Morphological changes of the internal carotid artery: prevalence and characteristics. A clinical and ultrasonographic study in a series of 19 804 patients over 25 years old

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Background and purpose: Morphological changes of the internal carotid arteries (McICA) are frequently found during cervical ultrasound studies. However, the etiology of McICA remains controversial. During this study, the prevalence and demographic characteristics of McICA, such as kinking, coiling or looping identified by Doppler ultrasound, were analysed and its relationship with vascular risk factors and stroke was assessed.

Methods: A retrospective study was performed by analysing 19 804 patients who were subjected to cervical ultrasonographic study between January 2000 and June 2012. The data were statistically analysed with SPSS® 20 and a multivariate logistic regression was performed. Statistical significance was accepted for $P < 0.05$ and 95% confidence intervals (CIs) were used.

Results: Morphological changes of the internal carotid arteries were present in 2678 patients (13.5%) and were unilateral in 61.6% of these cases. Carotid kinking was found in 80% of the patients, coiling in 16% and looping in 1%. In multivariate analysis, the presence of McICA was related to older groups (1.04; 95% CI, 1.04–1.05; $P < 0.01$), female gender (1.78; 95% CI, 1.64–1.94; $P < 0.01$), patients with hyperlipidemia (1.28; 95% CI, 1.17–1.40; $P < 0.01$), carotid thickness (1.22; 95% CI, 1.13–1.33; $P < 0.01$) and cardiac or cardioembolic disease (1.11; 95% CI, 1.01–1.21; $P = 0.02$). The results of this study indicate that kinking in the carotid artery was associated with ipsilateral cerebral ischemic events (1.43; 95% CI, 1.040–1.958; $P < 0.05$).

Conclusion: Morphological changes of the internal carotid arteries were associated with aging, female gender and patients with hyperlipidemia, hypertension, diabetes and heart disease. Kinking was associated with ipsilateral cerebral ischemia.

Introduction

Morphological variations in the course and geometry of the internal carotid artery are often found during cervical ultrasound studies [1]. Despite the common occurrence of morphological changes of the internal carotid arteries (McICA), conclusive evidence about their prevalence, characteristics and relationship with vascular risk factors remains controversial [1–7]. Different hypotheses are worthy of consideration as McICA have been frequently associated with embryological causes, fibromuscular dysplasia, shorter neck lengths and vascular risk factors [2–9]. However, more recent studies were based on small cohorts of patients with insufficient factual accuracy [7,8,10].

The incidence, mortality and cost of stroke will rise as the population ages and lifestyles change [2]. More clinical and vascular research is needed to assess risk

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factors, and to identify groups of individuals at higher risk for stroke. Carotid ultrasound study helps to assess the morphological and atherothrombotic risk of internal carotid arteries [3,4].

In general, McICA may be considered as a multifactorial disease with a genetic predisposition, which may cause changes in arterial wall thickness and significant hemodynamic disorder that may trigger stroke [7–9]. In some cases, patients with these changes were considered to be candidates for surgery [1–4]. We hypothesized that McICA may change blood flow within the vessel and cause ischemic events. Therefore, we investigated the prevalence and characteristics of McICA, and their possible association with ischemic stroke, carotid stenosis and vascular risk factors in a consecutive series of patients. The aim of this study was to assess the prevalence and characteristics of McICA and their possible association with vascular risk factors and ischemic stroke.

