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Risk Factors, Biomarkers, Etiologic Subtypes, Outcome and Prognosis of Posterior Circulation Ischemic Strokes

Posterior Dolaşım İskemik İnmelerinin Risk Faktörleri, Biyobelirteçleri, Etyolojik Alt Tipleri, Sonlanımları ve Prognozları

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Introduction: Acute infarcts in posterior circulation (AIPC) have been reported 16-39.8% of ischemic stroke patients in previous studies. The most frequent cause of AIPC was embolism from cardio-aortic, vertebra-basilar atherosclerosis or dissection, followed by large-artery atherosclerosis (LAA), small vessel disease and other causes. The aim of this study was to determine the etiologic subtypes of AIPC in our stroke registry.

Methods: We reviewed the charts of 554 patients who were admitted with acute ischemic stroke between the dates January 2011 and August 2014. The demographic data, the National Institutes of Health Stroke Scale (NIHSS) scores at admission and detailed investigations to determine etiologic focus of stroke were recorded. We determined etiologic stroke subtypes using the automated Causative Classification System (CCS). The modified Rankin Scale (mRS) scores were recorded in follow-up period.

Results: A total of 184 (40.6%) patients with AIPC (89 females [48.4%] and 95 males [51.6%]; mean age, 70.6±12.5 [25-92] years) and 268 (59.3%) patients with acute infarcts in anterior circulation (AIAC) (133 females [49.6%] and 135 males [50.4%]; mean age, 69.3±13.7 [28-103] years) were included in the study. History of diabetes and previous stroke were significantly more common in patients with AIPC compared to the patients with AIAC (p=0.04, p=0.009). The mean admission NIHSS score was 6.4± 4.6 (0-26) in patients with AIPC (Group 1) and 6.7±4.3 (0-23) in patients with AIAC (Group 2) (p=0.96). cardio-aortic embolism was more common in Group 2 compared to Group 1, but not significant (p = 0.12). There was no significant difference in the mean C-reactive protein (CRP) level between two groups (p=0.23). Mortality in hospital was 14.7% (n=27) in Group 1 and 8.6% (n=23) in group 2 (p = 0.04). The median mRS was 3 (0-6) in patients with AIPC and 2 (0-6) in patients with AIAC during follow up period (p=0.79). Recurrent stroke occurred in 1 (0.5%) patient with AIPC and 8 (3%) patients with AIAC (p=0.07).

Conclusion: AIPC was found in 40.6% of patients with acute ischemic stroke in this registry. Cardio-aortic embolism was the most common cause of AIPC group. Diabetes and previous stroke history appear to be the major risk factors for AIPC. Mortality in hospital was significantly higher in AIPC group.

Key Words: ***Acute Infarcts in Posterior Circulation, Risk Factors, Etiologic Subtypes, Outcome, Prognosis***

Giriş: Önceki çalışmalarda posterior dolaşımda akut infarktların (PDAİ) iskemik inmeli hastaların %16-39.8'inde görüldüğü bildirilmiştir. PDAİ'ın en sık sebepleri kardiyo-aortik sistemden embolism, vertebrobaziler ateroskleroz ve diseksiyondur. Bunları büyük arter aterosklerozu (BAA), küçük damar hastalığı ve diğer nedenler takip etmektedir. Bu çalışmanın amacı, inme ünitemizde görülen PDAİ'ların etyolojik alt tiplerinin belirlenmesidir.

Yöntem: Bu çalışmada Ocak 2011 ve Ağustos 2014 tarihleri arasında akut iskemik inme nedeni ile hastanemize başvurmuş 554 hastanın dosyası incelenmiştir. Hastaların demografik özellikleri, başvuru sırasındaki Ulusal İnme Sağlık Ölçeği (NIHSS) skorları, inme etyolojisine yönelik yapılmış olan ayrıntılı tetkikleri kaydedilmiştir. İnme alt tipleri, otomatize Causative Classification System (CCS) kullanılarak belirlenmiştir. İzlem sürecindeki modifiye Rankin Ölçeği (mRS) skorları kaydedilmiştir.

