Contributions

Digital fluoroscopy and intravenous cardiac angiography for the detection of coronary artery disease in selected subjects

A feasibility study

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Thirty-seven thin patients (height/weight ratio >2.2 cm/kg) without prior myocardial infarction underwent digital subtraction fluoroscopy and intravenous digital subtraction cardiac angiography one day before they were scheduled to undergo coronary angiography. Eighteen (49%) had at least a 50% obstruction of a major coronary artery as shown on selective coronary cineangiograms; eight of these (44%) had three calcified coronary arteries as visualized by digital fluoroscopy, five (28%) had diagnostic wall-motion abnormality by digital ventriculography, and 15 (83%) had intravenous angiographic evidence of at least one severe (>50%) coronary obstruction. Seventeen (94%) of the 18 with severe selective angiographic obstructions had at least one calcified artery detected by the digital study. Seventeen (89%) of the 19 without angiographic evidence of severe disease had none of these three abnormalities visualized on their digital intravenous images. Intravenous cardiac angiography was more accurate for predicting proximal coronary, right coronary, and left anterior descending branch obstructions, than for distal coronary and left circumflex artery obstructions.

Index terms: Coronary disease • Coronary vessels, angiography • Coronary vessels, fluoroscopy

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When evaluating patients with chest pain, tests that determine whether coronary disease exists are of special interest.[1-3] While intravenous digital cardiac angiography has been successfully applied to study chamber size and function, technical difficulties have prevented its use for evaluation of individual coronary arteries. Though these arteries can sometimes be visualized,[4] imaging is neither

See also the editorial by Moodie (p 123)

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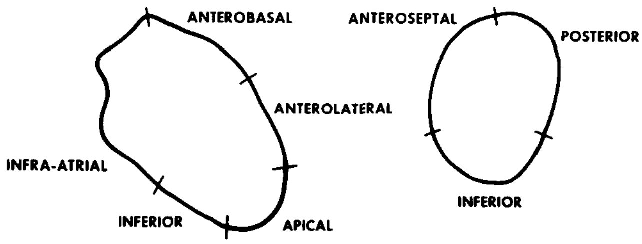

Fig. 1. Left ventricular diastolic outline (right anterior oblique and left anterior oblique projections), showing wall segments.

sufficiently resolute nor frequent enough for adequate disease localization and estimation of severity. Coronary obstructions, such as calcific deposits and wall-motion abnormalities, are usually multiple, however, and often leave their pathophysiological traces on fluoroscopic and ventriculographic images. This increases the probability that at least one such lesion can be detected. Thallium imaging, for example, has been somewhat successful because the multiplicity of coronary lesions allows the scintigrams more than one "chance" to detect disease.[5] Radionuclide angiography makes use of resting wall-motion abnormalities in order to noninvasively detect coronary disease.[6] Cardiac fluoroscopy detects atheroma because this condition usually involves the accumulation of calcium salts.[7] Intravenous digital angiography could exploit all three properties of coronary disease: its diffuse nature, ventricular wall-motion abnormalities caused by obstructions, and calcific deposits in coronary atheroma.

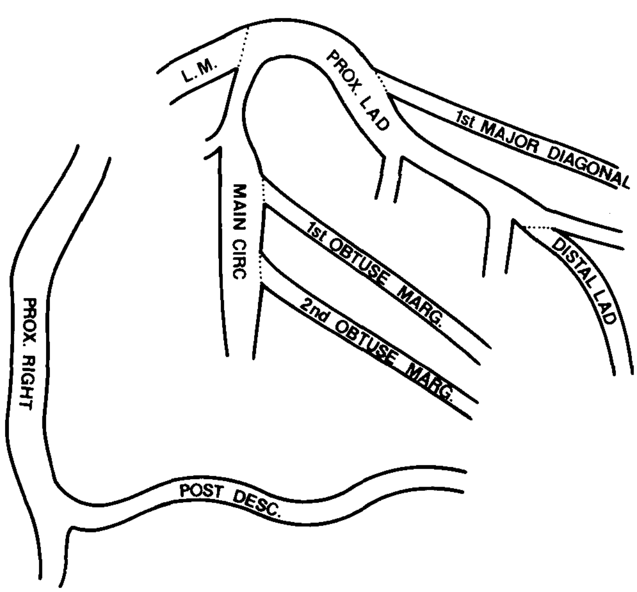

Fig. 2. Schema of coronary arterial tree, showing nine segments. *L.M.* = left main; *PROX.* = proximal; *LAD* = left anterior descending; *MARG.* = marginal; *CIRC* = circumflex; and *DESC.* = descending.

