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ASNC/JSNC JOINT SYMPOSIUM—REVIEW ARTICLE

The Report of ASNC-JSNC Joint Symposium in JSNC 33rd Annual Scientific Meeting

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Abstract

The JSNC-ASNC joint symposium in the 33rd JSNC annual meeting was held on Jun. 24th, and we invited Prof. Mouaz H. Al-Mallah, who was the president of ASNC and requested the lecture entitled "Comparison of MPI and FFR_{CT}". He introduced several cases and evidences reported previously, and summarized the current status of FFR_{CT}, especially about the diagnostic performance, prognostic value, and proper use, compared to MPI.
Keywords: FFR_{CT}, MPI, PET, SPECT
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With the continuation of the cooperative relationship between Japanese Society of Nuclear Cardiology (JSNC) and American Society of Nuclear Cardiology (ASNC), we hold a joint symposium at the JSNC annual meeting and invite a speaker from ASNC each year. JSNC-ASNC joint symposium has been one of the highlight sessions in JSNC annual meetings, since the participants can learn the trend and novel information of nuclear cardiology in USA, and recognize the differences between USA and Japan through the discussion in symposium.

The 33rd JSNC annual meeting in this year was held in Nagasaki, and its theme was "To boldly go where no cardiologist has gone before!" Since this conference was held as the face-to-face format for the first time in a long time as the COVID-19 pandemic subsided, the discussions of each session were very lively and fruitful. The JSNC-ASNC joint symposium was held on Jun. 24th, unfortunately, this program featured only video keynote lecture from ASNC, without the presentations by Japanese experts and discussions.

The theme of this symposium was focused on "FFR_{CT}," which was the noninvasive fractional flow reserve (FFR) derived from standard acquired coronary computed tomography angiography (CCTA). FFR_{CT} has been covered by health insurance since 2018 in Japan, and its usefulness has been recognized and its use is increasing year by year. However, the differences between myocardial perfusion imaging (MPI) and FFR_{CT} has not been well understood, and experiences and knowledges for proper use of both was also insufficient. Therefore, in this joint symposium, we invited Prof. Mouaz H. Al-Mallah, who was the president of ASNC and Houston Methodist DeBakey Heart and Vascular Center, and requested the lecture entitled "**Comparison of MPI and FFR_{CT}**".

I. Diagnostic accuracy of FFR_{CT}

Firstly, Prof. Al-Mallah introduced the case with intermediate stenosis and calcified plaque in left anterior descending artery (LAD) detected by CCTA. Although FFR_{CT} in this case showed significant decrease in LAD distal and the coronary calcium score was 330, PET MPI showed good cardiac function and preserved myocardial flow reserve (MFR) in LAD territory. He explained that the above case had a discrepancy between stress MPI and FFR_{CT}, but the patient was treated conservatively according to the guideline (1). After several months, there was no worsening of symptoms and any cardiac events.

Then he talked about the current achievement of the diagnostic accuracy of FFR_{CT}.

First of all, he explained that FFR_{CT} was the analysis by computer simulation, then, he introduced several evidences about the current status of FFR_{CT}.

1. In NXT trial, per-patient diagnostic performance of FFR_{CT}

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（≤0.8) for significant ischemia defined as FFR≤0.80, compared to CCTA (stenosis＞50%), was reported (2). FFR_{CT} was significantly better in specificity, positive predictive value (PPV), and accuracy. On the other hand, no significant difference in sensitivity and negative predictive value (NPV) between FFR_{CT} and CCTA was observed.

2. Cook, C. et al. reported that FFR_{CT} had wide gray zone of diagnostic accuracy (3). Especially, the accuracy was only 46% in the cases with FFR_{CT} range: 0.7-0.8. On the other hand, the diagnostic accuracy was high in the cases with FFR_{CT} below 0.6 (86%) and above 0.9 (98%).
3. In another report by Beg, F. and Al-Mallah, H. et al. the accuracy of detecting significant stenosis of more than 70% was good for FFR_{CT} >0.9 and <0.6, but poor for 0.6-0.8 (4).
4. The accuracy of FFR_{CT} <0.8 to detect the ischemia defined as invasive instantaneous wave-free ratio (iFR) ＜0.9 dropped to 50% in the cases with FFR_{CT} range 0.7-0.79.
5. In the study of the comparison between FFR_{CT} and the invasive FFR (5), the accuracy of FFR_{CT} for invasive FFR ≤0.8 was decreased as 32% in the cases with range of FFR_{CT}=0.71-0.80.
6. Mickley, H. et al. reported the diagnostic performance of FFR_{CT} in the stable coronary artery disease (CAD) patients with significant coronary calcification (coronary calcium score >400) (6). FFR_{CT} showed high sensitivity (95%), but low specificity (32%) and PPV (47%) for the diagnosis of hemodynamically significant CAD defined as invasive FFR ≤0.8.
7. The PACIFIC Trial (7, 8) showed that FFR_{CT} and PET-MPI with O-15 water were equivalent in primary analysis with AUC＝0.9. However, in the intention-to diagnose analysis, the AUC of PET-MPI was 0.90, which was superior to that of FFR_{CT}＝0.79. single-photon emission computed tomography (SPECT)-MPI and CCTA also have AUCs in the 0.7 range, which was similar to FFR_{CT}.
8. Fairbairn, T.A. et al. showed that the accuracy of FFR_{CT} was low in mild lesions (9).
   ① Normal vessels: 10% of the subjects showed FFR_{CT} <0.80
   ② 0-30% stenosis: 19% showed FFR_{CT} <0.80
   ③ 30-50% stenosis: 44% showed FFR_{CT} <0.80

