Association of Indicators of Dehydration and Haemoconcentration with the Coronary Slow Flow Phenomenon

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ABSTRACT

Objectives: The coronary slow flow phenomenon (CSFP), characterized by decreased distal progression of dye to coronary arteries, is a distinct angiographic phenomenon and little is known about its pathophysiology. Although several hypotheses have been suggested, the underlying mechanism of CSFP has not been well established yet. The aim of this study was to determine the roles of indicators of dehydration and haemoconcentration in CSFP which have blood flow abnormality effects.

Methods: The study consisted of 33 patients with CSFP (group 1), and 31 normal subjects as control group (group 2) detected by coronary angiography. CSFP was diagnosed by the TIMI frame count method. Serum electrolytes, osmolarity and haematological parameters were measured.

Results: Compared with control subjects, patient with CSFP had increased levels of calculated osmolarity, tonicity, sodium, glucose and blood urea nitrogen (BUN). Significant differences were also observed in the hematocrit, haemoglobin concentration, and calculated osmolarity but not in total cholesterol and albumin.

Conclusions: The results of the present study indicate that the markers of haemoconcentration and dehydration are significantly associated with CSFP. The markers may be important in the coronary blood flow anomaly.

Key Words: Coronary slow flow phenomenon, haematocrit, haemoconcentration, osmolarity, tonicity.

ÖZET

Koroner Yavaş Akım Fenomeniyle Dehidratasyon ve Hemokonsantrasyon Belirteçlerinin İlişkisi


Yöntemler: Çalışmaya anjiografik olarak 33 KYAF'si olan hasta (grup 1) ile 31 normal olan kontrol grubu hasta alınmıştır. KYAF tanısı TIMI frame sayım metodu ile konmuştur. Serum elektrolit, osmolarite, ve hematolojik parametreler ölçülmüştür.

Bulgular: KYAF hastalarında kontrol grubuna göre hesaplanmış osmolarite, tonisite, sodyum, glukoz, ve kan üre nitrojen düzeyi daha yüksek saplanmıştr. Ayrıca total kolesterol, albumin hariç hematokrit, hemoglobin ve hesaplanmış osmolarite de anlamlı fark saplanmıştr.

Sonuç: Bu çalışmamızKYAF ile hemokonsantrasyon ve dehidratasyon belirteçlerinin anlamlı olarak ilişkili olduğunu göstermiştir. Bu belirteçler koroner kan akım anomalisinde önemli olabilir.

Anahtar Kelimeler: Koroner yavaş akım fenomeni, hematokrit, hemokonsantrasyon, osmolarite, tonisite.

INTRODUCTION

The coronary slow flow phenomenon (CSFP), characterized by decreased distal progression of dye to coronary arteries, is a distinct angiographic phenomenon and little is known about its pathophysiology. Frequently, abnormally high small vessel resistance and increased microvascular tone have been suggested as the cause of this unique angiographic finding (1-3). It has been previously reported that brachial artery vascular endothelial functions are impaired in these patients (4). The vascular endothelium is injured by blood flow abnormalities aggravated by different risk factors. The viscoelastic nature of blood flow plays a major role in this process and depends on

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corpuscular and biochemical components of the blood (5, 6).

Haemoconcentration describes conditions under which the relative ratio of cellular and biochemical blood components to plasma volume increases (7). Haematocrit (Hct), haemoglobin (Hb) and total protein concentrations are indirect parameters commonly used as indices of the degree of haemoconcentration (8, 9). In addition, serum osmolality and sodium concentration are indicators of the status of extracellular fluid, as well as total body hydration (10, 11). It has been shown that haemorheological parameters, such as blood and plasma viscosity, Hct and Hb levels, are related to the incidence of cardiovascular disease (12-15).

Thus, in this study, we studied the relationship between the indicators of haemoconcentration and CSFP.

