

# Matrix Metalloproteinase Levels in Cervical and Intracranial Carotid Dolichoarteriopathies

Yıldız Arslan, MD,\* İlker Burak Arslan, MD,† Yeliz Pekçevik, MD,‡  
Ufuk Şener, MD,\* Şükran Köse, MD,§ and Yaşar Zorlu, MD\*

---

*Background:* Matrix metalloproteinases (MMPs) are enzymes suggested as a possible candidate for pathogenesis of arterial dolichoarteriopathy (DA). We aimed to investigate the relationship between MMP levels and DA of intra- and extracranial carotid arteries. *Methods:* This study included 88 subjects admitted with headache, vertigo, or pulsatile tinnitus and those who underwent computed tomography angiography. The study group (n = 70) consisted of patients with kink-coiling (group I, n = 41) and patients with tortuosity (group II, n = 29). The control group (n = 18) had normal angiography results. The diameter, course, and geometry of the carotid artery were analyzed. Serum MMP-1, -2, -3, and -12 levels were measured in all subjects. Vascular risk factors for DA were also noted. *Results:* MMP-2 levels were significantly higher in the kink-coiling and tortuous groups than in the control group. In the study group (n = 70), MMP-12 levels were also significantly higher in patients with atheromatous plaques than in those without plaques. Diameters of arteries were meaningfully wider in the kink and tortuous groups than in the control group. Among vascular risk factors, hypertension and diabetes mellitus were more common in the kink group than in the control group, and there were significant differences between them. *Conclusions:* MMP-2 plays a role in the etiology of DA, and MMP-12 levels increase in carotid atherosclerotic lesions and may lead to plaque formation. We demonstrated that dilatation and tortuosity occur together. **Key Words:** Dolichoectasia—MMP levels—cervical and intracranial carotid arteries—tromboembolic stroke.

© 2016 National Stroke Association. Published by Elsevier Inc. All rights reserved.

---

---

From the \*Izmir Tepecik Education and Research Hospital Neurology Clinic, Izmir, Turkey; †Izmir Tepecik Education and Research Hospital Head and Neck Surgery Clinic, Izmir, Turkey; ‡Izmir Tepecik Education and Research Hospital Radiology Clinic, Izmir, Turkey; and §Izmir Tepecik Education and Research Hospital Microbiology and immunology Clinic, Izmir, Turkey.

Received March 15, 2016; revision received May 12, 2016; accepted May 21, 2016.

Address correspondence to Yıldız Arslan, MD, İzmir Tepecik Education and Research Hospital Neurology Clinic, Yenişehir mah, Konak, 35120 Izmir, Turkey. E-mail: [dryildizarslan@yahoo.com](mailto:dryildizarslan@yahoo.com).

1052-3057/\$ - see front matter

© 2016 National Stroke Association. Published by Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.05.028>

## Introduction

Dolichoarteriopathy (DA) is an arterial phenotype characterized by elongation, tortuosity, and/or dilatation that can affect the intracranial and extracranial arteries, and can be asymptomatic or manifest in conjunction with compressive and/or vascular symptoms.<sup>1</sup> DA most frequently involves the vertebrobasilar artery, but also occurs less frequently in the intracranial carotid artery (CA) and middle cerebral artery. DA of the extracranial carotid artery (ECA) is particularly rare, but may be the source of cerebral emboli or intermittent stenosis.<sup>2,3</sup> The prevalence rates of DA among individuals with stroke have been reported as 3.1% in a population-based sample and 12% in a hospital-based sample.<sup>4,5</sup>

The dysregulation of matrix metalloproteinases (MMPs) and a variety of other predisposing genetic factors related to collagen, elastin, or extracellular matrix (ECM) health are associated with the development of DA.<sup>1,4</sup> In fact, it has been suggested that MMPs are a possible candidate for the pathogenesis that underlies this type of arterial dilatation.<sup>6,7</sup> MMPs are an enzyme family of more than 20 zinc-dependent endopeptidases that exert proteolytic activity against ECM components, such as collagen, proteoglycans, and elastin or fibronectin, and numerous proteins that mediate ECM turnover via their involvement in angiogenesis and cell migration, growth, and apoptosis.<sup>8-11</sup> Further, MMPs influence arterial remodeling and capillary permeability, and thus play a critical role in tissue and vascular homeostasis.<sup>12,13</sup> In addition to their physiological functions, MMPs also play important roles in several pathological processes including atherosclerosis, inflammation, aneurysmal dilatation, disruption of the blood-brain barrier, and neoplasia.<sup>11,13</sup>

Based on such evidence, it was hypothesized that MMPs play a role in the etiology of DA or that DA may increase serum levels of MMPs. Therefore, MMP-1, -2, -3, and -12 were chosen from different MMP subgroups to determine their associations with the pathophysiological mechanisms involved in the DA process, and the effects of vascular risk factors were also analyzed.