Thin people are nearly ideal for radiographic screening. Therefore, this investigation attempts to establish the feasibility of digital subtraction fluoroscopy and intravenous digital subtraction cardiac angiography for detecting angiographically significant coronary disease in thin individuals.

Materials and methods

Our study sample consisted of 37 consecutive subjects who were referred for coronary arteriography and who had a height/weight ratio of >2.2 cm/kg. Patients with evidence of prior myocardial infarction, valvular or cardiomyopathic disease, renal insufficiency, or a serious allergic reaction to contrast media were excluded.

Apparatus and imaging technique

Cardiac imaging equipment (Philips Polydiagnost C), coupled to a digital image processor (Philips DVI 1), was used. Careful attention was paid to brass-plate "bolusing" of the x-ray tube to eliminate bright spots from the image and reduce x-ray scatter. X-ray tube voltage was set at 70 kV in order to approach the iodine K edge and enhance the visualization of small contrast-medium-filled structures. Tube currents of <200 mA were used for all studies. The face of the image intensifier was positioned at least 15 cm from the patient's thorax to reduce x-ray scatter and provide magnification.

The imaging system was set in the continuous fluoroscopic mode. A 320-msec pre-injection mask image was obtained at a tube current of 150–200 mA prior to injection of contrast media. Tube current was then reduced for low-dose imaging of the dextrophase. When left ventricular opacification was noted, the tube current was again raised to the initial level, and frame-by-frame subtraction from the original pre-injection mask was done. The subtracted image frames were recorded on ¾-inch (1.9-cm) videotape. Frames were obtained two to three seconds after left ventricular opacification for late mask re-subtraction, which partially corrects motion mis-registration.

Imaging protocol

A 5-F pigtail or hockey-stick sidehole catheter was passed through an antecubital vein into the right atrium. Digital subtraction fluoroscopic images (30° right anterior oblique and 60° left anterior oblique projections) were obtained without injection of contrast media to visualize coronary calcifications.[8] The patient inhaled amyl nitrite for three to five seconds to increase cardiac output and decrease the time between mask acquisition and left ventricular opacification, thus decreasing contrast-medium dispersion and motion misregistration. Digital subtraction angiographic imaging of the left ventricle and coronary arteries (30° right anterior oblique projection) was then performed with the patient holding his or her breath, while Renografin 76 (meglumine diatrizoate) (45 mL) was injected at a flow rate of 25 mL per second into the right atrium. Amyl nitrite inhalation and contrast-medium injection were repeated before obtaining an image of the heart (60° left anterior oblique projection).

Test review and analysis

The digital subtraction fluoroscopic finding of three calcified coronary arteries is highly specific for identifying subjects with severe (>50%) coronary obstructions.[8] Likewise, the finding of a severely hypokinetic wall segment[9,10] by digital subtraction ventriculography has been found to be specific for severe coronary obstructions and to correlate well with conventional left ventriculography.[10,11] To maintain high specificity, the following abnormalities were required for defining an abnormal fluoroscopic or intravenous angiographic result:

1. Calcification of three major coronary arteries noted on digital fluoroscopy,
2. Severe hypokinesis, akinesis, or dyskinesis in one of the eight left ventricular wall segments as defined by the American Heart Association classification[9] (*Fig. 1*), and
3. A >50% obstruction of one of the nine major coronary arterial segments (*Fig. 2*).

Two observers independently carried out a blind review of the digital subtraction studies to determine the numbers of calcified coronary arteries (*Fig. 3*), the presence or absence of severe left ventricular segmental wall-motion abnormalities, and the presence of coronary artery segmental abnormalities suggesting >50% obstruction (*Fig. 4*). If the two observers disagreed about the presence of three calcifications or any ventricular wall segment or arterial segment, a third observer then did a blind review and decided the issue.

Selective coronary angiography

Sensitivities and specificities for the prediction of any obstruction >50% were calculated for the finding of (*a*) three coronary calcifications shown by digital fluoroscopy, (*b*) a severely hypokinetic left ventricular wall segment, (*c*) any severely obstructed (>50%) coronary segment as visualized on the intravenous angiogram, and (*d*) any one of these three findings. Sensitivities and spec-

