Predictive Value of ^{68}Ga -FAPI-04 PET/MR for Left Ventricular Remodeling in Patients with Acute Myocardial Infarction

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Research Article

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Abstract

Purpose

To observe longitudinal changes of myocardial fibroblasts activation by ^{68}Ga -labeled fibroblast activation protein inhibitor (^{68}Ga -FAPI-04) PET/MR in patients with ST-segment elevated myocardial infarction (STEMI), and assess its predictive value for late left ventricular remodeling (LVR).

Methods

Forty-two patients with STEMI were included in the study. ^{68}Ga -FAPI-04 PET/MR was performed at baseline (5.1 ± 3.0 days) and at 12 months (12.0 ± 1.1 months) after STEMI. The extent of activated myocardial fibroblasts were quantified using ^{68}Ga -FAPI-04 uptake volume (UV). Infarct size was expressed as late gadolinium enhancement (LGE) volume. LVR was defined as $> 10\%$ increase in left ventricular end-systolic volume (LVESV) from baseline to 12 months measured by echocardiography.

Results

Baseline ^{68}Ga -FAPI-04 uptake volume (UV) was a significant predictor of the change in LVESV ($B = 0.083$, $p = 0.023$) from baseline to 12 months after AMI. The LVR group demonstrated higher ^{68}Ga -FAPI-04 UV at baseline than the non-LVR group ($p = 0.013$). The area under the curve (AUC) of ^{68}Ga -FAPI-04 UV at baseline for predicting the LVR reached 0.833 ($p = 0.019$), with sensitivity of 100.0% and specificity of 60.0%.

Conclusion

^{68}Ga -FAPI-04 PET/MR is a useful tool to non-invasively quantify myocardial fibroblasts activation, and baseline ^{68}Ga -FAPI-04 UV in the early stage of STEMI may have predictive value for the late LVR.

Introduction

Heart failure after acute ST-segment elevated myocardial infarction (STEMI) causes complex and long-term structural cardiac changes known as left ventricular myocardial remodeling (LVR), and may be associated with poor prognosis. Myocardial fibrosis after acute myocardial infarction (AMI) plays a key role in LVR [1]. Fibroblasts are the primary mediators of this response. Following AMI, activated fibroblasts migrate to the infarcted myocardium and produce large amounts of extracellular matrix proteins, promoting the repair and maintaining the structural integrity of the affected tissue. Although initial replacement of dead cardiomyocytes and fibrosis are essential to prevent ventricular wall rupture

after ischemic injury, severe myocardial fibrosis increases ventricular stiffness and chamber dilatation, leading to late LVR and cardiac dysfunction and heart failure.

Fibroblast activation protein (FAP) is a membrane-bound serine protease highly expressed in activated fibroblasts in the infarcted myocardium [2]. Positron emission computed tomography (PET) with Gallium 68-labeled FAP inhibitor (^{68}Ga -FAPI) targeting activated myocardial fibroblasts may provide a visual monitoring tool to help understand the pathogenesis of AMI. Recent studies have showed that ^{68}Ga -FAPI uptake increased on the myocardium of patients with a history of coronary artery disease [3], pulmonary arterial hypertension [4], dilated cardiomyopathy [5], type II diabetes, other diseases associated with myocardial injury, and after chemotherapy or chest radiotherapy [6]; nonetheless, uptake was low in normal myocardium and myocardial scars [7]. Furthermore, a pioneering study in a rat model [8] and clinical studies in patients with AMI [7, 9, 10] showed intense focal uptake of ^{68}Ga -FAPI at the site of occlusion, and suggested a significant correlation between the extent of myocardial fibroblasts activation and myocardial injury in the early post-infarction period [10]. However, there is still lack of data from a longitudinal study to reveal the predictive value of myocardial fibroblast activation by ^{68}Ga -FAPI PET in the early phase of STEMI for late LVR.

Our prospective study using hybrid PET/MR with ^{68}Ga -labeled FAP inhibitor-04 (^{68}Ga -FAPI-04) aimed to quantitatively assess longitudinal changes in myocardial fibroblasts activation, and explore its predictive value for late LVR at 12 months after AMI.

