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Original article

Metabolic disturbances after acute vascular events: A comparative study of acute coronary syndrome and ischaemic atherothrombotic stroke

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Abstract

Objective. – This pilot study aimed to compare metabolic disturbances, particularly insulin resistance (IR) and cardiovascular risk factors (CRFs), following two types of acute vascular atherothrombotic disease events: ischaemic atherothrombotic stroke (AS); and acute coronary syndrome (ACS).

Design and methods. – A total of 110 non-diabetic patients presenting with either AS ($n = 55$) or ACS ($n = 55$) were included in our prospective comparative study, and matched for age and gender. IR was determined using the homoeostasis model assessment of insulin resistance (HOMA-IR) method, and each patient's personal and family history were also recorded.

Results. – IR was significantly higher in the ACS *vs* AS group (HOMA-IR index 2.17 ± 1.90 *vs* 1.50 ± 0.81, respectively; $P = 0.03$). The AS group had a significantly higher prevalence of personal history of hypertension (51% *vs* 31%; $P = 0.03$), while current smoking was more prevalent in the ACS group (30% *vs* 18%; $P = 0.04$). There were no significant differences between the two groups as regards any other CRFs.

Conclusion. – The distribution of CRFs varied depending on the vascular event, and metabolic disturbances differed according to the atherothrombotic disease. IR was greater after ACS than AS.

Keywords: Metabolic syndrome; Insulin resistance; Acute coronary syndrome; Stroke; Atherothrombotic disease

Résumé

Perturbations métaboliques après un accident vasculaire aigu : étude comparative entre syndrome coronaire aigu et accident vasculaire cérébral ischémique d'origine athérothrombotique.

Objectif. – Comparer les perturbations métaboliques, en particulier la résistance à l'insuline (IR) et les facteurs de risque cardiovasculaire (FRCV) après deux événements vasculaires aigus de la maladie athérothrombotique : accident vasculaire cérébral ischémique athérothrombotique (AVC-IA) ou syndrome coronaire aigu (SCA).

Méthodes. – Dans une étude pilote, 110 patients non diabétiques qui avaient présenté une AVC-IA ($n = 55$) ou un SCA ($n = 55$) ont été inclus dans une étude prospective, comparative, appariés pour l'âge et le sexe. L'IR a été déterminée en utilisant la méthode du modèle d'homéostasie de la résistance à l'insuline (HOMA-IR) et, les antécédents personnels et familiaux ont été enregistrées.

Résultats. – L'IR était significativement plus élevée dans le groupe SCA que dans le groupe AVC-IA (HOMA-IR $2{,}17 \pm 1{,}90$ versus $1{,}50 \pm 0{,}81$, $P = 0{,}03$). Dans le groupe AVC-IA, il y avait une prévalence significativement plus élevée d'antécédents personnels d'hypertension (51 versus 31 %, $P = 0{,}03$). Le tabagisme actif était plus fréquent dans le groupe SCA (30 versus 18 %, $P = 0{,}04$). Il n'y avait pas de différence significative entre les deux groupes pour les autres FRCV.

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Conclusion. – La distribution des FRCV varie en fonction de l'événement vasculaire, les perturbations métaboliques sont différentes selon la maladie athérothrombotique, l'insulinorésistance étant plus importante après un SCA qu'à la suite d'un AVC-IA.

Mots clés : Syndrome métabolique ; Insulinorésistance ; Syndrome coronaire aigu ; Accident vasculaire cérébral ; Maladie athérothrombotique ; Facteurs de risque cardiovasculaire

1. Introduction

Cerebro- and cardiovascular events are the leading cause of morbidity and mortality in industrialized countries. While acute coronary syndromes (ACSs) are caused by coronary atherosclerosis in a vast majority of cases, the risk factors for acute ischaemic atherothrombotic stroke (AS) include mainly carotid atherosclerosis as well as the presence of cardioembolic disease.

