Doppler ultrasonography of splanchnic vessels in patients with familial Mediterranean fever

Ailesel Akdeniz ateş olan hastalarda splanknik damarların Doppler ultrasonografisi

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Abstract

Aim. In FMF patients, abdominal pain attacks commonly occur and affect the whole abdomen with all findings of peritoneal inflammation. The aim of the present study was to evaluate the selected arterial and venous ultrasonographic and Doppler ultrasonographic parameters including the peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), and pulsatility index (PI) of superior mesenteric and celiac arteries, and blood flow velocity of portal vein in FMF patients in remission.

Methods. Ultrasonographic and Doppler ultrasonographic examinations performed at our Radiology Service from January 2012 to February 2013 were reviewed retrospectively in 52 adult FMF patients in stable phase. Correlation analyses were performed to assess the association of clinical and Doppler ultrasonographic data.

Results. Overall, there was no meaningful association between clinical and Doppler ultrasonographic parameters obtained from the superior mesenteric and celiac arteries and portal vein.

Conclusions. In this study, we attempted to reveal the long-term effect of abdominal attacks on abdominal vessels that might be affected by experienced abdominal attacks related to long-term nature of FMF. According to our findings, FMF may not cause deterioration in blood flow of the superior mesenteric and celiac arteries and portal vein. These findings cannot be accepted as the evidence of absence of atherosclerotic changes developing in patients with long-term inflammatory disorders like FMF. Further studies are needed to shed light on the long-term effects of inflammation related to FMF on vascular system.

Keywords: Familial Mediterranean fever, Doppler ultrasonography, superior mesenteric artery, celiac artery, portal vein

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Özet

Amaç. FMF olgularında karn ağrısı atakları sıklıkla görülür ve peritoneal inflamasyon bulguları ile tüm karnın etkilenir. Bu çalışmamızın amacı FMF olgularında superior mezenterik ve çöliak arterler ile portal venin pik sistolik, end diastolik, pulsatilite, ve rezistif indekslerinin Doppler ultrasonografi ile değerlendirilmesidir.


Anahtar sözcükler: Ailesel Akdeniz ateş, Doppler ultrasonografi, superior mezenterik arter, çöliak arter, portal ven

Introduction

Familial Mediterranean fever (FMF) is one of the autosomal recessive diseases. It is characterized by unprovoked, recurring, self-limited short episodes of fever and serositis resulting in pain in the abdomen, chest, joints, and muscles; it is accepted as one of the most common of the periodic hereditary fevers [1]. FMF mainly affects Middle Eastern populations and other ethnic groups living around the Mediterranean basin, such as Jews, Armenians, Turks, and Arabs, with high prevalence (1/200–1/1000); also, it is not considered rare in Italy, Spain and Greece [2-5].

Although FMF patients in remission, subclinical inflammation might be present somewhat in the body widely for prolonged times [6-8]. During exacerbation, related to the acute-phase response, there are a marked increase in erythocyte sedimentation rate, white blood cell count, fibrinogen, C-reactive protein, serum amyloid-A, interleukin-6, and tumor necrosis factor alpha [6, 9-11]. The status of inflammation as assessed by biomarkers mentioned previously likely reflects the activity of the disease and thus may contribute to the individual’s risk for atherosclerotic process [12].

Doppler ultrasonography as a non-invasive technique provides invaluable diagnostic approach by contributing the diagnosis of a broad range of pathologies related to atherosclerosis. According to our knowledge, there are not sufficient data to determine the status of blood flow in the portal vein and superior mesenteric and celiac arteries in patients with FMF in stable phase. The aim of the present study was to assess the effect of FMF on the selected arterial and venous Doppler ultrasonographic parameters including the peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), and...
pulsatility index (PI) of superior mesenteric and celiac arteries, and blood flow velocity of portal vein in FMF patients with remission.

Materials and methods

In this study, Doppler ultrasonography examinations performed at our Radiology Service from January 2012 to February 2013 were reviewed retrospectively in 52 adult FMF patients in stable phase. These Doppler ultrasound examinations were requested by internists for the differential diagnosis of comorbidities. For each case, a detailed review was conducted to confirm the absence of any vascular pathology. Patients with a history of any type of vascular abnormalities were excluded. Bilateral vascular ultrasonography and Doppler ultrasonography of portal vein and superior mesenteric and celiac arteries were performed. Patients were examined while they were in a supine position. Heart rate and blood pressure were recorded prior to US examination. One radiologist performed all ultrasound examinations by an ultrasonography device (General Electric Logic 9; Waukesha, WI, USA) equipped with a 3.5 MHz convex transducer. Intraobserver reliability was determined as Kappa coefficient ranged from 0.77-0.83.

