Accuracy of Electronic Digital Calipers Compared With Quantitative Angiography in Measuring Coronary Arterial Diameter

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Background. Quantitative angiography is the accepted method for measuring coronary luminal diameter. Electronic digital calipers have been used to assess arterial diameters in vasomotor function studies and after interventional procedures. However, careful validation of calipers against quantitative angiography has not been described.

Methods and Results. We used digital calipers and quantitative angiography to measure 517 arterial diameters (88 nonstenotic segments) in 24 transplant patients undergoing vasomotor function studies with acetylcholine and nitroglycerin, 20 stenoses in 14 patients with coronary artery disease, and 15 stenoses in 15 patients before and after excimer laser-facilitated coronary angioplasty and at 6 months' follow-up. In nonstenotic arterial segments ranging in size from 0.6 to 3.5 mm, calipers overestimated diameters measured by quantitative angiography by 0.29±0.21 mm (mean±SD) (limits of agreement, −0.13 to 0.71 mm). However, when the vasomotor responses were expressed as percent diameter change, the two methods did not differ significantly (−1±10%; limits of agreement, −21% to 19%). In the 35 stenoses measured before intervention and 30 stenoses measured after intervention, calipers and quantitative angiography differed by 3±9% (limits of agreement, −15% to 21%) across a range of stenosis severity (11% to 80%). Repeat caliper measurements by the same observer of the percent diameter change in the transplant patients and the percent stenosis in the coronary artery disease patients led to standard deviations of the differences of 9.3% and 7.6%, respectively. Two different observers recorded percent diameter change and percent stenosis that differed with standard deviations of 9.6% and 7.8%, respectively.

Conclusions. Quantitative angiography and electronic digital calipers produce similar relative changes in arterial diameters and percent stenosis in a broad range of severities. Digital calipers thus are a rapid and convenient alternative to computerized quantitative angiography in certain research studies and clinical practice of assessing stenosis severity. (Circulation. 1993;88[part 1]:1724-1729.)

Key Words • stenoses • angiography

Quantifying coronary arterial diameter is of great importance in both research and clinical settings. Common uses in research include quantifying diameter changes during infusion of vasoactive substances like acetylcholine and nitroglycerin in testing endothelial- and nonendothelial-dependent vasomotor function1-4 and measuring stenosis severity (percent stenosis) in patients before and after coronary interventions for defining success and restenosis.5-7 In clinical practice, quantification of stenosis is used in the routine interpretation of coronary angiograms, and the results may influence therapeutic decisions.

The commonly used methods of quantifying stenosis severity include visual inspection,8 manual calipers,9 electronic digital calipers,10 quantitative angiography,11,12 and videodensitometry.13 Visual inspection of coronary diameters is of limited utility for quantifying vasomotor reactivity as changes in diameter exceeding 20% to 30% are required for reliable detection. Grading of stenosis severity, expressed as percent stenosis before and after interventions, results in a significant degree of interobserver and intraobserver variability, and these inaccuracies can only be reduced by a panel judgment.14 Most quantitative angiographic analysis systems require offline digitization, and the process can be costly and time consuming.12 Therefore, semiquantitative methods like manual handheld calipers have been used to quantify stenosis severity, and studies have shown good correlation of calipers with quantitative angiography in measuring stenosis severity. One study found specially constructed electronic calipers to be sufficiently accurate to be used to evaluate stenoses clinically while another study found that measurements made using manual calipers underestimated stenoses ≥75%, overestimated lesions <75%, and had poor reproducibility between observers.8,10

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Recently, there has been renewed interest in a new generation of electronic digital calipers for performing quantitative angiographic measurements because of their simplicity and low cost. However, the comparison of electronic digital calipers with automated edge detection using quantitative angiography in vasomotor function and interventional studies has been lacking. Therefore, the aim of this study was to compare electronic digital calipers with quantitative angiography in measuring coronary artery diameter changes during tests of vascular function and percent diameter stenosis in lesions before and after excimer laser-facilitated coronary angioplasty and at follow-up.

Methods

Patient Studies

Three patient populations were studied: (1) 24 cardiac transplant patients during their yearly cardiac catheterization including vasomotor function testing, (2) 14 coronary artery disease patients with a range of stenosis severity, and (3) a separate group of 15 patients with critical stenosis before and after excimer laser-facilitated angioplasty and at 6 months' follow-up.

