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Review of Using Cardiac Fluoroscopy in Symptomatic and Asymptomatic Patients

By

Kevin T. Mason

Impact, Tolerance, and Protection Division

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Fort Rucker, Alabama 36362-5292**

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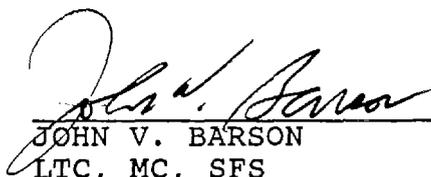
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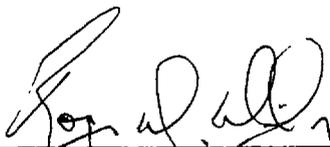
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Reviewed:



JOHN V. BARSON
LTC, MC, SFS
Director, Impact, Tolerance,
and Protection Division

Released for publication:



ROGER W. WILEY, O.D., Ph.D.
Chairman, Scientific
Review Committee



DAVID H. KARNEY
Colonel, MC, SFS
Commanding

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Introduction

The general medical community does not use cardiac fluoroscopy to find coronary artery calcifications associated with coronary artery disease. This standard of medical care conflicts with the use of cardiac fluoroscopy in the U.S. Armywide aircrew member cardiovascular disease prevention and detection program. The history of using cardiac fluoroscopy in symptomatic and asymptomatic populations is reviewed in this report with the goal of understanding and resolving this conflict.

History of techniques for finding coronary calcifications

Gross anatomy

Aided only by their eyes, sense of touch and dissection tools, classic gross anatomists of the 18th and 19th centuries described the deposition of calcium in coronary arteries and its association with coronary artery occlusions (Blankenhorn, 1961). Cruveilheir (1791-1874) found, ". . . a calcareous [chalk-like] infiltration of the mouth of the coronary artery, followed by a gangrenous myocardium." Some noted the relationship between chest pain and calcified coronary arteries. The colleagues of the anatomist Hunter (1728-1793), who was known to suffer from chronic chest pain, reported Hunter had on autopsy, "considerable ossification of his coronary arteries." Stokes (1804-1878) described his finding of a 68-year old man who suddenly died 6 weeks after the new onset of chest pain attacks. He noted, "The coronary arteries were so completely converted to bone as to be quite solid, having no perceptible cavity." Into the 20th century, the finding of calcification was considered pathognomonic of coronary artery sclerosis.

Clinical pathology

High power magnification devices with improved tissue fixation and staining techniques were introduced by the early 20th century. On postmortem studies, clinical pathologists found that coronary artery calcifications were always associated with atherosclerotic plaques involving the intima, which often occluded the vessel lumen. As an exception, pathologists reported rare cases of a rapidly fatal coronary artery and myocardial calcification of infants. They reported rare cases of calcified medial sclerosis (Monckeberg's sclerosis) of the coronary artery wall without vessel occlusion in young patients, (Blankenhorn, 1961; Rifkin, Parisi, and Folland, 1979).

Accepted dogma was that calcifications occurred in the advanced stages of atherosclerosis with coronary artery

occlusions of 70 percent or more. Following heavy deposition of cholesterol and lipids in the atherosclerotic plaques, calcification would complicate hemorrhagic or necrotic events. In 1936, Leary said, "Atheromatous calcification is a terminal process, a monumental deposit in dead and dying tissue" (Blankenhorn, 1961). The natural history of calcification was not entirely understood since patients with lesser degrees of coronary artery occlusion were not likely to die and undergo necropsy. Later, it was found by changing staining techniques and studying younger patients that coronary artery calcification also was associated with degeneration of elastic fibers in early atheromas. The evolution between this earlier stage of calcification and the previously described discrete calcifications of the advanced plaque were unknown. They were likely two independent processes (Blankenhorn, 1961).

Plain radiography

In the early to mid-20th century, pathologists did plain radiographs of necropsied hearts. They noted additional areas of coronary artery calcification not found by dissection alone. Calcifications as small as 1 millimeter were seen. The additional calcifications found by plain radiography were associated with arteriosclerotic disease by further pathologic dissection. By plain radiography, 40 to 53 percent of necropsied hearts had coronary artery calcifications. A more thorough survey of the arteries for arteriosclerotic disease was possible by this technique. Morgan, a pathologist, said, "Calcification is the very essence of coronary sclerosis" (Blankenhorn, 1961).

Coronary artery calcifications were noted in living patients using plain chest radiography by 1927 (Lieber and Jorgens, 1961). The heart shadow moved significantly during the plain radiograph exposure blurring the image. Only large calcifications were seen. Some improvement in image quality was noted by using shorter exposures employing a Buckey diaphragm and by refining positioning techniques (Blankenhorn, 1961; Rifkin, Parisi, and Folland, 1979; Kelley and Newell, 1983).

Cardiac calcifications were sporadically seen by this method. One series found 3 percent of the patients referred for suspected, symptomatic cardiac disease had cardiac calcifications on high-speed plain radiography (Habbe and Wright, 1950). Habbe said, "The examination for this pathologic process (coronary artery calcification) is best made by high-speed, aimed, multiple spot roentgenograms taken with the rays centered as accurately as possible over the coronary vessels."

Conventional fluoroscopy

From 1937 into the 1950s, investigators used conventional cardiac fluoroscopy to observe the living heart in motion for cardiac calcifications. Despite resolving the problem of blurred images caused by the beating heart, the technique lacked image intensification. The observer saw a dim image with 0.05 lux of brightness when at least 10 lux is required for adequate image visualization. The observer's visual acuity was less than 20/20 in this dim lighting. Visual acuity was compromised further if the observer was not dark adapted (Chen, 1983). The technique detected only large or extensive calcifications. At best, 3 percent of patients were found to have cardiac calcification, even when the study population was referred for symptoms of coronary artery disease. Conventional fluoroscopy was as inadequate as plain chest radiography for detecting coronary artery calcifications in the living patient (Habbe and Wright, 1950).

