

# Increasing Use of Cardiac PET/CT for Inflammatory and Infiltrative Heart Diseases in Korea

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Recently the incidence of inflammatory and infiltrative heart diseases is increasing in Korea. Cardiac PET/CT is a useful technology evaluating inflammatory and infiltrative heart diseases. This study analyzed trends in the use of cardiac PET/CT for evaluating inflammatory and infiltrative heart diseases in the Chonnam National University Hospital and Chonnam National University Hwasun Hospital. The general trend in Korea was also assessed based on the domestic nuclear medicine database. There was a common increasing trend in the number of F-18 FDG PET/CT for the evaluation of inflammatory and infiltrative heart diseases. A representative case with cardiac sarcoidosis is illustrated.

**Key Words:** Heart Diseases; Inflammation; Positron Emission Tomography

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## INTRODUCTION

Cardiac positron emission tomography (PET) has many advantages over single photon emission computed tomography, which include lower radiation doses, better image quality and quantitation of absolute myocardial blood flow, and coronary flow reserves.<sup>1</sup> Based on its diagnostic and prognostic values, myocardial perfusion imaging with PET has gained its clinical relevance in the management of coronary artery disease.<sup>2-4</sup>

The advantage of lower radiation exposure from PET ironically leads to the need for an on-site cyclotron. The requirement of representative short-living radioisotopes (RI) such as O-15 and N-13, the half-lives of which are 3 min and 10 min, respectively, limits its wide spread as the primary imaging study in the clinical fields. A Rb-82 with generator system may provide an answer, which is widely being used in the USA; but it has not been widely accepted in the Asian countries yet. Particularly in Korea, the cost of PET imaging and camera occupation (which is longer than oncology PET imaging) generally exceed the benefit from direct referral for invasive coronary angiography without functional testing. Moreover, the recent announcement of the negative results of the global large-scale prospective ISCHEMIA trial raised active controversies over the usefulness of functional testing itself in the manage-

ment of coronary artery disease.<sup>5</sup>

On the other hand, non-perfusion PET using F-18 fluorodeoxyglucose (FDG) is becoming more available in the fields of inflammatory and infiltrative heart diseases. Recently their incidences are increasing in Korea.<sup>6</sup> Despite the incremental clinical needs, the traditional diagnostic imaging tools are not sufficiently sensitive or specific to detect the molecular processes underlying these disease entities. To fill the unmet need, the recent clinical guidelines are being modified based on the clinical studies using FDG PET to detect infective endocarditis and cardiac sarcoidosis.<sup>7-9</sup>

Despite the usefulness of FDG PET/CT in inflammatory and infiltrative heart diseases, the actual clinical trends have not been elucidated in Korea.<sup>10</sup> The purpose of this paper is to investigate the recent trend of cardiac PET/CT usage in Korea, and use of FDG PET/CT for inflammatory and infiltrative heart diseases in the Chonnam National University Hospital (CNUH) and Chonnam National University Hwasun Hospital (CNUHH), and to discuss the further clinical applications of cardiac PET/CT.

## MATERIALS AND METHODS

### 1. Trends of cardiac PET/CT in Korea

The national-wide survey about the cardiac PET/CT was

performed by the Korean Society of Nuclear Medicine (KSNM). This survey data includes information about the cardiac PET/CT in 32 different hospitals in Korea from the 1990s to 2020. Firstly, we analyzed the overall numbers of cardiac PET/CT in each year. Secondly, we further categorized the cardiac PET/CT according to the radiopharmaceuticals. The N-13 NH<sub>3</sub> and F-18 FDG were used for cardiac PET/CT. We analyzed the proportional changes of both radiopharmaceuticals according to the year.

## 2. Trends of cardiac PET/CT for inflammatory and infiltrative heart diseases in CNUH and CNUHH

In addition to the national-wide survey of KSNM, we further analyzed the number of cardiac PET/CT in CNUH and CNUHH. The cardiac PET/CT scans were sorted according to the examined purpose. The number of PET/CT scan for inflammatory and infiltrative heart diseases was analyzed in the whole study period.