Materials and methods

Patients

From 3 January 2000 to 20 June 2012, 20 207 consecutive patients were examined at the Laboratory of Neurosonology, North Lisbon Hospital Center – Santa Maria Hospital, Lisbon, Portugal. We only considered patients over 25 years old and excluded repeated records and patients (Fig. 1). Within this 12-year period, the most common reasons for ultrasound study were ischemic stroke or transient ischemic attack (12 574), pre-operative investigation (4957), ischemic heart disease (489), subarachnoid hemorrhage (381), syncope (649), dizziness (37), dementia or other neurological conditions (407). A waiver of consent was granted because of the retrospective nature of this study.
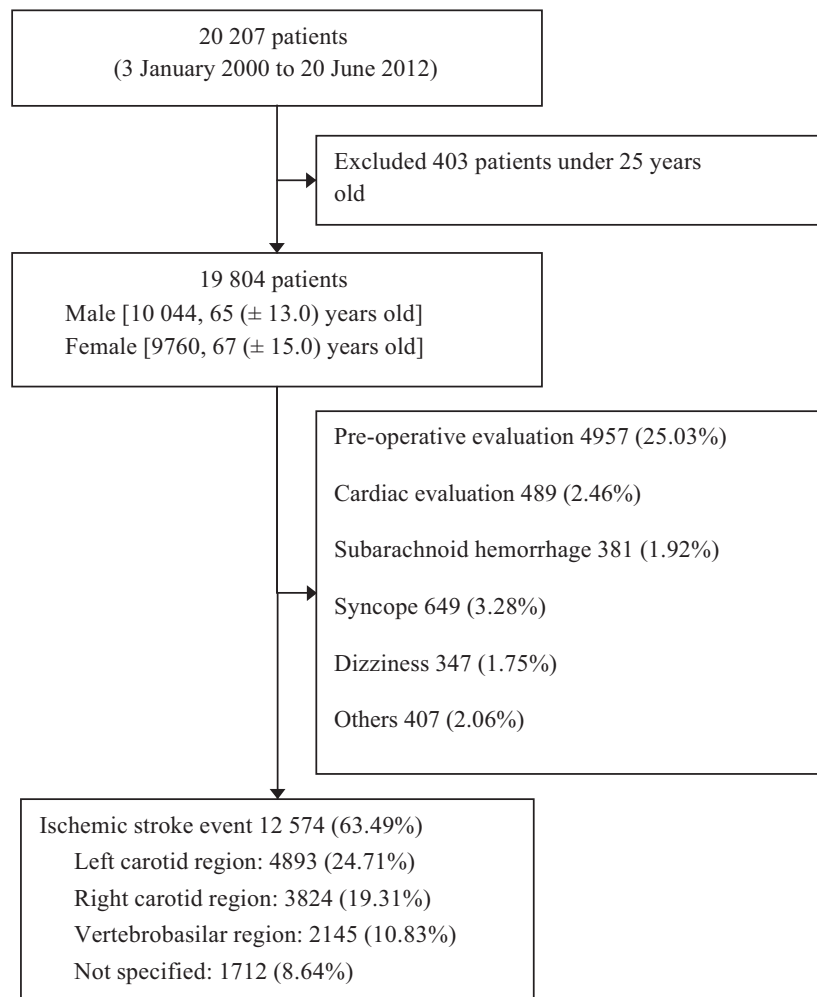

Figure 1 Characterization of the study population and reasons for conducting ultrasononographic examination.

Image analysis

We routinely scanned the arteries from the proximal common carotid artery, proceeding superiorly to the distal internal carotid artery and external carotid artery. Sagittal and transverse views were used to assess the presence of McICA. Cervical duplex sonography was performed by one of three experienced cardiovascular technicians who followed pre-established protocols. All of the technicians had more than 5 years of experience and were performing more than 1500 tests per year when they started to collect data. All of the ultrasound examinations were analysed and reviewed by a single senior neurologist to ensure the standardization of results.

The ultrasound equipment used in this study was, from the beginning of the study in 2000, the Philips ATL HDI 5000 Sono-CT (ATL) with linear probe (4–7 MHz) to which was added since 2011 the Logic E9 (GE) with linear probe (LD 9 MHz). The abnormalities in direction and course of McICA were assessed according to the criteria of Weibel–Fields and Metz modified by the authors. According to this classification, McICA were classified as kinking, coiling or looping. Kinking was defined as an acute angulation of one or more segments of the vessel, usually associated with functional or organic narrowing. Tortuosity was defined as any elongation of the vessel, creating an exaggerated S- or C-shaped curve of the vessel (coiling) or circular configuration (looping) [4–6].

