Admission insulin resistance index in nondiabetic patients with acute coronary syndrome: clinical and angiographic features

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Background
The clinical implication of insulin resistance has extended beyond diabetes mellitus to include ischemic heart disease, dyslipidemia, hypertension, and features of metabolic syndrome. Nondiabetic patients with acute coronary syndrome and elevated admission insulin resistance index (AIRI) may have certain clinical angiographic and therapeutic strategies.

Objectives
The study aimed to illustrate the value of AIRI in nondiabetic patients with acute coronary syndrome and identify the angiographic coronary artery disease severity in relation to AIRI.

Study design
This study was cross-sectional in design.

Patients and methods
This study included 120 nondiabetic patients presenting with acute chest pain who were admitted to the coronary care unit. Admission glucose and insulin concentrations were measured and the AIRI was calculated. ECG was carried out and the patients were grouped as follows: those with unstable angina (UA) (40 cases) and those with acute myocardial infarction (AMI) (40 cases). They were compared with 40 patients with stable angina (SA) and a group of controls (40 individuals). The studied participants were examined clinically stressing on the other criteria for insulin resistance syndrome. The following laboratory tests were undertaken, including random plasma glucose, HBA1-c, lipid profile, cardiac enzymes (CK-MB, LDH), and troponin T. An angiographic study was carried out for patients from each diseased group and for 20 patients who had suffered a first attack in the SA group.

Results
AIRI was significantly elevated in the AMI (3.9 ± 0.1) and UA (3.01 ± 0.2) groups when compared with the SA and control groups. AIRI was significantly higher in the AMI group when compared with the UA group. Coronary angiography revealed one coronary vessel involvement in 10, 20, and 10% of patients in the SA, UA, and AMI groups, respectively, whereas two-vessel involvement was detected in 0, 30, and 60% of patients in the SA, UA, and AMI groups, respectively. Three-coronary-vessel disease was not detected in the SA group but was evident in 5% of UA and 30% of AMI patients. The relation of AIRI in the studied groups on the basis of the χ^2-test revealed significant elevation of AIRI in the AMI and UA groups. Cases with three-vessel affection demonstrated higher AIRI.

Conclusion
Elevated AIRI can predict coronary artery events in nondiabetic patients with acute chest pain. Multiple coronary vessel involvement is common in such cases and suitable planned invasive therapeutic strategies have to be considered.

Keywords:
acute coronary syndrome, admission insulin resistance index, insulin resistance

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Introduction

Insulin resistance (IR) is one of the most important public health problems of the 21st century [1] and interest in identifying clinical syndromes with an IR background has increased since the availability of insulin sensitizer agents [2]. It is now considered the basic etiopathogenetic factor for coronary artery disease (CAD), hypertension, dyslipidemia, and endothelial dysfunction [3].

In response to IR, compensatory hyperinsulinemia takes place in a trial to prevent the onset of type 2 diabetes mellitus, although potentially predisposing to many cardiovascular diseases, essential hypertension, fatty liver disease, and sleep apnea syndrome [4].

Clavijo *et al.* [5] concluded that IR in nondiabetic patients with acute myocardial infarction (AMI) is associated with larger infarct size and more in-hospital complications.

Sinha *et al.* [6] concluded that homeostasis model assessment-insulin resistance (HOMA-IR) measurement in patients admitted with myocardial infarction (MI) is an important predictor of poor outcome and is superior to admission glucose measurement. Admission insulin resistance index (AIRI) is a method for measuring IR [admission serum insulin (μIU/ml) × admission plasma glucose (mmol/l)/22.5] [7]. AIRI is derived in the same way as the fasting IR, which correlates significantly with the HOMA of IR based on fasting plasma glucose and insulin concentrations [8].

Although it has been previously reported that patients admitted with IR carry a poor prognosis in coronary events [9,10,] the predictive effect of the degree of IR with its multiple confounding variables on the extent of CAD affection needs more confirmation.

Aims

The study aimed to illustrate the value of AIRI in nondiabetic patients with acute coronary syndrome (ACS), investigate the relationship of AIRI with other cardiovascular risk factors and components of metabolic syndrome (MS), and identify the angiographic CAD severity in relation to AIRI.

Design

This study was cross-sectional in design.

Subjects and methods

This study included 80 nondiabetic patients with ACS who were compared with 40 patients with stable angina (SA) and 40 control individuals. The patients presented with acute chest pain and underwent clinical examination and ECG and were admitted to the Cardiology Care Unit, Mansoura Specialized Hospital, during the period January 2010–January 2011. AIRI was calculated (plasma glucose mmol/l × plasma insulin μIU/22.5). The studied patients were examined clinically stressing on the other criteria for IRS including BMI, waist circumference, and mean arterial blood pressure (MABP). The following laboratory tests were undertaken, including random plasma glucose, HBA1-c, lipid profile [serum triglyceride (TG), cholesterol, LDL-cholesterol, HDL-cholesterol], cardiac enzymes (CK-MB, LDH), and troponin T; liver and kidney function tests were also carried out. The study protocol was approved by the cardiology ethical committee and informed consent was obtained. The patients were classified into four groups:

Group 1: SA (40 cases);
Group 2: unstable angina (UA; 40 cases);
Group 3: AMI (40 cases); and
Group 4: control volunteers of matched age and sex (40 individuals).

