The Headache and Neck Pain in Ischemic Stroke Patients Caused by Cervicocerebral Artery Dissection. A Case-Control Study

Yuhan Wang, MD,[1] Wenchao Cheng, MD,[1] and Yajun Lian, MD

Background and purpose: The symptom of headache and neck pain is common in patients with cervicocerebral artery dissection (CAD). We attempt to screen ischemic stroke patients with CAD based on the characteristics of the pain. *Methods:* Eighty-one consecutive ischemic stroke patients with CAD from 2010 to 2017 and 84 consecutive ischemic stroke patients with large artery atherosclerosis (LAA) were registered prospectively and observed in Zhengzhou, China. Those ischemic stroke patients complained of headache and neck pain were categorized into 2 groups. By analyzing the difference of headache and neck pain in 2 groups, we summarized characteristics of the pain secondary to CAD. *Results:* There were 34 patients in CAD group and 19 patients in LAA group. As for patients in CAD group, the pain could be located in the ipsilateral (41.9%), bilateral (41.9%), or contralateral (16.1%) side of the dissected artery, but in LAA group the pain was often in both sides (68.4%). When the dissected artery was involved in anterior circulation, 55.6% of CAD patients had pain in temporal and when involved in posterior circulation, 65.2% of CAD patients had pain in the occipital and neck. Patients with CAD had a higher prevalence of throbbing pain (30.0%), while pulsating pain (43.8%) was more common in LAA group. Patients often presented with severe pain (46.9%) in CAD group, while less frequently (11.8%) in LAA group, with a significant difference ($P = .003$). And there was a significant difference between the length (≥20 mm) of the involved artery and severity of the pain ($P = .028$) in CAD group. *Conclusions:* Ischemic stroke patients caused by CAD tend to suffer from headache and neck pain, which may be severe and throbbing, compared with those resulting from LAA. The anterior circulation dissection has a higher prevalence of temporal pain while posterior circulation dissection is typically more associated with occipital and neck pain.

Key Words: Cervicocerebral artery dissection—cerebral infarction—headache—neck pain—pain features

Introduction

Cervicocerebral artery dissection (CAD) refers to a tear in the wall of a cervicocerebral artery and can lead to both ischemic stroke (IS) and hemorrhagic stroke, recognized as one of the major causes of IS in young adults.[1,2] Previous studies reported that IS patients with headache, accounting for 16%-27%[3-6] of all IS patients and mainly determined by the location and etiology of IS,[7,8] had a better prognosis than those without.[4,9] Headache and neck pain are also considered as an early warning symptom of CAD,[10-12] however, the IS caused by CAD often needed specific endovascular treatment to prevent the progression of the disease. Therefore, in order to screen IS patients with CAD, we conducted a case-control study to analyze the difference of headache and

From the Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, People's Republic of China.

Received August 6, 2018; revision received October 2, 2018; accepted October 27, 2018.

Fundings: This study was supported by the grant from National Natural Science Foundation of China [No. 81771397].

Address correspondence to Yajun Lian, MD, Department of Neurology, The First Affiliated Hospital of Zhengzhou University, 1 Jianshe east Road, Zhengzhou, Henan Province 450052, People's Republic of China. E-mail: yajunlian369@163.com.

[1]These authors have contributed equally to this work.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.10.034

neck pain between IS patients attributed to CAD and LAA and summarized characteristics of the pain secondary to CAD.

Methods

Study Population and Case-Ascertainment

Eighty-one consecutive IS patients with CAD from January 2010 to December 2017 in Department of Interventional Neurology and 84 consecutive IS patients with large artery atherosclerosis (LAA) in Department of Neurology, the First Affiliated Hospital of Zhengzhou University were registered prospectively and observed. Those IS patients complained of headache and neck pain were categorized into CAD group and LAA group based on the reason for IS. Eventually, there were 34 patients in CAD group and 19 patients in LAA group. (1) Patients in CAD group: All IS patients were diagnosed by magnetic resonance imaging, including diffusion-weighted imaging; Patients were subjected to digital subtraction angiography, magnetic resonance angiography, and computed tomographic angiography with typical radiological signs, such as pearl-and-string sign, intimal flap, double lumen, and mural hematoma[13]; The infarction lesion was located in the blood supply area of the dissected artery. (2) Patients in LAA group: Acute IS was in the relevant territory of arterial stenosis on diffusion-weighted imaging; Atherosclerosis could be seen on angiography; There was no evidence of dissection, vasculitis, or other vascular disease on angiography; Patients with cardioembolic sources in LAA group and with large cerebral infarction in 2 groups were excluded. By comparing clinical manifestation of headache and neck pain in 2 groups, the pain characteristics of CAD patients were summarized. Patients were given informed consent before participating. The Ethics Committee of the First Affiliated Hospital of Zhengzhou University approved this study (Number: KW-2018-LW-006).

