Increased elastin content and decreased elastin concentration may be predisposing factors in dissecting aneurysms of human thoracic aorta

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Objective: The aim was to investigate whether changes in elastin distribution in the thoracic aorta are associated with occurrence of dissecting aneurysms. Methods: Ten thoracic aortas were obtained at necropsy from dissections (mean patient age 74.3 years, SD 7.3) and from 10 age matched controls (mean age 73.1 years, SD 6.9). Full wall thickness samples (1 cm diameter) were taken at 12 sites between heart and diaphragm from aortas of dissections and controls. Elastin content (total elastin per sample), concentration (mg·mg⁻¹ tissue dry weight), degree of cross linking, and amino acid composition were determined. Results: Comparison of areas of dissected aortas involved in dissection with corresponding areas of controls showed significant increases in content of elastin (p<0.05), content and concentration of proteins other than elastin and collagen (p<0.01), and a decrease in elastin concentration (p<0.01). Comparison of areas remote from dissection with corresponding areas in controls showed no significant differences except for decreased elastin concentration (p<0.05). There were no differences in elastin cross linking. Elastin from dissected aortas had a higher content of aspartate, threonine, serine, glutamate, and lysine and a lower content of glycine, alanine, and valine than elastin from controls (p<0.05). Conclusions: Biochemical changes in dissections are localised to the dissected area, with increased deposition of elastin, collagen, and other proteins. The altered matrix composition is likely to change the mechanical properties, possibly increasing the tendency to rupture.

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Dissecting aortic aneurysms are characterised by cleavage of the aorta by the blood along the laminar planes of the media, with the formation of a blood filled cavity or channel within the aortic wall. Subsequently, the blood may rupture outwards with fatal results, or may re-enter the lumen of the aorta. As the main strength of the large arteries resides in their medial layers, dissecting aneurysms have always been thought to be associated with some process that has weakened the media either generally or in localised areas.

Elastin and collagen, as key fibrous proteins of arterial walls, provide the integrity and resilience required to accommodate pressure variations. Elastin confers elasticity and is more prominent near the heart where pulsatile flow is marked, while collagen stiffens the wall, limiting its extensibility. The extent of cross linking within both collagen and elastin fibres is important in conferring adequate mechanical properties on the tissue.

Although fragmentation of the elastic laminae has been implicated in many vascular diseases, evidence suggests that the morphological changes and age related stiffening are not due to degeneration of the elastic network but to variations in the supramolecular organisation of the extracellular matrix. Altered elastin and/or collagen metabolism has been implicated in annulo-aortic ectasia, as have changes in the degree and type of elastin and collagen cross links in a variety of aortic diseases. Fragmentation of the elastica together with loss of elastin has been reported in abdominal aneurysms where destruction of elastic tissue occurs by increased elastase secretion. This is distinct from the lesion in dissections of the thoracic aorta, in which no loss of elastin is observed. Even in Marfan’s syndrome, in which patients suffer from dissecting aneurysms of the ascending aorta at an early age, no molecular defect in elastin has been identified. The weight of evidence now indicates that the primary lesion affects the microfibrillar protein fibrillin.

Our previous studies found no difference in pyridinoline cross linking of collagen in samples from dissected aortas and matched controls. However, there was a significantly increased collagen amount but decreased concentration in diseased tissue. We also observed significant increases in dry weight and total protein per sample site. Moreover, these changes were localised to the areas affected by dissection. The present investigation studied elastin from dissected aortas and matched controls.

Methods

Tissue source
Twenty human thoracic aortas, obtained at necropsy, consisted of two groups of 10 individuals (eight male, two female) aged between 63 and 90 years; the first group had dissecting aneurysms (mean age of 74.3 (SD 7.3) years) while the second group were controls (73.1 (6.9) years), with no evidence of dissection. The controls had usually died as a result of trauma and were selected to match the dissected group closely for age, sex, and degree of cardiac hypertrophy. Total heart weights, left ventricular (LV) and right ventricular (RV) weights, LV/RV weight ratios, and the degree of coronary atheroma were recorded.
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for each individual. Histological sections were routinely examined to exclude diseases such as giant cell arteritis and syphilis. Stains used were haematoxylin and eosin and the van Gieson stain for elastin.12

Aortic sample sites

Four circumferential bands (B1-B4) were selected along the thoracic aorta (figure) as previously described.13 Within each band, samples were taken at each of three sites (S1-S3) equally spaced around the aorta (fig. 1). Thus, in the main study, variables were determined at each of 12 sites for 20 individuals. However, for amino acid analyses, only samples from the S2 sites were taken.