Based on the above evidences, Prof. Al-Mallah summarized about the diagnostic accuracy of FFR_{CT} and its problems as follows:

① Diagnostic accuracy is not sufficient, especially in mild lesions
② Low quality studies, especially high rejection rate
   - 25% in PACIFIC trial
   - 13% in NXT trial
   - 33% in PROMISE of CTA with intermediate lesion
③ COST >900$: 3-4 folds reimbursement for CCTA in USA
④ It is unavailable to evaluate the patients with stents and coronary artery bypass graft (CABG)

II. The prognostic value and proper use of FFR_{CT}

Prof. Al-Mallah also introduced the case with intermediate stenosis and calcifying plaque in LAD. FFR_{CT} showed <0.5 in LAD, however, PET-MPI showed normal images, and MFR was maintained more than 2.0 in all coronary territories.

Then, he introduced several evidences regarding to the prediction of prognosis.

1. ADVANCE Registry showed that the cases with FFR_{CT} <0.8 had significant worse prognosis (10).
2. Ahmed, A.I. et al. reported about the difference of abnormal rates between machine learning FFR_{CT} (ML-FFR_{CT}) and SPECT-MPI, compared to CCTA anatomic assessment (11).
   ① ML-FFR_{CT} ＜0.8 was present in 41.6% of total subjects
   ② Ischemia on SPECT-MPI was present in 13.8% of total subjects
   ③ The large discrepancy between the positive rate of ML-FFR_{CT} and SPECT-MPI was observed.
   ④ The abnormal rate of ML-FFR_{CT} was high even in the group with low CAD-RAD.
3. In some studies, including the above report, the abnormal rate of FFR_{CT} was 40–60%, while that of SPECT-MPI was low (14–33%) (7, 11–14). Thinking from these results, which is the true, FFR_{CT} is over diagnostic or SPECT is under diagnostic?

As one of the solutions to this question, Prof. Al-Mallah introduced other case which was suspected the coronary lesion with calcified plaque in 3 branches, meaning multi-vessel disease, evaluated by CCTA. Although SPECT-MPI was normal, FFR_{CT} was slightly abnormal with left circumflex artery in the 0.7 range and right coronary artery distal at 0.84. The invasive coronary angiography showed no significant stenosis. Thinking from these results, this case was over diagnosed by FFR_{CT}.

4. Ahmed, A.I. et al, also reported the prognosis value of ML-FFR_{CT} comparison with MPI (11).
   ① There was a significant difference in the event rate of “Death and nonfatal MI,” between the group without and with ischemia by SPECT-MPI; 5.7% (normal MPI) vs 15.4% (with ischemia) (P=0.004)
   ② ML-FFR_{CT} showed no significant difference; 6.2%

(normal FFR_{CT}) vs 8.2% (FFR_{CT} <0.8), P=0.41.

③ Kaplan-Meier curve also showed better separation between the two arms in SPECT-MPI, but almost the same in ML-FFR_{CT}.

④ SPECT-MPI but not ML-FFR_{CT} added incremental prognostic information to CCTA-based anatomical assessment and clinical risk factors in predicting incident outcomes.

5. In the United Kingdom, CCTA has been used as the first approach for the patients with chest pain (15). However, the PPV of FFR_{CT} was low (49%) and the NPV was high (76%). Moreover, the cost was also expensive for FFR_{CT} at 2102 euros, but cheap for SPECT-MPI at 1242 euros (by the way, CMR is 1580 euros).
6. FFR_{CT} development is becoming increasingly competitive and crowded. For example, one software is developing in USA, and the other software is developing in China (onsite type). Totally, more than 5 other solutions are in development. In other words, FFR_{CT} will get better with time.

Based on the information above, Prof. Al-Mallah summarized about how to use FFR_{CT} properly as follows.

① Intermediate lesion on CCTA
② Not heavily calcified vessel
③ No stents or CABG
④ Good image quality, no motion artifacts
⑤ If FFR_{CT} is >0.8, then very reassuring; look at the gradient across lesion or just proximal and mid vessel
⑥ Alternative: stress testing and invasive hemodynamic

Finally, Prof. Al-Mallah concluded this lecture entitled "**Comparison of MPI and FFR_{CT}.**" as follows.

FFR_{CT}

Advantages

① No additional radiation
② Sensitive but not specific
③ Available in 5-10 hr.
④ Helpful for the CT reader

Disadvantages

① Significant additional cost
② Limited outcomes data
③ Cannot be done in patients with stents, CABG, or high calcium score
④ Cannot be done in 10-30% of cases, otherwise
⑤ Limited availability

MPI (PET or SPECT)

Advantages

① Can be done in all patients.
② Can be scheduled quickly
③ Highest accuracy
④ Can be done in patients with stents, CABG or high calcium score
⑤ Excellent validated prognostic value

Disadvantages

① Additional cost
② Additional radiation exposure
③ Limited availability for PET

His lecture was very meaningful for comprehension of the current status of FFR_{CT}, especially its diagnostic performance and prognostic value, compared to those of MPI. And it is also helpful for the proper use and the interpretation of the results of FFR_{CT} in the daily clinical practice.

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Conflicts of interest

None.

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