Image-intensified fluoroscopy

By the 1960s, the resolution of cardiac fluoroscopy images dramatically improved with the introduction of a cesium iodide image intensifier with focal spot tubes and adjustable shutters. Image brightness was intensified 10,000 times over conventional fluoroscopy (Chen, 1983). Investigators could find coronary artery calcifications as small as 2 millimeters approaching the resolution of plain radiography of necropsied hearts (Blankenhorn, 1961). Total radiation exposure dose and observation time were reduced compared to conventional fluoroscopy. The patient was viewed in the radiology suite by mirror optics or television relay, or later by cinefluorography on 16 or 35 millimeter, high-resolution film (Lieber and Jorgens, 1961; Rifkin, Parisi, and Folland, 1979; Green and Kelley, 1980). The technique became the standard for what is known today as cardiac fluoroscopy.

Multiple investigators began using the image-intensified method along with other emerging technologies, such as graded exercise treadmill test, thallium scan, and coronary artery angiography. They sought to find the clinical correlation between screening for coronary artery calcifications by cardiac fluoroscopy and anatomic coronary artery occlusion. Their methods and findings are discussed later in this report.

Computed axial tomography

Computed axial tomography (CAT scan) recently was introduced in the search for cardiac calcifications. CAT scan has improved contrast resolution compared to cardiac fluoroscopy with less

radiation exposure. CAT scan detects calcifications as small as 0.25 millimeters. The process is computerized and automated diminishing the variation caused by the varying degrees of observer skill. It requires less interpretation experience to diagnose cardiac calcifications (Schultz et al., 1989).

One study compared coronary angiography findings with heart examination by standard image-intensified cardiac fluoroscopy and with CAT scan imaging (Schultz et al., 1989). Fifty patients with suspected coronary artery disease were studied. CAT scan heart imaging was done with a 512-matrix, 10 millimeter thick slices, and 2-second scan time. Seventeen (34 percent) had coronary artery calcification by image-intensified cardiac fluoroscopy. All these patients had the calcifications detected by CAT scan. An additional 13 patients, for a total of 30 (60 percent), had coronary artery calcification by CAT scan. The positive predictive value of finding greater than 50 percent occlusion of a coronary artery by coronary angiography was 72 percent for both the CAT scan and the cardiac fluoroscopy. Though the positive predictive values were the same, the detection of calcification by CAT scan correlated with twice as many significant stenotic lesions as cardiac fluoroscopy as summarized in Table 1.

Table 1.

Correlation of coronary artery calcification by CAT scan and cardiac fluoroscopy with significant coronary artery stenosis.

Test finding coronary artery calcification	Total lesions**	≥50% Stenosis	<50% Stenosis
CAT scan	46	33 (72%)	13 (28%)
Cardiac fluoroscopy	22	16 (72%)	6 (28%)

* Adapted from Schultz et al., 1989

** Total patients, N=50

Image-intensified cardiac fluoroscopy methods

Preparation, equipment, and radiographic exposure

The proper interpretation of cardiac fluoroscopy findings requires a detailed knowledge of three-dimensional cardiac anatomy. The heart must be identified and separated from other chest structures that may contain calcium densities. Fluoroscopy

observers must differentiate coronary artery calcifications from valvular, pericardial, or large blood vessel calcifications (Bartel et al., 1974).

Use of barium swallow is not recommended for coronary artery calcification screening since the barium may hide calcium densities. Barium swallow is used only to better define the boundaries of the heart shadow in relation to mediastinal structures after the search for cardiac calcifications is complete (Margolis et al., 1980; Chen, 1983).

Cardiac fluoroscopy units have 6- to 10-inch cesium iodide image intensifiers with a 0.6 millimeter small focal spot tube, 1.0 millimeter large focal spot tube, and adjustable shutters. Some are equipped with video tape recorders or cinefluorography cameras (Kelley, Huang, and Langou, 1978; Chen, 1983).

The ability to detect small calcium densities depends on the proper balance of radiographic exposure factors to include mA, kV, and shutter opening. Excessive milliamperage (mA) diffuses a discrete density into a globe of glowing shadows. Excessive kilovoltage (kV) reduces contrast and image detail. Automatic brightness controls with photoelectric sensors at the output cesium iodine phosphor assist in maintaining optimum kV. The recommended exposure ranges include 1.5 mA to 3.5 mA, and 70 kV to 120 kV. Fluoroscopic unit shutters enhance the ability to see densities by limiting the field-of-view size to the area of interest. Adjusting the exposure factors briefly at each major patient position will increase the ability to see densities missed by observing the patient at a fixed exposure setting (Bartel et al., 1974; Green and Kelley, 1980; Chen, 1983).

Total examination exposure times vary from 1 to 4 minutes, with an average among two authors of 1.8 to 3.0 minutes (Loecker et al., 1992; Chen, 1983). The radiation dose is equivalent to two standard chest plain radiographs, about 5 rads skin entrance dose. The dose can be decreased by limiting the total fluoroscopy time and the use of shutters to limit the field of irradiation (Green and Kelley, 1980; Chen, 1983).