Frozen thoracic aortas were thawed at 4°C, opened out, and pinned to a board. A sharp cork borer was used to excise 1 cm diameter samples through the full thickness of the aortic wall at the predetermined sites. Each sample, varying in thickness from 2 to 10 mm, was crudely minced with scissors, frozen in liquid nitrogen, and shattered under pressure,2 giving a homogeneous, frozen powder from which subsamples were taken for biochemical analysis.

Lipid extraction

Chloroform/methanol extraction of lipids was used as previously described.14

Cyanogen bromide digestion

Cyanogen bromide digestion of tissue samples and elastin standards was carried out with modifications to the published methods.15 Tissue was incubated in 70% formic acid (c:1:100, v/v) for 30 min at 65°C, cooled, and flushed with oxygen free nitrogen. Because aortic tissue is highly cross-linked, samples were incubated with cyanogen bromide (~10 mg/ml) for 24 h at 37°C to ensure complete reaction. The digestion was terminated by dilution with 10 volumes of distilled water. The cyanogen bromide digested residue was recovered by centrifugation and subsequently washed twice with 0.1 M acetic acid to remove any adhering collagenous peptides. The amino acid composition of the elastin residue was determined as described below.

Collagenase digestion

Cyanogen bromide residues were digested16 with purified bacterial collagenase (Form III, Advanced Biofactors, Lynbrook, New Jersey, USA). Purified human aortic collagen standards (types I & III, prepared as described17-18) were used to monitor the collagenase digestion, while commercial elastin was digested for comparison. Following incubations in the absence and presence of elastase, samples were acid hydrolysed and the amino acid composition, especially hydroxyproline content, determined.

Acid-phenol extraction

The procedure of Davis and Mackle19 for the separation of insoluble collagen and elastin from small samples of blood vessels provided a second distinct set of aortic elastin samples for comparative amino acid analysis.

Tissue hydrolysis

Lipid free dry aortic tissue (2-5 mg ml-1 HCl) was acid hydrolysed as previously described.20

Amino acid analyses

Separation and quantitation of amino acids (including hydroxyproline) in whole tissue acid hydrolysates were achieved by liquid chromatography on an LKB Biotech Chrom 4400 amino acid analyser.21 Hydroxyproline was also assayed manually22 and the data treated as previously described.14-15

Differences between contents of amino acids in various groups were tested for statistical significance by Student’s t test.

Total protein was determined by summation of weights of anhydro- amino acids. The amount of protein other than collagen and elastin (non-collagen, non-elastin protein; NCNE protein) was determined by subtraction of elastin and collagen weights. The amount of collagen was determined as previously described.1 Scholz

Determination of desmosine and isodesmosine

The elastin specific cross linking amino acids, desmosine and isodesmosine, were separated and quantitated by a modification of the colorimetric procedure for acid hydrolysates.23 Purified standards of desmosine and isodesmosine were kindly donated by Dr S P Robins, Rowett Research Institute, Aberdeen. Separation was achieved on the tetol ILC-64H amino acid analyser using a 45 × 1.2 cm Dowex resin column equilibrated to pH 4.8 with a 0.1 M trisodium citrate buffer containing 0.01% (v/v) octanonic acid and 10% (v/v) BRJ 35. Calculation of moles desmosine-like cross links per mole elastin was based on a tropoelastin molecular weight of 72000.

Statistical analysis

The data were divided into two groups, dissections and controls, and within each group, there were 10 individuals. For each aorta, there were three sites within each of the four bands. Data were tested for normal distribution by the Kolmogorov-Smirnov one sample test. Either logarithmic or square root transformation was used where required to normalise data. However, for ease of understanding, data are presented in tables as arithmetic means. In the case of the hydroxyproline determinations, the results from two different methods were compared by the non-parametric Wilcoxon matched pairs signed ranks test.

