

Original Research

A Propensity Score-Based Comparison of Flat Panel Digital Detector Fluoroscopy Versus Digital Cinefluoroscopy for Coronary Artery Calcium Detection

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Introduction: Detection of coronary artery calcification (CAC) allows for a refined prediction of cardiovascular risk beyond global risk assessment algorithms. Newer-generation, high-resolution, flat-panel digital detector (FPDD) fluoroscopic systems may provide higher CAC detection rates compared with older fluoroscopic devices.

Methods: We compared the CAC detection rates of two fluoroscopic techniques in two different cohorts of asymptomatic individuals, analyzed within a two-decade time interval.

Results: FPDD detected CAC more frequently than the older fluoroscopy device, in the more recent and the older patient cohort of individuals, respectively. After propensity score matching to account for differences in age and risk factor prevalence, the adjusted rates of CAC detection remained higher in favor of FPDD (37.7% vs. 23.7%, $p=0.026$).

Conclusions: The ability of newer cine-fluoroscopic systems to identify CAC in a larger number of asymptomatic, intermediate-risk individuals may have implications for further risk stratification, management of risk factors and long-term prognosis.

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Coronary artery calcification (CAC) is highly specific for atherosclerosis, has a close association with cardiovascular (CV) risk factors and enables refined risk prediction beyond that provided by global risk assessment tools.¹⁻⁴ The absence of CAC on either multi-detector computed tomography (MDCT) or electron-beam computed tomography in adult populations identifies individuals at low risk for CV disease and CV events, thus precluding the need for further downstream testing and management.⁵ Furthermore, CAC scoring may potentially benefit asymptomatic individuals at intermediate CV risk by modifying risk prediction and al-

tering therapy.⁶ We have previously demonstrated that CAC detected with simple digital fluoroscopy in asymptomatic subjects with usual CV risk adds prognostic information over and above the usual risk factors.⁷ Newer-generation flat-panel digital detector fluoroscopic systems (FPDD) possess a higher resolution capacity than older fluoroscopic devices. We were recently able to show that FPDD, as compared with MDCT, accurately detects CAC with high sensitivity and negative predictive values for individuals with CAC scores ≥ 100 .⁸ The aim of this study was to assess whether the new technique can improve CAC detection rates compared with simple digital fluoroscopy. For

this reason, the two fluoroscopic techniques were compared in two different cohorts of asymptomatic individuals analyzed by the same operator in the same center and with a similar protocol within a two-decade time interval.

Methods

Study population

The older group of individuals consisted of 213 healthy volunteers aged 40-60 years who were analyzed between the years 1994-95. Results regarding risk factors, exercise tests and prognosis have been published previously.^{2,6} The more recently examined group included 163 individuals aged 40-60 years old.⁸ All volunteers were mainly hospital workers who responded to a campaign for CAC screening and were considered to be at intermediate CV risk. All subjects denied any history or symptoms of heart disease and had normal physical examinations and resting electrocardiograms. Systolic and diastolic blood pressure was measured and phlebotomy was performed for analysis of total cholesterol. Smoking history was determined and considered positive if the subject had been smoking in the past year. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, or if subjects were receiving antihypertensive treatment. Hypercholesterolemia was considered present if total cholesterol concentration was ≥ 220 mg/dL in the older series and > 200 mg/dL or treatment with statins in the more recent series of patients. Diabetes was defined according either to the older World Health Organization criteria or to the revised and stricter criteria in the recent series of patients (i.e. fasting plasma glucose ≥ 126 mg/dl).⁹ A family history of CAD was considered to be present if a parent or sibling aged ≤ 55 years had had documented CAD.

Cardiac cinefluoroscopy

In the older series of asymptomatic individuals digital cinefluoroscopy was performed in both the 30° right anterior oblique and 45° left anterior oblique views with 15° cranial angulation, using a Philips OM 200 X-ray tube, image intensifier, and a digital cardiac imaging unit with a 512 × 512 pixel matrix format. The image intensifier light output was focused on a video camera that allowed the playback of digitized cine loop images for immediate analysis.⁷

FPDD cinefluoroscopy

In the more recent cohort, FPDD imaging of CAC was obtained with a Philips Allura Xper FD10 system (Philips, Eindhoven, The Netherlands). The examinations were obtained in one view only (45° left anterior oblique, with 15° cranial angulation), stored on CD ROM, and reviewed with the Xcelera Lite Viewer (Koninklijke Philips Electronics N.V. 2003). All studies were independently analyzed by two investigators. In case of disagreement, a third opinion was sought. The cinefluoroscopy results were classified for the purposes of this study as having either absent or present CAC.^{7,8}

Subjects were informed about the calcium result and instructions were given to all for risk factor modification. The study was approved by the hospital ethics committee, and subjects gave informed consent.