Patient positioning and image viewing methods

Cardiac fluoroscopy begins with the patient standing in the left lateral position. The image intensifier or patient is rotated with the examination continuing in the posteroanterior, right anterior oblique, left anterior oblique, and left lateral positions. Some calcifications not seen in the standard views are seen during the slow rotation between views. The patient should suspend respiration during the examination, breathing small, shallow breaths only as required. The observer looks for

small densities moving synchronously with the heart in locations consistent with coronary artery anatomy (Bartel et al., 1974; Green and Kelley, 1980; Chen, 1983; Huang et al., 1985; Bobbio et al., 1988; Loecker et al., 1992). Small calcium densities in large or obese patients may be better visualized with the patient placed in the recumbent position displacing excess tissue from the field of view (Bartel et al., 1974; Chen, 1983).

The coronary arteries are embedded in the subepicardial fat stripes. Fat stripes are seen as light lines along the course of coronary arteries by cardiac fluoroscopy. The fat stripe pattern may help localize observed calcifications to a major coronary artery when the light fat stripe lines coincide in location and motion with dark, dense calcifications (Chen, 1983). Figures 1 through 4 graphically demonstrate the coronary artery and subepicardial fat stripe anatomy in four major cardiac fluoroscopy views.

The best view of left coronary artery calcifications is in the shallow left anterior oblique views from 25 degrees to 35 degrees of angle (Chen, 1983). Calcifications of the left main coronary artery may be difficult to separate from left anterior descending coronary artery calcifications, unless calcification is present separately in both artery segments (Green and Kelley, 1980).

Direct mirror optical viewing of the cardiac fluoroscopy image is the most accurate means for detecting small coronary artery calcifications. The disadvantage is that it is dependent on the observer skill and vision. It does not record the images for later review by other observers (Green and Kelley, 1980). A convenient, indirect observation method is by relaying the image to television. The procedure may be recorded on video tape. The disadvantage of television relay is that it degrades the image sharpness and contrast (Green and Kelley, 1980). Cinefluorography with 16 or 35 millimeter high resolution film detects small calcifications nearly as effectively as direct viewing, and records the procedure for review. The disadvantage of cinefluorography is that it increases the radiation dose to the patient by a factor of four because of longer examination times (Green and Kelley, 1980; Uretsky et al., 1988).

Indications and contraindications

Table 2 lists the medical indications for cardiac fluoroscopy (Chen, 1983). Table 3 lists the contraindications for cardiac fluoroscopy used in coronary artery disease screening programs (Department of the Army, 1991b).

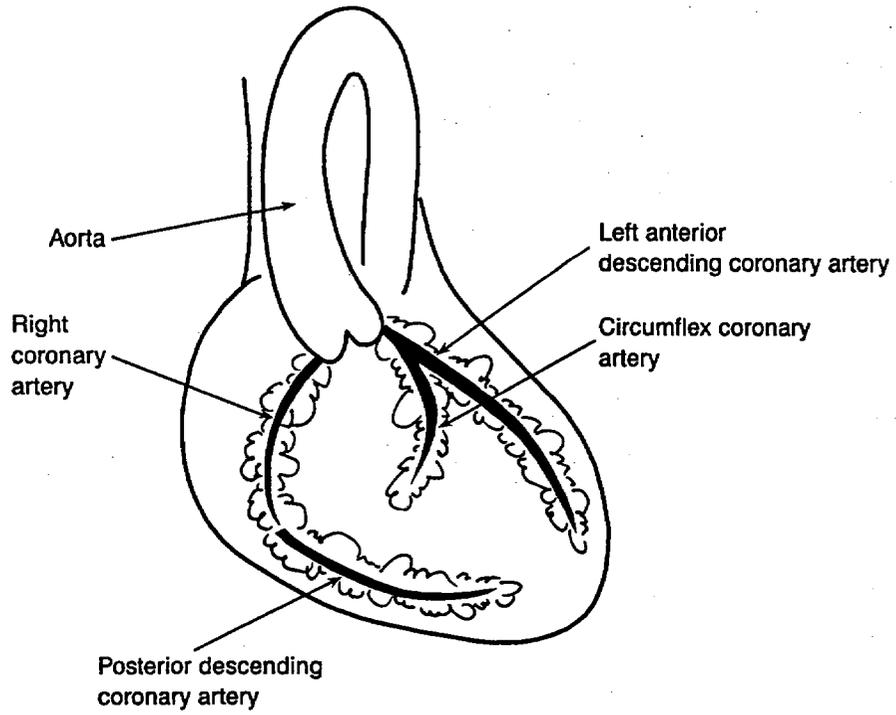


Figure 1. Posterior anterior view.

