Title
Correlation of minimum coronary lumen diameter with left ventricular functional impairment induced by atrial pacing

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To understand whether quantitative measurement of minimal coronary luminal diameter is a better method than percent diameter narrowing for assessing the functional impairment of myocardial contractility produced by coronary artery stenoses, measurements were made from 37 stenotic segments in 27 patients with coronary artery disease and from corresponding segments in 10 subjects without coronary artery narrowing. An assessment of the reliability of the 2 types of measurements was made by correlating them with the physiologic parameters of both segmental wall motion and global ejection fraction response induced by atrial pacing. Digitally acquired coronary angiograms were used to facilitate quantitative analysis. Measurements by edge detection and videodensitometry correlated closely \((r = 0.94)\). Percent diameter narrowing correlated moderately with the change in ejection fraction \((r = -0.41)\) or with the change in segmental wall motion \((r = -0.44)\). The measurement of minimal luminal diameter correlated with the change in global ejection fraction \((r = 0.61)\) and did so even better with the change in segmental wall motion \((r = 0.78, p < 0.05)\). A minimal luminal diameter of \(\geq 1.5\) mm identified patients likely to have a functional impairment during atrial pacing as assessed by either global ejection fraction or segmental wall motion defects. We conclude that minimal coronary luminal diameter provides a better method than percent diameter narrowing calculations to measure the anatomic severity of coronary artery narrowing. 

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The severity of coronary artery disease (CAD) is usually graded from angiograms by the percent narrowing between the stenotic segment and a more proximal normal portion.\(^1\,^2\) Therefore, percent diameter narrowing is a relative number that depends both on the size of the narrowed as well as the presumed normal segments. One problem with this method of measurement is that identification of the presumed normal region is arbitrary. In addition, pathologic studies indicate that atherosclerosis is present to a variable degree in a large portion of so-called normal segments.\(^3\) An alternative method of performing quantitative analysis of coronary angiograms is to measure the minimal luminal diameter instead of the percent diameter narrowing at the region of maximal arterial narrowing.\(^4\) Theoretically, this minimal lumen diameter would be a more accurate way of comparing studies or interpreting the results of coronary angioplasty. However, there have been no clinical studies demonstrating that measurements of minimal lumen diameter correlate better than percent diameter narrowing with functional determinations of the severity of disease. The purpose of this study was to assess the correlation of both percent diameter narrowing and minimal lumen diameter with functional measurements of global ejection fraction and segmental wall motion during ischemia induced by atrial pacing.

**Methods**

**Angiographic technique:** Coronary angiograms were obtained by on-line digital acquisition. Images were exposed on a 7-inch image intensifier at a nominal focal spot of 1.2 mm. The images were converted by an on-line video image processor [Fischer DA-100]...
into a 512 × 512 × 8 bit matrix and stored digitally on a 475 megabyte rapid parallel transfer disk (Fujitsu). Selective coronary angiograms were obtained in orthogonal right and left anterior oblique projections with cranial and caudal angulation. A more detailed description of our digital coronary acquisition and validation method as compared with 35-mm film cineangiography has been reported.5

Cardiac catheterization was performed by retrograde cannulation from the femoral artery and coronary angiograms were obtained and reviewed. A baseline digital subtraction left ventriculogram was then performed.6,7 If there were no contraindications, an atrial pacing study was carried out. Contraindications to atrial pacing included significant left main disease, unstable angina, recent myocardial infarction (<3 months), cardiomyopathy or valvular heart disease. Left ventriculograms were obtained in the 30° right anterior oblique projection to identify wall motion abnormalities in the distribution of the left anterior descending and right coronary arteries. To compare results of global ejection fraction and segmental wall motion in the right anterior oblique projection, no patients were included with predominant lesions in the circumflex artery (which would require left ventriculograms in the left anterior oblique projection to visualize lateral wall motion abnormalities).

**Pacing protocol:** After the resting digital left ventriculogram was obtained, 6Fr pacemaker electrode was inserted into the femoral vein and passed under fluoroscopic control to the lateral wall of the right atrium. The right atrium was stimulated at 2 mA initially at a rate of 10 beats/min above the patient's heart rate at rest. The rate was increased in increments of 10 beats/min every minute until chest pain developed or until a heart rate of 150 beats/min was reached. If atrioventricular Wenckebach block developed, 1 mg of atropine was administered intravenously and the pacing study continued. When the endpoint was achieved, another digital left ventriculogram was performed and the pacemaker was then turned off.