Sonuçlar: Çalışmaya 184 (%40.6) PDAİ'ı olan hasta (89 kadın [%48.4] ve 95 erkek [%51.6]; ortalama yaş, 70.6±12.5 [25-92] yıl) ve 268 (%59.3) anterior dolaşımda akut infarktı (ADAİ) olan hasta (133 kadın [%49.6] ve 135 erkek [%50.4]; ortalama yaş, 69.3±13.7 [28-103] yıl) çalışmaya dahil edildi. Diyabet ve geçirilmiş inme öyküsü PDAİ'ı olan hastalarda, ADAİ'ı olan hastalarla karşılaştırıldığında anlamlı olarak daha sık idi (p=0.04, p=0.009). Başvuru sırasındaki ortalama NIHSS skoru PDAİ'lı olan hastalarda (Grup 1) 6.4± 4.6 (0-26), ADAİ'ı olan hastalarda (Grup 2) 6.7±4.3 (0-23) olarak saptandı (p=0.96). Kardiyo-aortik embolizm Grup 2'de Grup 1'e kıyasla daha sık idi ama anlamlı değildi (p = 0.12). Ortalama C-reaktif protein (CRP) düzeyi açısından iki grup arasında istatiksel olarak fark bulunmamaktaydı (p=0.23). Hastanede mortalite Grup 1'de % 14.7 (n=27), Grup 2'de ise % 8.6 (n=23) idi (p = 0.04). İzlem sürecinde PDAİ'ı olan hastalarda ortalama mRS skoru 3 (0-6) iken ADAİ'ı olan hastalarda 2 (0-6) idi (p=0.79). Rekürren inme PDAİ'ı olan hastaların 1'inde (%0.5), ADAİ'ı olan hastaların 8'inde (%3) saptandı (p=0.07).

Sonuç: İnme ünitemizde takip edilen akut iskemik inmeli hastaların %40.6'sında PDAİ saptanmıştır. PDAİ'ı olan hastalarda en sık neden kardiyo-aortik embolizm idi. Diyabet ve geçirilmiş inme öyküsü PDAİ için majör risk faktörleri olarak saptandı. Hastanede mortalite PDAİ grubunda anlamlı olarak daha yüksek idi.

Anahtar sözcükler: ***Posterior Dolaşımda Akut Infarct, Risk Faktörleri, Etyolojik Alt Tipleri, Sonlanım, Prognoz***

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Acute infarcts in posterior circulation (AIPC) have been reported 16-39.8% in previous studies (1,3,5-7,9,10). The most frequent cause of AIPC was embolism from cardio-aortic, vertebra-basilar atherosclerosis or dissection, followed by large-artery atherosclerosis (LAA), small vessel disease and other causes.

The aim of this study was to determine the prevalence, etiologic subtypes, stroke severity and prognosis of patients with AIPC compared to acute infarcts in anterior circulation (AIAC) in our stroke registry.

Methods

The medical records of 554 consecutive patients who were admitted with acute ischemic stroke from January 2011 to November 2014 were retrospectively evaluated. Approval was obtained from the research ethic committee in advance of the study. Posterior circulation ischemic stroke (PCS) was defined as acute infarcts in isolated posterior circulations (Figure 1). The patients with PCS were selected based on diffusion weighted imaging (DWI). The patients were divided into two groups; group 1 included patients with AIPC and group 2 included patients with AIAC. The patients with acute multiple ischemic lesions located in anterior and posterior circulations and without performed DWI were excluded.

Patient demographics and medical risk factors, including history of hypertension, diabetes, hyperlipidemia, atrial fibrillation, congestive heart failure, coronary artery disease, previous transient ischemic attack, previous stroke, the National Institutes of Health Stroke Scale (NIHSS) scores at admission and C-reactive protein (CRP) level at admission were collected using a standard data collection form and entered into an institutional database. Hypertension was defined as blood pressure >=140/90 mmHg on repeated measurements or prior use of antihypertensive medication, diabetes mellitus (DM) as fasting blood glucose level >=126 mg/dL on repeated measurements or the use of medications to lower blood glucose, atrial fibrillation by previous history or if detected on ECG or Holter. Coronary artery disease included any history of angina, myocardial infarction or coronary revascularization.

A single rater (MHS) determined etiologic stroke subtypes using the automated Causative Classification System (CCS, available at https://ccs.mgh.harvard.edu) (11). The CCS subtypes included supra aortic large artery atherosclerosis, cardio-aortic embolism, small artery occlusion, other causes and undetermined causes. Etiologic work-up included vascular imaging studies, such as carotid Doppler ultrasonography, computerized tomography angiography, magnetic resonance angiography or digital subtraction angiography, transthoracic or transesophageal echocardiogram, 24-hour cardiac rhythm monitoring, and laboratory tests for hypercoagulability and vasculitis. The modified Rankin Scale (mRS) scores were recorded according to follow-up visits of the patients.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 16.0 version (SPSS Inc. Chicago, Illinois, USA). Descriptive statistics were expressed as means/standard deviations for normally-distributed continuous variables and median/interquartile range for non-normally distributed variables. Statistical analysis was performed to determine the prevalence and prognosis of the patients with AIPC and AIAS. The group rates were compared using a chi-squared test, and the means were compared using Student's t test; $p<0.05$ was considered to be statistically significant.

