

ORIGINAL ARTICLE

ARAŞTIRMA YAZISI

THE ASSOCIATION OF POSTERIOR COMMUNICATING ARTERY HYPOPLASIA WITH EARLY NEUROLOGICAL DETERIORATION IN PONTINE INFARCTS WITH BASILAR ARTERY STENOSIS

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ABSTRACT

INTRODUCTION: Early neurological deterioration (END) is a common problem of stroke practice. Although lacunar pontine infarcts are known with the high risk of END, such worsening can also be seen in patients with pontine infarcts attributed to basilar artery stenosis. Since the quality of collateral supply are considered one of the proposed mechanisms of END, we hypothesized that the pattern of posterior communicating arteries (PcoA) would be associated with END in pontine infarcts with basilar artery stenosis.

METHODS: Patients with acute pontine infarcts and having ≥ 50 basilar artery stenosis were included in the study. END was diagnosed as an increase of at least 2 points on the National Institutes of Health Stroke Scale from baseline during the 5 days. A diagnosis of PcoA hypoplasia was based on the presence of either a PcoA of less than 1 mm in diameter or the absence of a PcoA, based on computed tomography angiography (CTA). Univariate and multivariate analysis were performed to compare demographics, risk factors and the hypoplasia of PcoA between patients with END and those without END.

RESULTS: Of 60 patients included, 17 patients (28.3%) exhibited END. Demographics and vascular risk factors did not differ between groups. END was significantly higher in patients having at least one hypoplastic PcoA and those with bilateral PcoA hypoplasia as compared to patients without hypoplasia ($p=0.040$, $p=0.006$, respectively). In multivariate analysis, there was a trend for the development of END in patients with bilateral hypoplastic PcoA ($\beta = 1.9$, 95% CI 0.8-59; $p=0.073$).

DISCUSSION and CONCLUSION: Bilateral hypoplasia of PcoA might be associated with the development of END in pontine infarcts attributed to basilar arteries.

Keywords: Pontine infarct, basilar artery stenosis, early neurological deterioration, posterior communicating artery..

BAZİLER ARTER STENOZU OLAN PONTİN İNFARKLARDA ERKEN NÖROLOJİK KÖTÜLEŞME İLE POSTERİOR KOMÜNİKAN ARTER HİPOPLAZİSİNİN İLİŞKİSİ

ÖZET

GİRİŞ ve AMAÇ: Erken nörolojik kötüleşme (ENK) inme pratiğinde sık karşılaşılan bir problemdir. Lakuner pontin infarktlar ENK riski açısından bilinse de bu kötüleşme baziler arter stenozuna bağlı pontin infarktlarda da görülebilir. Kollateral akımın durumu ENK'in mekanizmalarından biri olarak düşünüldüğünden, bu çalışmanın hipotezi baziler arter stenozu olan pontin infarktlarda ENK'in posterior komunikan arterlerin (PcoA) durumu ile ilişkili olabileceğidir.

YÖNTEM ve GEREÇLER: Akut pontin infarktı ve ≥ 50 baziler arter stenozu olan hastalar alındı. ENK, NIHSS skorunda en az 2 puanlık artış olması olarak tanımlandı. PcoA hipoplazisi; BT Anjiyografide arterin hiç olmaması ya da 1 mm'den düşük çapta olması olarak tanımlandı. ENK olan ve olmayan hastalarda demografik özellikler, risk faktörleri ve PcoA hipoplazisi karşılaştırıldı.

BULGULAR: Çalışmaya dahil olan 60 hastanın 17'sinde (%28,3) ENK gelişti. Demografik özellikler ve risk faktörleri gruplar arasında değişmedi. ENK, en az 1 PcoA hipoplazisi ve bilateral hipoplazisi olanlarda, hiç hipoplazisi olmayanlara göre daha fazlaydı (sırasıyla $p=0.040$, $p=0.006$). Multivaryat analizde bilateral hipoplazi varlığı, ENK gelişimine etki etme trendi gösterdi ($\beta = 1.9$, 95% CI 0.8-59; $p=0.073$).

