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Serebral Lateralizasyon, Koroner Arter Hastalığı, Koroner Arter Anomalileri ve Koroner Arter Baskınlığı Arasındaki İlişki

Relationship Between Cerebral Lateralization, Coronary Artery Disease, Coronary Artery Anomalies and Coronary Arterial Dominance

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Öz

GİRİŞ ve AMAÇ: Koroner Arter Hastalığının (KAH) iyi bilinen klasik risk faktörleri ve yeni tanımlanan minör risk faktörlerinin yanı sıra; "geometrik risk faktörleri" olarak adlandırılan yeni risk faktörleri son zamanlarda araştırılmaktadır. Serebral lateralizasyonun (SL) diğer hastalıklarla ilişkisi daha önce tanımlanmıştı. Bu çalışmanın amacı, KAH ile SL, koroner arter anomalisi, koroner arter baskınlığı arasındaki ilişkiyi araştırmaktır.
YÖNTEM ve GEREÇLER: Kliniğimizde Mayıs 2009-Mart 2010 tarihleri arasında koroner anjiyografisi yapılan ardışık 1069 hasta çalışmaya dahil edildi. Koroner arter darlığının varlığı ve evresi, anatomik varyasyonlar ve koroner arter anomalileri, koroner arter baskınlığı ve RCA (S veya C) şekli tanımlandı. Hastaların SL'ye ilişkin el tercihleri "10 Maddeli Edinburg Anketi" ile tanımlandı ve denekler şu şekilde üç gruba ayrıldı: solak, sağ elini kullanan ve her iki eklini kullanan. Hastaların yaş, boy, kilo ve KAH risk faktörlerinin varlığı kaydedildi.
BULGULAR: Üç grup arasında KAH, koroner arter anomalileri ve koroner arter baskınlığı açısından istatistiksel olarak fark yoktu. Ortanca yaş, sağ elini kullananlara kıyasla sol elini kullananlarda önemli ölçüde daha düşüktü. Koroner arter anomalileri ve koroner arter baskınlığı açısından 38 sol el ile 38 sağ el arasında fark yoktu.
TARTIŞMA ve SONUÇ: Solak hastalarda daha düşük koroner arter darlığı oranları ve tutulan arter sayısının daha düşük olması sağ elini kullananların solaklara göre daha yüksek KAH riski altında olabileceğini düşündürmektedir.

Anahtar Kelimeler: Serebral lateralizasyon, Koroner Arter Hastalığı, Koroner arter baskınlığı, Koroner arter anomalisi.

Abstract

INTRODUCTION: Besides the well-known classic risk factors and newly described minor risk factors of Coronary Artery Disease (CAD); novel risk factors so-called "geometric risk factors" are recently being investigated. The association of cerebral lateralization (CL) with other diseases has been defined formerly. The aim of this study was to investigate the relationship between CL and CAD, coronary artery anomaly, coronary artery dominance.
METHODS: 1069 consecutive patients who underwent coronary angiography in our Clinics between May 2009 and March 2010 were included in the study. The presence and the stage of coronary arterial stenosis, the anatomic variations and coronary artery anomalies, coronary artery dominance and the shape of RCA (S or C) were defined. Hand preferences of the patients in regard to CL were defined with "10 Items Edinburgh Questionnaire" and subjects were divided into three groups as follows: left-handed, right-handed and mixed-handed. Age, height, weight and the presence of CAD risk factors of the patients were recorded.
RESULTS: There was no statistical difference between the three groups in terms of CAD, coronary artery anomalies and coronary artery dominance. The median age was significantly lower in the left-handeds compared to the right-handeds. There was no difference between 38 left-handeds and 38 right- handeds in terms of coronary artery anomalies and coronary artery dominance.
DISCUSSION and CONCLUSION: Lower rates of coronary artery stenosis and number of involved arteries were lower in the left-handed patients, suggesting that right-handed people may be at a higher risk of CAD than the left-handed ones.

Keywords: Cerebral lateralization, Coronary Artery Disease, Coronary artery dominance, Coronary artery anomaly.