## 3. F-18 FDG cardiac PET/CT imaging in CNUH and CNUHH

All patients were instructed to take a low-carbohydrate and high-fat diet for 48 hours followed by 12-18 hours fasting before PET/CT scanning to suppress physiologic myocardial glucose uptake as recommended in cardiac FDG PET/CT guidelines.<sup>11</sup> Blood glucose levels were measured to ensure that the glucose level did not exceed 150 mg/dL. The 50 IU/kg unfractionated heparin was injected 15 minutes before FDG injection. 3.7 or 5.55 MBq/kg of F-18 FDG were injected into the patients intravenously. All scans were performed on combined PET/CT systems (Discovery ST and Discovery ST 600, GE Medical Systems, Milwaukee, WI, USA) at 50 minutes after F-18 FDG injection. Images were reconstructed using a conventional ordered subset expectation maximization algorithm.

## RESULTS

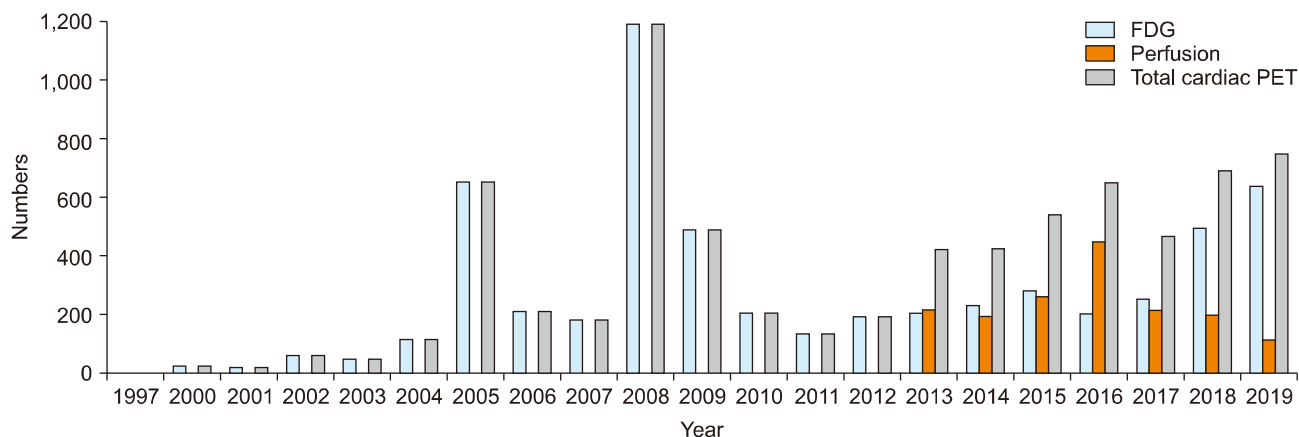
### 1. Trends in use of cardiac PET/CT in Korea

The use of cardiac PET/CT in clinical practice began in the 1990s, with the first official record in 1997, according to the Korean Society of Nuclear Medicine database. It continuously had grown 36-fold as of 2019 with 21 studies in 2000, 491 in 2010, and 749 in 2019. Cardiac FDG PET/CT had its highest clinical use in 2008 (1,192 studies) but showed a decreasing trend of usage until its nadir in 2011 (133 studies) (Fig. 1). The usage rebounded and gradually increased from 2012, reaching 637 studies in 2019. FDG became the main radiopharmaceutical in cardiac PET/CT as well as in oncology. This change mainly led the incremental trends of cardiac PET/CT use in Korea. Although FDG PET/CT is used to evaluate myocardial viability, it is less commonly used since cardiac magnetic resonance imaging has gained clinical relevance. The increase in the number of cardiac FDG PET/CT studies in Korea can be attributed to its use in inflammatory and infiltrative heart diseases.

Myocardial perfusion imaging (MPI) by PET/CT, on the other hand, is currently having its lowest utilization. Its clinical use first appeared in the official record in 2013 followed by a peak in 2016 (448 studies), but declined to 112 studies in 2019. The proportions of FDG PET/CT in cardiac PET/CT was 48% in 2013 (when perfusion PET first began). It decreased to 31% in 2016, when the number of MPI PET/CT was highest, but increased to 85% in 2019, reflecting the recent incremental use of FDG PET/CT in non-coronary heart diseases.

### 2. Trends in the use of cardiac PET/CT in inflammatory and infiltrative heart diseases in CNUH and CNUHH

The first use of cardiac PET/CT in inflammatory and infiltrative heart diseases was found in 2015, when only three studies were performed (Fig. 2). The number of cardiac



**FIG. 1.** Trends of cardiac PET/CT in Korea. The first cardiac PET study began in 1997. Parallel to its oncologic use, FDG PET (blue) peaked in 2008, most of which consisted of viability testing, and decreased to its nadir in 2011. It has again grown up to reach almost the second highest number of studies in 2019, mainly led by the incremental uses in inflammatory and infiltrative heart diseases. The first perfusion PET (orange) appeared on official records in 2013 which peaked in 2016. However, it rapidly declined largely due to its limited availability.