Clinical parameters

The clinical features of the patients included age, sex and risk factors for vascular disease such as hypertension, diabetes, hyperlipidemia and ischemic and hypertensive heart disease. All demographic characteristics were collected from direct interview and medical reports at our hospital by a physician certified in internal medicine who followed the adopted criteria.

The cardioembolic risk was defined as the presence of cardiac arrhythmia or atrial dilatation identified on echocardiography [11]. Arteriosclerosis is a general term for the thickening and hardening of arteries. Atherosclerosis is a type of arteriosclerosis characterized by formation of atherosclerotic plaques. Thickening was defined as evidence of arterial wall stiffness in the intima-media tissue identified by Doppler ultrasound [12].

Hypertension was defined as an elevated systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥ 90 mmHg or patient receiving antihypertensive medication as defined by the guidelines of the European Society of Cardiology [13].

Type 2 diabetes mellitus was defined as elevated serum glucose [fasting plasma glucose > 7.0 mmol/L (or 126 mg/dL) on repeated measurements or occasional plasma glucose > 11.0 mmol/L (or 198 mg/dL) or HbA1c ≥ 6.5%] or patient receiving antidiabetic therapy as defined by the guidelines of the International Federation of Diabetes [13,14].

Hyperlipidemia was defined as high levels of lipids or lipoproteins in the blood or in patients receiving therapy as defined by the guidelines of the European Society of Cardiology and the European Atherosclerosis Society [12,13].

Heart disease was considered to be present in both patients with past medical history of heart attack or with areas of akinesia/hypokinesia on echocardiography and patients with ventricular hypertrophy on echocardiography (ischemic and/or hypertensive) [15]. The risk of smoking in these patient groups was not analysed due to insufficient data.

In order to analyse the risk of ischemic stroke in patients with McICA, we only considered the patients with a cryptogenic cause of unilateral ischemic stroke.

Statistical analysis

Statistical analysis was performed with Microsoft Office Excel® 2007 and Statistical Package for Social Sciences (SPSS) software program (version 20; IBM SPSS Statistics, SPSS Inc, Armonk, NY, USA). We used Student's t-test for the evaluation of continuous variables, Fisher's exact and chi-square tests for evaluation of binomial variables, and binary regression multivariate logistic to compare binomial dependent variables. Continuous data are given as mean $\pm$ SD. We used odds ratio (OR) calculation and 95% confidence intervals (CIs). $P < 0.05$ was accepted as statistically significant. Multivariate logistic regression analysis was used to investigate cerebral risk factors.

Results

We analysed 19 804 patients, 10 044 (50.7%) of whom were men [mean age 66.00 $\pm$ 14.02 (range 25–99) years]. Among these 19 804 patients, 1139 (5.75%) had atrial fibrillation and 147 (0.74%) had foramen ovale patent. Cardioembolic disease was present in 6411 patients (32.37%), hypertension in 15 316 (77.34%), diabetes in 3826 (19.32%), hyperlipidemia in 5507 (27.81%) and heart disease in 6149 (31.05%) (Table 1).

Morphological changes of the internal carotid arteries were detected in 2678 patients (13.52%). Of these patients, kinking was detected in 2147 cases (80.17%), coiling in 426 cases (15.91%) and looping in 24 cases

Risk factor	With McICA	Without McICA	Odds ratio	P value
Age	72 ± 10.94	65 ± 14.21		<0.01
Women	1684 (63%)	8076 (47%)	1.898	<0.01
Cardioembolic and cardiac disease	1056 (39%)	5357 (31%)	1.430	<0.01
Arterial hypertension	2174 (81%)	13 142 (77%)	1.308	<0.01
Diabetes mellitus	575 (21%)	3251 (19%)	1.167	<0.01
Hyperlipidemia	843 (31%)	4664 (27%)	1.227	<0.01
Thickening	1380 (52%)	8423 (49%)	1.099	0.013
Total	2678	17 126		

Data are given as mean ± SD or n (%).