The data were analysed using the multivariate program (MANOVA) from the SPSS-X package. Each variable was analysed separately. The variables can be split up into (1) those where the explanatory variables are disease or control groups, band and site, and (2) those where the data were available from a single site (S2) and only the disease and control groups and band were used (see footnotes to tables I and II). In case 1, it was assumed that the results followed a multivariate normal distribution with correlated residuals over bands and sites within individuals in the disease and control groups. In case 2, it is assumed that the results followed a multivariate normal distribution with correlated residuals over bands. Details of the appropriate analysis making the above assumptions can be found in a paper by Bock.24 As there are only two groups, the effects of explanatory variables and of interactions between them can be tested using the F distribution with the appropriate degrees of freedom.

The data were also analysed using an analysis of variance approach similar to that described above, except that it was assumed that residuals were uncorrelated across bands and sites and across band only, as appropriate. Statistical results obtained using this approach
were broadly similar to those found on the assumption of correlated residues.

As dissections did not always extend along the aorta from heart to diaphragm, wall components in regions of dissection and at uninvolved sites above and/or below the lesion (table IV) in diseased aortas were compared with the equivalent regions of controls. As segregation of the sample sites in this way did not allow the ordered analysis provided by multivariate analysis, a range of tests was carried out: Student's t test, paired t test, and non-parametric Wilcoxon's signed rank test for both raw and normalised data. The results were remarkably similar irrespective of the chosen method of analysis, so the Student t test probabilities for differences between means of normalised data were selected for presentation since this method precludes exact pairing of samples (an advantage when dealing with a human population).

Presentation of data

It should be stressed that data presented in the tables as ratios (eg, mg·mg⁻¹ tissue) are the average of this ratio for the individual sample sites. Therefore, this average ratio, i.e., \( \frac{1}{n}(\sum x_i/y_i + \frac{1}{x_i y_i} + \cdots) \), will not be equal to the quotient of the meaned numerator and meaned denominator, i.e., \( \frac{\bar{x}}{\bar{y}} \). Thus in table I, the average amount of elastin divided by the lipid extracted dry weight does not equal values given for average elastin concentration.

Results

Pathological variables for the 10 dissected aortas have already been reported and discussed, as have the differences in lipid free dry weight between dissections and controls and the profiles of lipid free dry weight along and around the aorta.

Amino acid analyses of human aortic elastin prepared by acid-phenol extraction, cyanogen bromide digestion and bacterial collagenase digestion of cyanogen bromide residues

<table>
<thead>
<tr>
<th>Mean residues(1000 residues)</th>
<th>Published data</th>
<th>Acid-phenol</th>
<th>CNBr residues</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(control)</td>
<td>(aorta)</td>
<td>Diss (d)</td>
</tr>
<tr>
<td>Hyp</td>
<td>8</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Asp</td>
<td>6</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Thr</td>
<td>13</td>
<td>23</td>
<td>22*</td>
</tr>
<tr>
<td>Ser</td>
<td>11</td>
<td>25</td>
<td>25*</td>
</tr>
<tr>
<td>Gly</td>
<td>20</td>
<td>47</td>
<td>45*</td>
</tr>
<tr>
<td>Ala</td>
<td>239</td>
<td>183</td>
<td>181</td>
</tr>
<tr>
<td>1/2 Cys</td>
<td>4</td>
<td>113</td>
<td>109</td>
</tr>
<tr>
<td>Met</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ile</td>
<td>25</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>Tyr</td>
<td>21</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Phe</td>
<td>24</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Hyl</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>His</td>
<td>1</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Lys</td>
<td>17</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Arg</td>
<td>7</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Des/isodes</td>
<td>4</td>
<td>nd</td>
<td>3</td>
</tr>
</tbody>
</table>

+Coll=collagenase digestion; -Coll=no collagenase digestion; nd=not determined; n=not stated; T=trace amounts only. *p<0.05; **p<0.01.

are shown in table I. When compared with accepted analyses for human aortic elastin from younger subjects (column a), our control values (columns b and c) were higher in hydroxyproline, aspartate, threonine, serine, glutamate, lysine, and arginine and lower in glycine, alanine, and valine (table I). Hydroxyproline content was not reduced by digestion with bacterial collagenase (columns e and f).