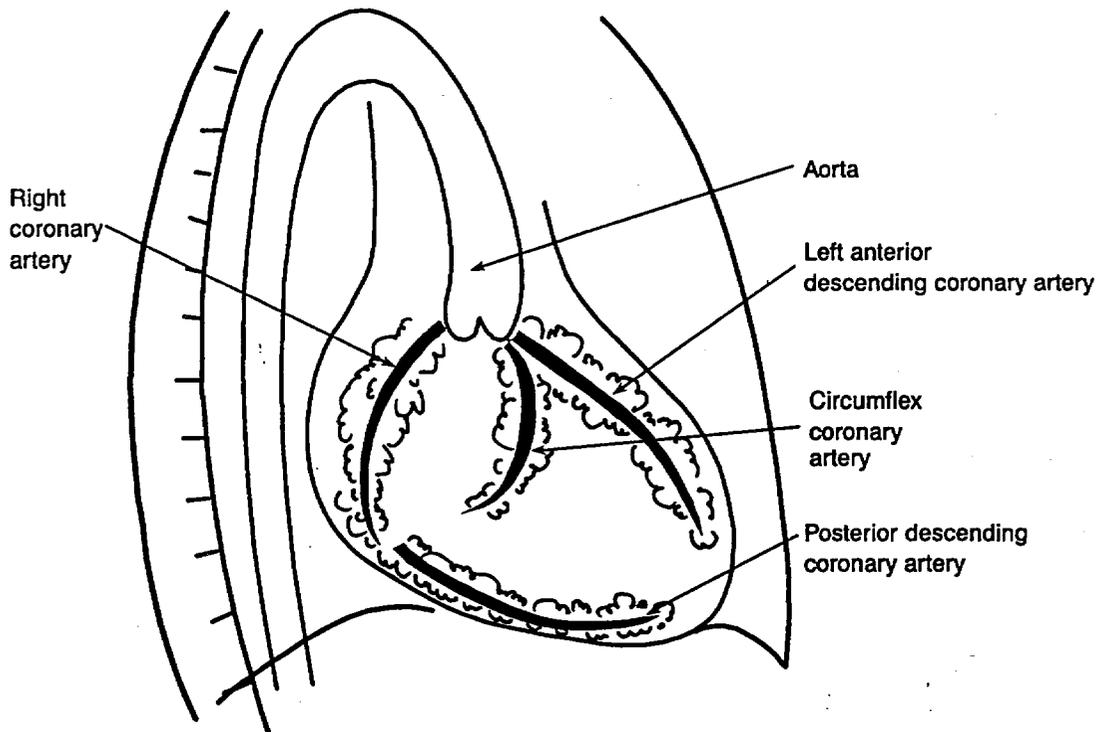


Figure 2. Right anterior oblique view.

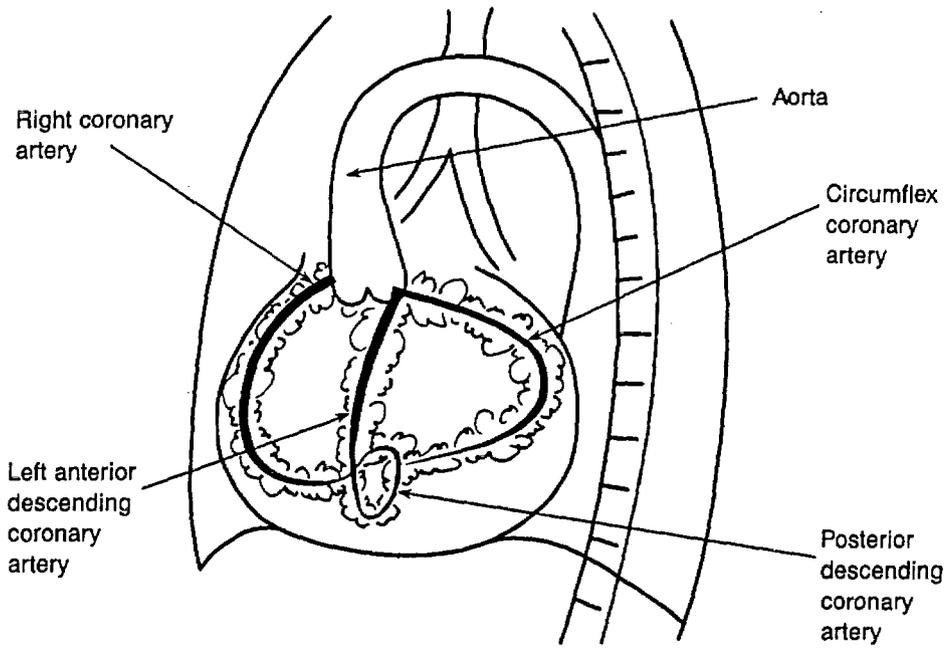


Figure 3. Left anterior oblique view.

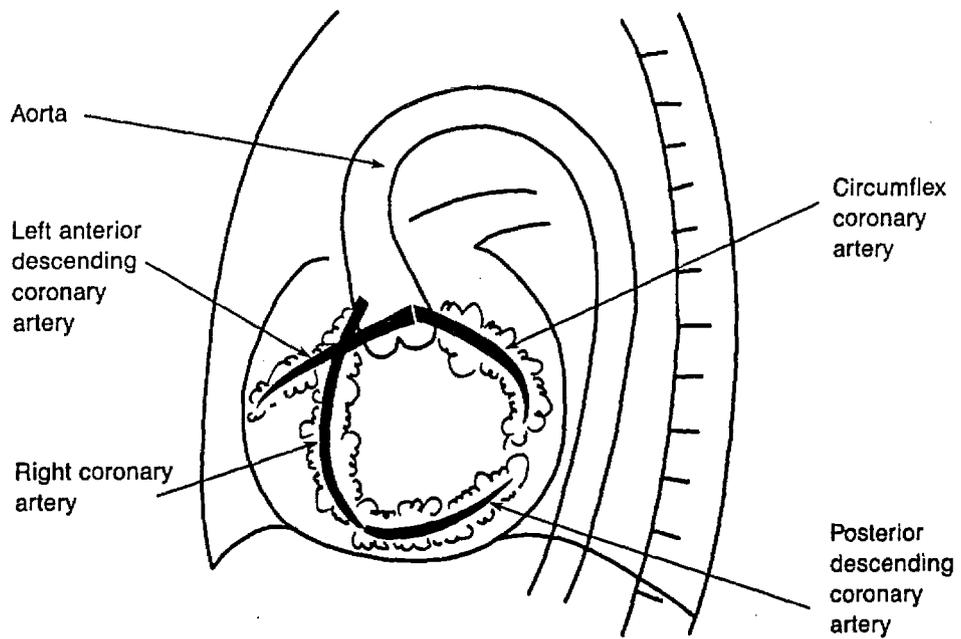


Figure 4. Left lateral view.

Table 2.

Indications for cardiac fluoroscopy.

Evaluate cardiovascular dynamics.
Detect cardiac calcifications.
Visualize the delicate subepicardial fat lines.
Differentiate cardiac from noncardiac disease.
Evaluate cardiac pacemakers, valve prostheses, and other radiopaque foreign bodies.
Guide angiography catheters.

