Regression of Coronary Atherosclerosis
Angiographic Perspective

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Summary

The influence of dietary or pharmacological intervention on coronary atherosclerosis can best be assessed by performing serial coronary arteriography on patients at high risk for coronary disease progression who are randomised into controlled trials. Changes in coronary artery lesion diameter of less than 20% cannot be accurately assessed by visual interpretation, because of inter- and intra-observer variability. The introduction of quantitative, computer-assisted measurements of coronary lesions has reduced variability and greatly improved the precision of measurements. Both cholestyramine and colestipol-niacin have been shown to reduce the rate of progression of coronary atherosclerosis; however, in both studies coronary lesions were assessed visually and no quantitative measurements were reported. A marked reduction in serum cholesterol appears to be the intervention that is most likely to prevent the progression or induce regression of coronary atherosclerosis. Quantitative angiographic measurement techniques should be used in clinical trials designed to assess cholesterol-lowering interventions.

Morbidity and mortality from coronary heart disease are the ultimate results of progression of coronary atherosclerosis. When these end-points are used in clinical trials to assess the effect of an intervention, large numbers of patients and long periods of follow-up are required if a benefit is to be demonstrated. The number of patients required and the length of the study are greatly reduced by the use of coronary arteriographic end-points to assess interventions. Therapies that could delay the progression of coronary atherosclerosis, or even induce regression of lesions, would have a profound clinical impact.

1. Angiographic Assessment of Changes in Coronary Lesions

Visual interpretation of coronary arteriograms is plagued by a high degree of inter- and intra-observer variability (Detre et al. 1982; Zir et al. 1976). There is general agreement that changes of 20% or more in the diameter of a stenosis can be detected with a high degree of confidence, but that the accuracy of the interpretation of smaller changes may be affected by technical or observer variability. In previous studies (Moise et al. 1983, 1984a,b, 1985), coronary disease progression has been defined as an increase in the diameter of a stenosis of 20% or
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more in a lesion at least 50% narrowed, or 30% or more in a lesion narrowed by < 50% (e.g. a 30% stenosis becoming 60%). Regression was defined as a decrease in the percentage diameter of a stenosis to the same extent.

The problem of assessing progression from serial coronary arteriograms was studied in detail by the investigators in the National Heart, Lung and Blood Institute Type II Coronary Intervention Study (Brensike et al. 1984; Detre et al. 1982), who concluded that a consensus of a panel of 3 experienced readers decreased variability. Three separate panels each consisting of 3 experts interpreted the study films without knowledge of treatment assignment or the order of films. Change, either progression or regression, was classified as 'definite' or 'probable' but no quantitation of the degree of change, expressed either by percent stenosis or by another measurement, was reported in this study. Similarly, the beneficial effect of colestipol-niacin on coronary lesions reported by Blakenhorn et al. (1987) was demonstrated only with qualitative and not quantitative measurements of coronary lesion changes.

The development of quantitative coronary arteriography has eliminated most of the problems associated with visual interpretation. The Cardiovascular Angiographic Analysis System (CAAS) developed by Reiber et al. (1985) digitises the selected cine-frame and corrects for distortion. The image is calibrated using the known dimensions of the cardiac catheter, and an automatic edge detection program determines the arterial contour and calculates both the vessel diameter over a region of interest and the degree (%) of stenosis (fig. 1).

The reproducibility of repeat measurements using this system is excellent (Waters et al. 1987); however, the variability of measurements over a period of months or years has not yet been well documented. Reiber et al. (1985) reported a standard deviation of 0.36mm for minimum diameter and 6.5% for diameter stenosis when angiograms recorded 90 days apart were compared. Our experience showed that a minimum diameter change \( \geq 0.4 \text{mm} \) or a diameter stenosis change \( \geq 10\% \) are indicators of progression or regression.

Variations in coronary tone from one angiogram to the next are an important source of variability when serial arteriograms are compared. At-