Elastin concentration was decreased in dissections compared to controls (p<0.01, table II). In contrast to the amount of collagen, the average amount of elastin per sample site did not differ significantly between dissected or control aortas (table II) or between any one band and another along the thoracic aorta (table III). The concentration of elastin also remained relatively constant along the thoracic aorta (table III). Within each band there were no significant differences between sites S1, S2 and S3 around the aorta in either elastin amount or concentration (results not shown).

Dissected aortas showed a decrease in the concentration but not in the amount of both the isomeric elastin specific cross links, isodesmosine and desmosine. The decrease in cross link concentration paralleled that of elastin between dissections and controls (table II), and in relation to distance from the heart (table III), i.e., there was no change in cross link/elastin ratio.

Dissections of the thoracic aorta resulted in an overall increase in concentration and amount of the non-collagen non-elastin (NCNE) protein components of the aortic wall (table II). However, distance from the heart, in the presence or absence of a dissection, did not alter the concentration or amount of NCNE protein significantly (table III). No circumspect data are available.

The elastin to collagen ratio was not significantly different in dissections and controls (table II).

Since in a number of the cases studied the thoracic aortic wall was not dissected completely from heart to diaphragm...
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**Table III** Overall mean(SEM) values for a range of variables measured at specific anatomical locations in both dissected and control human thoracic aortas.

<table>
<thead>
<tr>
<th>Bands</th>
<th>Ascending aorta</th>
<th>Arch</th>
<th>Descending aorta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid free dry weight (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissections</td>
<td>118(14)</td>
<td>162(27)</td>
<td>159(19)</td>
</tr>
<tr>
<td>Controls</td>
<td>69(12)</td>
<td>78(8)</td>
<td>84(6)</td>
</tr>
<tr>
<td>Amount of elastin (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissections</td>
<td>141(1)</td>
<td>21(5)</td>
<td>20(2)</td>
</tr>
<tr>
<td>Controls</td>
<td>15(3)</td>
<td>16(2)</td>
<td>15(1)</td>
</tr>
<tr>
<td>Elastin concentration (mg-mg(^{-1}) dry tissue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissections</td>
<td>0.13(0.01)</td>
<td>0.14(0.01)</td>
<td>0.13(0.01)</td>
</tr>
<tr>
<td>Controls</td>
<td>0.22(0.02)</td>
<td>0.20(0.01)</td>
<td>0.18(0.01)</td>
</tr>
</tbody>
</table>

**Table IV** The extent of dissection in 10 aortas from individuals who suffered a fatal dissecting aneurysm of the thoracic aorta, showing the age (years) and sex (M or F) of the individuals and their matched controls: 26 of the bands (B1-4, fig 1) from which samples were taken were affected by dissection (+) and 13 were not (\(-\)).

<table>
<thead>
<tr>
<th>Age and sex</th>
<th>Areas affected by dissection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>B1</td>
<td>B2</td>
</tr>
<tr>
<td>63M</td>
<td>+</td>
</tr>
<tr>
<td>66M</td>
<td>+</td>
</tr>
<tr>
<td>70M</td>
<td>+</td>
</tr>
<tr>
<td>71M</td>
<td>+</td>
</tr>
<tr>
<td>73M</td>
<td>+</td>
</tr>
<tr>
<td>79M</td>
<td>+</td>
</tr>
<tr>
<td>85M</td>
<td>+</td>
</tr>
<tr>
<td>90M</td>
<td>+</td>
</tr>
</tbody>
</table>

* Data from this area (saccular aneurysm) were not included in our analysis.

Preparations had an increased proportion of hydroxyproline and polar amino acids and a decreased proportion of some non-polar amino acids when compared with analyses published for human aortic elastin. Others have reported similar observations. The proportion of contaminating polar protein, which cannot be extracted by chaotrophic solvents, increases with age and correlates with the degree of calcification but not with the degree of atheroma. Histidinoalanine is believed to link acidic structural proteins covalently to both elastin and collagen. Our results show that the polar protein component cannot be removed by cyanogen bromide digestion.