Exclusion criteria

Individuals with diabetes, smokers, and those with thyroid disorders, muscle disease, and clinically evident renal or hepatic disease were excluded from the study.

Angiographic studies were undertaken at random for each diseased group and for 20 patients of the SA group who had suffered their first attack. The extent of CAD was measured according to the number of major coronary arteries affected by CAD [11]. CAD was defined as stenosis of at least 50% in at least one major coronary artery [11]. The extent of CAD lesions was quantified using the number of vessels with at least 50% stenosis. Management of coronary artery lesions was undertaken individually by coronary stent or coronary artery bypass graft. Thrombolytic therapy was not tried as the patients presented more than 12 h after the onset of chest pain.

Statistical analysis

Statistical analysis was performed using the statistical package for social science program (SPSS Inc., Chicago, Illinois, USA) version 16. Qualitative data were presented as frequency and percentages. Quantitative data were examined using the Kolmogorov–Smirnov test for normal distribution of the data and when parametric, expressed as mean and SD. The Student *t*-test was used to test for difference in normally distributed quantitative data between the two groups. The Mann–Whitney *U*-test was used for comparison between two groups when data were not normally distributed. Significance was considered when the *P* value was less than 0.05.

Results

A total of 120 patients (40 cases of SA, 40 cases of UA, and 40 cases of AMI) were compared with 40 controls of matched age and sex.

The age of the studied patients ranged from 49.7 ± 3.6 to 53.9 ± 1.1 years, being significantly higher in the infracted group and the unstable (US) angina group. There were no significant differences between the SA group and the control group.

BMI was 30.1 ± 1.5 kg/m^2 in the UA and 30.4 ± 1.9 kg/m^2 in the AMI group, being significantly higher when compared with the reference and SA groups. No significant differences between the UA group and the AMI group were detected.

Waist circumference was significantly larger in the UA and AMI groups when compared with the SA and reference groups. However, an insignificant difference between the two groups with ACS was observed.

MABP was significantly increased in both UA and AMI groups when compared with the SA and control groups.

The biochemical changes in serum cholesterol, TG, HDL-C, LDL-C, and HbA1-c were insignificantly different among the studied groups. Random plasma glucose and plasma insulin were significantly higher in the UA and AMI groups when compared with the reference and SA groups.

There was insignificant difference on comparing the SA group with the control group.

The AIRI was significantly higher in the UA and AMI groups when compared with the SA and control groups ($P<0.001$). However, patients with AMI revealed significantly higher AIRI when compared with the UA group ($P<0.02$). There was insignificant difference on comparing the SA group with the control group.

Coronary angiography was performed on all patients with UA and AMI and on 20 patients from the SA group who had suffered their first attack. Significant CAD was considered when the narrowed CA was at least 50% and the number of vessels and degree of narrowing were estimated. One-coronary-vessel affection was detected in 10, 20, and 10% of patients in the AMI, UA, and SA groups, respectively. Two-vessel disease was observed in 60% of patients in the AMI group, 30% of patients in the UA group, and in 0% of individuals in the SA group. Three-vessel disease was recorded in 30% of AMI and 5% of UA patients and was not detected in the SA group. Insignificant narrowing of coronary vessels was detected in 45% of UA cases, whereas it was not detected in the AMI group.

The AIRI (Tables 1–3) was highest (3.9 ± 0.1) in the AMI group, whereas it was 3.01 ± 0.2 in the UA and 1.5 ± 0.13 in the SA group. The calculated χ^2 showed that the higher the AIRI, the more severe the state of myocardial ischemia as regards the number of observed coronaries. The number of coronary vessels was significantly higher (three) with higher AIRI (Table 4).

Discussion

Caccamo *et al.* [12] reported that IR quantified by the HOMA index is considered the 'primum movens' for the development of MS.

IR was reported to predict cardiovascular diseases independently of other risk factors. Stubbs *et al.* [7] concluded that AIRI is significant in identifying the state of IR in nondiabetic patients with ACS. In the present study many components of MS revealed insignificant changes on comparing the different groups. Esam *et al.* [13] found an insignificant correlation between AIRI, MABP, TG, HDL-C, and serum cholesterol.