INTRODUCTION

Besides known classical risk factors and recently described minor risk factors in the development of coronary artery disease (CAD), there are newer risk factors that have been more recently studied and defined as "geometrical risk factors" (1-4). It has been reported that certain aspects of the

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vascular geometry that mediate both flow dynamics and wall mechanics may be risk factors of coronary atherosclerosis (5). The fluid dynamic environment in the arterial wall relies on both the geometry and the movement of the channel where the fluid flows, and the geometries with adverse hemodynamics may be an additional risk factor for the disease. Left and right cerebral hemispheres are known to have different roles in the regulation of cardiovascular function. Whereas the right hemisphere modulates sympathetic cardiovascular activity, the left hemisphere more contributes to parasympathetic. Studies have reported cerebral lateralization (CL) in the cardiac autonomic control (6). Numerous studies have reported an association between left-handedness and diseases including migraine, epilepsy, autism, attention deficit, hyperactivity disorder, schizophrenia, Alzheimer's disease, obsessive compulsive disorder, allergic diseases, immune system diseases, autoimmune diseases, antisocial behavior disorders, drug and alcohol abuse (7-11).

It was thought that evaluation of the geometry of human coronary arteries with CL may be a potential tool for predicting the risk of CAD. Therefore, the objective of this study was to evaluate the relationship of CL with CAD, coronary artery anomalies and coronary artery dominance.

METHODS

A total of 1069 patients who underwent coronary angiography examination in the cardiology department of an University Medical Faculty between May 2009 and March 2010 were prospectively included in the study. The indications of coronary angiography included stable angina pectoris, unstable angina pectoris, myocardial infarction (MI), prognostic reasons following MI, atypical chest pain and significant valvular disease. Patients with unsatisfying coronary artery images were excluded from the study. Patients' demographic features such as age and gender, and risk factors including the presence of hyperlipidemia, hypertension, diabetes mellitus, smoking status and obesity, which was determined with body mass index were recorded.

Coronary angiography protocol

All patients were percutaneously catheterized through the femoral artery with standard Judkins technique or via the right brachial artery with Sones technique. The coronary angiograms were visually interpreted by two separate specialists. The atherosclerotic lesions of the left main coronary artery (LMCA), left anterior descending (LAD) artery, circumflex (Cx) artery and right coronary artery (RCA) were determined. The presence of ≥50% lesions in each artery was described as vascular lesions. More than 50% stenosis of the luminal diameter observed during systole compared to diastolic phase was defined as myocardial bridge (MB). Congenital coronary artery anomalies were detected. Coronary dominance was defined according to branching of posterior descending artery (PDA). RCA supplying PDA was defined as right dominant, Cx branching PDA as left dominant, and both RCA and Cx supplying PDA as balanced (12). The criteria of a luminal diameter < 2mm and not supplying PDA were used to define rudimentary RCA (13). Patients without any angiographic lesion were defined as not having CAD or normal. More than 50% dilatation of an arterial luminal diameter was defined as ectasia (14).

Determination of shape of the right coronary artery

In order to determine the shape of the right coronary arteries, we used a single-frame angiogram acquired during end-diastole of the cardiac cycle at 23-35 degrees left anterior oblique projection, generally without cranio-caudal angle. A perpendicular line combining two points at the lateral margin of the artery was plotted and the longest perpendicular width

between this line and the artery was measured. The arteries were categorized as sigma (S) (Figure 1) if the width measured was wider than the maximal arterial diameter, and those with only one lateral point or the arteries that did not meet criterion of categorization as S were classified as C (Figure 2) (15).