PET/CT for inflammatory and infiltrative heart diseases has constantly grown until it reached 37 in 2020. FDG PET/CT was used for evaluating cardiovascular inflammation (e.g. sarcoidosis, pericarditis) or infection (e.g., infective endocarditis, vascular graft infection) in all cases. A representative case of a female with systemic sarcoidosis and cardiac involvement is summarized in Fig. 3, for whom FDG PET/CT contributed not only to the diagnosis and disease activity evaluation, but also to the follow-up of treatment response.

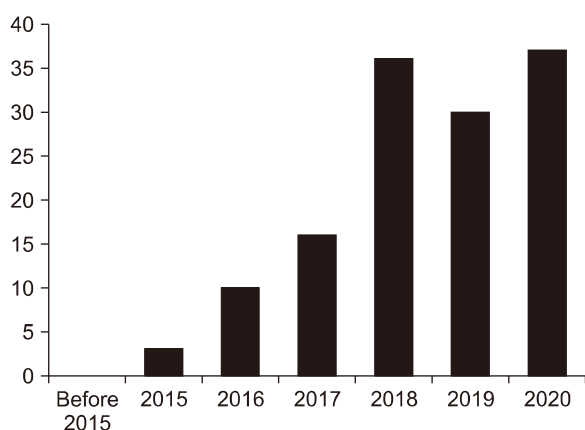
## DISCUSSION

The present study showed that the usage of cardiac PET/CT in inflammatory and infiltrative cardiac diseases has increased, which has paralleled the decreasing tendency of myocardial perfusion PET. This trend was mirrored in both domestic database and our institutional database.

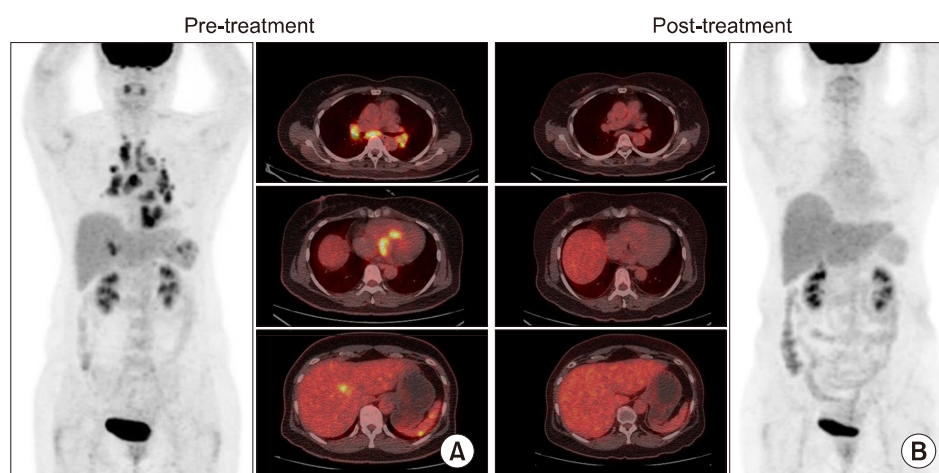
The main cause of changing trend of cardiac diseases in Korea is the rapid aging of Korean population. Increases

of valvular heart disease and arrhythmia were faster than that of coronary artery diseases. The number of patients with arrhythmia increased 57% in 7 years (from 232,547 in 2010 to 365,461 in 2017). The number of patients with valvular heart disease increased 55% in the same period (from 29,308 in 2010 to 45,581 in 2017). The increasing number is notable in aortic valve disease, which was 88% in the same period (from 14,058 in 2010 to 26,448 in 2017). An increase of patients with coronary artery diseases was only 30% in the same period.<sup>6</sup> Non-rheumatic valvular heart diseases became the main cause of valvular heart diseases.<sup>12</sup> In the nationwide database, the use of cardiac FDG PET/CT had two phases of rise in number. The first one was mainly based on its use for myocardial viability testing. This trend did not continue as the prospective clinical trials evaluating myocardial viability testing with FDG PET failed to show its value in the decision of revascularization for ischemic heart failure.<sup>13,14</sup> The use of cardiac FDG PET/CT, which was almost used for viability testing, decreased in the late 2000s and early 2010s. Another emerging imaging study, cardiac magnetic resonance (MR) imaging also accelerated the decreasing use of FDG PET in viability testing, taking advantage of the late gadolinium enhancement (LGE) imaging technique.