Table 3.

Contraindication for cardiac fluoroscopy in screening programs.

Absolute	Relative contraindications
None	Pregnancy. Age less than 35 years old. History of abnormal cardiac fluoroscopy. History of a normal cardiac fluoroscopy within the last 3 years. History of anatomic coronary artery occlusion found by coronary angiography. History of no coronary artery occlusions found by coronary angiography in the last 5 years.

Cost

The cost of cardiac fluoroscopy ranges did not exceed 75 dollars in military and civilian hospitals according to the accounting departments of five hospitals located in southern Alabama, Atlanta, and Chicago (author). Green says, "With the expenditure of a small amount of time and minimal radiation, many patients could be screened inexpensively" (Green and Kelley, 1980).

General findings by image-intensified cardiac fluoroscopy

Location and patterns of calcification

Coronary artery calcifications seen by image-intensified cardiac fluoroscopy usually are located in the proximal 40 millimeters of the artery (Rifkin, Parisi, and Folland, 1979). Table 4 lists the patterns of cardiac calcification seen by image-intensified cardiac fluoroscopy and correlates the pattern with possible clinical findings (Blankenhorn, 1961). Table 5 combines the findings of five reports in the literature that noted the location of coronary artery calcifications by image-intensified cardiac fluoroscopy (Lieber and Jorgens, 1961; Frink et al., 1970; Bartel et al., 1974; Kelley, Huang, and Langou, 1978; Aldrich et al., 1979).

Table 4.

Patterns of coronary artery calcification
observed by cardiac fluoroscopy.

Pattern of calcification	Possible clinical correlation
Discrete, punctate shadows with 1 to 10 millimeter diameters; most common pattern.	The smallest of these may be associated with largest of artery occlusions.
Dense, linear, blocky shadows outlining artery wall for 6 to 30 millimeters; next most common pattern by fluoroscopy; usual pattern detected by plain radiography; some appearing as a double tube pattern.	Many of these arteries are stiff, enlarged, and not always associated with artery occlusion, but still associated with sudden death syndrome.
Series of punctate, railroad-like shadows along the artery wall; least common pattern.	Most often associated with long, irregular, flattened artery occlusions.

Table 5.

Location of coronary artery calcifications
by cardiac fluoroscopy.

Coronary artery with calcification	Frequency (percent)
Left main and left anterior descending	401 (46%)
Circumflex	252 (29%)
Right coronary artery	212 (25%)

False positive and false negative findings

Table 6 summarizes factors that may result in false positive findings by image-intensified cardiac fluoroscopy (Green and Kelley, 1980; Chen, 1983; Loecker et al., 1992). Table 7 summarizes factors that may result in false negative findings by image-intensified cardiac fluoroscopy (Lieber and Jorgens, 1961, Schultz et al., 1989).

Table 6.

Factors contributing to false positive
cardiac fluoroscopy findings.

Early calcification of a coronary artery that has not developed atheromatous occlusion of the artery lumen.

Viewing a normal coronary artery en face, creating the illusion of coronary artery calcification shadows.

Calcifications within structures overlying coronary arteries:

Left atrium or ventricular myocardium.

Pericardium.

Heart valves.

Left ventricular thrombi.

Right and left atrial myxomas.

Pulmonary artery.

Pulmonary hilum.

Table 7.

Factors contributing to false negative
cardiac fluoroscopy findings.

Calcification size is less than 2 millimeters.
Obesity.
Cardiomegaly.
Pulmonary congestion with or without effusion.
Pulmonary or pleural disease overlying heart shadow.
Valvular calcification overlying coronary artery calcification.
Failure to examine the heart in all positions.
Failure to observe the heart during rotation between positions
Inattentiveness or image fixation by the observer.
Inexperience on diagnosing calcification by the observer.

Methods of literature review analysis

The literature correlating coronary artery calcification with coronary artery disease in symptomatic and asymptomatic patients was reviewed from 1960 to the present. The data found in these studies was analyzed using SAS[®] Proc Freq (SAS[®] Institute, Incorporated, 1991) as required when current techniques of analysis were not used in the paper. The odds ratio is a test of the strength of association between outcomes. Each odds ratio is reported with its 95 percent confidence interval (C.I.).

Coronary artery calcification and symptomatic patients

Correlation with autopsy findings

Postmortem cardiac plain radiography

Frink searched for cardiac calcifications by plain radiography in 200 hearts randomly obtained at autopsy (Frink et al., 1970). The patients were 30 years of age or older. No attempt was made to select hearts of patients with clinical coronary artery disease. After radiographic survey, the coronary arteries were dissected.

Frink found coronary artery calcification was invariably associated with arteriosclerosis. Calcification was noted in artery segments with fibrosis and degenerative changes whether lumen occlusion was present or not.

Table 8 shows a correlation between calcification of the coronary arteries and increasing age. Table 9 shows there was a

significant correlation between coronary artery calcification and coronary artery occlusion greater than or equal to 50 percent by dissection regardless of the patient gender.

Table 8.

Coronary artery calcification correlated with age at autopsy.

Age group by year	Total cases	Cases with calcification seen
30-39	14	3 (21%)
40-49	24	6 (25%)
50-59	35	25 (71%)
60-69	60	46 (77%)
70-79	44	36 (82%)
80+	23	22 (96%)
Totals	200	138 (69%)

* Adapted from Frink et al., 1970

Table 9.

Correlation of coronary artery calcification with artery occlusion by autopsy.