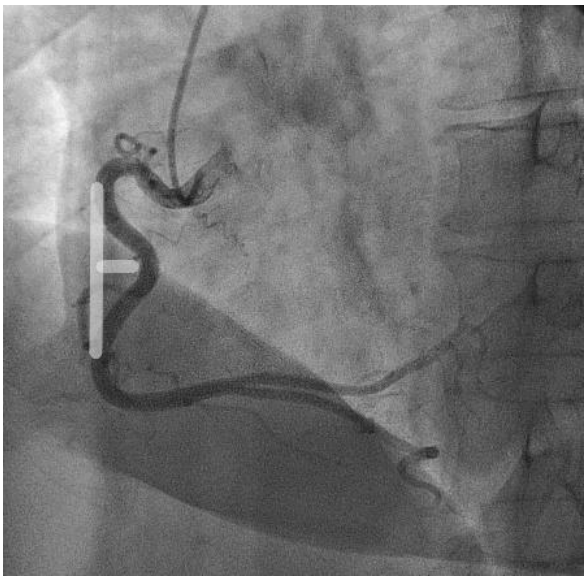

Figure 1. Angiographic view of S shaped right coronary artery

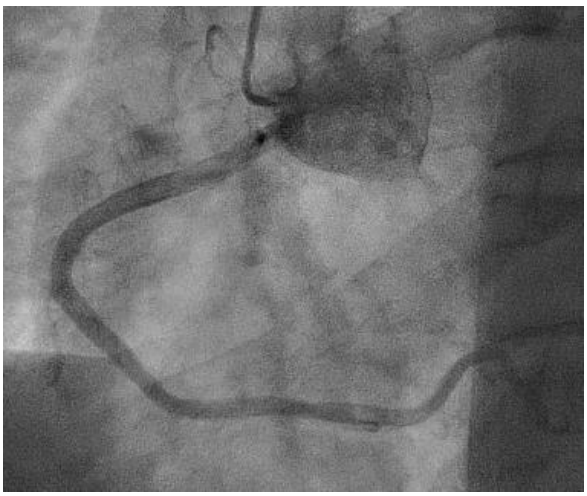

Figure 2. Angiographic view of C shaped right coronary artery

Determination of cerebral lateralization

Ten-question Edinburgh Handedness Inventory was used to determine hand preference in CL (16). The patients were asked to answer the ten questions that determine their hand preference during several activities including writing, drawing, throwing (ball), holding scissors, toothbrush, knife, spoon, brooming, striking match and opening box. They were told to put "+" mark to the column related to the hand that they use during the activity. The patients were asked to put "++" if they strongly use that hand, "+" if the preference is not much strong, and "+" to both columns if they use both hands equally. The score was obtained by counting "+" marks of the relevant columns. (Left hand column = X, Right hand column = Y) Cumulative total (CT) = X + Y, Difference (D) = Y – X, Score = (D/CT) x100. The patients were defined as left-handed: for scores <-40, mixed handed: for -40 ≤ score ≤ +40, and right handed: for scores > +40.

In the statistical analysis, descriptive statistics were evaluated with ANOVA variant analysis, Chi-square test and student's t test. The statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 16.0.

RESULTS

A total of 1069 patients who underwent diagnostic coronary angiography in the cardiology department of Izzet Baysal University Medical Faculty were included in the study. The patients were divided into three groups based on the hand preferences. As a result of the scoring, patients with a score > +40 points were defined as right-handed (Group 1), those with a score < -40 points as left-handed (Group 2) and those with a score between -40 and +40 points as mixed handed (Group 3). Accordingly, 92% of the patients were right-handed, 3.5% left-handed and 4.5% as mixed handed. There was no significant difference between the groups in terms of gender ($p>0.05$). The mean age of the left-handed patients was significantly lower than the right-handed patients ($p<0.05$). The mean age of mixed-handed patients tended to be less than that of right-handed patients ($p=0.055$).

When risk factors were examined according to the groups; no significant difference was found in terms of the incidences of hypertension, diabetes mellitus, hyperlipidemia, active smoking, family history of premature CAD and obesity (for all p>0.05). Clinical and demographic characteristics of patients are given in Table 1.

The groups were compared in terms of the rates of coronary artery involvement and coronary artery anomalies. No significant difference was found between the three groups in terms of the number of diseased vessels (p>0.05). In addition, there was no significant difference in regarding the stenosis of LMCA, LAD, Cx and RCA (for all p>0.05).