Data Collected

We collected data of age, gender, and clinical manifestations such as headache, dizziness, and focal neurological deficits of all patients. Especially for patients with headache and neck pain, the location, nature, intensity, frequency of pain, the initial symptom, and the length of the involved artery were collected by specialized neurologists through a routine neurological questionnaire face to face in the first days after hospital arrival. According to the visual analog scale (VAS), the intensity of the pain was classified as mild: VAS 1-3, moderate: VAS 4-6, and severe: VAS 7-10.

Statistical Analysis

With the help of Excel, the patient database was established. Quantitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed in terms of frequency and percentage. Differences in 2 groups were examined by means of chi-square test, Fisher's exact test or Wilcoxon rank sum test, when appropriate. All data were analyzed using SPSS22.0, and $P < .05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 165 patients with acute cerebral infarction were registered in present study, including 81 CAD patients, of which the average age was (51.56 ± 12.40) years, 58 (71.6%) were males, and 34 (42.0%) patients presented with headache and neck pain, and 84 LAA patients, of which the average age was (55.45 ± 8.06) years, 58 (69.0%) were males, and 19 (22.6%) presented with headache and neck pain. There was a significance difference in the prevalence of the pain between IS patients attributed to CAD and LAA ($P = .008$). Those IS patients complained of headache and neck pain were categorized into CAD group and LAA group based on the reason for IS.

Analysis of Headache and Neck Pain Characteristics in 2 Groups

The pain characteristics in CAD group

(1) Location: There were 32 patients with complete description of the pain location. When the dissected artery was involved in anterior circulation, 55.6% (5/9) of the patients had pain in the temporal regions, and when the dissection was in the posterior circulation, 65.2% (15/23) of the patients had pain in the occipital and neck. Except for 1 patient with basilar artery dissection, headache and neck pain could be located in the ipsilateral (41.9%), bilateral (41.9%), or contralateral (16.1%) side of the dissection.
(2) Nature: There were 30 patients with complete description of pain nature, consisted of throbbing (30.0%), pulsating (16.7%), dull (23.3%), stabbing (13.3%), constrictive (13.3%) and electrical (3.3%).
(3) Intensity: There were 32 cases with complete description of pain intensity, 15 (46.9%) with severe pain, 12 (37.5%) with moderate pain, and 5 (15.6%) with mild pain. In CAD patients with severe pain, there were 7 (46.7%) patients with the length of the involved artery greater than or equal to 20 mm, and 2 (11.8%) patients with the length of the involved artery greater than or equal to 20 mm in CAD patients with moderate

or mild pain. The statistical analysis displayed that there was a significant difference between the length (≥20 mm) of the involved artery and severity of the pain ($P = .028$).

(4) Frequency: There were 33 patients who could completely describe the frequency of the pain, of which 17 (51.5%) were intermittent and 16 (48.5%) were continuous.

(5) Initial symptom: There were 7 (20.6%) patients only with headache and neck pain as the initial symptom.

The pain characteristics in LAA group

(1) Location: There were 13 patients (68.4%) with unilateral infarction, of which 7 patients presented with bilateral pain, 3 ipsilateral pain, 2 contralateral pain, and 1 was unavailable. And there were 6 patients (31.6%) with bilateral infarcts, and the pain sites were located bilaterally.

(2) Nature: There were 16 patients with complete description of pain nature, consisted of throbbing (18.8%), pulsating (43.8%), dull (25.0%), and stabbing (13.3%).

(3) Intensity: There were 17 patients with complete description of pain intensity, 2 with severe pain (11.8%), 6 with moderate pain (35.3%), and 5 with mild pain (52.9%).

(4) Frequency: There were 17 patients who could completely describe the frequency of the pain, of which 10 (58.8%) were intermittent and 7 (41.2%) were continuous.

(5) Initial symptom: There were 2(10.5%) patients only with headache and neck pain as the initial symptom.

Analysis of intensity and frequency of pain in 2 groups

The results displayed that there was a significant difference in the pain intensity ($P = .003$), while no statistically significant difference was found in the frequency ($P = .623$; Tables 1 and 2).