## Materials and Methods

### Study Subjects

The 88 study subjects were selected from patients admitted to outpatient clinics with the symptoms of headache, vertigo, or pulsatile tinnitus and who underwent head and neck computed tomography (CT) angiography between March 2014 and January 2015. CT angiography images were reviewed by a radiologist and patients with aneurysms, artery dissections, arteriovenous malformations, and CA stenosis including nonsignificant stenosis (<50%), vertebrobasilar system (VBS) dolichoectasia (diameter >4 mm), and deviation of more than 90° (kink and coiling) were excluded from the study.

These patients were recalled and examined by a neurologist and a head and neck surgeon. Patients who had any cervical, skeletal, or soft tissue pathologies that may have led to tortuosity or kinking were eliminated. Patients who had ischemic cerebrovascular diseases except chronic lacunar infarcts, subarachnoid hemorrhage, cerebral hematoma, atrial fibrillation, ischemic cardiomyopathy (myocardial infarction, rheumatic heart disease, or a prosthetic valve), severe infections (pneumonia or tuberculosis for <1 month), and/or neoplasia were excluded. Additionally, patients who had undergone radiotherapy or chemotherapy, had major surgery, had major renal or hepatic diseases, had experienced major trauma within the last 6 months, or had vasculitis, collagen diseases, rheumatic diseases, severe chronic

obstructive lung disease, or asthma were also excluded from the study.

Consequently, the control group included 18 patients with normal CT angiography scans and the study group included 70 patients with cervical CA tortuosity, kink, or coiling (with or without intracranial DA). All patients in the study group had tortuosity in the VBS, but not kink or coiling (deviation < 90°).

### Image Analysis

All CT examinations were performed using a 64-slice CT scanner (Aquilion 64; Toshiba Medical Systems, Tochigi, Japan) and were independently reviewed with respect to the course and geometry of the internal carotid artery (ICA). The course and geometry of the cervical CA were classified based on the modified criteria of Paulsen et al<sup>5</sup> as follows: straight, less than 15° curvature; tortuosity, a deviation between 15° and 70°; kinking, a deviation between 90° and 145°; and coiling, a loop of 360°.

We divided the study group into two:

**Group I:** Patients with kink and coiling and curvatures between 145° and 360°.

**Group II:** Patients with tortuosity and curvatures between 70° and 90°.

A curvature smaller than 15° (straight) was included in the control group.

We also measured the diameters of cervical CA to demonstrate the ectasia of arteries. Diameters of the common carotid artery were measured 20 mm below the bifurcation and diameters of the ICA were measured 20 mm above the carotid bulb, at the plaque-free portions of the vessels.

The presence of an intracranial carotid DA was noted in Groups I and II and, in addition to DA, atheromatous plaques of the CA were also assessed in all patients. In the control group, there were no atheromatous plaques or any cases of stenosis, but in the study group, atheromatous plaques without any stenosis were analyzed.

Furthermore, vascular risk factors of DA, gender, stroke, coronary artery disease (CAD), hypercholesterolemia (HC), hypertension (HT), diabetes mellitus (DM), smoking, mild or moderate chronic obstructive lung disease, and asthma, were investigated.

### Laboratory Assessments

The MMP levels were independently measured using an enzyme-linked immunosorbent assay (ELISA) by 2 microbiologists blinded to the conditions. Each subject provided a 5 mL blood sample that was drawn from the antecubital vein directly into serum separator tubes by forming mild stasis. The serum was allowed to clot in the tube (over approximately 2 hours) at room temperature and was centrifuged at 2000 × g for 15 minutes. To analyze all serum samples together, samples were frozen and stored at -80°C. After collection, the serum samples

Download English Version:

<https://daneshyari.com/en/article/2703664>

Download Persian Version:

<https://daneshyari.com/article/2703664>

[Daneshyari.com](https://daneshyari.com)