TARTIŞMA ve SONUÇ: Bilateral PcoA hipoplazisi baziler arter stenozuna bağlı pontin infarktlarda ENK gelişimi ile ilişkili olabilir.

Anahtar Sözcükler: Pontin infarkt, baziler arter stenozu, erken nörolojik kötüleşme, posterior komunikan arter..

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INTRODUCTION

Early neurological deterioration (END) after acute ischemic stroke is seen in about 10%-40% of patients and often leads to worse clinical outcome (1, 2). Although the underlying pathophysiology of END is not completely understood, several studies demonstrated that hemodynamic factors are important in neurological worsening during early stages of acute ischemic stroke (3). Posterior communicating arteries (PcoA) are important parts of Willis polygon which may supply blood flow in either direction between the anterior and posterior circulations (4). In a recent study, the presence of bilateral PcoA on pretreatment Computed Tomography Angiography (CTA) was found to be associated with more favorable outcomes in acute ischemic stroke patients with basilar artery occlusion treated with endovascular thrombectomy (5). In another study assessing the arterial status in both anterior and posterior circulation stroke, a significant association with END was detected for not only arterial occlusion but also arterial stenosis and this association was strongest for posterior circulation stroke (6). Based on these considerations, we aimed to investigate the association of the hypoplasia of PcoA with END in acute pontine infarctions attributed to basilar artery stenosis. Our hypothesis was that END would be more commonly found in patients with poor PcoA collateral patterns.

MATERIAL AND METHODS

Between April 2012 and April 2017, we retrospectively identified patients with acute pontine infarction who were admitted within 24 hours of the clinical presentation and hospitalized for at least 5 days in our stroke department. All patients had a 64-slice scanner CTA with a slice thickness of 1.25 mm and acquisitions in axial, sagittal and coronal planes with 3D reformations. Of all patients, those who had a stenosis of at least 50% lumen diameter in the basilar artery corresponding to etiological subtype of large artery atherosclerosis according to TOAST criteria were included into the study (7). The degree of stenosis in basilar artery was defined according to WASID (Warfarin-Aspirin Symptomatic Intracranial Disease) criteria (8). Patients with a potential cardiac source or other etiologies of

embolism and those who met the criteria for lacunar infarction were excluded from the study. The study was approved by Local Ethical Committee.

Demographical characteristics, vascular risk factors and follow-up variables were retrieved from medical records. The following criteria were used for vascular risk factors: a history of hypertension (HT) or an observed arterial blood pressure >140/90 mmHg; presence of a history of diabetes mellitus (DM) or a fasting glucose exceeding 126 mg/dl other than that measured during the acute phase; a positive history of hyperlipidemia or a fasting total cholesterol >200 mg/dl, low-density protein >130 mg/dl, and/or a triglyceride >180 mg/dl. Data for the presence of coronary artery disease, smoking and previous history of stroke were retrieved from patients' medical records.

The National Institutes of Health Stroke Scale (NIHSS) was assessed in the first day when patients were admitted to the hospital and in the following days at least twice a day. Patients were defined as having END if their NIHSS scores increased by ≥ 2 unites between the maximal and initial neurological deficits in the first 5 days of clinical presentation. Neurological deteriorations caused by extracerebral illnesses such as infection, aspiration pneumonia, metabolic changes, respiratory or cardiac failure were not recorded as neurological deterioration.

The diameter measurements of PcoA were taken at proximal, mid-point and distal segment of the artery, and the average of those measurements were considered as the diameter of PcoA. The diagnosis of PcoA hypoplasia was based on the presence of either a PcoA of less than 1 mm in diameter or the absence of a PcoA, as in the literature (9). The criteria for hypoplasia were a PcoA external diameter of <1mm or an absent vessel because it might be difficult to distinguish between PcoA hypoplasia (in diameter) and agenesis (absence of the PcoA).