Gender	Total artery segments	Segments with calcification and occlusion $\geq 50\%$	Odds ratio	95% C.I.	p
Male	518	144	8.5	(5.16, 14.08)	$<10^{-6}$
Female	292	65	10.5	(4.85, 20.23)	$<10^{-6}$

* Adapted from Frink et al., 1970.

Premortem cardiac fluoroscopy

Lieber and Jorgens followed 630 Veterans Administration Hospital patients with known or suspected coronary artery disease for 19 months (Lieber and Jorgens, 1961). Each patient was examined by cardiac fluoroscopy. Twenty-one patients died and underwent postmortem examination for coronary artery disease. Table 10 shows that among the deceased patients, those with coronary artery calcifications by cardiac fluoroscopy were significantly more likely to have coronary artery disease by dissection (Fisher's Exact test, $p=0.005$).

Table 10.

Correlation of autopsy findings of coronary artery disease with premortem history of abnormal cardiac fluoroscopy.

Cardiac fluoroscopy outcomes	Autopsy outcomes		Totals
	CAD** present	CAD absent	
Calcification seen	13	2	15
No calcifications seen	1	5	6
Totals	14	7	N=21

* Adapted from data in Lieber and Jorgens, 1961.

** CAD is coronary artery disease by dissection.

Correlation with coronary angiography findings

Hamby compared the cardiac fluoroscopy findings of 500 patients undergoing coronary angiography (Hamby et al., 1974). Of the 500 cases, 250 had at least one coronary artery occlusion greater than or equal to 50 percent, and the other 250 had occlusions less than 50 percent. The patients were all referred for signs and symptoms of coronary artery disease.

In both groups, the likelihood of finding coronary artery calcifications increased with age. Hamby found that multivessel calcification was related to multivessel coronary artery disease. Table 11 shows the finding of coronary artery calcification correlated significantly with the finding of coronary artery occlusion greater than or equal to 50 percent by coronary angiography regardless of age or gender.

The age group greater than 70 years of age deviated from these conclusions. In this age group, the positive predictive value of an abnormal cardiac fluoroscopy for coronary artery occlusion greater than or equal to 50 percent was only 43.8 percent (7 of 16). The odds ratio for this age group was not significant at 0.77 with 95 percent C.I. of 0.04 and 14.75 (calculated from the data found in Hamby et al., 1974). This was likely due to the group's high prevalence of coronary artery calcifications (15 of 16).

Table 11.

Correlation of coronary artery calcification with coronary artery occlusion greater than or equal to 50 percent.

Factor controlling for	Odds ratio*	95% C.I.
Age group by decade and gender	11.72	(7.36,18.68)
Age group by decade only	13.62	(8.87,20.89)
Gender only	10.64	(6.94,16.31)

* Calculated from the data found in Hamby et al., 1974

A cohort of 800 patients with suspected coronary artery disease underwent cardiac fluoroscopy. They were referred for coronary angiography (Bartel et al., 1974; Margolis et al., 1980) was followed for up to 5 years. Ninety-one percent of the cohort presented angina and 6 percent had a likely history of myocardial infarction.

Table 12 shows there was a significant correlation between coronary artery calcification by cardiac fluoroscopy and the finding of significant coronary artery occlusions greater than or equal to 75 percent. The odds ratio was 9.7 with 95 percent C.I. of 5.37 and 17.87 (calculated by the data presented in Margolis et al., 1980). The positive predictive value of coronary artery calcification by cardiac fluoroscopy for significant coronary artery occlusion was 94.4 percent (236 of 250). However, the false negative rate was 63.5 percent (349 of 550), showing the absence of coronary artery calcification does not exclude significant coronary artery occlusion.

Table 12.

Correlation of coronary artery calcification with coronary artery occlusion greater than or equal to 75 percent.

Fluoroscopy outcome	Coronary angiography outcome		Totals
	Occlusion \geq 75%	Occlusion 0-74%	
Calcification seen	236	14	250
No calcification seen	349	201	550
Totals	585	215	N=800

A similar study by Bobbio et al. (1988) confirmed the findings of Margolis. Five hundred and six patients with symptoms consistent with coronary artery disease underwent cardiac fluoroscopy and coronary angiography. There was a significant correlation between coronary artery calcification by cardiac fluoroscopy and the finding of significant coronary artery occlusions greater than or equal to 75 percent. The odds ratio was 2.5 with 95 percent C.I. of 1.19 and 5.42 (calculated from the data presented in Bobbio et al., 1988). The positive predictive value of coronary artery calcification by cardiac fluoroscopy for significant coronary artery occlusion was 87.6 percent (85 of 97). The false negative rate was 73.7 percent (115 of 156).

Although Hamby et al. 1974; Bartel et al. 1974; Margolis et al., 1980; and Bobbio et al. 1988, found cardiac fluoroscopy a useful screening tool for predicting anatomic coronary artery occlusions, Huang said a dissenting opinion (Huang et al., 1985). One hundred and seventy-one men with chest pain underwent cardiac fluoroscopy, exercise treadmill testing, thallium scan, and coronary angiography. Patients with established histories of heart disease were excluded, to include those with a history of myocardial infarction, coronary artery bypass surgery, valvular heart disease, and cardiomyopathy. The positive predictive value of coronary artery calcifications for at least one coronary artery occlusion greater than or equal to 70 percent was 83.7 percent (87 of 104). Huang noted that the results of the cardiac fluoroscopy did not add additional information after the results of the exercise treadmill test and thallium scan were known. He felt the false negative rate of screening tests should not exceed 5 to 10 percent as a diagnostic threshold. Since the false negative rate of the cardiac fluoroscopy exceeded these thresholds, Huang said, "In symptomatic men, cardiac fluoroscopy

is an ineffective test [diagnostic test as opposed to screening test] when compared to exercise ECG [exercise treadmill test] and thallium scan."

