Background / Hypotheses

- Homocysteine has been discussed as a cardiovascular risk factor in patients with chronic kidney disease (CKD).
- However, randomized trials in which homocysteine was lowered via vitamin B supplementation failed to demonstrate a survival benefit.
- The homocysteine metabolite S-Adenosylhomocysteine (SAH; Figure 1) is a potent inhibitor of methylation reactions and thus a central epigenetic regulator.
- Vitamin B supplementation, which lowers homocysteine, does not reduce SAH.
- Against this background, we aimed to investigate the prognostic value of SAH in chronic kidney disease.

Figure 1: C1 metabolism (schematic overview; Zawada et al. NDT 2013)

Methods / Results

- Plasma homocysteine (fluorescence polarization immunoassay) and SAH (tandem mass spectrometer) concentrations were assessed among 297 CARE FOR HOMe participants who suffered from CKD (KDIGO G 1- G 5; Table 1).
- Participants with more advanced GFR categories had higher plasma homocysteine and SAH concentrations (Figure 2 & 3).
- eGFR correlated more strongly with plasma SAH (r = 0.497) than with plasma homocysteine (r = 0.424).
- Participants with prevalent cardiovascular disease had higher plasma SAH than patients without prevalent cardiovascular disease (p = 0.007; Figure 4 & 5).
- In logistic regression analyses, however SAH did not independently predict prevalent CVD (Table 2).
- During a follow-up period of 2.5 ± 0.7 years, 33 participants experienced the predefined cardiovascular endpoint (Kaplan Meier analysis, Figure 6).

Table 1: Baseline characteristics of CARE FOR HOMe participants.

<table>
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<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>67.0 ± 12.5</td>
<td>117 (39.4 %)</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>30.6 ± 5.6</td>
<td>Active smoking (yes) 32 (10.8 %)</td>
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<td>Systolic blood pressure (mmHg)</td>
<td>146 ± 21</td>
<td>Prevalent CVD (yes) 61 (20.5 %)</td>
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<td>eGFR (MDRD) (ml/min/1.73 m²)</td>
<td>44 ± 19</td>
<td>Diabetes mellitus (yes) 106 (35.7 %)</td>
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Table 2: Logistic regression analyses: independent variables: SAH, age, gender, eGFR and cardiovascular risk factors; dependent variable: prevalent cardiovascular disease. BP: blood pressure; LDL-C = low density lipoprotein-cholesterol.

Discussion

In CKD, plasma SAH predicts cardiovascular events. Further studies are needed to identify strategies to lower plasma SAH, after B vitamins failed to reduce plasma SAH levels.