**Quantitative analysis:** After the catheterization was completed, the coronary angiographic images were recalled from computer memory. An individual frame was chosen from either the right anterior oblique or left anterior oblique projection which most clearly demonstrated the stenotic segment. Studies were chosen for analysis if the stenosis involved the proximal half of the right coronary artery or the left anterior descending coronary artery. This digital image was in an unsubtracted format, all calculations of the severity of coronary artery narrowing being made from the unsubtracted image so that measurement errors due to misregistration would not be introduced. The observer chose the stenotic portion of the image and the computer digitally magnified the area of interest 4-fold. Two different methods of quantifying the stenosis were used. The first was an edge-detection method with the operator choosing the diameter boundaries of the presumed normal and stenotic arterial segments. The image was magnified so that the catheter was displayed on the monitor screen and edges of the catheter were defined by the operator. The routine angiographic catheters had been measured by Vernier calipers and these known measurements were used to calibrate the pixel dimensions of the digital image. Because the image was already in a digital X-Y coordinate matrix, the measurements of relative percent stenosis as well as absolute lumen dimensions could be quickly derived.

The second method of measurement of the stenosis was by videodensitometry (Figure 1). Because the unsubtracted digital images were logarithmically amplified to correct for exponential x-ray absorption, the digital number in each pixel corresponded to the thickness of the contrast material that the x-rays traversed. The observer chose the normal and stenotic segments by placing a rectangular region of interest over portions of the coronary image. The underlying background densities not due to contrast media in the arterial lumen were subtracted out by a linear averaging method, with the densities at the 4 corners of the region of interest used to estimate the underlying background.8 In order to assure that a reasonable background measurement was obtained, the computer displayed the density profile of the arterial segment across the width of the artery. The observer could then alter the width of the region of interest so that it was just beyond the densitometric edge of the image as determined by the sharp inflection of the density profile. After subtracting out background densities, the density within each region of interest corresponded to the volume of contrast within the lumen. When divided by the height of the region of interest, this number corresponds to the cross-sectional area. The ratio of the densities at the stenotic and presumed normal segments was used to compute the percent area stenosis.

![FIGURE 1. This digital coronary angiogram of a right coronary artery demonstrates a severe obstruction in the middle segment. Two regions of interest are defined at the obstruction and at a more proximal (assumed normal) segment. Because the image is already in a computerized format, the density of contrast within the lumen is calculated and plotted with the Y axis representing relative density and the X axis corresponding to a 50-pixel wide segment perpendicular to the long axis of the artery. The densitometric boundary of the artery is then chosen and the percent area stenosis is calculated.](image-url)
In order to compare videodensitometric results with the edge detection method, the percent diameter narrowing was derived from the percent area stenosis by assuming a circular cross section for the 2 segments. The minimum lumen diameter was then derived by using the width of the catheter to calibrate the distances in the image. The measurements of all the stenoses were performed by 2 independent observers. The first observer identified the regions of the artery to be measured and recorded their location with Polaroid® film so that both observers would derive measurements from approximately the same segments.

The digital left ventriculograms were analyzed by standard area-length methods for calculating volumes and ejection fraction. The images were recalled from computer memory and processed by mask mode subtraction using a 10 to 15 frame blurred mask to enhance contrast. The operator outlined the boundary of the end-diastolic and end-systolic images using the cursor of the computer graphics system. A separate wall motion analysis was performed on the ventricular boundaries using the method developed by Alderman et al. In this analysis, the perimeter of the left ventricle in the right anterior oblique projection was divided into 5 segments (anterobasal, anterior, apical, diaphragmatic and posterobasal). The wall motion in these segments along radians was calculated and a percent of area segmental motion derived.

The relative amount of radial area shortening can be compared to a graph of wall motion based on normal subjects. For the purpose of this study, the percent of segmental area shortening was calculated at rest and during atrial pacing. The value at rest was subtracted from the value during pacing so that an increase in contractility during pacing would appear as a positive number and a decrease in contractility as a negative number. Similarly, the change in global ejection fraction was calculated as the value at rest subtracted from the value during pacing; thus, a fall in ejection fraction during pacing would appear as a negative value.

