CORRELATION BETWEEN BLOOD RHEOLOGICAL PROPERTIES AND RED BLOOD CELL INDICES (MCH, MCV, MCHC) IN HEALTHY WOMEN


18th Conference of the European Society of Clinical Hemorheology and Microcirculation
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5. – 8. June 2016
Introduction

- From a physical point of view, blood is a two phase suspension of cells in plasma, which is an aqueous solution of organic molecules, proteins and salts.

- Blood viscosity depends on existing shear forces, hematocrit, plasma viscosity, interactions between Red Blood Cells (RBCs) and their mechanical properties.

- The deformability of the RBCs, i.e., the ability to change shape in response to deforming forces, improves the RBC flow in microcirculation and protects them against cell disruption under bulk flow conditions and when passing through capillary vessels.
Background

- The extend of the reversible RBC deformability is influenced by their viscoelastic properties, internal viscosity and surface area to volume ratio.

- Extreme external shear forces and pathologic conditions of several diseases, such as metabolic syndrome, diabetes mellitus, iron deficient anemia, hemoglobinopathy, pre-eclampsia/HELLP-Syndrome and autoimmune diseases can cause irreversible plastic deformations of the RBC membrane.

- Here changes in MCV, MCHC and hemoglobin content are found to correlate with impaired RBC deformability.
Objectives of the study

The intention of this community based trial was to investigate the physiological associations between blood rheological parameters - and deformability in particular - and RBC indices in healthy middle-aged women prior to elective gynecological surgeries.
Laboratory Methods

Blood rheological parameters and platelet function:

- **Plasma viscosity:** Capillary tube viscometer (KSVP-4)
  Fresenius, Bad Homburg Germany

- **RBC aggregation:** Aggregometer (MA1)
  Myrenne, Roetgen, Germany

- **RBC deformability:** Rheodyn SSD shear stress
  diffractometer
  Myrenne, Roetgen, Germany

- **Platelet function:** Platelet Function Analyzer (PFA-100)
  Siemens, München, Germany
Patients

- Acquisition period: June – December 2014.
- Women prior to elective gynaecological surgery.
- Exclusion of women with known pregnancy, malign-, infective- and chronic - diseases, extreme BMI (<16; >40kg/m²), or receiving permanent medication.
- Blood sampling took place along with pre-operative routine between 8:00 and 10:00 a.m.
- Signed informed consent.
- Anonymized data acquisition via questionnaire.
- Vote of Ethik Kommission.
Statistical analysis

- Descriptive analysis.

- Two-sided Pearson’s correlation.

- $P$ values $< 0.05$ were considered statistically significant.

- PSPP-project version 0.7.9; February 2012.

- In cooperation with the Institute for Clinical Epidemiology and Biometry; Maximillians-University Würzburg.
## Results

### Descriptive statistics of characteristics of 286 women

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>48.54</td>
<td>46.5-50.59</td>
<td>17.578</td>
<td>286</td>
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<tr>
<td>Weight (kg)</td>
<td>70.6</td>
<td>68.82-72.37</td>
<td>15.124</td>
<td>282</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166.46</td>
<td>165.76-167.16</td>
<td>6.018</td>
<td>283</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>25.46</td>
<td>24.85-26.07</td>
<td>5.211</td>
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</tbody>
</table>
### Blood rheological parameters

#### Means and standard deviations

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma viscosity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pv (mPa s)</td>
<td>1.1749</td>
<td>1.1604-1.1895</td>
<td>0.12422</td>
<td>283</td>
</tr>
<tr>
<td><strong>RBC aggregation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E1</td>
<td>17.930</td>
<td>17.072-18.788</td>
<td>7.3206</td>
<td>282</td>
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<tr>
<td><strong>RBC deformability %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBC 1.2</td>
<td>11.291</td>
<td>10.958-11.625</td>
<td>2.8576</td>
<td>285</td>
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<tr>
<td>RBC 3.0</td>
<td>22.878</td>
<td>22.483-23.273</td>
<td>3.3874</td>
<td>285</td>
</tr>
<tr>
<td>RBC 6.0</td>
<td>30.919</td>
<td>30.560-31.278</td>
<td>3.0789</td>
<td>285</td>
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<tr>
<td>RBC 12</td>
<td>37.196</td>
<td>36.845-37.547</td>
<td>3.0127</td>
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<tr>
<td>RBC 30</td>
<td>43.586</td>
<td>43.214-43.957</td>
<td>3.1854</td>
<td>285</td>
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<tr>
<td>RBC 60</td>
<td>47.131</td>
<td>46.736-47.525</td>
<td>3.3832</td>
<td>285</td>
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</tbody>
</table>