PATIENTS and METHODS
Thirty three patients (17 males and 16 females, mean age 51 ± 7 years, group 1) with CSFP detected by coronary angiography by the TIMI "frame count" method were included in this study. Gender and age-matched 31 control subjects with no coronary or valvular disease (15 males and 16 females, mean age 49 ± 8 years, group 2) were included in this study. In both groups, coronary arteriography was performed since the subjects were suffering from intractable symptoms such as angina and angina-like chest pain, shortness of breath and palpitation, and their symptoms could not be adequately clarified with noninvasive tests.

Exclusion criteria were as follows: coronary artery disease including spasm, plaque, ectasia or obstructive lesion, positive family history of hyperlipidemia, known peripheral vascular disease, diabetes mellitus, congestive heart failure, valvular heart disease, hypertrophic, restrictive and dilated cardiomyopathy, left ventricular hypertrophy, vasculitis, pulmonary, renal, and hematologic disorders and use of medications known to alter plasma lipid profile.

All participants underwent two-dimensional echocardiographic evaluation by an experienced research echocardiographer using commercially available echocardiography machines equipped with 3.5 MHz transducers (Vivid System Five, GE Vingmed Horten, Norway). Measurements were made according to the American Society of Echocardiography guidelines by a single cardiologist (16). Left ventricular ejection fraction (LVEF) was measured from the apical four-chamber and two-chamber views using the modified Simpson method (16).

Definition of Slow Coronary Flow
Coronary flow was quantified by using the thrombolysis in myocardial infarction (TIMI) frame count method (17). All patients with a TIMI frame count (TFC) greater than 2 standard deviations (SD) from the published normal range for the particular vessel were accepted as having CSFP while those whose TFC fell within 2 SD of the published normal range were considered to have normal coronary flow (17).

Measurement of TIMI Frame Count
Coronary angiography was performed via femoral approach using the standard Judkins technique and iopromide (Ultravist-370, Schering AG, Berlin, Germany) as the contrast agent (cine angiographic equipment: Philips Integris H 3000, Holland; cine frame:30 fps). The angiograms were recorded on a compact disc in DICOM format. We measured the number of cine frames required for the contrast to first reach standard distal coronary landmarks in the left anterior descending coronary artery (LAD), left circumflex artery (Cx), and right coronary artery (RCA). The first frame is defined as the one where the column of nearly or fully concentrated dye is seen extending across at least 70% of the arterial lumen with antegrade dye motion, and the last frame counted is that in which contrast first appears in the distal predefined landmark branch, but full opacification of the branch is not necessary (18). The distal coronary landmarks used for analysis were the distal bifurcation at the apex of the LAD (the mustache, pitchfork, or whale's tail), the distal bifurcation of the major obtuse marginal or the main Cx, whichever was larger, and the site of origin of first branch at the crux or its posterolateral extension for RCA. The cine film was run past the initial opacification of the end branch and then was moved forward by frame in reverse until the end branch disappeared before catching the last frame. Then the frame count for each artery was done by subtracting the first frame from the last frame. The LAD frame count was corrected by dividing with 1.7 to derive a corrected TIMI frame count (CTFC) (18).

Biochemical measurements
Blood samples were taken after overnight (12 h) fasting on the day prior to angiography. All measurements were performed on fresh serum. Serum lipids, were measured on a Roche Hitachi 911 (Roche Diagnostics, Indianapolis, IN, Germany) system using Roche cholesteryl, Triglycerides/GB, LDL-C and HDL-C plus reagents. The standard deviation for osmolarity measurements from triple samples was less than 1 mOsmol/kg H2O. Sodium and potassium were determined by fully-selective system for Clinical Chemistry, ISE (Roche/Hitachi 902, Germany).

Serum osmolarity was calculated using the following equation: (10) Serum osmolarity= 1.897[Na^+] + glucose + BUN + 13.5 [19] where BUN is blood urea nitrogen. Serum glucose concentrations were determined by the enzymatic glucose oxidase method (Roche Hitachi analyzer), creatinine was determined by creatinine Roche Jaffe method (Roche/Hitachi 902) and urea was determined by the kinetic UV assay method (Hitachi/Roche Urea, Germany).