Statistical analysis: The measurements of percent diameter narrowing by the edge detection and videodensitometric techniques were compared by a linear regression analysis. The measurements of percent diameter narrowing and minimal lumen diameter were correlated to the change in global ejection fraction as well as to the change in segmental wall motion by separate linear regression analyses. Volumetric parameters at rest were compared with the values during pacing by a paired t test. Differences between groups of patients were compared with an unpaired t test.

**Results**

There were 41 patients who underwent atrial pacing studies. Four of these studies were excluded because either the resting or pacing left ventriculogram was not sufficiently opacified or it had multiple premature ventricular contractions which could have affected the wall motion analysis. There were 10 patients with chest pain syndromes who were found to have normal coronary angiograms and had atrial pacing studies performed. In the 27 patients with coronary artery narrowing, 22 were men and 5 women. The mean age was 54 ± 10 years. There were 35 narrowed coronary segments measured. There were 19 patients with 1-vessel disease and 8 with narrowed segments in both the left anterior descending and right coronary arteries; however, the second stenosis measured <50% and was judged not to be significant angiographically. Patients with complete occlusions or those with evidence of collateral blood supply were excluded. Of the 27 primary stenoses analyzed, 18 were in the left anterior descending, 8 in the right coronary artery and 1 was in a large diagonal artery. In the 27 patients with stenoses, the atrial pacing study induced chest pain in 15 (56%) and positive electrocardiographic criteria for ischemia was induced in only 8 (35%).

The mean percent diameter narrowing of the 27 primary lesions was 60 ± 16% when measured by the edge detection technique and it was not significantly different when measured by videodensitometry (60 ± 18%). The minimal lumen diameter was calculated to be 1.4 ± 0.6 mm by the edge detection method and 1.4 ± 0.7 mm by the densitometric technique (p = not significant). There was a close correlation (r = 0.94) between measurements of individual stenoses by edge detection and videodensitometry over the 0.4 to 2.8 mm range. In addition, interobserver variability was very close with either edge detection (r = 0.90) or videodensitometric technique (r = 0.89). There was no difference in the mean measurement of minimal lumen diameter for the left anterior descending artery obstructions (1.2 ± 0.4 mm) versus the right coronary artery obstructions (1.6 ± 0.6 mm).

The mean age of the 10 patients without CAD was 53.6 years (range 36 to 65), which was not different than the mean age of the patients with CAD. The mean ejection fraction at rest was 66 ± 7% and increased to 72 ± 5% at peak pacing (p < 0.001). The results of the ventricular volumetric measurements for the 27 patients with CAD are listed in Table 1. The mean resting global ejection fraction was 64 ± 15%. At the peak heart rate achieved during atrial pacing, the mean ejection fraction fell to 54 ± 20% (p < 0.001).

Segmental wall motion was quantified for the portion of the ventricular perimeter in the right anterior oblique projection expected to be affected by the ste-
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Figs. 2 to 6 relate segmental (SEG) wall motion changes to Lumen Diameter (mm) changes. The primary stenosis in patients with coronary disease was measured and analyzed. The effect of atrial pacing in patients with CAD was compared to the effect of pacing on the change in Lumen Diameter (mm) in the 10 normal subjects (Fig. 4).

The results of patients with coronary disease (n = 27) and those with angiographically normal coronary arteries (n = 10) are demonstrated. The measurement of the stenotic lumen or the normal arterial diameter in normal subjects is compared with the effect of pacing on the change in segmental (SEG) wall motion shortening.
shown in Figure 6 for the segmental areas perfused by the left anterior descending coronary artery and in Figure 7 for the areas perfused by the right coronary artery. A minimal arterial diameter of \( \leq 1.5 \) mm tended to identify those patients likely to have an abnormal response in segmental wall motion during atrial pacing. The normal response to pacing revealed a mean increase in segmental area shortening of \( 18 \pm 11\% \) in the area perfused by the left anterior descending artery and \( 8 \pm 9\% \) in the area perfused by the right coronary artery \((p < 0.05)\). The minimal lumen diameter of \( \leq 1.5 \) mm significantly separated the patients with abnormal responses for both the right coronary artery and left anterior descending artery. However, there was some overlap among patients with left anterior descending artery narrowing between 2.2 and 1.6 mm. Moreover, there was no difference from normal segmental motion in the patients with right coronary artery narrowing between 2.2 and 1.6 mm.