Table 1. *Comparison of pain intensity in both groups*

Intensity (n, %)	CAD (n = 32)	LAA (n = 17)	Total (n = 49)	*P* value
Severe	15 (46.9%)	2 (11.8%)	17 (34.7%)	
Moderate	12 (37.5%)	6 (35.3%)	18 (36.7%)	
Mild	5 (15.6%)	9 (52.9%)	14 (28.6%)	.003

CAD, cervicocerebral artery dissection; LAA, large artery atherosclerosis.

Table 2. *Comparison of frequency in both groups*

Frequency (n, %)	CAD (n = 33)	LAA (n = 17)	Total (n = 50)	*P* value
Intermittent	17 (51.5%)	10 (58.8%)	27 (54.0%)	
Continuous	16 (48.5%)	7 (41.2%)	23 (46.0%)	.623

CAD, cervicocerebral artery dissection; LAA, large artery atherosclerosis.

Discussion

Compared with large artery diseases, patients with artery dissection were more likely to present with headache and neck pain,[14] which could be the initial symptom of CAD patients.[15] In present study, there were 20.6% of patients in CAD group with headache and neck pain as the initial symptom. In addition, it has been reported that the proportion of headache and neck pain in cerebral infarction patients with artery dissection was 2 times higher than patients without.[16,15] In agreement with previous studies, there were 42.0% (34/81) of all CAD patients and 22.6% (19/84) of all LAA patients with headache and neck pain in present study.

According to reports, headache in patients with cerebral infarction or CAD was both mainly related to the trigeminovascular framework.[17,18] Cerebral infarction caused headaches by facilitating the activation of perivascular nerve fibers.[19] van OS et al found that headache in the early phase of IS tended to occur less often in patients with atherosclerosis than patients without atherosclerosis in the large cerebral arteries. This finding indicated that wall elasticity was an essential factor in the occurrence of headache during acute IS.[20] Mitsias et al suggested that the integrity of the vessel wall may also be an important factor.[19] Therefore, the tear and haematoma in the wall may be the direct reason for the pain secondary to CAD, and it may be explained by stretch, distortion, and ischemia of the perivascular innervations around the dissected artery.[21] Fisher reported that the site of pain caused by CAD could occur in any part of the head and neck. Although the pain was usually located in the same side of the dissection, the bilateral and diffuse headache could also occur.[22] In present study, the pain was more common bilateral (68.4%) whether the infarction was bilateral or unilateral in LAA patients. However, 41.9% of patients in CAD group had pain in the same side of the dissected artery and 41.9% in both sides. When the dissection was involved in anterior circulation, 55.6% of the patients had pain in temporal, and when involved in the posterior circulation, 65.2% of the patients had pain in occipital and neck. Hence, the pain could be helpful in determining the location of the dissection, although there could be much variation. In CAD group, the pain could be described like throbbing, pulsating, dull, constrictive, and stabbing,[23,24] of which the throbbing pain was more common. However, in

patients without dissection, it was more common to have a pulsating pain. According to the literature, the pain caused by CAD was usually associated with a sudden onset of severe pain, and most patients described this attack as unique and unusual.[25-27] In this study, CAD patients were more likely to present with severe pain (46.9%), LAA patients were more likely to present with mild pain (52.9%), there was a significant difference in pain intensity between the 2 groups ($P = .003$). In addition, when the length of the involved artery greater than or equal to 20 mm, CAD patients was more prone to severe pain ($P = .028$).

This study includes some patients who do not have complete headache characteristic informations. But our study also has several strengths. Our study is exhaustive, continuous and prospective registry of patients in the 2 groups, and with clinically meaningful outcome measures.

Conclusions

IS patients caused by CAD tend to suffer from headache and neck pain, which may be severe and throbbing, compared with those resulting from LAA. The anterior circulation dissection has a higher prevalence of temporal pain while posterior circulation dissection is typically more associated with occipital and neck pain. Therefore, when meeting ischemic patients with above characteristics, we should attach greater importance to the timely investigation of CAD, if necessary, interventional treatment should be performed to prevent the development of the disease.

Conflict of Interest

The authors declare that there is no conflict of interest.

Author Contributions

All authors were involved in the study conception and design, acquisition of data, and analysis and interpretation of data; drafted and revised the manuscript for intellectual content; approved the final version to be published; and agree to be accountable for all aspects of the work.

Acknowledgment: The authors thank the patients for their collaboration. Thanks to all of my friends for their contributions to the design, implementation, data processing, drafting, and revision of this study. Thanks to my tutor and my lover for their encouragement and care to me.

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