Assessment of vascular ultrasound and Doppler ultrasound parameters

The participants underwent ultrasonography of the portal vein and superior mesenteric and celiac arteries for the measurement of vessel diameters and Doppler flow parameters including the peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), and pulsatility index (PI) of superior mesenteric and celiac arteries, and blood flow velocity of portal vein. All measurements were made by using angle correction.

Statistical analysis

Selected clinical data and Doppler ultrasonographic data were collected from the patient charts. Data were expressed as mean ± SD and median (min-max). Correlation analyses were performed to assess the association of clinical and Doppler ultrasonographic data. Significance was determined at the p<0.05 level.

Results

Table 1 presents age, gender, age at diagnosis, duration of disease, interval between attacks, and body mass index. Ultrasonographic data as vessels diameters and Doppler ultrasonographic data as measurements of PSV; EDV; RI; PI, and blood flow velocity were also presented in Table 1. As seen in Table 1, in the study population, considerable number of patients affected by FMF as a long-term disorder. We found no vascular abnormality related to vessel diameters.
**Table 1. Selected clinical and Doppler ultrasonographic data.**

<table>
<thead>
<tr>
<th>Clinical data (n=52)</th>
<th>Median (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>22 (16-46)</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>40/12</td>
</tr>
<tr>
<td>Age at diagnosis (y)</td>
<td>19.5 (1-45)</td>
</tr>
<tr>
<td>Duration of disease (y)</td>
<td>3.5 (1-24)</td>
</tr>
<tr>
<td>Interval between attacks (m)</td>
<td></td>
</tr>
<tr>
<td>&lt;1 months</td>
<td>21%</td>
</tr>
<tr>
<td>1-3 months</td>
<td>73%</td>
</tr>
<tr>
<td>&gt;3 months</td>
<td>6%</td>
</tr>
<tr>
<td>BMI</td>
<td>22.9 (17.7-34.4)</td>
</tr>
</tbody>
</table>

**Doppler ultrasonography (Mean±SD)**

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter (mm)</th>
<th>PSV (cm/sec)</th>
<th>EDV (cm/sec)</th>
<th>RI</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior mesenteric artery</td>
<td>6.27±1.30</td>
<td>68±22</td>
<td>14±7</td>
<td>0.79±0.08</td>
<td>2.24±0.78</td>
</tr>
<tr>
<td>Celiac artery</td>
<td>6.91±1.36</td>
<td>72±21</td>
<td>17±10</td>
<td>0.78±0.09</td>
<td>2.17±0.73</td>
</tr>
<tr>
<td>Portal vein</td>
<td>11.15±2.56</td>
<td>21±9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; PSV, peak systolic velocity; EDV, end diastolic velocity; RI, resistive index; PI, pulsatility index.

Table 2 shows the correlation coefficients calculated for the assessment of the association between the status of FMF and Doppler ultrasonographic findings of selected abdominal vessels. Overall, there was no meaningful association between clinical and Doppler ultrasonographic parameters obtained from the superior mesenteric and celiac arteries and portal vein.

