Plasma homocysteine and calcific aortic valve disease

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Plasma homocysteine and coronary atherosclerotic disease both demonstrate histological features of endothelial disruption and subendothelial accumulation of lipid, lipoprotein, and inflammatory cells. These entities also share acknowledged risk factors, including hypercholesterolaemia, hypertension, and diabetes mellitus, believed to cause disease at least partly via endothelial injury. Data suggest that raised homocysteine concentrations, also associated with endothelial damage, may be an independent risk factor for coronary artery disease. Whether raised homocysteine is a risk factor for calcific aortic valve disease is unknown. We hypothesised that increasing homocysteine concentrations might predict the prevalence of calcific aortic valve disease, specifically aortic sclerosis and aortic stenosis, in a group of patients undergoing cardiac surgery.

METHODS

We retrospectively analysed 76 patients with a mean (SD) age of 66 (13) years, (65% male) who underwent cardiac surgery at the Cleveland Clinic Foundation with intraoperative transoesophageal echocardiography. The patients were originally recruited for a prospective study assessing the relation between plasma homocysteine and aortic atheroma. Exclusion criteria were chronic renal failure, rheumatic heart disease, and known malignancy. All subjects gave informed consent and our institutional review board approved the study. All patients had fasting plasma homocysteine concentrations obtained on the day of their preoperative evaluation or on the morning of surgery. Venous blood was placed into a heparinised tube on ice, centrifuged within 10 minutes of blood being drawn, and analysed using a microparticle enzyme immunoassay. Normal plasma homocysteine ranges in our laboratory are 6.4–13.7 μmol/l for men and 3.4–12.9 μmol/l for women.

The following baseline clinical characteristics were recorded: age, sex, serum creatinine concentration, and history of hypertension, hypercholesterolaemia, tobacco use, and diabetes mellitus. All patients underwent intraoperative transoesophageal echocardiography at the time of surgery with 5.0 MHz biplane or multiplane probes. The aortic valve was coded as normal, aortic sclerosis (thickening and calcification of aortic leaflets without left ventricular outflow obstruction) or aortic stenosis (thickening and calcification of aortic leaflets, impaired systolic mobility, and a mean transvalvar gradient > 10 mm Hg). A staff echocardiographer, blinded to homocysteine concentrations, ascertained the degree of aortic valve disease. Continuous variables are expressed as medians with interquartile ranges (IQR). Categorical data appear as frequencies and percentages. Kruskal-Wallis tests were utilised for bivariate analyses of continuous data. χ² Tests were employed for bivariate analyses of categorical data.

RESULTS

Clinical characteristics appear in table 1. Median (IQR) homocysteine concentration was 11.7 (8.8–15.2) μmol/l. In bivariate analyses, plasma homocysteine concentrations were significantly higher with worsening aortic valve disease (table 1). Other bivariate predictors included age, hypercholesterolaemia, and serum creatinine. No association was found between homocysteine concentrations and sex, smoking, or hypertension. In multivariate analysis, after adjusting for age, hypercholesterolaemia, and serum creatinine, increasing plasma homocysteine was not associated with aortic sclerosis (p = 0.40) or stenosis (p = 0.25). Increasing age (p = 0.002) and serum creatinine (p < 0.001), however, remained significant independent predictors of aortic valve disease.

When comparing patients with aortic stenosis to those without stenotic aortic valves (that is, normal aortic valve or aortic sclerosis, n = 59), plasma homocysteine concentration was significantly higher in those with aortic stenosis compared to those without aortic stenosis (10.4 (8.5–12.9) μmol/l, p = 0.001). Patients with aortic stenosis, on average, were older (p < 0.001) and had higher serum creatinine concentrations (p = 0.008). In multiple logistic regression models, however, plasma homocysteine concentrations failed to predict aortic stenosis (p = 0.28), whereas increasing age remained a significant predictor (p < 0.001).

|                         | Normal valve (n = 27) | Aortic sclerosis (n = 32) | Aortic stenosis (n = 17) | p Value |
|-------------------------|----------------------|--------------------------|-------------------------|---------|
| Age (years)             | 57 (49–70)           | 68 (60–74)               | 78 (71–83)              | <0.001  |
| Female (%)              | 30                   | 34                       | 47                      | 0.49    |
| Hypertension (%)        | 52                   | 50                       | 53                      | 0.98    |
| Hypercholesterolaemia (%)| 48                  | 81                       | 41                      | 0.006   |
| Diabetes mellitus (%)   | 22                   | 28                       | 12                      | 0.42    |
| Tobacco use (%)         | 63                   | 56                       | 47                      | 0.58    |
| Serum creatinine concentration (mg/dl) | 0.9 (0.8–1)      | 1.0 (0.9–1.2)           | 1.2 (1–1.3)             | 0.004   |
| Plasma homocysteine concentration (μmol/l) | 9.2 (8.2–14.6) | 11.3 (9.3–12.8)          | 16.6 (12.7–17.8)        | 0.003   |

Continuous variables are expressed as medians (interquartile ranges)
A novel streamlined “anchored” anatomical approach to ablation of AVNRT

A practical approach to slow pathway ablation for the treatment of atrioventricular nodal re-entrant tachycardia (AVNRT) is to use a combined anatomical and electrogram technique to identify target sites. The efficacy and safety of radiofrequency (RF) ablation depend on the stability of the ablation catheter during RF energy delivery. Unusual anatomy, abrupt rhythm changes during RF application, and intraprocedural catheter and patient movement can pose significant challenges. Inadvertent AV block remains a concern occurring in approximately 1% of cases.

A 42-year-old woman with a narrow complex regular tachycardia that had a pseudo r in V1 during tachycardia but not during sinus rhythm underwent a diagnostic electrophysiological study followed by RF ablation for cure of her AVNRT. The patient’s own anatomy was leveraged not only as a means to localise an ablation target, but most importantly, as a stabilising factor during performance of slow pathway ablation. This highly streamlined approach can be performed safely, successfully, and rapidly entirely from the left femoral vein, through a single sheath, and with only two catheters in appropriately selected supraventricular tachycardia (SVT) patients.

A 12 French long sheath was introduced into the femoral vein and guided fluoroscopically to the base of the right atrium. A 6 French Bard EP-XT catheter was inserted into the coronary sinus (CS). Next, a 6 French EPT Blazer II ablation catheter was directed to the His and then, after confirming the diagnosis of AVNRT, moved to the putative anatomic region of the slow pathway. During three RF applications, the efficacy of the “sheath-catheter-catheter” complex led to excellent electrogram and ablation catheter stability by taking advantage of the “collaring” effect of the 12 French sheath which was in turn “anchored” to the diagnostic catheter placed in the CS. No further tachycardia was inducible or has occurred clinically in follow up.