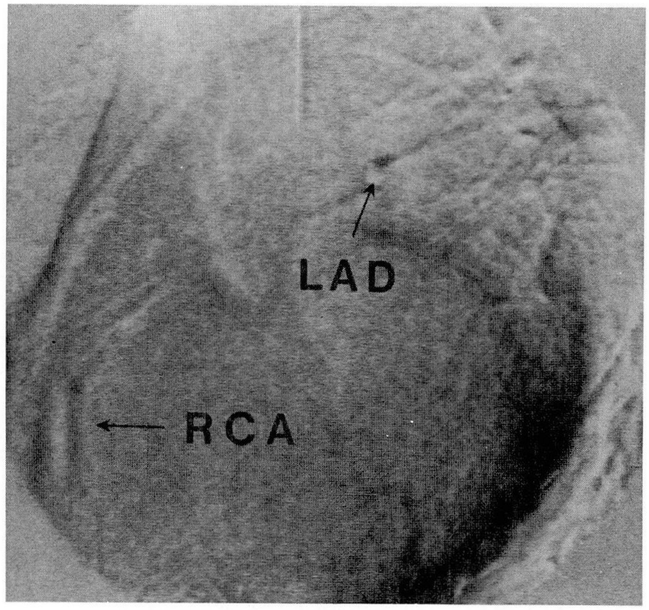

Fig. 3. Digital subtraction fluorograph (right anterior oblique projection), showing calcific deposits in these arteries. *LAD* = left anterior descending and *RCA* = right coronary artery.

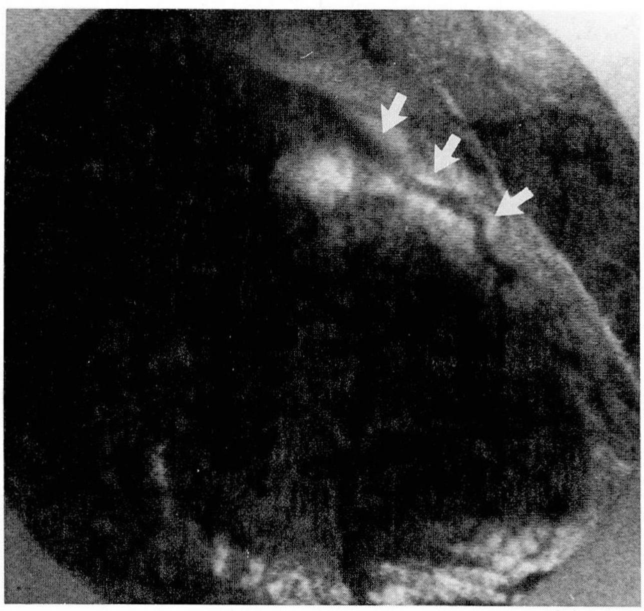

Fig. 4. Intravenous digital subtraction angiography, showing a normal proximal left anterior descending coronary artery and diagonal branch.

Table 1. Visualization and discordance of interpretation

	% visualized	% discordance
Left main (N = 37)	84 (31)	0 (0)
Proximal segments		
Anterior descending (N = 37)	92 (34)	19 (7)
Circumflex (N = 37)	60 (22)	3 (1)
Right (N = 37)	100 (37)	5 (2)
All proximal segments (including left main) (N = 148)	84 (124)	7 (10)
Distal segments		
Diagonal (N = 37)	57 (21)	3 (1)
Anterior descending (N = 37)	78 (29)	3 (1)
First obtuse marginal (N = 37)	11 (4)	0 (0)
Second obtuse marginal (N = 37)	14 (5)	0 (0)
Posterior descending (N = 37)	84 (31)	3 (1)
All distal segments (N = 185)	49 (90)	2 (3)
All segments (N = 333)	64 (214)	4 (13)

Numbers of segments are in parentheses.

ificities of the intravenous coronary angiographic finding of a severe (>50%) coronary segmental obstruction for the prediction of a >50% selective angiographic obstruction were calculated for all the arterial segments and for the proximal segments alone. Only coronary segments for which visualization was considered adequate by two observers were included in the analysis. Interobserver discordance occurred when two observers disagreed concerning the presence of coronary calcification, the abnormality of segmental wall motion, or the presence of a >50% obstruction of a coronary arterial segment.

Results

Clinical data

Thirty-seven subjects (18 men and 19 women) were evaluated. The mean age was 57 years (SD = 8.4). Their mean height was 167 cm (SD = 8.0), and the mean weight was 65 kg (SD = 7.3). The mean height/weight ratio was 2.58 cm/kg (SD = 0.28). Nineteen of these subjects (51%) had a history of typical angina pectoris, 15 (41%) had atypical angina or non-anginal pain, and three (8%) did not have chest pain but were referred for angiography because of abnormal stress tests.

Selective coronary angiographic results

Eighteen of the 37 subjects (49%) had at least one >50% coronary artery obstruction. Eight subjects had single-vessel coronary artery disease, seven had double-vessel disease, and three had triple-vessel disease.