Recently, inflammatory and infiltrative heart diseases have become the novel targets of cardiac FDG PET/CT. Inflammatory changes follow many pathologic processes including valvular heart diseases and some infiltrative heart diseases such as cardiac sarcoidosis. Infective endocarditis particularly following prosthetic valve insertion is a deadly disease.<sup>15</sup> Recently, FDG PET/CT is being increasingly used for detection and treatment response evaluation in inflammatory and infiltrative heart diseases. Clinical and imaging guidelines on such diseases stresses the use of cardiac PET/CT and its genuine values in their recommendations. These disease entities include infective endocarditis (particularly prosthetic valve endocarditis), infected cardiac implantable electronic devices, vascular graft infection, large vessel vasculitis, atherosclerosis and valvular disease, cardiac sarcoidosis, and cardiac amyloido-



**FIG. 2.** Number of F-18 FDG PET/CT studies for inflammatory and infiltrative heart diseases in Chonnam National University Hospital and Chonnam National University Hwasun Hospital.



**FIG. 3.** F-18 FDG PET/CT findings in a 56-year-old female with systemic sarcoidosis before (A) and after (B) corticosteroid treatment. (A) Multiple hypermetabolic lesions were observed in the mediastinal lymph node stations, heart, liver, and spleen, indicating the presence of active inflammation. (B) After 6 months of corticosteroid treatment, systemic inflammation was completely resolved.

sis.<sup>7,16-21</sup>

Cardiac MR can be a valuable alternative for evaluating inflammatory and infiltrative heart disease.<sup>22</sup> The LGE of cardiac MR can detect small myocardial involvement lesions in a patient with cardiac sarcoidosis.<sup>23</sup> Therefore, the international expert consensus statement suggests cardiac MR or FDG PET as an advanced imaging technique to patient where cardiac sarcoidosis with abnormal initial screening test results is suspected.<sup>24</sup> In addition, the diffuse subendocardial LGE of cardiac MR is the distinct pattern in cardiac amyloidosis.<sup>25,26</sup> Not only the diagnostic impact, but the presence of transmural LGE is also an independent poor prognostic marker of cardiac amyloidosis patients.<sup>27</sup>

The most important practical consideration for imaging inflammatory and infiltrative heart diseases is suppression of physiologic myocardial FDG uptake. Low-fat high-carbohydrate diet and prolonged fasting for at least for 12 hours were sometimes combined with heparin injection are key factors for suppression of myocardial glucose uptake.<sup>7,16-21</sup> This imaging technique is well accepted in the Korean community of cardiologists and cardiac surgeons as demonstrated in this paper.

The illustrated case shows that FDG PET/CT clearly shows cardiac involvement of sarcoidosis, and the response to steroid therapy (Fig. 2). Although sarcoidosis mostly involves the lungs, cardiac involvement develops in 25% and becomes major cause of death.<sup>28</sup> If the sarcoidosis patient has one or more abnormalities, such as palpitation, syncope, abnormal electrocardiographic or echocardiographic findings, the patient is indicated to undergo imaging studies including FDG PET/CT.<sup>24</sup> FDG PET/CT is mandatory when isolated cardiac sarcoidosis is suspected without evidence of systemic involvements.<sup>29</sup>

This paper has limitations. First of all, the number of cardiac PET/CT is small in authors' institutions and also in Korea. Only data from CNUH and CNUHH was analyzed for inflammatory and infiltrative heart diseases. Analysis of nationwide data is through the use of radiopharmaceutical, which can be reasonably used to assume the application of cardiac PET/CT for inflammatory and infiltrative diseases because FDG is the main radiopharmaceutical for this purpose. Secondly, a comparative analysis with global data was not done. We cited references instead of direct comparison. Despite these limitations we could show an increasing use of cardiac PET/CT for inflammatory and infiltrative heart diseases in Korea. Third, the nationwide survey in Korea is based on voluntary data collection from the domestic institutions, without obligation on strict data quality control. We authors categorized the studies in a highly specific manner, but potential biases during the data input had not been excluded.

In conclusion, cardiac PET/CT tailored for detection of inflammatory processes is useful for both detection and therapy while monitoring inflammatory and infiltrative heart disease. Fusion imaging of PET and CT enhances localization and characterization of even small lesions. Clinical

use of cardiac PET/CT for inflammatory and infiltrative heart diseases is increasing in Korea.

## CONFLICT OF INTEREST STATEMENT

None declared.

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