejun Jiang, Jun Liu.

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