In the present study, risk factors for coronary atherosclerosis were evident. These factors are among the criteria for diagnosing MS according to the National Cholesterol Education Program and the Adult Treatment Panel III (NCEP-ATP III 2001) [14] (Table 1).

Caccamo *et al.* [12] concluded that IR detected by HOMA has an important prognostic role, with worst prognosis. Clavijo *et al.* [5] also reported that IR in AMI is associated with larger infarct size, more complications of AMI, and an increase in acute renal failure. In the present study, the AMI group had more significant elevation of CK-MB in relation to the control, SA, and US groups (Table 1).

Table 1 Demographic and biochemical characteristics of the studied groups

Parameters (mean ± SD)	Group 1 SA (40 cases)	Group 2 UA (40 cases)	Group 3 AMI (40 cases)	Group 4 conrol (40 cases)	P_1-P_2	P_1-P_3	P_1-P_4	P_2-P_3	P_2-P_4	P_3-P_4
Age (years) (range)	49.7 ± 3.6 (47–55)	50.1 ± 2.1 (46–55)	53.9 ± 1.1 (51–55)	50.2 ± 1.2 (46–54)	0.545	<0.001	0.407	<0.001	0.794	<0.001
BMI(kg/m^2) (range)	28.2 ± 1.9 (24–32)	30.1 ± 1.5 (27–33)	30.4 ± 1.9 (26–34)	25.1 ± 2.2 (21–29)	<0.001	<0.001	<0.001	0.435	<0.001	<0.001
WC (cm) (range)	105.6 ± 6.5 (92–118)	110.7 ± 7.8 (96–118)	112.2 ± 8.8 (96–128)	91.2 ± 1.8 (87–95)	<0.001	<0.001	<0.001	0.422	<0.001	<0.001
MABP (mmHg) (range)	88.4 ± 10.6 (68–108)	98.2 ± 16.4 (66–130)	100.2 ± 15.8 (70–130)	86.2 ± 10.8 (66–106)	0.002	<0.001	0.361	0.580	<0.001	<0.001
Serum cholesterol (mg/dl) (range)	158.1 ± 15.4 (128–188)	161.7 ± 19.4 (123–199)	162.1 ± 20.4 (122–202)	153.7 ± 19.4 (115–191)	0.361	0.325	0.264	0.928	0.069	0.063
TG (mg/dl) (range)	127.8 ± 17.4 (93–161)	128.2 ± 20.8 (80–168)	129.3 ± 23.4 (83–175)	120.7 ± 16.4 (88–152)	0.925	0.745	0.064	0.825	0.077	0.061
HDL-C (mg/dl) (range)	49.7 ± 8.2 (33–65)	48.7 ± 8.4 (32–64)	48.1 ± 6.1 (36–60)	50.1 ± 3.4 (43–57)	0.592	0.325	0.776	0.716	0.331	0.074
LDL-C (mg/dl) (range)	85.4 ± 12.2 (61–109)	86.1 ± 13.2 (63–112)	89.1 ± 14.9 (60–119)	83.4 ± 15.4 (53–113)	0.806	0.228	0.522	0.343	0.402	0.096
HbA1-c (%) (range)	5.5 ± 0.2 (5.1–5.9)	5.5 ± 0.4 (5.3–5.7)	5.5 ± 0.9 (5.4–5.8)	5.5 ± 0.1 (5.3–5.7)	1	1	1	1	1	1
RPG (mmol/l) (range)	5.8 ± 0.02 (5.75–5.84)	5.9 ± 0.01 (5.88–5.92)	6.0 ± 0.01 (5.98–6.02)	5 ± 0.3 (4.4–5.6)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Plasma insulin (μIU/ml) (range)	8.9 ± 3.9 (2–13.7)	10.9 ± 1.1 (8–14.2)	11.8 ± 2.4 (7.8–16.6)	8.7 ± 3.8 (1.7–14.9)	0.002	<0.001	0.817	0.034	<0.001	<0.001
AIRI (range)	1.5 ± 0.13 (1.24–1.71)	3.01 ± 0.2 (2.6–3.41)	3.9 ± 0.1 (3.7–4.1)	1.3 ± 0.9 (1.8–2.2)	<0.001	<0.001	0.168	0.026	<0.001	<0.001
Creatine kinase MB (range)	8.1 ± 1.1 (6–10.1)	15.3 ± 3.1 (9–22)	85.1 ± 7.1 (61.1–99)	6.1 ± 2.1 (2–10)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

AIRI, admission insulin resistance index; AMI, acute myocardial infarction; MABP, mean arterial blood pressure; RPG, random plasma glucose; SA, stable angina; TG, triglyceride; UA, unstable angina; WC, waist circumference.

