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Research paper

Dynamic CT myocardial perfusion imaging identifies early perfusion abnormalities in diabetes and hypertension: Insights from a multicenter registry

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ABSTRACT

Background: To identify patients with early signs of myocardial perfusion reduction, a reference base for perfusion measures is needed.
Objective: To analyze perfusion parameters derived from dynamic computed tomography perfusion imaging (CTPI) in patients with suspected coronary artery disease (CAD), and relationship with risk factors.
Methods: In this multicenter study, coronary CT angiography (cCTA) and dynamic CTPI were performed by second-generation dual-source CT in patients suspected of CAD. Risk factors were collected from hospital records. Patients with visual perfusion defects on CTPI, previous coronary intervention, or

List of abbreviations: CAD, Coronary artery disease; CT, Computed tomography; cCTA, Coronary computed tomography angiography; CTPI, Computed tomography perfusion imaging; ECG, Electrocardiographic; K^{trans}, Volume transfer constant; MBF, Myocardial blood flow; MBV, Myocardial blood volume; MRI, Magnetic resonance imaging; SPECT, Single-photon emission computed tomography; PET, Positron emission tomography; SD, Standard deviation.

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missing risk factor details were excluded. This analysis included 98 patients (mean age ± standard deviation [SD], 59.0 ± 8.6yrs; 73 male). Global measures of left ventricular myocardial blood flow (MBF), myocardial blood volume (MBV) and volume transfer constant (K^{trans}) were calculated.

Results: Mean MBF was 139.3 ± 31.4 mL/100 mL/min, MBV 19.1 ± 2.7 mL/100 mL, and K_{trans} 85.0 ± 17.5 mL/100 mL/min. No significant differences in perfusion parameters were found by gender or age category. Hypertension and diabetes mellitus resulted in lower perfusion parameters (hypertension vs normotension: MBV 18.5 ± 3.0 vs 19.7 ± 2.3 mL/100 mL and K^{trans} 82.0 ± 18.0 vs 89.0 ± 16.0, $p < 0.05$; diabetes vs no diabetes: MBF 128.5 ± 31.5 vs 144.0 ± 30.5 mL/100 mL/min and MBV 17.9 ± 2.4 vs 19.4 ± 2.8 mL/100 mL, $p < 0.05$). In patients with hyperlipidemia, MBF was higher (146.8 ± 34.4 vs 130.7 ± 24.3 mL/100 mL/min, $p < 0.05$). Smoking and family history did not show perfusion parameter differences.

Conclusions: Dynamic CTPI identifies early perfusion disturbances in conditions like diabetes and hypertension. With further standardization, absolute perfusion measures may improve CAD risk stratification in patients without visual perfusion defects.

1. Introduction

Coronary computed tomography angiography (cCTA) is the preferred non-invasive imaging test to interrogate the coronary arteries for plaque and stenosis. The presence of coronary stenosis alone does not suffice to diagnose hemodynamically relevant coronary artery disease (CAD), especially for luminal narrowing between 30 and 70%.[1,2] Additional imaging-based information is needed to determine whether the coronary stenosis leads to reduced perfusion of the myocardium. While in the past, a second imaging modality such as single-photon emission computed tomography (SPECT) would be needed to evaluate myocardial ischemia, recent meta-analyses show the potential of adenosine stress CT to assess myocardial perfusion.[3,4] Different stress CT techniques are studied for the detection of myocardial perfusion defects, such as static arterial first pass imaging,[5] and dynamic CT perfusion imaging (CTPI).[6] A particular strength of dynamic CTPI is the fact that quantitative measures of myocardial perfusion are obtained, including absolute blood flow values, owing to the linear relationship between myocardial iodine attenuation and tissue perfusion.[7,8] This distinguishes CTPI from other imaging modalities like magnetic resonance imaging (MRI).[9,10]

There are different reasons for the interest in quantification of myocardial perfusion. In case of three-vessel disease, visual analysis of relative perfusion, such as in SPECT, can miss balanced ischemia.[11] Quantification of myocardial blood flow allows for diagnosis of globally reduced perfusion.[12] On the other hand, early blood flow disturbances without gross myocardial perfusion defects, can be missed in visual evaluation of relative myocardial perfusion, but likely also on dynamic CTPI color map displays as these subtle deviations may be invisible for the human eye. By quantifying myocardial perfusion, it may be possible to identify patients with early signs of myocardial blood flow reduction, and thus improve the diagnosis of hemodynamically significant CAD. Furthermore, myocardial perfusion may already be impaired due to cardiovascular risk factor effects on microvasculature, but without anatomical CAD.[13,14] Detection of early global myocardial perfusion disturbances could help to stratify CAD risk in patients without overt myocardial ischemia, who may benefit from optimized medical therapy.[15]

In order to distinguish normal from abnormal values, a reference base for measures of myocardial blood flow and blood volume is needed. Previous studies have identified cut-off values for ischemic myocardium in CTPI,[16,17] but there is scarce evidence on the range of myocardial perfusion parameters in the typical population referred for CAD imaging but without overt perfusion defects.[12,18] Also, information on relationships between cardiovascular risk factors and CTPI-derived perfusion parameters is scarce. Thus, the purpose of our study was to evaluate global myocardial perfusion parameters based on dynamic CTPI and its relationship to cardiovascular risk factors in patients with suspected CAD but without myocardial ischemia.

2. Materials and methods

2.1. Patient population

We used data from a multicenter registry of individuals included in single-center studies in Asia, Europe and the United States between November 2009 and July 2011.[16,17,19] The individuals in the registry were symptomatic patients with suspected or known CAD, who prospectively underwent cCTA and dynamic CTPI in the individual studies as part of research protocols. All patients had stable chest pain, with an indication for further evaluation by (non-) invasive imaging. In some of the studies, there was an indication for cCTA with CTPI as added investigation,[19] while in others the entire CT examination was for research purposes.[16,17] In case of known contraindications to CT, iodinated contrast medium or adenosine, patients were not included in the local studies. The local institutional review board approved each respective study protocol and all patients provided written informed consent. Presence of cardiovascular risk factors (diabetes mellitus, hypertension, hyperlipidemia, current or past smoking, family history of CAD) was ascertained from the patient's hospital records. For the current analysis, patients with a history of coronary artery bypass grafting or percutaneous coronary intervention, and those with missing risk factors were excluded. Only patients without visual perfusion defects on dynamic CTPI were included, to limit the analysis to cases without hemodynamically significant CAD (see further description of dynamic CTPI evaluation below).

2.2. CT image acquisition

Second-generation dual-source CT systems (Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany) were used for image acquisition. For cCTA, 50–80 mL of contrast medium (concentration 300–370 mg I/mL) was injected at a flow rate of 4–5 mL/s. No rate-controlling drugs were administered. Depending on the patient's heart rhythm and heart rate, cCTA was performed with prospectively electrocardiographically (ECG)-triggered high-pitch acquisition (in case of sinus rhythm and heart rate up to 60 bpm), prospectively ECG-triggered sequential acquisition (in