(0.90%), and 81 patients had concurrent changes (3.02%). McICA were unilateral in 1650 patients (61.61%) mostly in the left internal carotid artery [957 (58.00%)]. This change had unknown laterality in seven patients (0.26%).The prevalence of McICA increased similarly in all age groups for both men and women. However, it was significantly higher among women in all age groups and this difference increased for older age groups (25–39 years old, $P = 0.036$; >40 years old, $P < 0.01$) (Fig. 2). It is important to note that we identified a second peak of incidence in patients under 25 years old.

For all age groups the prevalence of McICA was more frequent in kinking, followed by coiling and more rarely looping. These differences were more pronounced for ages above 50 years (Fig. 3).

The prevalence of kinking and looping was higher in women than in men for any carotid affected (kinking: OR, 1.759; $P = 0.000$; coiling: OR, 2.446; $P = 0.000$; looping: 2.147; $P = 0.026$) (Fig. 4). In univariate analysis, patients with McICA were older than those without McICA ($72 ± 10:94$ vs. $65 ± 14.21$ years; $P = 0.000$) and they were more frequently women (OR, 1.898; 63%; $P = 0.000$). The presence of McICA also proved to be associated with heart and cardioembolic diseases (OR, 1.430; 39%; $P = 0.000$), arterial hypertension (OR, 1.308; 81%; $P = 0.000$), diabetes (OR, 1.167; 21%; $P = 0.001$) and hyperlipidemia (OR, 1.227; 31%; $P = 0.000$). The atherosclerotic thickening was also associated with a higher P value (OR, 1.099; 52%; $P = 0.013$) (Table 1).

In multivariate logistic regression analysis (Fig. 5), with the inclusion of all previously analysed variables, it was found that McICA were associated with age (OR, 1.045; 95% CI, 1.038–1.045; $P = 0.000$), female gender (OR, 1.782; 95% CI, 1.636–1.941; $P = 0.000$), heart disease (OR, 1.107; 95% CI, 1.013–1.209; $P = 0.024$), hyperlipidemia (OR, 1.280; 95% CI, 1.169–1.402; $P = 0.000$) and atherosclerotic plaque (OR, 1.224; 95% CI, 1.126–1.331; $P = 0.000$). The
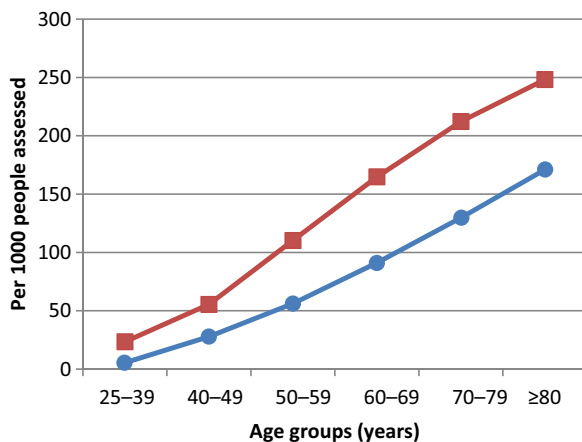

Figure 2 Prevalence of morphological changes of the internal carotid arteries according to age and gender per 1000 people assessed. ■, men; ●, women. [Colour figure can be viewed on wileyonlinelibrary.com].
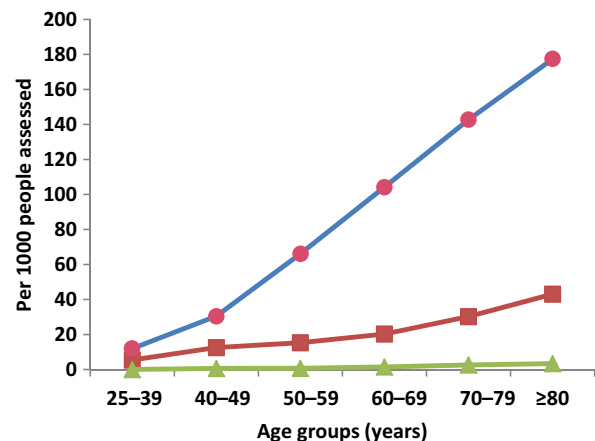