Statistical Analyses
Statistical analysis was performed with SPSS for Windows, version 16.0 (SPSS Inc, Chicago, Illinois). Data are presented as mean ± standard deviation. For continuous variables unpaired Student t test was used. A p value <0.05 was considered to indicate statistical significance.

RESULTS
The baseline characteristics of the study groups, TIMI frame count for each artery, in the use of antihypertensive medication are shown in Table 1.

Koşuyolu Kalp Dergisi
Association of Indicators of Dehydration ...
Table 1: The baseline characteristics of the study groups, TIMI frame count for each artery, in the use of antihypertensive medication are shown.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>51 ± 7</td>
<td>49 ± 8</td>
</tr>
<tr>
<td>Male/Female</td>
<td>17 / 16</td>
<td>15 / 16</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>73 ± 7</td>
<td>69 ± 8</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>120 ± 13</td>
<td>123 ± 12</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>79 ± 7</td>
<td>78 ± 9</td>
</tr>
<tr>
<td>Smoking, n</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>29±3</td>
<td>28±4</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>65 ± 3</td>
<td>66 ± 2</td>
</tr>
<tr>
<td>CTFC-LAD, frames/sec</td>
<td>31±10</td>
<td>16±4</td>
</tr>
<tr>
<td>RCA TFC, frames/sec</td>
<td>33±9</td>
<td>15±4</td>
</tr>
<tr>
<td>Cx TFC, frames/sec</td>
<td>27±8</td>
<td>17±3</td>
</tr>
<tr>
<td>Mean TFC, frames/sec</td>
<td>30±7</td>
<td>16±3</td>
</tr>
<tr>
<td>Calcium antagonists, n</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>ACE inhibitors, n</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>


The corrected TIMI frame count, Cx frame count, and RCA frame count were significantly higher in CSFP than control subjects. There was no difference between the two groups in terms of sex, age, heart rate, systolic blood pressure (BP), diastolic BP, body mass index (BMI), smoking, echocardiographic parameters and the use of angiotensin-converting enzyme inhibitors and calcium channel blockers.

The biochemical and haematological parameters of the study groups are shown in Table 2.

Table 2: The biochemical and haematological parameters of the study groups are shown.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated osmolarity (mOsmol/kg H2O)</td>
<td>298.5± 9.2</td>
<td>286.1 ± 7.6</td>
</tr>
<tr>
<td>Serum toxicity (mOsmol/kg H2O)</td>
<td>295.2± 9.1</td>
<td>282.5 ± 7.4</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>139.8 ± 3.6</td>
<td>137.4/ 4.5</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.7± 0.42</td>
<td>4.59 ± 0.35</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>108 ± 20</td>
<td>100 ± 14</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>19.4 ± 6.7</td>
<td>16.2 ± 5.9</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.97 ± 0.16</td>
<td>0.85± 0.19</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>43.4±5.4</td>
<td>40.5±4.4</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>14.6 ± 1.7</td>
<td>13.8 ± 1.5</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>16±6</td>
<td>14 ±6</td>
</tr>
<tr>
<td>Platelet count (X109/L)</td>
<td>242±89</td>
<td>258±53</td>
</tr>
<tr>
<td>Partial prothrombin time (s)</td>
<td>27±2</td>
<td>26±3</td>
</tr>
<tr>
<td>Prothrombin time (s)</td>
<td>12.6±2.5</td>
<td>11.6±1.2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>194±36</td>
<td>187±42</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>132±88</td>
<td>117±83</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>128±29</td>
<td>121±33</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>39±9</td>
<td>41±7</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.41±0.43</td>
<td>4.36±0.45</td>
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</table>

BP: blood pressure, BMI: body mass index, LVEF: left ventricle ejection fraction, LDL: low-density lipoprotein, HDL: high-density lipoprotein, CTFC-LAD: corrected TIMI frame count, Cx TFC; right coronary artery TIMI frame count, Cx TFC; circumflex artery TIMI frame count.