**Discussion**

Assessment of the severity of coronary artery narrowing is made primarily by angiographic determination of the percent of diameter narrowing relative to an assumed normal portion of the artery. This determination may be misleading for several reasons. Of greatest importance, pathologic studies have demonstrated that atherosclerosis is a diffuse process and even when the angiogram only demonstrates a single stenosis, \(<25\%\) of the length of the arteries will be free of disease and truly normal.\(^3\)\(^,\)\(^12\) In addition, stenoses commonly occur at bifurcations so that it may be difficult to identify a normal proximal portion of the same arterial segment. Consistent with these observations, the study of White et al.\(^3\) reported that measurements of percent diameter narrowing correlate very poorly with a physiologic assessment of stenosis severity determined by hyperemic flow response after temporary coronary occlusion during open heart surgery. Legrand and coworkers\(^4\) found a similar poor correlation between mea-
measurements of percent stenosis and coronary blood flow reserve, as measured by digital flow maps after a hyperemic stimulus.

For these reasons, percent diameter narrowing measurements are flawed as a quantitative method of assessing the severity of CAD. In addition, there is frequent disagreement between observers about the severity of a stenosis and it has been suggested that minimum lumen dimensions (either cross-sectional area or linear diameter) would be preferable to using percent diameter narrowing to assess the severity of CAD. Harrison et al found that the minimal lumen diameter correlated better with the hyperemic flow velocity response after 20 seconds of occlusion of the left anterior descending artery. Our data, using the changes in wall motion during atrial pacing in conscious patients, are very similar to their results. In addition, both studies found that an arterial diameter of <1.5 mm was predictive of an abnormal physiologic response. Our data extend these findings to the right coronary artery as well as the left anterior descending.

In addition, the data show that measurements of minimal lumen dimensions predict clinical results better than does percent diameter narrowing.

In the present study, atrial pacing stress tests were used as a functional assessment of stenosis severity for comparison with coronary angiographic determinations of stenosis severity. In the 27 patients with CAD, measurements of percent diameter narrowing and lumen diameter by edge detection or videodensitometry correlated closely (r = 0.94). Both percent diameter narrowing and minimal lumen diameter correlated with the change in global ejection fraction (r = -0.41 and r = 0.61, respectively). However, it was recognized that the correlation may have been reduced when using global ejection fraction as the measured parameter because the myocardial wall supplied by the normal nonstenotic segments may compensate for diminished motion in the affected myocardium. Localized segmental wall motion was analyzed to isolate the effect of ischemia due to a specific stenosis. The result was a correlation of percent diameter narrowing with segmental wall motion (r = -0.44), similar to that obtained with global ejection fraction (r = -0.41). This result may be explained because percent diameter narrowing is a relative number that does not truly represent the functionally effective resistance to coronary flow. The Poiseille equation for laminar flow indicates that resistance to flow is inversely proportional to the fourth power of the radius. Thus, a 50% reduction of a 2-mm vessel will have a much greater resistance to flow than a 50% reduction in a 4-mm vessel. When the effect of atrial pacing on segmental radial wall motion was analyzed, there was a clear difference between the 2 methods of measurement of CAD. Whereas percent diameter narrowing was correlated with segmental wall motion with a coefficient of r = -0.44, minimum lumen diameter correlated much more closely (r = 0.78, p <0.05). The improved correlation suggests that the lumen diameter predicts more accurately the functional impairment induced by pacing because the absolute diameter is more directly related to the resistance to flow than percent narrowing.

With regard to the amount of narrowing, our data indicated that the narrowing of an epicardial coronary artery to a diameter <1.5 mm increased the likelihood of a functional impairment induced by atrial pacing in the myocardium supplied by the narrowed artery. Narrowing of the artery to <1.5 mm in diameter increased the probability of a positive study both by global ejection fraction and segmental wall motion. Thus, a minimum lumen diameter <1.5 mm may be useful as a predictor of which patients will be symptomatic during stress.

As demonstrated in Figure 3, there was a close linear correlation between the minimal lumen diameter and the affected segmental wall motion for the patients with CAD. As the stenotic lumen diameter increased, the effect on wall motion leveled off into the range of normal subjects. Our data emphasize the finding that patients with mild disease may not have a functional impairment induced during stress. An exact linear relation between lumen diameter and functional impairment should not be expected because other
influences such as the length of coronary narrowing, vasomobility and the presence of sequential stenoses also impede blood flow.21-23

References