Uretsky et al. (1988) studied 600 patients with suspected coronary artery disease who underwent cardiac fluoroscopy and coronary angiography. Uretsky correlated the number of calcified coronary arteries by cardiac fluoroscopy with the angiography outcome. He found the sensitivity of the test for coronary artery occlusions greater than 49 percent was less for one vessel calcification (61 percent) than for multivessel calcification (78 percent in two vessel calcification, and 91 percent in three vessel calcification) in all age groups. Single vessel calcification mostly involved the left main or proximal left anterior descending coronary artery. He confirmed the significant positive predictive value of coronary artery calcification by cardiac fluoroscopy for coronary artery occlusions by coronary angiography.

One study noted the cardiac fluoroscopy outcomes of 24 patients with cardiomyopathy who underwent a diagnostic coronary angiography. All 10 patients with ischemic cardiomyopathy had coronary artery calcification by cardiac fluoroscopy while 14 patients with nonischemic cardiomyopathy had no coronary artery calcification (Johnson, Laiken, and Shabetai, 1978).

Correlation with mortality

Margolis followed 792 out of 800 in the cohort described in Table 12, for up to 8 years (Margolis et al., 1980). The finding of coronary artery calcification was significantly associated with an increase in mortality rates over a period of 5 years whether the patient had coronary artery occlusion by coronary angiography or not. At the end of 5 years, the 5-year mortality rate was 13 percent for patients without coronary artery calcification compared to 42 percent for patients with coronary artery calcification. Margolis stratified the data into subgroups for gender, decade of age, graded exercise treadmill test results, degree of coronary artery disease, ventriculogram results, left ventricular function, and arteriovenous oxygen difference. The increased mortality rate was significantly increased in all subgroups. He concluded cardiac fluoroscopy is an important prognostic indicator of mortality.

Coronary artery calcification and asymptomatic patients

General population

Patients in coronary artery disease screening programs are generally asymptomatic since symptoms usually develop between screening evaluations. Researchers studied the usefulness of cardiac fluoroscopy in asymptomatic patients, mostly in screening programs.

Kelley studied 108 asymptomatic, middle-aged office workers who volunteered for screening by cardiac fluoroscopy and graded exercise treadmill test (Kelley, Huang, and Langou, 1978). He found that 34 percent had cardiac calcifications. There was a significant correlation between the finding of coronary artery calcifications and one millimeter or greater ST segment depression on graded exercise treadmill test. The odds ratio was 12.3 with 95 percent C.I. 12.28 and 41.88 (calculated from the data presented in Kelley, Huang, and Langou, 1978). The meaning of this relationship is unknown since the patients did not undergo coronary angiography.

Aldrich studied 93 asymptomatic patients referred for hypercholesterolemia (Aldrich et al., 1979). All were free of other significant diseases. Patients underwent coronary angiography if their screening cardiac fluoroscopy or graded exercise treadmill tests were abnormal. The graded exercise treadmill test was abnormal if there was 1 millimeter or more of ST segment depression below baseline. There was a significant correlation between the finding of coronary artery calcification by cardiac fluoroscopy and coronary artery occlusions of 50 percent or more. The odds ratio was 3.94 with a 95 percent C.I. of 1.21 and 13.57 (calculated from the data presented in Aldrich et al., 1979). There was also a significant correlation between the finding of coronary artery calcification and any degree of coronary artery occlusion. The odds ratio was 4.02 with 95 percent C.I. of 1.28 and 12.90. Table 13 shows the summary findings stratified by two methods of grouping the degree coronary artery occlusion.

Table 13.

Correlation of abnormal cardiac fluoroscopy with coronary angiography outcomes in 93 asymptomatic patients.

Fluoroscopy	Coronary angiography outcomes			
	Any degree of occlusion		Occlusion \geq 50%	
	Yes	No	Yes	No
Abnormal	56	9	30	35
Normal**	17	11	5	23
Positive predictive value	86.2%		46.2%	
False negative rate	60.7%		17.9%	

* Calculated from the data presented in Aldrich et al., 1979

** All patients with normal fluoroscopy had an abnormal graded exercise treadmill test.

One hundred and twenty-nine men volunteered for screening by cardiac fluoroscopy and graded exercise treadmill test (Langou et al., 1980). They were middle-aged with ages ranging from 41 to 56 years old. They had no history of chronic illness or symptoms. Thirteen had abnormal cardiac fluoroscopy and abnormal graded exercise treadmill test. They were referred for coronary angiography. The positive predictive value of the abnormal cardiac fluoroscopy and abnormal graded exercise treadmill test for any degree of coronary artery occlusion was 100 percent. The positive predictive value of the abnormal tests for coronary artery occlusion greater than 50 percent was 92 percent. The cohort was followed for 3 years. Five patients developed angina. Four of the five had a history of abnormal cardiac fluoroscopy.

Nineteen hundred asymptomatic U.S. Army soldiers over 40 years of age were divided into low and high risk groups for coronary artery disease by primary screening history, resting electrocardiogram, cholesterol profile, and Framingham Risk Index (Wortham et al., 1990). The 781 found at high risk were referred for secondary screening. In secondary screening, 700 completed a graded exercise treadmill test and cardiac fluoroscopy. Sixty had coronary artery calcifications by fluoroscopy. These patients were referred for coronary angiography only if they had an abnormal graded exercise treadmill test. One hundred percent

of the patients with an abnormal cardiac fluoroscopy and abnormal graded exercise treadmill test (N=34) had some degree of coronary artery occlusions.