The hydroxyproline content of our cyanogen bromide residues could not be decreased by digestion with bacterial collagenase. A similar observation was made by Spina et al., who argued that this hydroxyproline did not indicate a collagen contamination but was a component of the polar protein. Our analyses show a small amount of hydroxylysine, indicating slight collagen contamination. Possibly collagenous peptides persist which are either resistant (eg, high molecular weight terminal regions of type IV collagen) or inaccessible to bacterial collagenase. Correction for this contamination can be made, based on the hydroxylysine content, but an appreciable hydroxyproline content in excess of that expected for pure elastin remains. The calculated hydroxyproline content of the polar protein component is 22 residues per 1000 amino acids. Our results show significant differences in amino acid composition between the control cyanogen bromide residues and residues from dissected aortas. Very similar results were previously reported in cases of aortic dilatation and dissection, again with high hydroxyproline values. These analyses therefore show that there is significantly more polar protein component in dissected tissue than in age matched control tissue. The accumulation of this component with age

**Table V** Overall mean(SEM) values for a range of variables derived from both the dissected (DR) and non-dissected (NDR) regions of diseased thoracic aortas and for the equivalent regions of the controls (CEDR for DR, CENDR for NDR).

<table>
<thead>
<tr>
<th>Lipid free dry weight (mg)</th>
<th>DR (n=26)</th>
<th>CEDR (n=26)</th>
<th>(p^2)</th>
<th>NDR (n=13)</th>
<th>CENDR (n=13)</th>
<th>(p^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of elastin (mg)</td>
<td>18(2)</td>
<td>13(2)</td>
<td>&lt;0.05</td>
<td>15(1)</td>
<td>15(1)</td>
<td>NS</td>
</tr>
<tr>
<td>Elastin concentration (mg-mg(^{-1}) dry tissue)</td>
<td>0.13(0.01)</td>
<td>0.20(0.01)</td>
<td>&lt;0.01</td>
<td>0.15(0.01)</td>
<td>0.20(0.01)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Elastin cross links (mol-mol(^{-1}) elastin)</td>
<td>2.97(0.43)</td>
<td>3.26(0.34)</td>
<td>NS</td>
<td>2.77(0.48)</td>
<td>2.54(0.39)</td>
<td>NS</td>
</tr>
<tr>
<td>Elastin cross links (µg-mg(^{-1}) elastin)</td>
<td>21.1(3.1)</td>
<td>23.2(2.4)</td>
<td>NS</td>
<td>19.7(3.4)</td>
<td>18.1(2.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Amount of NCNE protein (mg)</td>
<td>78(14)</td>
<td>15(3)</td>
<td>&lt;0.01</td>
<td>31(5)</td>
<td>26(6)</td>
<td>NS</td>
</tr>
<tr>
<td>NCNE protein concentration (mg-mg(^{-1}) dry tissue)</td>
<td>0.47(0.03)</td>
<td>0.27(0.03)</td>
<td>&lt;0.01</td>
<td>0.30(0.04)</td>
<td>0.26(0.04)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Elastin was prepared by cyanogen bromide digestion. See table II for abbreviations. 

\(p^2=DR \times CEDR; p^2=NDR \times CENDR\) (Students t test)
may lead to altered mechanical properties of the aortic wall, and increasing liability to rupture at lower stress and strain values. The presence of a polar protein component might interfere with the establishment or maintenance of the hydrophobic domains necessary to allow elastin to function by the "oiled coil" mechanism. The aorta might therefore suffer a permanent and inappropriate dilatation, increasing its tendency to rupture.

While the events described above have been suggested as reasons for morphological changes and stiffening associated with aging, it should be pointed out that earlier reports proposed that these age changes were due to fragmentation of elastic laminae, loss of elastin, and increased collagen content. However, other investigators proposed a decreasing elastin but constant collagen content with aging. A more recent study supports a concomitant increase in collagen and other proteins with age, while in contrast elastin amount remained relatively constant. However, the elastin concentration decreased due to an increase in the concentration of other tissue components as the tunica media thickened with increasing age. The differences which we found between dissected and control aortas parallel these latter findings (except for our observation of increased elastin content) but disagree with the other reports of decreased content. If the findings of Spina et al. are correct, the similarity of our results suggests that premature aging of the aortic wall may be a contributory factor in the aetiology of dissecting aneurysms.