Hematologic parameters and RBC indices

Means and standard deviations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>N</th>
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</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>13.2</td>
<td>13.0 - 13.4</td>
<td>1.4</td>
<td>277</td>
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<tr>
<td>Hct (%)</td>
<td>39.3</td>
<td>38.8 - 39.7</td>
<td>3.9</td>
<td>277</td>
</tr>
<tr>
<td>Leu (/µL)</td>
<td>7,819</td>
<td>7,492 - 8,147</td>
<td>2,769</td>
<td>277</td>
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<tr>
<td>Thr (/µL)</td>
<td>281,079</td>
<td>271,834 – 290,325</td>
<td>78,022</td>
<td>276</td>
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<tr>
<td>MCV (fL)</td>
<td>89.8</td>
<td>89.1-90.5</td>
<td>6.1</td>
<td>277</td>
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<tr>
<td>MCHC (g/dL)</td>
<td>33.7</td>
<td>33.6-33.8</td>
<td>1.1</td>
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</tr>
<tr>
<td>MCH (pg)</td>
<td>30.3</td>
<td>30.1-30.6</td>
<td>2.0</td>
<td>277</td>
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Blood rheological parameters, age and BMI

Bivariate Pearson correlation between rheological parameters, age and BMI

<table>
<thead>
<tr>
<th></th>
<th>Pv</th>
<th>E0</th>
<th>E1</th>
<th>RBC 1.2</th>
<th>RBC 3.0</th>
<th>RBC 6.0</th>
<th>RBC 12.0</th>
<th>RBC 30</th>
<th>RBC 60</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>r</td>
<td>0.165</td>
<td>0.131</td>
<td>0.185</td>
<td>0.046</td>
<td><strong>0.132</strong></td>
<td>0.145</td>
<td><strong>0.158</strong></td>
<td>0.147</td>
<td>0.131</td>
</tr>
<tr>
<td>p</td>
<td><strong>0.005</strong></td>
<td><strong>0.028</strong></td>
<td><strong>0.002</strong></td>
<td>0.443</td>
<td><strong>0.026</strong></td>
<td><strong>0.014</strong></td>
<td><strong>0.007</strong></td>
<td><strong>0.013</strong></td>
<td><strong>0.027</strong></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
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<td>N</td>
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<td>281</td>
<td>281</td>
<td>281</td>
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</tr>
<tr>
<td>r</td>
<td>0.144</td>
<td>0.182</td>
<td>0.224</td>
<td>0.012</td>
<td>0.047</td>
<td>0.096</td>
<td>0.113</td>
<td>0.094</td>
<td>0.075</td>
</tr>
<tr>
<td>p</td>
<td><strong>0.016</strong></td>
<td><strong>0.002</strong></td>
<td><strong>0.001</strong></td>
<td>0.846</td>
<td>0.435</td>
<td>0.110</td>
<td>0.058</td>
<td>0.115</td>
<td>0.213</td>
</tr>
</tbody>
</table>

Correlation between MVC and RBC deformability

Low shear

Moderate shear

High shear

$r = 0.128, p = 0.034$

$r = 0.209, p = 0.001$

$r = 0.197, p = 0.001$

$r = 0.198, p = 0.001$

$r = 0.214, p = 0.001$

$r = 0.160, p = 0.008$
Correlation between MCH and RBC deformability

**Low shear**

- $r = 0.108, p = 0.073$
- $R^2_{\text{Linear}} = 0.012$

**Moderate shear**

- $r = 0.201, p = 0.001$
- $R^2_{\text{Linear}} = 0.04$

**High shear**

- $r = 0.161, p = 0.008$
- $R^2_{\text{Linear}} = 0.026$

**Correlation between MCH and RBC deformability**

- $r = 0.183, p = 0.002$, $R^2_{\text{Linear}} = 0.034$
- $r = 0.198, p = 0.001$, $R^2_{\text{Linear}} = 0.039$
- $r = 0.122, p = 0.043$, $R^2_{\text{Linear}} = 0.015$
Correlation between MCHC and RBC deformability

- **Low shear**
  - $r = -0.145$, $p = 0.016$
  - $r = -0.160$, $p = 0.008$

- **Moderate shear**
  - $r = -0.155$, $p = 0.010$
  - $r = -0.176$, $p = 0.003$

- **High shear**
  - $r = -0.200$, $p = 0.001$
  - $r = -0.202$, $p = 0.001$
Summary

- Cell volume and hemoglobin content have a strong impact in apparently healthy middle-aged women on RBC Deformability.

- There is a strong correlation between RBC deformability and MCV, most remarkable during moderate and high shear force exposure.

- RBC deformability continuously decreases with increasing MCHC, with the strongest negative correlation at high shear force exposure.

- All blood rheological parameters are closely correlated with the age of the women with a trend towards hyper viscosity, while an increase in RBC aggregation and plasma viscosity correlated with advancing BMI.
Conclusion

- The RBC hemoglobin content and its biochemical characteristics primarily determine the intracellular fluid viscosity, which itself shows no elastic properties and correlates inversely with RBC deformability.

- The combination of a high degree flexibility of RBC membrane and a high surface area to cell volume ratio in the presence of a low intracellular fluid viscosity provides optimal constellation for maximal cell deformability, which is needed in the microcirculation and for passing through the spaces between the endothelial cells of the splenic sinusoids.