Numerous factors contribute to the development of atherosclerosis. The main ones are hypertension, dyslipidaemia, smoking, diabetes, age, male gender and abdominal obesity. There is a difference in the distribution of cardiovascular risk factors (CRFs) according to the site of the atherothrombotic complications, with hypertension more significant in the onset of ischaemic stroke [1], whereas dyslipidaemia plays a greater role in coronary patients [2]. Although the role of the metabolic syndrome (MetS) in the onset of a cardiovascular event is still being debated [3] and there are several different definitions of the syndrome, its pathophysiology is primarily linked to insulin resistance (IR). Several cohort studies have demonstrated that the MetS is associated with an increased risk of stroke [4] and coronary heart disease [5]. However, the relationship between atherothrombotic disease in the acute phase and IR is less well known. To our knowledge, no study has compared the metabolic disturbances following the two principal types of acute atherothrombotic events.

For this reason, the main objective of the present study was to compare metabolic disturbances in patients who had suffered two different consequences (AS and ACS) of a single disease (atherothrombosis). The hypothesis was that the two groups differed not only in 'conventional' CRFs, but also at the level of IR, as determined by homoeostasis model assessment (HOMA-IR), with possible prognostic implications.

2. Design and methods

This was a prospective, comparative, single-centre pilot study conducted at Grenoble University Hospital between November 2005 and November 2009. A total of 110 patients of both genders, aged 40 to 70 years (to avoid selection of a particular atherothrombotic profile) and presenting with completed AS ($n = 55$) or ACS ($n = 55$), were enrolled. As a pilot study, calculation of the number of patients in both groups could not be based on a dataset. Taking into account the capacity to recruit patients at our institution, it was decided that a total of 110 patients (55 in each group) should be included in the study. Matched for age and gender, none of them had diabetes mellitus. Diagnosis of ischaemic stroke was made on the basis of the patients' interview data, physical examination and imaging examinations (computed tomography [CT] and/or magnetic resonance imaging [MRI] scans) showing the absence of haemorrhage, but with direct signs of ischaemia. Conventional neurological tests, including ultrasound of the supra-aortic arteries, electrocardiography (ECG) monitoring and cardiac ultrasound, identified an atherothrombotic mechanism as defined by:

(1) the presence of atherosclerotic thrombosis or stenosis ($\geq 50\%$ diameter reduction, or $< 50\%$ but with plaque ulceration) in the clinically relevant extracranial or intracranial artery;
(2) the absence of acute cerebral infarction in a vascular territory other than the one pertaining to the stenosed or occluded artery;
(3) the absence of any other possible mechanism particularly in the light of normal 48-h ECG monitoring, normal transthoracic and transesophageal echocardiography, and the absence of coagulopathy.

Patients with an arterial disease other than atherosclerosis (such as arterial dissection, vasculitis or arterial spasm) were excluded. Also excluded were patients presenting with lacunar stroke.

These criteria were inspired by the Causative Classification of Stroke system, an evidence-based classification algorithm for acute ischaemic stroke [6]. An ACS with persistent ST-segment elevation was diagnosed on the basis of patient interview data and ECG signs of acute myocardial ischaemia. Calculation of the US National Institutes of Health Stroke Scale (NIHSS) was done for each AS patient to evaluate the severity of the ischaemic stroke [7]. Ethical approval was obtained from the local ethics committee, and all participants gave their informed consent. The registration (ClinicalTrials.gov) trial number for this study was NCT00926874.

The non-inclusion criteria were:

(1) for patients in the ACS group, stroke within the previous 6 months (to diminish the role of acute biological and vascular modifications arising in the initial phase of the two types of atherothrombotic events) or coronary bypass performed between the start of hospitalization for ACS and inclusion;
(2) for patients in the AS group, cardioembolic disease (diagnosis left to the assessment of the neurologist who treated the stroke) or ACS within the previous 6 months;
(3) for all patients, haemodynamic instability, atrial fibrillation or flutter, frequent extrasystoles (> 10/min, to obtain valid 24-h ambulatory blood pressure monitoring [ABPM]) and