Statistical analysis

We first conducted a univariate analysis of the patients' baseline characteristics according to the method used for detection of calcification, using a t-test for continuous variables and a chi-square test for categorical variables. Propensity score-matching analysis was used to adjust for potential biases.¹⁰ The predicted probability of early CAC was estimated with the use of a logistic regression model fit with all the variables listed in Table 1. Greedy, nearest neighbor 1:1 matching was used to match subjects with a caliper width of 0.2 of the standard deviation of the logit of the propensity score.¹¹ Each matched pair was unique and patients without a suitable match were excluded from further analysis. Standardized differences of the mean $< 10\%$ were taken to indicate good balance in the matched sample.¹² Using the matched pairs, we conducted McNemar's test to compare calcium detection rates between the two methods. All tests were two-sided and the criterion for statistical significance was a p-value < 0.05 . The SPSS for windows software package (version 16.0; SPSSInc., Chicago IL, USA) was used for statistical analysis.

Results

As already reported, the inter- and intra-observer agreement for FPDD results were 92.7% and 93.4%, with weighted kappa coefficients of 0.852 and 0.853 respectively.⁸ The subjects' demographic characteristics are presented in Table 1. The recent group of individuals who underwent examination with the FPDD

Table 1. Demographic characteristics of the study population.

	Overall (N=376)	Digital cinefluorography (N=213)	FPDD cinefluorography (N=163)	p
Age	51.07 ± 6.9	50.01 ± 6.3	52.4 ± 7.6	0.001
Male gender	218 (58.0)	116 (54.5)	102 (62.6)	0.14
Smoking	160 (42.6)	77 (36.2)	83 (50.9)	0.005
Hyperlipidemia	162 (43.1)	67 (31.5)	95 (58.3)	<0.001
Hypertension	92 (24.5)	32 (15.0)	60 (36.8)	<0.001
Diabetes mellitus	25 (6.6)	5 (2.3)	20 (12.3)	<0.001
Family history of CAD	95 (25.3)	42 (19.7)	53 (32.5)	0.006

CAD – coronary artery disease; FPDD – flat panel digital detector.

Variables are expressed as mean ± SD or N (%). The p-value refers to comparisons between individuals who underwent digital cinefluorography and FPDD cinefluorography.

system exhibited a higher prevalence of all CV risk factors with the exception of gender, as compared with the older series of individuals. Digital cinefluorography and FPDD fluoroscopic system detected calcification in 42 (19.7%) and 71 (43.6%) individuals, respectively ($p < 0.001$). All baseline individual characteristics displayed in Table 1 were included in the logistic regression model as covariates. The propensity scores for the two groups differed significantly (0.36 ± 0.17 digital cinefluorography vs. 0.53 ± 0.21 for FPDD; $p < 0.001$). Propensity score matching resulted in 114 pairs of patients. The standardized difference between the two groups was less than 10% for all variables (Table 2, Figure 1). In the propensity-matched sample there was a statistically significant difference in the adjusted rates of calcium detection between digital cinefluorography and FPDD cinefluorography (Figure 2).

Discussion

In the current study we investigated the CAC identification rates of FPDD compared with digital cinefluorography in two temporally separated groups of asymptomatic individuals with different CV risk factor

profiles. In order to adjust for the well-known strong influence of risk factors on CAC prevalence, propensity score matching was performed, which showed a higher CAC detection rate in favor of the newer generation fluoroscopy system. The clinical relevance of this finding is the potential of newer FPDD cinefluoroscopic systems to identify CAC in a larger number of asymptomatic, intermediate-risk individuals, which has implications for further risk stratification, management of risk factors and long-term prognosis.⁶⁻⁸ In our recent work we have shown that FPDD in comparison with MDCT as a reference method has both a high sensitivity in detecting and high specificity in excluding CAC in such subjects.⁷ Notably, the sensitivity and negative predictive values for CAC Agatston scores > 100 were excellent. Although the prognostic value of a zero CAC score has been disputed in the setting of acute coronary syndromes, i.e. among patients with a high pretest disease probability,¹³ it appears that asymptomatic, intermediate-risk populations with scores of < 100 exhibit a very low annual estimated risk of death or myocardial infarction (i.e. $< 0.5\%$).⁷ Therefore, even if some individuals with scores 10-99 are left unidentified by the FPDD method they are likely to need no further CAC quantification, as they represent a low-risk category for future vascular episodes.