Forty (12%) of the 333 coronary arterial segments were reported by the coronary angiographers as >50% obstructed. Twenty-five (63%) of these obstructions were proximal (13 [52%] occurred in left anterior descending coronary arteries, 8 [32%] were in right coronary arteries, and 4 [16%] were in circumflex coronary arteries). There were no severely obstructed left main coronary arteries.

Interobserver discordance and frequency of coronary segment visualization

There were no disagreements concerning the number of coronary calcifications or the presence and severity of ventricular wall-segment abnormalities.

Two of the observers agreed that visualization was adequte for 214 (64%) of the 333 coronary arterial segments. Visualization was best for the proximal right coronary artery (100%), the proximal left anterior descending coronary artery (92%), and the left main coronary artery (84%). Only 60% of the proximal circumflex segments and 48% of all the distal segments were visualized adequately. Of the 119 nonvisualized arterial segments, 106 (89%) were free of any >50% obstruction based on selective angiograms. Interobserver discordance was highest in the proximal anterior descending coronary artery (19%). Because the observers agreed unanimously concerning the nonvisualization of most of the distal segments, total disagreements in this area were less frequent (2%). Discordance for all 333 coronary segments was 4%. These results are summarized in *Table 1.*

Digital fluoroscopic and intravenous ventriculographic results

None of the 19 subjects without a >50% selective angiographic obstruction had calcifications of three coronary vessels as shown by digital fluoroscopy (specificity = 100%). Eight (44%) of the 18 subjects with a >50% obstruction had digital fluoroscopic evidence of calcification in three coronary vessels (sensitivity = 44%) (*Fig. 3*). Five (28%) of the 18 had ventriculographic

Table 2. Overall sensitivity and specificity of combined fluoroscopic and intravenous angiographic cardiac examinations

Examination	Sensitivity	Specificity	Predictive value (positive)	Predictive value (negative)
Digital fluoroscopy	44% (8)	100% (19)	100% (8/8)	65% (19/29)
Intravenous ventriculography	28% (5)	100% (19)	100% (5/5)	59% (19/32)
Intravenous coronary angiography	83% (15)	89% (17)	88% (15/17)	85% (17/20)
Digital fluoroscopy or intravenous ventriculography	67%* (12)	100% (19)	100% (9/9)	68% (19/28)
Digital fluoroscopy or intravenous ventriculography or intravenous coronary angiography	94%* (17)	89% (17)	89% (17/19)	94% (17/18)
Typical angina pectoris by history	83% (15)	79% (15)	79% (15/19)	83% (15/18)

* $P = 0.04$ for difference between 67% and 94% (McNemar's test).
Numbers in parentheses represent the number of patients.

evidence of severe segmental wall-motion abnormality (sensitivity = 28%). All subjects with ≤50% coronary artery obstruction as visualized by selective angiography had no evidence of severe segmental wall-motion abnormality (specificity = 100%). These results are summarized in *Table 2*.

Intravenous coronary angiographic results

Twenty-seven (13%) of the 214 visualized coronary arterial segments had >50% luminal obstruction as shown by selective coronary cineangiography.

Review of the intravenous cardiac angiograms resulted in 23 reported coronary artery segmental abnormalities thought to represent >50% obstructions (*Fig. 4*). Of these, eight were not confirmed and 15 were confirmed by selective coronary cineangiography. The overall sensitivity of the method in predicting coronary artery segmental obstructions was thus 15/27 (56%). The specificity was 179/187 (96%). All of the 15 correctly identified diseased segments were proximal segments. Of the 103 visualized proximal segments that were normal according to selective angiograms, 97 (94%) were normal based on intravenous coronary angiograms. The sensitivity and specificity for proximal segments were thus 71% and 94%, respectively. These results are summarized in *Table 3*.

Overall sensitivity and specificity

Fifteen (83%) of the 18 subjects with selective angiographic evidence of >50% coronary obstructions also had intravenous coronary angiographic evidence of such an obstruction. Seven-

Table 3. Sensitivity and specificity for coronary segments

	Sensitivity	Specificity
Left main		31/31 (100%)
Proximal segments		
Anterior descending	9/11 (82%)	20/23 (87%)
Circumflex	1/2 (50%)	20/20 (100%)
Right	5/8 (63%)	26/29 (90%)
All proximal segments (including left main)	15/21 (71%)	97/103 (94%)
Distal segments		
Diagonal		21/21 (100%)
Anterior descending	0/3 (0%)	26/26 (100%)
First obtuse marginal	0/1 (0%)	2/3 (67%)
Second obtuse marginal		5/5 (100%)
Posterior descending	0/2 (0%)	28/29 (97%)
All distal segments	0/6 (0%)	82/84 (98%)
All segments	15/27 (56%)	179/187 (96%)

teen (89%) of those free of severe (>50%) selective angiographic disease had no severe coronary obstruction visualized by intravenous angiography. *Table 2* shows that when the intravenous coronary angiographic results are included with the fluoroscopic and ventriculographic results, the sensitivity increases significantly from 67% to 94% with an insignificant drop in specificity (100% to 89%). Also, the combined test was a more accurate indicator of disease than a history of typical angina pectoris.