**Table 2. Correlations of clinical and Doppler ultrasonographic data.**

<table>
<thead>
<tr>
<th></th>
<th>Age (y)</th>
<th>Duration (y)</th>
<th>Age at diagnosis (y)</th>
<th>Interval between attacks (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior mesenteric artery</td>
<td>0.11 (p=0.54)</td>
<td>0.13 (p=0.46)</td>
<td>-0.00 (p=0.99)</td>
<td>0.04 (p=0.83)</td>
</tr>
<tr>
<td>PSV</td>
<td>0.24 (p=0.17)</td>
<td>-0.19 (p=0.27)</td>
<td>0.29 (p=0.09)</td>
<td>-0.01 (p=0.97)</td>
</tr>
<tr>
<td>EDV</td>
<td>-0.18 (p=0.30)</td>
<td>0.32 (p=0.06)</td>
<td>-0.33 (p=0.05)</td>
<td>-0.07 (p=0.70)</td>
</tr>
<tr>
<td>RI</td>
<td>-0.08 (p=0.66)</td>
<td>0.21 (p=0.22)</td>
<td>-0.19 (p=0.28)</td>
<td>-0.05 (p=0.78)</td>
</tr>
<tr>
<td>PI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celiac artery</td>
<td>-0.13 (p=0.53)</td>
<td>-0.17 (p=0.41)</td>
<td>-0.01 (p=0.94)</td>
<td>0.17 (p=0.44)</td>
</tr>
<tr>
<td>PSV</td>
<td>-0.08 (p=0.68)</td>
<td>-0.05 (p=0.79)</td>
<td>-0.04 (p=0.84)</td>
<td>0.18 (p=0.40)</td>
</tr>
<tr>
<td>EDV</td>
<td>0.10 (p=0.65)</td>
<td>-0.09 (p=0.66)</td>
<td>0.13 (p=0.53)</td>
<td>-0.20 (p=0.35)</td>
</tr>
<tr>
<td>RI</td>
<td>0.00 (p=0.99)</td>
<td>0.03 (p=0.88)</td>
<td>-0.02 (p=0.93)</td>
<td>-0.00 (p=0.99)</td>
</tr>
<tr>
<td>PI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Portal vein</td>
<td>-0.34 (p=0.05)</td>
<td>-0.17 (p=0.32)</td>
<td>-0.15 (p=0.41)</td>
<td>0.17 (p=0.34)</td>
</tr>
<tr>
<td>Velocity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Salk et al.: Doppler ultrasonography in FMF**

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**Discussion**

Of the 52 FMF patients, Doppler ultrasonography of the superior mesenteric and celiac arteries and portal vein were performed. This is the first study in the pertinent literature evaluating the impact of FMF on the blood flows of superior mesenteric and celiac arteries and portal vein according to duration of disease in patients during remission. Overall, we found no abnormal blood flow pattern in the selected vessels and there was no association between clinical and Doppler ultrasonographic parameters obtained from the superior mesenteric and celiac arteries and portal vein.

In FMF patients, abdominal attacks commonly occur and they affect the whole abdomen with all findings of peritoneal inflammation. In this study, we attempted to reveal the long-term effect of abdominal attacks on abdominal vessels that might be affected by experienced abdominal attacks related to long-term nature of FMF. Recent studies strongly suggest that there are some inflammatory activities between attacks [12].

Systemic inflammation is an important role for the onset and development of atherosclerosis. Ridker et al. [13] reported that baseline CRP levels had a prognostic value for future vascular risk. Yang et al. [14] assessed adipocytes and noted that they played an important factor in systemic inflammation and might be related to atherosclerosis. Schillinger et al. [15] showed correlation between progressive atherosclerosis and C-reactive protein (CRP) and serum amyloid-A (SAA) levels.

Chronic disorders with ongoing subclinical inflammation, like systemic lupus erythematosus, rheumatoid arthritis, and diabetes mellitus, are now accepted as increasing the risk of early structural vascular alteration and atherosclerosis because of long-term inflammation [16-19]. At this perspective, patients need to be followed up over a life-long period, like other chronic inflammatory disorders.

Peru et al. [12] investigated the long-term effect of FMF on carotid intima-media thickness in children and its association with premature atherosclerosis with several inflammatory markers. They noted that in FMF patients, the carotid intima-media thickness was increased compared to the healthy controls; however, there were no correlations between carotid intima-media thickness and SAA, CRP, homocysteine, and lipoprotein-a. They noted that several factors contribute to the development of atherosclerosis and there was a need for further studies revealing the association of carotid intima-media thickness and inflammatory markers. They suggested that carotid intima media-thickness as a test might have a place in the follow-up of pediatric patients with FMF.

There were some limitations for this study. The study has a small sample size. Further, preferably multicenter, investigations should be designed to reach a more reliable result in FMF patients grouped according to colchicine use, severity of clinical course and increase in inflammatory markers between attacks.
In conclusion, according to our findings, FMF may not cause deterioration in blood flow of the superior mesenteric and celiac arteries and portal vein. These findings cannot be accepted as the evidence of absence of atherosclerotic changes developing in patients with long-term inflammatory disorders like FMF. In clinical practice, during differential diagnosis of patients with an attack of abdominal pain, Doppler ultrasonography may be needed for the screening of arterial thromboembolic pathologies. In the absence of a contributing abnormality related to abdominal vessels, the knowledge about the normal blood flow of studied abdominal vessels might help during differential diagnosis of disorders with abdominal pain.

**Conflict of Interest**

The authors declare that there is no conflict of interest.

**References**


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