Table 2 Frequency of affection of coronary arteries in the studied groups

	N (%)					
	SA group 1 (20 cases)	UA group 2 (40 cases)	AMI group 3 (40 cases)	P_1-P_2	P_1-P_3	P_2-P_3
One-coronary-vessel significant stenosis	2/20 (10)	8/40 (20)	4/40 (10)	0.331	1	0.210
Two coronary vessel significant stenosis	0/20 (0)	12/40 (30)	24/40 (60)	0.006	<0.001	0.007
Three-coronary-vessel significant stenosis	0/20 (0)	2/40 (5)	12/40 (30)	0.313	0.006	0.003
One-coronary-vessel insignificant narrowing	18/20 (90)	18/40 (45)	0/40 (0)	<0.001	<0.001	<0.001

AMI, acute myocardial infarction; SA, stable angina; UA, unstable angina.

Table 3 Calculated χ^2 of admission insulin resistance index in the studied groups

	SA group 1 (40 cases)	UA group 2 (40 cases)	AMI group 3 (40 cases)	Control group 4 (40 cases)	P_1-P_2	P_1-P_3	P_1-P_4	P_2-P_3	P_2-P_4	P_3-P_4
Number of cases with normal AIRI	36	16	8	40	<0.001	<0.001	0.041	0.052	<0.001	<0.001
Number of cases with elevated AIRI	4	24	32	0	<0.001	<0.001	0.041	0.052	<0.001	<0.001

AIRI, admission insulin resistance index; AMI, acute myocardial infarction; SA, stable angina; UA, unstable angina.

Table 4 The relation of number of vessels affected to admission insulin resistance index

	One CV affection 1 (12 cases)	Two CV affection 2 (36 cases)	Three CV affection 3 (14 cases)	P_1-P_2	P_1-P_3	P_2-P_3
AIRI	1.7 ± 0.1	3.3 ± 0.1	3.8 ± 0.8	<0.001	<0.001	0.023

AIRI, admission insulin resistance index; CV, cardiovascular.

In the present study, age was significantly higher in the AMI group compared with the control, SA, and US groups. Older age with increased visceral fat was associated with higher IR [15].

The significant elevation in MABP compared with the SA group in the present work is in agreement with previous reports [16,17]. It can be explained by the suggestions of McFarlane *et al.* [16] and Michinori [17] who hypothesized it to be secondary to sympathetic nervous system activation by stress of admission, to salt and water retention effects of hyperinsulinemia, and to stimulation of the renin–angiotensin system.

The significant increase in BMI and waist circumference in the ACS group and the SA group in comparison with the control group is usually associated with decreased insulin sensitivity in peripheral tissues and with reduced ability of insulin to suppress hepatic glucose production and stimulate glucose disposal in peripheral tissues. Campbell and Gerich [18] found that euglycemia is inversely correlated with BMI.

The insignificant increase in serum cholesterol, serum TG, and serum LDL-C and insignificant decrease in HDL-C in the AMI and UA groups compared with the control group are in accordance with the results of Reaven *et al.* [19], who discussed CAD in the absence of hypercholesterolemia.

The significant high elevation in AIRI in ACS is in agreement with the results of Stubbs *et al.* [7,] who found that AIRI is a simple measure of IR that correlated well with other IR indices. This simple measurement of an admission IRI makes it suitable for large-scale studies [7].

In the present study, all patients with ACS and 20 cases with first attack from the SA group underwent coronary angiography. The extent of CAD was quantified using the number of vessels with more than 50% stenosis [11]. Yoon *et al.* [10] assessed the value of IR scores in relation to angiographic CAD severity.

Sinha *et al.* [6] concluded that HOMA-IR measurement of patients admitted with AMI provides an important predictor of poor outcome and is superior to admission glucose measurement. The present study revealed that the higher the AIRI, the more the affection of coronary vessels. This is in accordance with the results of Yoon *et al.* [10], who found a higher prevalence of multiple-vessel CAD in patients with higher AIRI.

Significant angiocardiographic findings of multivessel CAD in relation to elevated AIRI may help to identify patients who could benefit from alternative early invasive strategies [6].

Cardiac myocytes in patients with CAD have resistance to insulin-mediated glucose disposal [20]. This may expose the cardiac myocytes to double jeopardy, not only to rapid depletion of low glycogen stores but to impaired glucose delivery to ischemic myocardium as well, by the IR-mediated glucose disposal. The DIGAMI study examined the effects of metabolic support using glucose–insulin–potassium infusion and subsequent infusion of insulin in diabetic patients sustaining a MI and reported a better prognosis [21].

Kragelund *et al*. [9] reported that, although AMI induces a transient decline in insulin secretion induced by an increase in the activity of the sympathoadrenal system, the high insulin level in the present study is most likely a measure of severe IR before MI.

Conclusion

AIRI is a simple measure to identify IR states. The presence of IR in ACS may have a role in identifying the extent of coronary vessel affection in nondiabetic patients, and suitable planned invasive therapeutic strategies have to be considered.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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