Letter to the Editors

Atherosclerosis, type I collagen cross-linking and homocysteine

Patients with homocystinuria have several connective tissue manifestations, the most severe being atherosclerosis. Furthermore, elevated plasma homocysteine concentrations correlate with atherosclerosis without other features of homocystinuria [1]. Homocysteine has been shown to interfere with collagen cross-linking, although the exact biochemical mechanism is unclear [2]. Moreover, the serum level of carboxyterminal telopeptide of human type I collagen (ICTP), the degradation product of type I collagen, decreases in patients with homocystinuria [3]. Thus, the decreased tensile strength of the connective tissue may be at least partially responsible for the clinical manifestations of homocystinuria. We have recently shown that the ICTP assay detects only degradation of mature, trivalently cross-linked type I collagen [4]. We, therefore, wanted to study if there really is a negative correlation between serum homocysteine and ICTP concentrations in patients with severe coronary atherosclerosis.

Serum samples were obtained from 109 consecutive patients (75 men, 34 women, mean age 62 ± 9) before coronary artery bypass grafting at the Oulu University Hospital. Forty-nine of the patients had previously suffered a myocardial infarction and 70 patients had three-vessel disease. The collection of the samples was approved by the local ethics committee. Homocysteine (reference range 4.5–12.4 μmol/l) and ICTP (reference range 1.6–4.6 μmol/l) were measured by commercially available methods (Abbott Laboratories and Orion Diagnostica, respectively). Spearman’s rank correlation was used for the correlation analyses.

The mean ICTP and homocysteine concentrations were 3.3 ± 1.3 and 14.4 ± 4.8 μg/l, respectively. These correlated significantly with each other (r = 0.260, P = 0.006) (Fig. 1). However, both ICTP and homocysteine also correlated significantly with the age of the patients (r = 0.265, P = 0.005 and 0.310, P = 0.001, respectively).

We did not find the expected negative correlation between serum ICTP and homocysteine concentrations, which suggests that cross-linking of type I collagen does not decrease in the presence of increasing homocysteine concentrations, although the observed homocysteine levels were not very high in the present series. Both ICTP and homocysteine also correlated significantly with age. Atherosclerosis, in addition to aging, possibly accelerates the turnover of type I collagen, which may mask the effect of homocysteine on collagen cross-linking. Type I collagen is the major constituent of mineralised bone, and thus part of the circulating ICTP could be derived from bone turnover via the matrix metalloproteinase (MMP) pathway [4]. Measurements of type III collagen metabolism with respect to, for instance, plaque rupture might be more relevant, since type III collagen is very abundant in atherosclerotic plaques and vessel walls [5], being absent in bone.

References


Fig. 1. Correlation between serum concentrations of homocysteine and ICTP in patients with coronary atherosclerosis (n = 109).

Abbreviations: ICTP, cross-linked carboxyterminal telopeptide of type I collagen.


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