When the groups were compared in terms of coronary artery anomalies, 12 patients (1%) with anomalies were found in Group 1. Among these patients, absence of LMCA was found in 6, single coronary artery in 1, dual LAD in 1, RCA originating from the left sinus valsalva in 1, Cx arisen from RCA in 1 and coronary fistula in 2 patients. Absence of LMCA was observed in 1 patient (4%) in Group 2. There was no coronary anomaly in Group 3. The rates of coronary artery involvement and coronary artery anomalies are shown in Table 2

When the groups were compared in terms of coronary dominance, 56 patients excluded from the evaluation because their RCAs were totally obstructed. In Group 1, 178 (19%) patients were Cx dominant, 583 (63%) patients were RCA dominant, and 169 (18%) were in balance. In Group 2, 10 (27%) patients were Cx dominant, 24 (65%) patients were RCA dominant, and 3 (8%) were in balance. In Group 3, 11 (24%) patients were Cx dominant, 26 (57%) patients were RCA dominant, and 9 (19%) were in balance. There was no statistically significant difference between the groups in terms of coronary dominance (p>0.05).

Tablo 1. Clinical and demographic characteristics of patients

	Right-Handed (Group 1) n:981	Left-Handed (Group 2) n: 38	Mixed-Handed (Group 3) n=50	P Value
Age	62±12	57±13	58±10	0.003*
Gender/Female	549 (%56)	21 (%56)	32 (%64)	0.432
Height (cm)	165±8	166±8	166±7	0.771
Weight (Kg)	77±14	77±15	76±12	0.719
Obesity	314 (%32)	11 (%30)	14 (%28)	0.706
Hyperlipidemia	441 (%46)	19 (%49)	22 (%44)	0.876
DM	275 (%28)	8 (%22)	17 (%33)	0.629
HT	579 (%59)	22 (%59)	25 (%49)	0.504
Smoking	216 (%22)	8 (%22)	13 (%26)	0.796
Family history	294 (%30)	18 (%35)	16 (%31)	0.790

Tablo 2. The rates of coronary artery involvement and coronary artery anomalies

	Right-Handed (Group 1) n=981	Left-Handed (Group 2) n= 38	Mixed-Handed (Group 3) n=50	P Value
Number of Diseased vessel	1.01	0.75	1.33	0.102
Rudimentary RCA	76 (%8)	3 (%9)	4 (%8)	0.987
Myocardial bridge	5 (%05)	1 (%3)	0	0.209
Coronary anomaly	12 (%1)	1 (%4)	0	0.549
Shape of RCA (C)	700/930 (75%)	26/38 (68%)	35/46 (76%)	0.518
Slow coronary flow	41/981 (4%)	3/38 (8%)	0/50 (0%)	0.182
Coronary artery ectasia	78/981 (8%)	3/38 (8%)	3/50 (6%)	0.889
LMCA stenosis	16 (%2)	0 (0%)	4 (%8)	0.111
LAD stenosis	397 (%40)	12 (%32)	25 (%50)	0.328
Cx stenosis	295 (%30)	9 (%24)	19 (%38)	0.627
RCA stenosis	285 (%29)	7 (%19)	19 (%38)	0.234

In addition, left-handed patients were matched with 38 right-handed patients for age and gender. The same parameters were compared between these two groups. No significant difference was found between the two groups in terms of coronary artery anomalies and coronary dominance ($p>0.05$). However, the rate and presence of stenosis in LMCA, and in RCA were statistically significantly higher in the right-handed patients than in the left-handed patients ($p<0.05$). The number of involved arteries tended to be higher in the right-handed patients (1.34 vs 0.84, $p=0.069$).

DISCUSSION

Cerebral lateralization refers to different abilities of a cerebral hemisphere in gaining, performing, and controlling some specific neurologic functions (17). Cerebral dominance is the dominance of one cerebral hemisphere on the other in performing and controlling some neurologic functions (18). Dominant laterality refers to a dominant extremity or emotion in performing complex psychomotor activities. Laterality may manifest both as right-handedness and left-handedness that are functionally equal and symmetric in performing activities. The most accepted theory for the onset of lateralization is genetic theory. Accordingly, organization asymmetry models of the brain are strongly genetically determined (19).

