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Original article

Quantification of myocardial perfusion reserve using dynamic SPECT images of patients with chronic kidney disease

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ABSTRACT

Background: Chronic kidney disease (CKD) is an independent risk factor for cardiovascular disorders. The aim of this study was to examine whether the quantitatively measured myocardial blood flow (MBF) or myocardial perfusion reserve (MPR), calculated by dynamic single photon emission computed tomography (SPECT) analysis using a cardiac cadmium zinc telluride (CZT) gamma camera, was related to renal dysfunction in patients with normal myocardial perfusion imaging (MPI) findings.
Methods: The study population consisted of 46 patients with CKD and 46 individuals without CKD (controls). Their MPR index was quantitatively measured using adenosine MPI with a cardiac CZT gamma camera. All assessments were with a single tissue compartment kinetic model. The K1 value was calculated on stress and at-rest images. To obtain the MPR index we divided K1 stress-by K1 at-rest values.
Results: The at-rest K1 value was significantly higher and the MPR index was significantly lower in patients with CKD than those without CKD [CKD vs. controls: at-rest K1 value, 0.21 (0.17–0.25) vs. 0.19 (0.16–0.22), $p = 0.040$; MPR index, 1.86 (1.69–2.22) vs. 2.19 (1.93–2.41), $p < 0.001$]. The stress K1 values were not significantly different.
Conclusion: The MPR index is significantly lower in CKD patients; this is considered as being mainly due to an increase in the at-rest K1 value.

Introduction

Chronic kidney disease (CKD) is an independent risk factor for cardiovascular disease. The incidence of cardiac events and the mortality rate in patients with severe CKD is high [1–4]. Cardiovascular events associated with cardiovascular stenosis and other factors unrelated to coronary stenosis have been reported and the possibility of coronary microvascular dysfunction has been suggested [5].

Assessment of coronary flow reserve (CFR), myocardial perfusion reserve (MPR), and myocardial flow reserve (MFR) has been suggested as a useful approach for the diagnosis of microvascular dysfunction [6–10]. Generally, the CFR, the ratio of maximal hyperemic to basal coronary blood flow, an integrated measure of the flow through both large coronary arteries and microcirculation [6,9,11,12] is used when the coronary blood flow is measured by coronary angiography [6,9,12,13] or Doppler ultrasound [14,15]. MPR and MFR defined as the ratio of the maximal hyperemic to the baseline resting myocardial blood flow (MBF) [7,16] are indicators similar to CFR. MPR and MFR can be used when the MBF is assessed on positron emission tomography (PET) or single photon emission computed tomography (SPECT).

Radionuclide myocardial perfusion imaging (MPI) is widely used to detect cardiovascular diseases and to predict the prognosis [17] of patients with such diseases. Acquisition of the MPR on dynamic PET images is well established [10,16]. Although their high quantitative accuracy, sensitivity, and resolution facilitate the

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accurate measurement of the kinetic behavior of radiotracers in the body, PET instrumentation is costly and a cyclotron and facilities for radiolabeling ligands near the PET scanner are required. On the other hand, SPECT scanners are widely available and the longer half-life of SPECT radiotracers obviates the need for production facilities close to the SPECT scanner. However, MPR measurements are not typically acquired with standard SPECT cameras because of low sensitivity, poor resolution, and the need to rotate around the patient for obtaining three-dimensional (3D) images.

A novel cardiac SPECT system that features solid-state semiconductor detectors is now available. Since its sensitivity and spatial resolution are higher than those of conventional SPECT instruments [18], this system allows the calculation of indices to describe the MBF and MPR [19,20]. Using this system, we earlier identified a decrease in the MPR index of coronary left main stem lesions and in patients with multi-vessel disease [21]. In the current study, we performed quantitative measurements of the MBF and MPR indices, calculated on human dynamic SPECT images using a cardiac cadmium zinc telluride (CZT) gamma camera, in the presence and absence of CKD.

Patients and methods

Study population

This study was approved by our institutional ethics board. All study procedures were in accordance with the Statement of Human and Animal Rights. Prior informed consent for inclusion in the study was obtained from all patients or their legal representatives.