The transplant patients underwent the following protocol as described previously. 2 Briefly, after completion of the diagnostic catheterization, a guiding catheter was positioned in the ostium of the left coronary artery. A 2.5F infusion catheter was advanced into the proximal portion of the left anterior descending coronary artery. Serial infusions of acetylcholine (10 -9 to 10 -6 mol/L final estimated concentration) and nitroglycerin were made. At the end of each infusion, nonionic contrast medium was injected into the left coronary artery using a power injector to achieve optimal opacification. The coronary angiograms were analyzed using quantitative angiography and electronic digital calipers. A total of 517 coronary diameters were measured by both methods in 88 coronary segments (see “Appendix I”).

Twenty stenoses were measured in 14 patients after a routine diagnostic catheterization using both methods. Five lesions were in the left anterior descending coronary artery, six in the circumflex artery, eight in the right coronary artery, and one in saphenous vein graft. The angiographic view that showed the most severe stenosis was used for the measurements.

Fifteen stenoses in the group of 15 patients undergoing excimer laser-facilitated angioplasty were measured before and after angioplasty and at 6 months' follow-up, as previously described. 6 Ten patients had a stenosis in the left anterior descending coronary artery, and five had a stenosis in the right coronary artery. The angiographic view that revealed the stenosis optimally was used for subsequent measurements.

Phantom Study

Thirteen holes were precision-drilled in a Lucite block using a water-cooled drill at the Bioengineering Department of the Brigham and Women's Hospital. The diameters of the holes varied from 0.6 to 3.8 mm. A brass rod (3.175 mm) was also imbedded into the block for calibration. The holes were then filled with contrast and sealed. The block was placed under 30 cm of water, and a cine film was obtained using a focal spot of 0.6 mm and tube height of 28 cm without skew or angulation.

Quantitative Coronary Angiography

The quantitative angiography program was previously validated by Kirkkeide et al 15 and has been used extensively in our laboratory. 1,2,4,6 Each coronary segment of interest was centered on a Vanguard projector, and the single-frame cine images were optically magnified sevenfold to eightfold with the use of a video camera (Cohu, San Diego, Calif). This image was then digitized into a 512×512 matrix of pixels (40 to 50 μm per pixel). Image-processing equipment (Recognition Concepts Inc) with a dedicated Microwx II (Digital Equipment Corp, Maynard, Mass) was used to search for the vessel edges and the segmental diameter using the first derivative of the densitometric profile computed according to a least-squares convolution technique. Four end-diastolic frames were digitized to obtain the mean diameter of the segment at the selected position. Anatomic features were used to identify the region of interest (ROI) in each segment so that the same segment could be studied by electronic digital calipers. Calibrated grids were used to scale these measurements to millimeters in the transplant population. The diameters at the site of maximum reduction and in the normal adjacent areas were measured to obtain percent diameter stenosis in the coronary artery disease patients. Similar measurements were made of the 13 phantom diameters (four frames each) using the brass rod diameter as calibration.

Electronic Digital Calipers

A handheld electronic digital caliper (Mitutoyo Corporation, Tokyo, Japan) was used to measure coronary diameters for each lesion displayed on the screen of a Vanguard projector. The cine frame analyzed was the first frame used in quantitative coronary angiography analysis. Particular care was taken to ensure that the measurements with the calipers and quantitative angiography were taken from exactly the same vessel segments using the anatomic landmarks identified during quantitative angiographic analysis. Each segment was measured at the ends and the center of each ROI. The mean of these measurements represented the diameter of each segment. The calibrated grid was measured using the same method, and the measurements were scaled to millimeters. Similarly, the diameters at the site of maximal reduction and in the normal adjacent areas were measured to obtain percent stenosis in the coronary artery disease patients. Similar measurements were made of the 13 phantom diameters using the brass rod diameter as calibration.