Our findings of undiminished elastin content in dissected thoracic aortas distinguishes this condition markedly from aneurysms of the abdominal aorta where decreased elastin due to excessive elastase activity is well documented. Other studies on aneurysms have been rare, but those that have been published have found that in many cases the elastin concentration was decreased compared with controls, which agrees well with our results. Neither of these studies measured total elastin or protein.

The amount of elastin was increased in dissected aortas only in areas affected by dissection, while the concentration of elastin was decreased over the whole aorta, although its decrease in dissected areas was greater than that in non-dissected areas. Decreased elastin concentration could not be accounted for by the increased amount of collagen alone but more obviously by the increase in NCNE protein. The decreased elastin concentration in areas not affected by dissection is probably due to the combined effect of small increases in collagen and non-collagen non-elastin protein.

Distribution of elastin along the thoracic aorta from valve to diaphragm showed no gradient in amount or concentration, neither was there any significant variation circumferentially. While previous reports have pointed out the decreasing elastin component of the abdominal as compared to the thoracic aorta, we are unaware of any other published data for the detailed elastin distribution within the human thoracic aorta. Our results indicate that the diaphragm seems to be the dividing line between an elastic vessel in the thorax and a more collagenous one in the abdomen. The elastin to collagen ratios showed no significant differences between dissections and controls because both variables increased in dissection. The elastin to collagen ratios show that in the thoracic aorta of mildly hypertensive individuals in the eighth decade collagen predominates over elastin. The highest ratios occur, as expected, in the ascending aorta.

In the previously published study, we found no differences in the number of pyridinoline cross links per collagen molecule between dissected and control aortas. Thus there is no evidence that aortic wall weakness in dissection is due to decreased collagen cross linking. Similarly, the findings reported here show that there was no change in the degree of elastin cross linking by desmosine and isodesmosine in dissected tissue relative to controls, or from heart to diaphragm. No definitive studies have been published on elastin cross links in aortas affected by aneurysms, so ours is the first study to provide detailed information.

All differences between dissections and controls were accentuated within areas affected by dissection, whereas few differences from controls were seen in areas unaffected by dissection. Indeed, in the overall comparison of dissected aortas and controls there was no significant difference in total elastin. However, on reanalysing the data so that dissected regions were compared with corresponding regions, a significant increase in total elastin in dissected aortas was revealed. More importantly, the value of this analytical approach was shown by the lack of differences (with the exception of elastin concentration) between non-dissected areas of dissected aortas and corresponding areas of controls. Thus there is some factor which stimulates deposition of elastin, non-collagen non-elastin protein, and collagen in areas "susceptible" to dissection, suggesting an imbalance between synthesis and degradation. Since full thickness samples from the aortic wall were taken in this study, any blood proteins occluded within the cleavage plane would be included in the analysis. It is therefore likely that those are at least partly responsible for the increase in non-collagen non-elastin protein. However, collagen and elastin are not blood proteins and must therefore have increased in amount prior to dissection. If changes in these matrix components affect one layer only, e.g., media, then analysis of full thickness samples would mean that such changes would be less obvious. The decreased elastin and collagen concentrations must be due to influx of plasma proteins and/or to increased deposition of non-collagen non-elastin proteins. The latter could, of course, be due to increase in smooth muscle cell protein. However, these matrix changes could conceivably have arisen secondarily to a generalised defect, the latter perhaps causing continuous trauma, particularly in areas of high stress. Tissue repair in these areas could then have produced a structurally weaker matrix than in other parts of the aorta, so leading to dissection.

It is possible that changes in fibre orientation may be important. It has been suggested that dissection is initiated by the processes of injury and repair in the aortic wall, and that this process would lead to gradual dilatation of the aorta and, according to Laplace's law, a vicious circle would lead to further complications such as rupture and complete or incomplete dissection. The repair processes might produce inappropriate fibre orientation. Studies on fibre orientation in dissected aortas therefore would need to be in three dimensions but to our knowledge have not been carried out.

Finally, it should be recognised that dissecting aneurysms of the thoracic aorta, like other connective tissue diseases, may result from several different primary lesions. Thus the changes which we have defined may not necessarily originate from identical defects in different patients.

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Key terms: elastin; thoracic aorta; dissecting aneurysm.


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