SPSS (Statistical Package for Social Sciences) for Windows Version 23 software was used for statistical analyses. Mean, minimum, maximum, and percentage values were calculated for descriptive data. The Pearson chi-square test was used to compare the differences in categorical

variables. Student t-test or Mann-Whitney U test was used for numerical variables, as appropriate. Multivariate regression analysis was performed to determine the independent factors associated with the development of END and the model included variables with $p < 0.1$ in univariate analysis. Statistical significance was set at a p value of < 0.05 .

RESULTS

The cohort study consisted of 60 patients. The median age was 66 (IQR: 62-74) and 65% of the patients were male. The median NIHSS at onset was 5 (IQR: 4-7.7). Of all patients, 86.7% had HT, 63.3% had DM, 50% had HL, 26.7% had CAD, 35% had a history of smoking and 25% had a history of ischemic stroke. Of all infarcts, 52 (86.7%) were located in the medial pons, while 8 (13.3%) were in the lateral pons. 33 (55%) of them were in the right side, 26 (43.3%) were in the left and 1 (1.7%) was bilaterally located. Of all, 35 (58.3%) patients had infarcts extending beyond pons while 25 (41.7%) had isolated pontine infarct.

Of all, 17 patients (28.3%) exhibited END while the remaining 43 patients (71.7%) did not.

All of the ENDs occurred within 3 days after the acute event. The maximum increase in NIHSS score was 8 units and overall median of NIHSS increase in patients with END was 4 (4-5). Age, initial NIHSS and the presence of vascular risk factors did not differ between groups with and without END (Table I).

There was no PcoA hypoplasia in 35 patients (58.3%) while 25 patients (41.7%) had hypoplasia of which at least one was PcoA. The hypoplasia of both PcoAs was present in 11 (18.3%) patients. The development of END was significantly higher in patients having at least 1 hypoplastic PcoA as compared to patients without PcoA hypoplasia. Moreover, END was more significantly developed in patients with bilateral PcoA hypoplasia as compared to patients without any hypoplastic PcoA (Table II).

In regression analysis, the development of END was not found to be associated with the hypoplasia of at least one PcoA ($\beta = 0.092$, 95% CI 0.1-5; $p = 0.92$). However, there was a trend for the development of END in patients with two hypoplastic PcoAs ($\beta = 1.9$, 95% CI 0.8-59; $p = 0.073$).

Table I. Comparison of demographics and vascular risk factors between patients with END and those without END.

	Patients with END (n=17)	Patients without END (n=43)	p
Age, median (IQR)	65 (62.5-74)	68 (61-74)	0.837
NIHSS, median (IQR)	5 (3-7.5)	6 (4-8)	0.631
Sex, male n (%)	9 (52.9)	30 (69.8)	0.243
Hypertension, n (%)	14 (82.4)	38 (88.4)	0.676
Diabetes mellitus, n (%)	11 (64.7)	27 (62.8)	1.000
Hyperlipidemia, n (%)	12 (70.6)	18 (41.9)	0.084
Coronary artery disease, n (%)	2 (11.8)	14 (32.6)	0.120
Smoking, n (%)	5 (29.4)	16 (37.2)	0.765
History of ischemic stroke, n (%)	5 (29.4)	10 (23.3)	0.743

IQR: Interquartile range; NIHSS: National Institutes of Health Stroke Scale; END: Early neurological deterioration.

Table II. Comparison of the presence of hypoplastic PcoA between patients with END and those without END.

	Patients with END (n=17)	Patients without END (n=43)	p
PcoA hypoplasia			
≥ 1 PcoA	11 (64.7)	14 (32.6)	0.040
None	6 (35.3)	29 (67.4)	
PcoA hypoplasia			
Both	7 (53.8)	4 (12.1)	0.006
None	6 (46.2)	29 (87.9)	

END: Early neurological deterioration; PcoA: Posterior communicating artery.