Digital Calipers Intraobserver and Interobserver Variabilities

Intraobserver and interobserver variabilities of the caliper measurements were calculated using 51 diameters selected at random from 517 measurements in the transplant patients and 30 stenoses in the angioplasty patients. The first observer analyzed these segments on four separate occasions, each separated by a minimum of 7 days. The second independent observer analyzed the segments on only one occasion, and these measurements were compared with those made by the first observer. For intraobserver variability, the four observations by the same observer were analyzed using a
one-way analysis of variance, with the patient as the single factor. The resulting variance estimate was multiplied by two (since the difference of two measurements has twice the variability of a single measurement), and then the square root was calculated to capture the standard deviation of the differences between two measures by the same observer. For interobserver variability, a two-way analysis of variance with patient and observer as the two factors was performed. In this case, the systematic mean difference between observers was subtracted from the data before the calculation of the standard deviation of the difference between two measures by two observers. These estimates of interobserver and intraobserver reliabilities determine in part the stability of data collected with calipers; the implications for study design are discussed in “Appendix II.”

Statistical Analysis

The agreement between computerized quantitative angiography and digital calipers was assessed by plotting the difference between methods against the mean of the measurements following the technique described by Bland and Altman.16 This procedure allows visual inspection of the deviation from the mean over the full range of measurement. This analysis was performed for each stage of drug infusion in the first group of patients; after routine angiography in the second group; and for preangioplasty, immediate postangioplasty, and at follow-up in the third group. The range of agreement between the two methods is given as the mean difference ±2 standard deviations; this interval will contain 95% of the measurement differences. If the range is small and clinically acceptable, then the two methods can be used interchangeably. A systematic difference between the two methods of measurement is estimated by the mean difference. Similar analyses were performed for the phantom diameters with the quantitative angiographic and calipers measurements plotted against the true diameters. All data were expressed as mean±SD.

Results

Vasomotor Function Testing

In the measurements of 517 coronary diameters in 88 segments, there was a consistent bias with electronic digital calipers overestimating quantitative angiography by 0.29±0.21 mm across all vessel sizes (0.6 to 3.5 mm) (Fig 1A). The limits of agreement were −0.13 to 0.71 mm. There was a small increase in differences as the vessel size increased (vessel size <1.5 mm: 0.21±0.18 mm; vessel size 1.5 to 2.5 mm: 0.29±0.21 mm; vessel size >2.5 mm: 0.44±0.24 mm). The mean difference between the two methods represented a discrepancy of 21% for a 1-mm vessel or a discrepancy of 14% for a 3-mm vessel. These systematic differences, however, were not obvious from the linear regression (Fig 1B) with a slope of 1.09 (95% confidence interval, 1.06 to 1.13, r=.94).

Both methods showed good agreement in detecting directional changes elicited by infusion of vasoactive drugs. When responses were expressed as percent diameter change from baseline after each drug infusion (acetylcholine, nitroglycerin), there was no significant difference between caliper and quantitative angiography measurements in segments that dilated to maximal dose of acetylcholine (difference: −2±13%) and segments that constricted to acetylcholine (difference: 0±11%). Nitroglycerin response was not different between that measured by calipers and quantitative angiography (difference: 0±13%) (Table 1). The overall difference between the two methods of measurement for percent change (n=429) was −1±10% with limits of agreement from −21% to +19%.

Stenoses and Angioplasty Follow-up

Caliper measurements overestimated the quantitative angiographic measurements of the 35 stenoses (range, 35% to 80%) in the coronary artery disease (20) and preangioplasty (15) patients by 5±7% (Table 2). The limits of agreement were from −9% to 19%.

After excimer laser-facilitated angioplasty and at follow-up, the difference between the two methods became negligible, 1±9% and −1±11%, respectively (Table 2). In the 65 stenoses measured, quantitative angiography and digital calipers differed by 3±9% across all severity (range, 11% to 80%) with the limits of agreement of −15% to 21% (Fig 2A). Again, these differences were not obvious from the linear regression with a correlation coefficient of .89 (Fig 2B).