Figure 3 Prevalence of morphological changes of the internal carotid arteries (McICA) according to its classification and age of diagnosis per 1000 people assessed. All results shown in this figure are related to the number of McICA identified (2752) and not to the number of patients with these changes (2678). ●, kinking; ■, coiling; ▲, looping. [Colour figure can be viewed on wileyonlinelibrary.com].
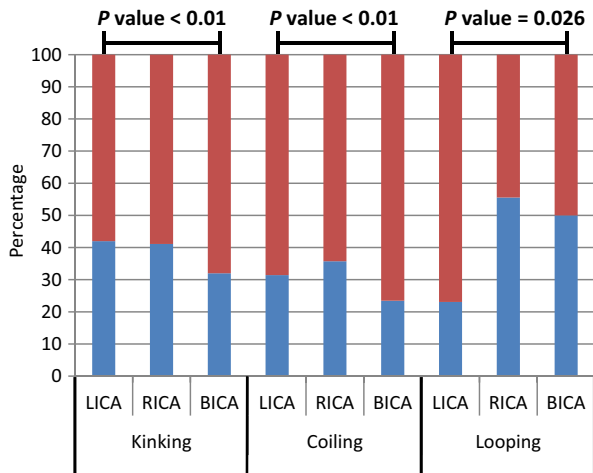
Figure 4 Prevalence of morphological changes of the internal carotid arteries (McICA) according to the classification and carotid affected. All results shown in this figure are related to the number of McICA identified (2752) and not to the number of patients with these changes (2678). BICA, both internal carotid arteries; LICA, left internal carotid artery; RICA, right internal carotid artery; ■, men; ■, women. [Colour figure can be viewed on wileyonlinelibrary.com].

variables hypertension and diabetes were excluded from the regression model.

Discussion

In the present study, the prevalence of McICA is similar to those reported in previous studies but prevalence rates range from 7% to 58% [2–6,10]. Nevertheless, this may have been underestimated because of diagnostic challenges with ultrasound acquisition and interpretation. The prevalence is higher with computed tomography and magnetic resonance imaging [10]. However, there have been an increasing number of reports of McICA in recent years. Ultrasound is a fast, cheap and non-invasive examination that allows an evaluation of the morphology and blood flow of extracranial arteries. This reflects both a growing familiarity with this clinical entity and a significant improvement in ultrasound devices for detection of this condition [2–7].

As suggested by previous studies, we found that internal carotid abnormality was associated with women and older patients [2–7]. A more severe alteration in vessel wall elasticity may also be related to post-menopausal women due to the hormonal process, without excluding a bias related to the competitive comorbid conditions in men.

We also found that internal carotid change was associated with hypertension, hyperlipidemia, diabetes, heart disease and arterial thickening, which was previously identified in only some studies [3,9]. The difference in prevalence rates may be explained by different biases, such as diagnostic techniques, selection criteria of the population, classification of McICA, definition of each risk factor and ethnic differences [4,7,8]. Nevertheless, this is the largest group of McICA analysed in the literature, which evidently illustrates the accuracy of the results to a large extent.

We admit that the prevalence of McICA in older patients is affected by the arteriosclerosis process. Arteriosclerosis is a general cause of the thickening and hardening of arteries and it affects the intima layer of large and medium-sized arteries, such as the aorta, carotid and coronary arteries. It is a condition in which plaque, made of cholesterol, fatty substances and other products, builds up inside the arteries [16,17] and it is believed that atherosclerotic plaque begins when the intima becomes damaged due to elevated levels of cholesterol and triglycerides in the blood, high blood pressure and smoking. This is a complex, systemic and chronic inflammatory process. Despite beginning in childhood, the main syndromes related to atherosclerotic disease manifest after the fourth decade of life.