DISCUSSION

The neurological deterioration of acute ischemic stroke patients in the early days after stroke is a serious condition potentially affecting short- and long-term outcomes of the patients. The incidence of END was reported for between 5% and 40% of acute ischemic stroke patients depending on the definition criteria used (10). The NIHSS was the most widely used scale and ≥ 2 point neurological deterioration was reported as a sensitive indicator of poor outcome and in-hospital mortality in acute ischemic stroke (11). Therefore, we defined END as an increase by ≥ 2 units in motor scores of NIHSS between the maximal and initial neurological deficits during follow-up period. It was reported that the development of END was observed during the first 48 or 72 hours after onset (12, 13). The development of END also occurred within the first 3 days in all of our patients, although we reviewed the first 5 days after the onset of acute stroke.

In our study, 28.3% of the patients represented END. In the previous studies, the incidence of END was reported for between 22% to 32% in patients with pontine infarcts (14-16). These studies, however, included patients with all etiological subtypes of ischemic stroke or were limited to patients with lacunar infarction. Although lacunar stroke etiology in pontine infarcts is widely known with progressive course, the patients with basilar artery stenosis are also at high risk for END (17, 18). However, few studies investigated the incidence and factors associated with the END in particular group of patients with atherosclerotic etiology. In a recent study investigating clinical, laboratory and radiological factors associated with early neurological deterioration (END) in symptomatic basilar artery stenosis (≥ 70 stenosis); CRP level of at least 1.5 mg/dL, NIHSS score of at least 4, and proximal FLAIR-hyperintense vessel were significantly associated with END (19). In our study, demographics, NIHSS and vascular risk factors did not differ between the patients with and without END.

The exact mechanism of END is probably multifactorial, including hemodynamic factors and inflammatory mechanisms (3, 13). Hemodynamically, the presence of good collaterals is known as an important factor in early improvement in acute ischemic stroke patients (20). Moreover, the failure of collateral flow was

found to be associated with infarct growth in anterior ischemic stroke patients (21) and the rate of clinical worsening was found to be nearly 4 times greater in patients with proximal middle cerebral occlusion without sufficient collaterals (22).

PcoAs are important collaterals providing retrograde filling of the basilar artery. The hypoplasia/agenesis of PcoA was reported in 21% of general population (23). In our study, the presence of at least one PcoA hypoplasia was 41.7%. Because it is not easy to distinguish between agenesis and hypoplasia of PcoA through CTA, the PcoA hypoplasia was defined as 'the absence of the artery or having a diameter lesser than 1 mm', similar to previous studies (9). Previous studies investigating the effect of PcoA in the outcome of brain stem infarcts are conflicting. One study investigating basilar artery occlusion infarcts provided no relation of PcoA hypoplasia or vertebral artery configuration with functional outcome (24). Another study, on the other hand, showed an association between PcoA hypoplasia and poor functional outcome at the end of 1st month (25). Our study, to the best of our knowledge, is the first study investigating the association of PcoA hypoplasia with END in patients with basilar artery stenosis. We found that the hypoplasia of both PcoAs was associated with a trend to the development of END in pontine infarcts with basilar artery stenosis. These results suggest that the insufficient collateral retrograde flow might be related to neurological deterioration of patients in the early stages.

The present study has a lot of limitations. First, this study was a retrospective study and had a small sample size. We only used NIHSS to evaluate the progression, since our main purpose was to evaluate the effect of PcoA hypoplasia on the clinical worsening. However, the analysis of infarction volume in a longitudinal basis should be included in further studies to evaluate the radiological deterioration as well. Another limitation was that we did not analyze the configuration of other arterial structures such as vertebral arteries and posterior inferior cerebellar arteries. Moreover, we did not evaluate the factors that can cause hypoperfusion such as blood pressure at onset, the presence of hypovolemia or anemia. Another significant limitation was that the lack of information on the choice of early

treatments of the patients. Although there is no consensus in the prevention of END, early dual antiplatelets, low molecular weight heparin or intravenous thrombolytic treatment were found to reduce END in patients with acute ischemic stroke (26-28). Further studies should be conducted to examine these issues.

In conclusion, the bilateral hypoplasia of PcoA might be associated with neurological worsening in pontine infarcts attributed to basilar arteries. Therefore, it could be important to evaluate PcoA to predict END. Future studies with larger sample size are required.

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