Aircrew member population

Loecker et al. (1992) studied 1,466 asymptomatic U.S. Air Force pilots referred to a tertiary aeromedical consultation service with possible cardiac problems after primary screening for cardiovascular disease at the local flight surgeon's office. They underwent a complete noninvasive cardiac evaluation, to include cardiac fluoroscopy. All 239 patients with an abnormal cardiac fluoroscopy were referred for coronary angiography. Fifty-six declined catheterization and were removed from flying duties since obstructive coronary artery disease could not be ruled out by noninvasive tests alone. The remaining 183 patients with abnormal cardiac fluoroscopy completed coronary angiography. A total of 430 aircrew members with normal cardiac fluoroscopy completed coronary angiography (total studied equals 183 + 430, N=613). The positive predictive value of the abnormal cardiac fluoroscopy for any degree of coronary artery occlusion was 68.9 percent and for occlusions greater than or equal to 50 percent was 37.7 percent. The false negative rate for any degree of occlusion was 19.1 percent. Among all patients undergoing angiography, there was a significant correlation between the finding of coronary artery calcification by fluoroscopy and coronary artery obstruction by angiography as shown in Table 14.

Table 14.

Correlation of abnormal cardiac fluoroscopy with coronary angiography outcomes in 613 asymptomatic pilots with suspected cardiac disease.

Fluoroscopy	Coronary angiography outcome			
	Any degree of occlusion		Occlusion $\geq 50\%$	
	Yes	No	Yes	No
Abnormal	126	57	69	114
Normal	82	348	35	395
Odds ratio	9.38		6.83	
95% C.I.	(6.21, 14.2)		(4.22, 11.1)	

* Adapted from the data in Loecker et al., 1992.

Discussion

Since the "gold standard" test, coronary angiography, was not applied to all subjects in these studies, the sensitivity and specificity of cardiac fluoroscopy are unknown. Thus the value of cardiac fluoroscopy as a diagnostic tool is unknown. But the studies of living patients primarily used cardiac fluoroscopy as a screening test and not a diagnostic test. Cardiac fluoroscopy was used together with other screening methods to make decisions on which subjects would undergo coronary angiography. In this context, the positive predictive value and the false negative rate of the screening test are important factors in making decisions on the utility of the test. Due to its high positive predictive value, cardiac fluoroscopy assists screening program managers in dividing subjects into low and high risk groups for underlying disease when the test is positive. Knowing the false negative rate of cardiac fluoroscopy is increased helps screening program managers understand disease may still exist despite a negative test.

In 1987, the managers and consultants of the U.S. Army Aeromedical Cardiovascular Disease Prevention and Detection Program (Aeromedical Policy Letter 28) significantly modified the program. The modification was based on literature review and an evolving standard of care in the aeromedical and military preventive medicine communities. Cardiac fluoroscopy was a new test added to the secondary level of the stratified screening program

(Department of the Army, 1988; Department of the Army, 1989; Department of the Army, 1991a; Department of the Army, 1991b; Hickman, 1987; Loecker et al., 1992). A related technical report discusses the coronary angiography findings of 82 asymptomatic U.S. Army aircrew members with a history of cardiac calcifications by fluoroscopy (Mason, Shannon, and Celio, 1993).

My observations as manager of this screening program from 1988 to 1992 are that the general medical community does not widely understand, practice, or accept using cardiac fluoroscopy in screening programs to identify coronary artery calcifications as an indicator of probable coronary artery disease. Clinicians hesitated even more to use the test as an indication for coronary angiography when the patient is asymptomatic. A majority of the aircrew members in the Army screening program are asymptomatic. The conflicts between screening program directives and referral clinicians' opinions created confusion and turmoil when aircrew members were referred for cardiac fluoroscopy. As a result of this review, I have found no reasons for doubting the value of using cardiac fluoroscopy in stratified coronary artery disease screening programs.

Summary

Anatomists and pathologists have linked coronary artery calcification to the coronary atherosclerotic process. The finding of coronary artery calcification is associated with a significant increase in mortality risk (3.2 fold increase in risk) compared to patients without coronary artery calcifications regardless of the patient's age or outcome of other cardiovascular disease tests.

Plain radiography and conventional fluoroscopy of the living patient are poor tests for finding coronary artery calcification. They do not have the resolution required to find coronary artery calcifications which are often only millimeters in size.

Image-intensified cardiac fluoroscopy can find coronary artery calcifications as small as 1 to 2 millimeters. There is a strong association between the finding of coronary artery calcification by cardiac fluoroscopy and anatomic occlusions of the coronary arteries, especially in patients under 60 years of age. It is an independent predictor of coronary artery disease with a high positive predictive value of the test for significant occlusive coronary artery disease (80-100 percent). The high positive predictive value makes cardiac fluoroscopy an excellent test as an adjunct to graded exercise treadmill test in the secondary level of testing for stratified coronary artery disease screening programs.

Users of image-intensified cardiac fluoroscopy must remain aware that significant occlusive disease may exist when no coronary artery calcifications are seen by cardiac fluoroscopy due to the moderate false negative rate of the test (18-61 percent). Perhaps it is this finding that has made the test unpopular in the general medical community as a diagnostic tool.

The CAT scanner is emerging as a better tool to detect coronary artery calcifications. CAT scan can find smaller and more calcifications than image-intensified cardiac fluoroscopy while maintaining a high degree of positive predictive value for correlating calcifications to anatomic coronary artery occlusions. It remains to be decided if CAT scan would be a cost-effective tool in a large cardiovascular disease screening program.

In summary, it was best said by Uretsky in 1988, "Cardiac fluoroscopy has an important contribution to make in the assessment of coronary artery disease. Lack of familiarity with the method of performing the examination and with the interpretation of the findings rather than the lack of efficacy, may explain the present disinterest of clinicians in fluoroscopy" (Uretsky et al., 1988).

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