False positives and false negatives

False-positive test results occur when an abnormality seems to be present but disease is absent; false negatives occur when the test result is negative but the disease is present. Digital subtraction fluoroscopy resulted in 10 false negatives and no false positives; in eight false-negative cases, at least one calcified artery was identified by digital fluoroscopy. Intravenous ventriculography resulted in 13 false negatives (two of which showed some evidence of segmental hypokinesis, which was judged to be mild) and no false positives.

Intravenous coronary angiography resulted in three false negatives and two false positives. All three false negatives involved patients with single-vessel coronary disease. One of these was correctly identified on intravenous ventriculography as an akinetic ventricular wall segment. This subject had an 80% obstruction in the proximal anterior descending coronary artery. Another false-negative result was corrected by the subsequent discovery of three calcified coronary arteries. The third false negative resulted when 80% proximal right coronary obstruction was not discovered; no abnormality was identified by the fluoroscopic or intravenous studies. One of the false-positive intravenous angiograms was of a patient with a 40% proximal right coronary obstruction; the other false positive was judged retrospectively to be due to artifacts from vessel overlap.

Discussion

This pilot project resulted in a sensitivity of 94% and a specificity of 89%. This compares well with other diagnostic tests done at The Cleveland Clinic Foundation. Exercise thallium scintigraphy, for example, had a sensitivity and specificity of only 73% and 79%, respectively, while exercise electrocardiography was only 66% and 72%.[7]

Intravenous and intra-arterial digital subtraction angiography have been used for visualization of the cardiac anatomy[12] and peripheral arteries.[13] Several investigators[14-16] have applied digital subtraction angiographic techniques to the visualization of coronary arteries after an injection of contrast media into the aortic root. This approach may be beneficial because of its relative safety, simplicity, and cost-effectiveness. Magotteaux et al[16] have reported a failure to adequately visualize the coronary anatomy after injections of contrast media into the venous circulation. Our results confirm that much of the coronary circulation is inadequately visualized after injections of contrast media into the right atria of subjects with optimal thoracic radiographic properties. However, our findings also suggest that intravenous coronary angiography may detect the presence of severe proximal coronary obstruction in selected subjects. Two explanations for this apparent paradox may be that coronary disease usually occurs in more than one vessel and obstructions are more often proximal than distal.[17] Successful disease detection in individual patients is therefore possible without visualization of all of the vessels. Digital subtraction fluoroscopy[8] and intravenous digital subtraction ventriculography[18] also contribute information toward the diagnosis of coronary artery disease in subjects without prior myocardial infarction. *Table 1* demonstrates that at least three coronary calcifications of a severely hypokinetic left ventricular wall segment had a specificity of 100% and a sensitivity of 67%. The intravenous coronary angiogram improved the sensitivity to 94%, while specificity decreased minimally to 89%. Coronary visualization was adequate and clinically useful for identifying patients with severe coronary obstructions.

The results of this investigation are encouraging, but the subjects, all of whom had a height/weight ratio of >2.2, were optimal candidates for almost any radiological procedure, whether radiographic or scintigraphic. It is conceivable that radionuclide myocardial perfusion imaging would also have been successful. Radionuclide examinations are safer than cardiac angiography and provide important functional as well as anatomic information. In order to compete with radionuclide methods, an angiographic technique must be significantly more accurate. Technologic improvements in digital imaging, such as energy subtraction,[19] beam attenuation,[20] and gated- or phase-matched masking,[21] may improve the quality of digital angiographic images and the intravenous angiographic diagnosis of coronary artery disease.

Our study sample was restricted to subjects with a height/weight ratio of at least 2.2, which eliminated approximately 60 patients referred to The Cleveland Clinic Foundation for coronary arteriography. This restriction was imposed because of the physical limitations of the x-ray tube and because the generator components operated at 70 kV. Had we included heavier patients in our protocol and used high voltages, we might not have obtained comparable results.

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