The higher CV risk factor prevalence in the recent as compared with the older series of patients is most probably the result of the enrolment of two temporally remote populations of healthy subjects with slightly different definition criteria for two of the risk factors, as both hypercholesterolemia and diabetes mellitus were more strictly defined in the recent than in the older cohort of patients. The retrospective, non-randomized analysis of the newer data with

Table 2. Standardized differences (%) before and after propensity matching.

Covariate	Before (%)	After (%)
Age	34.95	3.31
Male gender	16.5	9.11
Smoking	29.97	-1.8
Hyperlipidemia	55.94	-3.6
Hypertension	51.37	0
Diabetes mellitus	39.17	0
Family history of coronary artery disease	29.46	0

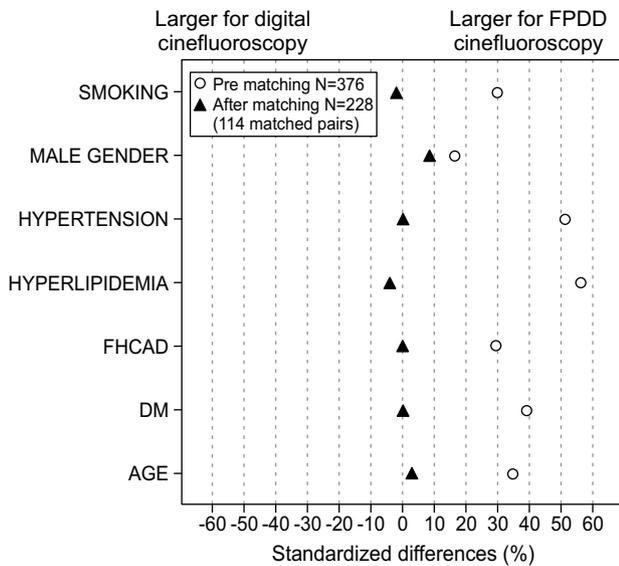


Figure 1. Percentage standardized differences in patients' baseline characteristics before and after matching by propensity score. DM – diabetes mellitus; FHCAD – family history of coronary artery disease. FPDD – flat panel digital detector fluoroscopy.

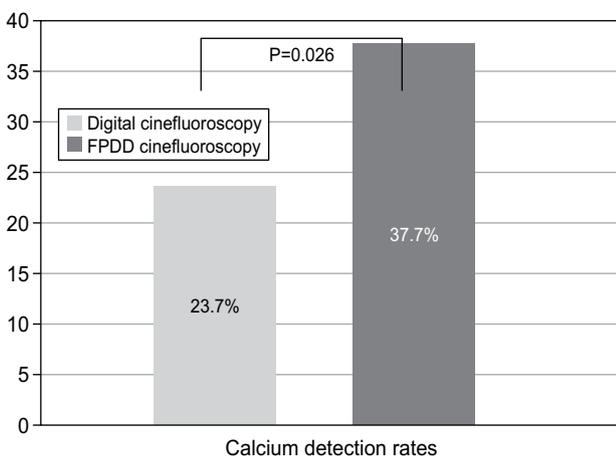


Figure 2. Adjusted rates of calcium detection in the propensity-matched sample.

those from two decades earlier is a clear limitation of the current study.

The strengths and uncertainties of CAC identification by virtue of FPDD devices relative to MDCT include the patient's convenience, less radiation exposure (0.26 ± 0.13 vs. 1.8 ± 0.09 mSv)⁸ and lack of prognostic data. Large-scale, population-based longitudinal trials are needed in this regard to validate this semi-quantitative, simpler, logistically favorable and quite accurate CAC detection method in terms of prognostic merits beyond the clinical risk factor infor-

mation. In fact, no studies have yet shown a net effect of CAC scoring on health outcomes.⁶ Although cost-effectiveness analyses do not appear to support the liberal use of sophisticated CAC detection devices,¹⁴ a recent trial demonstrated that CAC scanning was associated with better coronary artery disease risk factor control as compared to CAC scanning without increasing downstream medical testing.^{15,16}

Conclusions

The ability of newer cine-fluoroscopic systems to identify CAC in a larger number of asymptomatic, intermediate-risk individuals may have implications for further risk stratification, management of risk factors and long-term prognosis.

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