Results

A total of 184 (40.6%) patients with AIPC (89 females [48.4%] and 95 males [51.6%]; mean age, 70.6±12.5 [25-92] years) and 268 (59.3%) patients with AIAC (133 females [49.6%] and 135 males [50.4%]; mean age, 69.3±13.7 [28-103] years) were included in the study. Patient demographics and vascular risk factors, including history of hypertension (n=311, 68.8%), diabetes (n=129, 28.5%), hyperlipidemia (n=104, 23%), atrial fibrillation (n=97, 21.5%), congestive heart failure (n=56, 12.4%), coronary artery disease (n=111, 24.6%), previous transient ischemic attack (n=24, 5.3%) and previous stroke (n=78, 17.3%) are shown in Table 1.

History of hypertension, hyperlipidemia, AF, congestive heart failure, coronary artery disease or previous transient ischemic attack was not different between Group 1 and Group 2 ($p>0.05$). However, history of diabetes and previous stroke were significantly more common in the patients with AIPC compared to the patients with AIAC ($p=0.04$, $p=0.009$) (Table 1).

The mean admission NIHSS score was 6.4± 4.6 (0-26) in the patients with AIPC and 6.7±4.3 (0-23) in the patients with AIAC ($p=0.96$) (Table 1). The mean CRP level was 21.15±36.4 mg/dl in Group 1 and 24.71±39.6 mg/dl in Group 2 at admission ($p=0.23$).

The etiologic stroke subtypes in Group 1 were large-artery atherosclerosis (LAA) in 52 (28.3%) patients, cardio-aortic embolism in 73 (39.7%) patients, small artery occlusion in 12 (6.5%) patients, other causes in nine (4.9%) patients and undetermined causes in 38 (20.7%) patients. The etiologic stroke subtypes in Group 2 were large-artery atherosclerosis (LAA) in 62 (23.1%) patients, cardio-aortic embolism in 124 (46.3%) patients, small artery occlusion in 12 (4.5%) patients, other causes in 15 (5.6%) patients and undetermined

causes in 55 (20.5%) patients. Cardio-aortic embolism was more common in Group 2 compared to Group 1, but not significant (p = 0.12) (Table 2).

Mortality in hospital was 14.7% (n=27) in Group 1 and 8.6% (n=23) in group 2. It was significantly higher in Group 1 compared to Group 2 (p = 0.04). The follow-up information was accessible for 308 patients. The median follow-up time was nine (1-32) months. The median mRS score was 3 (0-6) in patients with AIPC and 2 (0-6) in patients with AIAC during this period (p=0.79). Recurrent stroke occurred in one (0.5%) patient with AIPC and in eight (3%) patients with AIAC. There was no significant difference between the groups (p=0.07) (Table 1).

On logistic regression analysis, DM, previous stroke history and mortality in hospital were significantly associated with AIPC, see Table 3.

Table 1: Epidemiologic and clinical characteristics of patients with AIPC and AIAC

	AIPC n=184	AIAC n=268	P
Age, year, *Mean±SD*	70.6±12.5	69.3±13.7	0.34
Sex, *n(%)*			
Female	89 (48.4)	133 (49.6)	0.79
Male	95 (51.6)	135 (50.4)	
Medical history			
- Hypertension, *n(%)*	135 (73.4)	176 (65.7)	0.08
- Diabetes mellitus, *n(%)*	62 (33.7)	67 (25)	**0.04**
- Atrial fibrillation, *n(%)*	35 (19)	62 (23.1)	0.29
- Hyperlipidemia, *n(%)*	36 (19.6)	68 (25.4)	0.15
- CAD, *n(%)*	26 (14.1)	30 (11.2)	0.35
- CHF, *n(%)*	51 (27.7)	60 (22.4)	0.19
- Previous TIA history, *n(%)*	10 (5.4)	14 (5.2)	0.92
- Previous stroke history, *n(%)*	42 (22.8)	36 (13.4)	**0.009**
CRP,mg/l	17.9±30.9	23.1±38.5	0.23
Admission NIHSS, *Mean±SD*	6.4±4.6	6.7±4.3	0. 96
Mortality in hospital, *n(%)*	27 (14.7)	23 (8.6)	**0.04**
Follow up mRS, *Mean±SD*	2.7±2.4	2.4±2.3	0.79
Recurrent stroke, *n(%)*	1 (0.5)	8 (3)	0.07