Between April 2013 and March 2016, 734 patients underwent pharmacologic SPECT-MPI with a cardiac CZT gamma camera at our hospital. Of those, we enrolled 214 patients with normal SPECT-MPI results [summed stress score (SSS) ≦3] and no history of myocardial infarction, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG)- heart valve-, or pacemaker implantation surgery, and no history of cardiomyopathy, myocarditis, cardiac amyloidosis, or arrhythmia with heart failure. Additionally, in those patients, thirty-nine individuals had undergone coronary angiography, and 4 patients with left main or 3-vessel coronary artery disease (CAD) were also excluded. After application of a multivariate matched sampling method that incorporates the propensity score, we selected 92 subjects and divided them into a control group ($n = 46$) and a CKD group ($n = 46$). Matching criteria included clinical profile [age, gender, body mass index (BMI), Brinkman index, dyslipidemia, diabetes mellitus, hypertension and family history of CAD] and hemodynamics (baseline heart rate, blood pressure, and ejection fraction). The estimated glomerular filtration rate (eGFR) was above 60 ml/min/1.73 m^2 in the controls and below that value in CKD patients (Fig. 1).

Their coronary risk factors (advanced age, gender, BMI, Brinkman index, dyslipidemia, diabetes mellitus, and hypertension) were recorded at the time of SPECT-MPI assessment. Blood biochemical tests results [eGFR, triglyceride (TG), low- and high-density lipoprotein (LDL, HDL) cholesterol, brain natriuretic peptide (BNP), HbA1c, and hemoglobin] recorded in electronic medical charts were the parameters used for analysis. We also recorded the systolic and diastolic blood pressure and the heart rate under stress- and at-rest conditions upon completion of the SPECT-MPI studies. The stress and at-rest left ventricular (LV) ejection fraction were calculated with Cedars-Sinai quantitative-gated SPECT software on electrocardiography-gated SPECT scans.

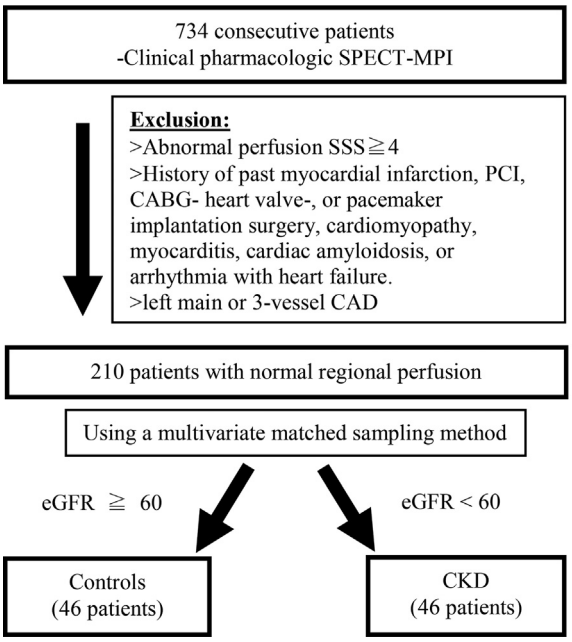

Fig. 1. Flow chart showing our patient selection criteria. CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MPI, myocardial perfusion imaging; PCI, percutaneous coronary intervention; SPECT, single photon emission computed tomography; SSS, summed stress score.

SPECT-MPI

All study participants underwent pharmacologic SPECT-MPI examination using a cardiac CZT gamma camera (Discovery NM530c; GE Healthcare, Waukesha, WI, USA); injectable 111 MBq ^{201}Tl (Nihon Medi-Physics Co., Ltd., Tokyo, Japan or FUJIFILM RI Pharma Co., Ltd, Tokyo, Japan) was the solution used.

Stress SPECT-MPI

Pharmacologic vasodilator stress was induced in all subjects through the intravenous administration of adenosine (0.120 mg/kg/min for 6 min). At peak stress, a bolus radiotracer (55.5 MBq) was injected. Dynamic imaging was performed within a 6-min acquisition protocol in list mode. A temporal series of 3D axial volumes ($70 \times 70 \times 50$ voxels, $4 \times 4 \times 4$ mm) was reconstructed from the acquired raw data using maximum a posteriori-expectation maximization. This technique generated 72 3D volumes integrating 5-s time frames in the course of 360 s. Routine summed cardiac and gated stress images were acquired in list mode after dynamic imaging.

At-rest SPECT-MPI

Routine gated at-rest images were obtained 3 h after stress SPECT-MPI. For at-rest dynamic imaging, a 30-s scan was first acquired to obtain a baseline pre-scan image. Then the radiotracer (55.5 MBq) was injected and list-mode scans were obtained in a similar manner. To evaluate the at-rest findings, the baseline pre-scan images from the list-mode dynamic scans were subtracted. Routine gated at-rest imaging was then added.

SPECT image and quantitative analysis

The images were reformatted using Lister on a Xeleris workstation (GE Healthcare) and then reconstructed with a

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