Digital Calipers Intraobserver and Interobserver Variabilities

The standard deviation of the intraobserver differences was 0.148 mm while measuring absolute diameters in the transplant patients. In comparing two observers, we found a systematic mean difference of 0.14 mm. After allowing for this systematic difference, the standard deviation of the interobserver differences was 0.149 mm. When the diameters were expressed as percent change from baseline, the standard deviation of
TABLE 1. Comparison of Electronic Digital Calipers With Computerized Quantitative Angiography in Vasomotor Function Studies

<table>
<thead>
<tr>
<th>Response to maximal ACH</th>
<th>Measured by QA, %</th>
<th>Measured by Calipers, %</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilation (n=30)</td>
<td>Mean 13</td>
<td>11</td>
<td>−2</td>
</tr>
<tr>
<td></td>
<td>SD 9</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Constriction (n=58)</td>
<td>Mean −16</td>
<td>−16</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>SD 16</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Response to TNG (n=88)</td>
<td>Mean 24</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>SD 16</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Response of all segments (n=429)</td>
<td>Mean 3</td>
<td>2</td>
<td>−1</td>
</tr>
<tr>
<td></td>
<td>SD 17</td>
<td>19</td>
<td>10</td>
</tr>
</tbody>
</table>

QA indicates quantitative angiography; ACH, acetylcholine; TNG, nitroglycerin; and SD, standard deviation.

Discussion

This study shows that electronic digital calipers can provide accurate directional and magnitude changes during vasomotor function studies as expressed as percent diameter change and before and after angioplasty as expressed as percent stenosis. Significant discrepancy exists between the two methods in measuring absolute diameters.

The comparison of a new method against an established one often has been evaluated inappropriately by the correlation coefficient between the results of the two methods as an indicator of agreement. Correlation coefficients measure the strength of a relation between two variables, not the agreement between them. Moreover, correlation depends on the range of the variables measured, with wider ranges leading to better correlation. Most often, two methods measuring the same variable will be related, and thus the test of significance is irrelevant to the question of agreement. Thus, a correlation coefficient of .94 may still harbor sufficient disagreement to render a new method an unsuitable...
substitute for an established standard. The analytical method of Bland and Altman as used in our study is more appropriate in evaluating a new method of measurement against an established one. No such evaluation has been performed in comparing electronic digital calipers against quantitative angiography in vasomotor function testing and in the follow-up of angioplasty results.

**Vasomotor Function Testing**

In the transplant patients, this study shows that electronic digital calipers cannot provide accurate measurements of the absolute diameters due to a systematic overestimation especially in vessels >2.5 mm (0.44±0.24 mm) compared with quantitative angiography. This systematic bias is most likely due to the different edges used by the two methods to measure the diameters. Quantitative angiography measures the points of maximal rate of change of the videodensity while visual diameters are measured from arbitrary borders where the human eye identifies a gradient change. This border is likely to occur before the maximal rate of change and thus leads to overestimation of the diameter. The visual borders used for caliper measurements are different for different observers and thus also account for the systematic interobserver bias (0.14 mm).

When the measurements are expressed as percent diameter changes, the caliper method, on average, accurately reflects the response to acetylcholine and nitroglycerin as measured by quantitative angiography with little systematic bias (−1±10%). We have shown that measuring a single percent diameter change can result in a discrepancy between calipers and angiography approximately ±20%. However, when multiple diameter changes are measured as would be done in a research setting with many subjects, the mean percent diameter change measured by calipers would be much closer to the mean percent diameter change measured by quantitative angiography. The averaging process reduces the variability and allows one to use calipers or quantitative angiography relatively interchangeably in measuring percent diameter change. The exact sample size needed will depend on the precision required (see “Appendix II”).

**Stenoses and Angioplasty Follow-up**

In measuring stenosis severity, calipers and quantitative angiography differed by 5±7%. The limitations are that calipers tend to overestimate the stenosis severity (95% confidence of 9% underestimation or 19% overestimation), and this may be critical in measuring moderate lesions of 50% to 60%. Other methods like quantitative angiography and videodensitometry may be needed to clarify the severity in these stenoses.

After angioplasty and at follow-up, there are no systematic differences (0±10%) between the mean stenosis severity measured by the two methods. As stated earlier, a standard deviation of the differences of 10% means that a single measurement by calipers may differ from the measurement by quantitative angiography by 20%. Thus, trials using calipers to measure results or follow-up of angioplasty must have sufficient sample size to be confident about the actual results.