DISCUSSION

The results of the present study indicated that some of the markers of haemoconcentration and dehydration are significantly associated with the CSFP. Although the pathophysiological mechanisms of CSFP remain uncertain, there are several hypotheses that have been suggested: for example, a form of early phase of atherosclerosis (20), small vessel dysfunction (21), Hagen–Poiseuille’s equation model (22), imbalance between vasoconstrictor and vasodilatory factors (23-25), inflammation (26), platelet function disorder (27,28), and interaction of plasma homocysteine and thyroid hormone concentrations (29).

It has also been reported that brachial artery vascular endothelial function was impaired in these patients (4).

Haematocrit, Hb, serum total protein, osmolality, sodium, the density and viscosity of blood and plasma have been used as measures of the cellular and constituent mass to plasma volume ratio. However, the extent to which of these variables are indicative of haemoconcentration differs. Haematocrit and Hb concentration, routinely reported along with other haematological variables, are widely used as indicators of haemoconcentration (8,9). Because the Hct is the ratio of red cells to plasma volume, in order for the measure of Hct to provide an accurate estimate of changes in plasma volume, both a constant number of red blood cells and a constant volume of cells are assumed. Plasma or serum total protein concentration is also often measured concurrently with Hct and/or Hb to confirm haemoconcentration. Yet, total plasma protein is not sufficient by itself to estimate changes in plasma volume as accurately as Hct owing to the movement of small proteins across capillary membranes. Furthermore, because albumin is a negative acute-phase reactant and is reduced in cardiovascular disease patients, the total serum protein concentration does not increase significantly under these conditions.

In this study, we found for the first time that some of the haemoconcentration markers are significantly high in CSFP. High levels of some of the haemoconcentration markers have been reported to be associated with tachycardia (30), reduced oxygen transport (31), reduced myocardial perfusion (32) and increased risk of coronary thrombosis (33,34).

Moreover, when red blood cells (RBCs) pass through the microcirculation, they release vasodilatory compounds, such as ATP or nitric oxide (NO), that enhance blood flow to hypoxic tissues (35,36) causing the imbalance between vasoconstrictor and vasodilatory mechanisms.
In our study, increased TFC values in patients with CSFP might be caused by cardiac effects of haemoconcentration markers.

The findings of the present study indicated that CSFP patients have statistically significant dehydration when compared to control subjects. The results showed that serum osmolality was increased in CSFP patients. The major determinants of serum osmolality, namely sodium, glucose and BUN, were higher in SCFP patients although it was statistically insignificant. Even though serum osmolality and sodium are indicators of the hydration status of the body, their relationship is influenced by glucose and BUN, as seen in equation 1. The effect of sodium on cardiovascular disease is mainly exerted through its effects on blood pressure (37). However, recent animal studies, as well as clinical/therapeutic trials, have shown that Na+ has pressure-independent injurious effects on the arterial wall (37, 38). Most outcomes in diabetes mellitus patients are due to insulin insufficiency, but hyperglycaemia itself, as an independent variable, has deleterious effects, such as glycosylation of tissue proteins and hyperosmolality (39, 40).

Few prospective studies of CAD risk have evaluated the coagulation activation markers, and shortened coagulation times, were thereafter limited and inconclusive (41, 42).

In our study, platelet count, partial prothrombin time and prothrombin time were similar in both groups. The Thrombolysis in Myocardial Infarction (TIMI) flow grading system is a valuable and widely used qualitative measurement for CSFP. However, the measurement of TFC from coronary angiograms is operator-dependent to some extent. Important variables that can significantly affect the TFC exist. For example, nitrate use, heart rate, and the phase of the cardiac cycle in which dye is injected have a significant effect on TFC (43). The corpuscular and biochemical components play a major role the viscoelastic nature of blood flow (5, 6).

Some of dehydration and haemoconcentration marker should be taken into account when using TFC method in conditions which are responsible for CSFP such as myocardial microvascular disorder and endothelial dysfunctions.

Study Limitations

Whole-blood and plasma viscosity were not examined in the present study. Coronary blood flow was not measured invasively.

CONCLUSION

In conclusion, the results of the present study indicate that the markers of haemoconcentration and dehydration are significantly associated with CSFP. The markers may be important in the coronary blood flow anomaly.

REFERENCES