AIPC; acute infarcts in posterior circulation, AIAC; acute infarcts in posterior circulation, SD; Standard Deviation, CAD; Coronary Artery Disease, CHF; Congestive heart failure, TIA; transient ischemic attack, CRP; C-reactive protein, NIHSS; National Institutes of Health Stroke Scale, mRS; modified Rankin Scale

Table 2: Etiologic stroke subtypes of AIPC and AIAC

	AIPC	AIAC	p
CCS classification, *(%)*			
- Large-artery atherosclerosis	52 (28.3)	62 (23.1)	0.22
- Cardio-aortic embolism	73 (39.7)	124 (46.3)	0.12
- Small artery occlusion	12 (6.5)	12 (4.5)	0.34
- Other rare causes	9 (4.9)	15 (5.6)	0.74
- Undetermined causes	38 (20.7)	55 (20.5)	0.97

AIPC; acute infarcts in posterior circulation, AIAC; acute infarcts in posterior circulation, CCS; Causative Classification System

Table 3: Logistic regression analysis of AIPC

	OR	95%, CI	p
DM, *n(%)*	1.46	1.013 - 2.987	**0.037**
Previous stroke history, *n(%)*	1.81	1.003 – 2.997	**0.022**
Mortality in hospital, *n(%)*	1.66	1.012 – 2.989	**0.044**

DM; diabetes mellitus

Discussion

AIPC were reported 16-39.8% of ischemic stroke patients in previous studies (1, 3, 5, 6, 7, 9, 10). In our registry, AIPC was found in 184 (40.6%) patients. It was higher than the other studies (1, 3, 5, 6, 7, 9, 10).

In some of previous studies, the most common vascular risk factor was hypertension followed by smoking, DM, hyperlipidemia, cardiac disease and previous stroke history in patients with AIPC, but they did not compare with AIAC group (7, 8).

Miyamoto et al. found that younger age and hyperlipidemia were significantly associated with AIPC group (5). In another study by Tao et al., male gender and DM was significantly associated with AIPC (3). Otherwise, most of studies showed that AF was higher in patients with AIAC (1, 3, 5). Conversely, Sato et al. did not find any significant difference between patients with AIPC and AIAC (6). In our study, DM and previous stroke history were significantly associated with AIPC.

In previous studies, the most frequent stroke subtype was LAA in AIPC group (5, 6, 7, 8, 9, 10). Otherwise, we found that cardio-aortic embolism was the most frequent stroke subtype in patients with AIPC.

Miyamoto et al. reported that LAA was higher in AIPC group and cardio-aortic embolism (CE) was higher in AIAC group (5). De Marchis et al. showed that small artery disease was significantly more frequent in patients with PCS than patients with anterior circulation ischemic stroke (1). On the other hand, Sato et al. did not find any significant difference between AIPC and AIAC group (6). There was no significant difference between two groups in our study.

Most of previous studies reported that lower NIHSS score at admission was significantly associated with AIAC group (1, 3, 6, 7). In our study, the mean admission NIHSS score was lower in patients with AIPC than patients with AIAC, but the difference was not statistically significant.

Sato et al. reported that the mRS scores at 3th month were lower in patients with AIPC than in patients with AIAC (6). But, De Marchis et al. found no statistically relevant difference in outcome or mortality between patients with AIPC and AIAC (1). Lee et al. did not find any significant difference with regard to the proportion of patients with clinical improvement or clinical worsening during hospitalization and in-hospital mortality between AIPC and AIAC groups, too (7).

Mortality in hospital was significantly higher in AIPC group compared to AIAC group in our study. Otherwise, there was no significant difference in follow up mRS scores and recurrent stroke prevalence between two groups.

There are several limitations of our study, including its retrospective design, unavailable data of clinical findings and hemodynamic parameters on admission, and a relatively short follow up duration. In addition, this is a restriction of the cohort to a single medical center. However, all of our patients underwent a detailed work-up for determining causative mechanism of ischemic stroke. Acute ischemic lesions were identified with diffusion weighted imaging in all patients. In contrast to the previous studies, etiologic subtypes of AIPC have been determined systematically according to the CCS in our patients.

In conclusion, AIPC was found in 40.6% of patients with acute ischemic stroke in this registry. Cardio-aortic embolism was the most common cause of AIPC group opposite to previous studies. DM and previous stroke history appear to be the major risk factor for AIPC. Mortality in hospital was significantly higher in AIPC group.

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