**Phantom Study**

The phantom study confirms the overestimation of absolute diameters by calipers when compared with the true measurements. Also, increased overestimation with larger vessel size is seen. This most likely is due to the blurring of the vessel edges and the ability of the human eye to pick up subtle densitometric changes before the actual vessel edge. Also, since the human eye detects densitometric changes nonlinearly, this may account for the larger absolute error in larger vessels. Parallax may also be a significant source of error. The quantitative angiography persistently underestimated the true diameters, especially in the smaller vessels, which is consistent with the original results of Kirkeide et al. This most likely is due to the first derivative algorithm used in the program. Since the phantom was imaged using the best imaging conditions, the differences between the two methods and the true diameters are small (0.05 and 0.08 mm). The mean differences and standard deviation between the two methods (0.13±0.09 mm) is 44% and 43% of the patient studies (0.29±0.21 mm), respectively. The larger and more variable differences in the patients study probably can be attributed to angulation, motion, penetration, nonuniform opacification, and pin-cushion distortion.

**Study Limitations**

The interobserver standard deviation of mean differences between the two observers reported in this study is smaller than that reported from manual calipers (7.8% versus 12.4%). This may be due to the difference in precision of electronic digital calipers versus manual calipers. The absolute diameters of stenoses are not measured in this study since we do not have accurate calibrations in these routine angiograms. Presumably, the calipers will also overestimate the absolute sizes of the vessels and will be subject to the same constraints mentioned above. We also have not addressed the issue of whether percent stenosis measurement after angioplasty is an accurate reflection of the stenosis severity due to the presence of dissection and tears; presumably, these difficulties will affect both the caliper method and quantitative analysis. The population of angioplasty patients studied may have less intimal abnormalities since an excimer laser was used and generally better angiographic results can be achieved.

In conclusion, this study suggests that in a sufficiently large sample size, electronic digital caliper measurements can provide a rapid, low-cost approach to assessing relative changes in vessel sizes in research. Also, it can provide acceptable accuracy estimates of percent diameter stenosis before and after intervention.
Appendix I

For the transplant population, 24 patients were studied. For each patient, two vasomotor studies were performed over a mean of 2.7±1.2 years (range, 1 to 5 years). In each study, an average of two segments—one proximal and one in the distal left anterior descending coronary artery—were analyzed. A total of 88 segments were analyzed (24×2×2=96; eight studies had only one segment analyzed, 96–8=88). Multiple measurements of these 88 segments were taken after increasing doses of acetylcholine and after nitroglycerin, making a total of 517 measurements. Eighty-eight segments were measured at baseline and at 10⁻⁴ and 10⁻³ mol/L acetylcholine, and 77 segments were measured at 10⁻¹ mol/L (11 segments did not receive this highest dose of acetylcholine due to severe vasoconstriction to 10⁻³ mol/L). The 88 segments were measured again at recontrol and after nitroglycerin (88×5+77=517 diameters).

Appendix II

The results in this article are presented in terms of the variability of the differences between two measurements. For example, if $x$ represents percent diameter change as measured by calipers, and $y$ represents a measurement of the same artery using quantitative angiography, then the report resulted was:

$$\sqrt{\text{Variance}(x-y)} = 11\%$$

leading to 95% confidence intervals of ±(1.96) (11%) or ±22%. This variability is a combination of the interobserver and intraobserver variabilities we have noted in caliper measurements, as well as intrinsic variability in the technique.

If the angiographic measure $y$ is the “truth” (or at least a measure with much smaller variability than $x$), then the results imply that a single caliper measurement can deviate as far as ±22% from the truth. Therefore, single caliper measurements may not provide sufficiently precise information.

However, in research or clinical studies involving multiple patients, the group average caliper measurement, $\bar{x}$, will be much closer to the “true” angiographic mean, $\bar{y}$. Either decreasing the caliper variability or increasing the sample size will lead to studies with greater statistical power. Assuming $n$ subjects in the study,

$$\sqrt{\text{Variance}(\bar{x}-\bar{y})} = \sqrt{\text{Variance}(x-y)/n} = 11%/\sqrt{n}$$

so that the 95% confidence interval reduces to ±(1.96) (11%)/$\sqrt{n}$ where $t$ depends on the sample size and can be read from standard statistical tables. As an example, from a sample of 50 patients, the average percent diameter change measured by calipers would be within 3% of the angiographic “truth,” whereas 100 patients would lead to an estimate within 2% of the “truth.” This minor loss of precision compared with quantitative angiography will often be offset by the ease with which caliper measurements can be made.

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