Because hand preference reflects asymmetric structure of the brain, cerebral asymmetry is genetically structured. However, since the relationship between genetic factors and left-handedness could not been clearly demonstrated, research has focused on environmental factors affecting left-handedness. It is obvious that cognitive functions of the brain are not related only with the development of both cerebral hemispheres. The brain has two hemispheres, about only one consciousness.

These to cerebral hemispheres are connected with nervous fibers. One of them is informed immediately about the other's activity. Therefore, persons with high intelligence also have an excellent communication between the right and left hemispheres (20).

Right hand dominance is seen by 85-90% in the general population. Considering mixed-handed people, this rate may change as 66% right-handedness, 30% mixed-handedness and 4% left-handedness (21). Left-handedness has been found to be 1-2% more common among men (22).

Starting from 1860s, today significant improvements have been noted in CL as a result of anatomical, embryological, pathological, chemical, hormonal and psychological studies. Many of behavioral asymmetries resulted from hemispheric asymmetry have been described. The most prominent asymmetry is hand preference. Hand preference, and thus dominant cerebral region for hand preference are used for determination of lateralization (21).

Left-handed people live 8-10 years less on average. There are some diseases associated with left-handedness. The most focused among these diseases are migraine, epilepsy, autism, attention deficit hyperactivity disorder, schizophrenia, Alzheimer's disease, obsessive compulsive disorder, allergic diseases, immune system diseases, autoimmune diseases, antisocial behavior disorders, drug and alcohol abuse (7).

Although the etiology of CAD or atherosclerosis has not been fully understood, besides genetic and familial factors, acquired risk factors such as smoking, hypertension, diabetes mellitus and hyperlipidemia are also associated with this disease.

Studies have reported associations between skull-recorded temporal lobe activity and autonomic regulation or cardiovascular function (23). Again, there are studies reporting association between left-handedness and sudden death from CAD (24). Recently, hemispheric lateralization has been described in decreased cerebral blood flow and autonomic defects in heart failure (25).

In our study, we evaluated the relationship between CL and CAD, major risk factors, coronary artery anomalies and coronary arterial dominance. Of the 1069 patients evaluated; 981 patients (92%) were right-handed, 38 patients (3.5%) left-handed and 50 patients (4.5%) mixed-handed. When coronary angiographic, laboratory and clinical parameters were compared between the groups; no statistically significant difference was found between the groups in terms of the severity of CAD and risk factors ($p>0.05$). However, the mean age was significantly lower in 38 left-handed patients compared to right-handed ones ($p<0.05$). This result suggests that although there was no significant difference in terms of CAD and lesion severity at first sight, left-handed patients experience CAD in a younger age and probably develop early atherosclerosis. However, when equal number of left-handed patients were matched with right-handed ones for age and gender, the picture shows some difference. Total 38 left-handed patients in our study may be seen as a limitation; however, compared to the right-handed patients left handed-ones had lower rates and percentages especially in terms of right coronary stenosis and lesion percentage. Similarly, left main coronary artery stenosis and lesion percentage were also higher in the right-handed patients. Although not statistically significant, the incidence of diabetes mellitus was higher in the right-handed patients compared to the left-handed ones. The rate of ectatic vessel segments was 8% in the left-handed patients, and the difference was close to statistical significance ($p=0.092$). The number of involved arteries was higher in the right-handed patients (1.34 vs 0.84) and the difference was close to statistical significance ($p=0.069$).

There was a difference close to significance

between mixed-handed patients and right handed ones in terms of age (p=0.055). No significant difference was found between the groups in terms of coronary artery anomalies and coronary dominance (p>0.05).

Lack of a significant difference between left-handed, right-handed and mixed-handed patients in terms of coronary artery anomalies and dominance supports that the variations in cardiac embryogenesis are not associated with cerebral lateralization.

Conclusion

According to the results of the present study, no significant difference was found between left-handed, right-handed and mixed-handed patients in terms of cardiovascular risk factors, coronary anomalies and coronary dominance. However, lower rates of coronary artery stenosis and number of involved arteries were lower in the left-handed patients, suggesting that right-handed people may be at a higher risk of CAD than the left-handed ones.

Further clinical studies including larger series evaluating the possible association of CL with CAD and coronary anatomy are warranted.

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