vWF-Antigen correlates with severity of portal hypertension

Stephanie Hametners, Rainer Schoff 1, Alexander Ziechehabiti, Thomas Hufnagl2, Doris Trubert-Exinger3, Andreas Maieron1
1 Internal Medicine IV, Gastroenterology / Hepatology, Elisabethinen Hospital Linz, Austria
2 Siemens diagnostics 3 Institute of Laboratory Medicine, General Hospital St. Pölten, Austria

Background
Clinically significant portal hypertension (CSPH), defined by hepatic venous pressure gradient (HVPG) > 10 mmHg causes major complications in cirrhotic patients such as hepatic decompensation. To improve the survival of cirrhotic patients an early diagnosis of portal hypertension (PH) leading to adequate therapy is crucial. The diagnosis of PH by HVPG measurement is not comprehensively available. Neither are any biomarkers widely available for the prediction of CSPH. vWF-Ag has shown significant ability for the diagnosis of CSPH and is a predictor for mortality. vWF-Ag is released by activated endothelial cells and therefore represents an indicator of endothelial cell activation and plays a crucial role in high shear stress depending primary haemostasis. The endothelium plays a crucial role in many vascular diseases and endothelial dysfunction is a fundamental component of the increased hepatic vascular tone of cirrhotic livers. vWF-Ag is under investigation as a valuable marker for prediction of varices, portal hypertension and mortality in patients with liver cirrhosis. ELF-test, consisting of a panel of direct biomarkers such as hyaluronic acid (HA), procollagen III N-terminal propeptide (PIIINP) and inhibitor of metalloproteinase 1(TIMP-1) can detect liver cirrhosis adequately in most cases. Therefore we analysed whether there is a correlation between vWF-Ag and ELF-test throughout different stages of liver disease.

Methods
Data of 51 patients with liver cirrhosis of different aetiology were included. The diagnosis of cirrhosis was established by either liver biopsy, transient elastography (TE) or typical clinical signs such as ascites. All patients underwent HVPG measurement and vWF-Ag and ELF-test were analysed. Blood samples were obtained during HVPG measurement. Portal haemodynamics were assessed by HVPG measurement. Patients’ data were collected to evaluate Child Pugh Score (CPS), MELD score and patients were classified according to D’Amico staging system. Statistical analyses were performed using SPSS 19.0.

Results
51 patients (female: 10, median age 60, IQR: 53-67) with liver cirrhosis underwent 63 HVPG measurements and were included. The aetiology of liver cirrhosis was distributed as shown in figure 1.

Figure 1 Aetiology of liver cirrhosis

CPS A n=36 (57,1%), CPS B n=23 (36,5%) and CPS C n=4 (6,35%). The median MELD was 9,3, IQR: 7.1-12. Median MELD in CPS A was 7,9, IQR: 5,8-9,4; in CPS B 11,6, IQR: 9,3-16,6 and in CPS C 28, IQR: 24,1-28,6. According to D’Amico classification n=28 (44,4%) were compensated and n=33 (55,6%) were decompensated. Only 2 (3,16%) patients showed no CSPH, 61 (96,83%) showed CSPH. vWF-Ag levels and ELF-test correlate with Child Pugh Stage. vWF-Ag and ELF-test increase significantly according to progression of CPS (p<0.05). The medians, IQRs and significance of vWF-Ag and ELF test depending on CPS are summarized in table 1.

Table 1 median, IQR and significance of vWF-Ag and ELF depending on CPS

<table>
<thead>
<tr>
<th>CPS Group</th>
<th>vWF-Ag (mg/l)</th>
<th>ELF*100/plt</th>
<th>significance p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child A n=28</td>
<td>205 (120-330)</td>
<td>14,7 (10,8-15,9)</td>
<td>0,01 0,00 0,00</td>
</tr>
<tr>
<td>Child B n=22</td>
<td>235 (120-420)</td>
<td>16,4 (14,1-19,5)</td>
<td>0,01 0,01 0,01</td>
</tr>
<tr>
<td>Child C n=5</td>
<td>250 (183-295)</td>
<td>16,4 (14,1-19,5)</td>
<td>0,01 0,01 0,01</td>
</tr>
</tbody>
</table>

vWF-Ag level increases significantly in the group of decompensated patients according to D’Amico as shown in figure 4. The median vWF-Ag is 241%, IQR: 201-399 in compensated and 328% IQR: 236-651 in decompensated patients (p<0.05).

Figure 4 shows ELF and HVPG in relation to compensated/decompensated liver cirrhosis.

Conclusion
vWF-Ag helps evaluating the severity of PH. vWF-Ag significantly correlates with CPS, PH and D’Amico staging. Our data supports the published evidence that vWF-Ag is a key indicator in assessing the diagnosis of PH. ELF test correlates significantly with CPS and D’Amico classification and identifies each patient with cirrhosis adequately, but does not show significant correlation with vWF-Ag, which might due to the low number of available ELF tests.