As cases of McICA were detected in patients under 25 years old, we cannot exclude that some McICA were congenital or due to some diseases that are more prevalent in infants. However, the increased prevalence of carotid changes in older patients supports the hypothesis that McICA occur more often later in life,

Figure 5 Risk factors associated with morphological changes of the internal carotid arteries (multivariate analysis with the regression method 'backward stepwise'; calculated using SPSS). CI, confidence interval; OR, odds ratio.
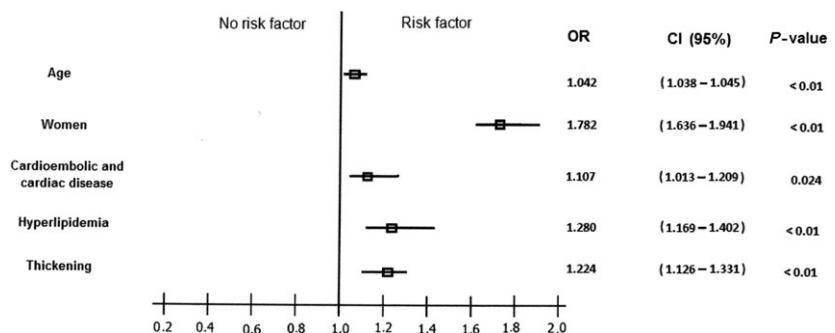
probably due to the low elasticity and degeneration of the vascular wall caused by hyperlipidemia, diabetes and hypertension [18–21]. The association between McICA and cardioembolic or heart disease probably arises as a marker of vascular disease and not as a risk factor itself for McICA.

Although hypertension and diabetes appear to be risk factors for McICA in a univariate analysis, when we performed multivariate logistic regression these variables were excluded from the regression model ('backward stepwise'). This is probably justified by the fact that artery thickening is caused by many other variables, in addition to diabetes and hypertension, that are not included in this study. Atherosclerosis is not only an accumulation of cholesterol but a complex interaction of environmental risk factors and genetically mediated components, such as the immune system, hematological and endothelial cells, clotting factors and inflammatory mediators [18,19].

An increased prevalence of kinking in patients with arterial hypertension was also previously reported [3,4]. It is probably related to raised endoluminal pressure and increased parietal tension caused by arterial hypertension that favors the thickening. Nitric oxide produced by the endothelium is a substance that has vasodilator and antiatherogenic properties. In diabetic patients, nitric oxide production is impaired by the blockage of the endothelial nitric oxide synthase enzyme that activates nitric oxide, which contributes to atherosclerosis [22,23].

In the present series, the multivariate analysis shows a relationship between McICA and vascular risk factors. This study suggests that kinking is important as a stroke risk factor of vascular disease. Moreover, kinking may produce significant hemodynamic disorders, potentially related to the occurrence of embolic phenomena in the central nervous system. From an anatomical point of view, coiling and looping have greater impacts on hemodynamic blood flow [10]. However, only kinking was significantly associated with stroke, probably due to the small number of patients analysed with coiling and looping. Further investigation is required using hemodynamic parameters to clarify this finding.

Advantages and limitations of the study

This study is well designed with important conclusions. It has a practical application in real medical practice. The advantages of this study are related to the large sample analysed and the extensive experience of the technicians in performing cervical ultrasound.

Some of the limitations of this study are related to its clinical design. This is a retrospective study, which makes a proper assessment of data more difficult, and not all of the required information may have been collected. Furthermore, it was not possible to include other variables related to atherosclerosis (such as smoking) and hemodynamic flow. A prospective randomized multicenter trial is needed for a broader assessment. Also, the specific localization of the McICA, neck length and degree of stenosis were not evaluated.

Conclusion

Morphological variations in the course and geometry of the internal carotid artery are often found during cervical ultrasound study. According to this study, their presence was associated with aging, female gender and vascular risk factors as hyperlipidemia, diabetes, hypertension and thickening. The results of this study also indicate that kinking is associated with ipsilateral cerebral ischemia.

Disclosure of conflicts of interests

The authors declare no financial or other conflicts of interest.

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