Materials And Methods

Patients

Forty-two patients (39 men and 3 women; average age, 63.4 ± 9.2 years) with ST-segment elevation myocardial infarction were recruited from August 2020 to November 2021 and underwent primary percutaneous coronary intervention (PCI) within 12 h of symptom onset. All patients underwent baseline cardiac ^{68}Ga -FAPI-04 PET/MR scans at 5.1 ± 3.0 days after STEMI. Laboratory tests, including serum N-terminal pro-brain natriuretic peptide (NT-pro-BNP), high-sensitivity C-reaction protein (hsCRP), low-density lipoprotein cholesterol (LDL-C), glycated hemoglobin (HbA1c), creatine kinase MB (CK-MB), and troponin I (TnI) were performed 24h after AMI. Baseline Echocardiography was performed at the day before discharge. Among all 42 patients, 21 patients had completed follow-up echocardiography and NT-pro-BNP test at 12.0 ± 1.1 months after AMI, while 19 of 21 patients underwent follow-up ^{68}Ga -FAPI-04 PET/MR scans at the same time. The study flow chart was shown in Figure 1.

All procedures involving human participants were conducted in accordance with the ethical guidelines of the Declaration of Helsinki and national regulations. The study was approved by the Research Ethics Committee of Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine (2020CER152) and was registered at ClinicalTrials.gov (NCT04723953). All patients gave written informed consent.

⁶⁸Ga-FAPI-04 PET/MR image acquisition

All patients underwent ⁶⁸Ga-FAPI-04 PET on a Biograph mMR system (Siemens, Erlangen, Germany), and no preparation was required. The FAPI precursor DOTA-FAPI-04 was purchased from CSBio Ltd. (Shanghai, China) and radiolabeled as previously described [11]. A 30-min PET scan was performed approximately 60 min after the intravenous injection of 162.1 ± 48.8 MBq of ⁶⁸Ga-FAPI-04. Images were reconstructed using the point-spread function algorithm with 172×172 pixels, four iterations, 21 subsets, and a filter with a full width at half maximum of 2 mm.

Short- and long-axis T2-weighted short-tau inversion recovery (STIR) and late gadolinium enhancement (LGE) images were acquired. STIR images (repetition time, 750 ms; echo time, 140 ms; slice thickness, 8.0 mm; acquisition matrix, 270×270 ; field of view, 256×256 mm; voxel size $1.1 \times 1.1 \times 8.0$ mm) were used to show the anatomy of the heart. A phase-sensitive inversion recovery gradient-recalled echo sequence (repetition time, 930.40 ms; echo time, 1.55 ms; slice thickness, 8.0 mm; acquisition matrix, 256×164 ; field of view, 350×263 mm; voxel size, $1.4 \times 1.4 \times 8.0$ mm) was performed 10 min after the administration of the contrast agent (0.04 mmol/kg; Magnevist, Bayer) to produce LGE images.

PET/MR Image data analysis

PET and MR images were transferred to a Syngo.via workstation (Siemens, Erlangen, Germany) for data registration, integration, and measurement and were reviewed by two experienced nuclear medicine physicians blinded to clinical and biological data of patients.

A volume of interest (VOI) was placed on the left ventricle (LV) to obtain the maximum standardized uptake value (SUV_{max}) of ⁶⁸Ga-FAPI-04 on the infarcted myocardium. The uptake volume (UV) of enhanced ⁶⁸Ga-FAPI-04, defined as the extent of activated myocardial fibroblasts, was automatically calculated using a threshold above mean SUV ($SUV_{mean} \pm 2$ standard deviations in the reference tissue (left ventricular blood pool)). The SUV_{mean} of the infarcted myocardium was obtained by calculating the average activity within the UV. The intensity of myocardial fibroblasts activation was quantified using the maximum and mean target-to-background ratio (TBR_{max} and TBR_{mean}), which were equal to the SUV_{max} and SUV_{mean} of the infarcted myocardium divided by the SUV_{max} and SUV_{mean} in the reference tissue, respectively.

LGE images were analyzed using Segment version 3.1 (<http://segment.heiberg.se>) [12]. Endocardial and epicardial borders were traced manually, excluding papillary muscles. Infarct size (IS) was expressed as LGE volume and the percentage of LGE volume (LGE%) in the LV, and was automatically calculated using the expectation-maximization, weighted-intensity, a priori information (EWA) algorithm [13]. The extent of microvascular obstruction (MVO%), defined as the percentage of low signal area in the LV on LGE images, was also automatically calculated.

The change rate of imaging parameters was defined as the percentage of the difference between the follow-up and the baseline relative to the baseline.

Echocardiography

Echocardiography (GE vivid E9, GE Healthcare, USA) was performed within one week before or after PET/MR scans by an experienced researcher in our hospital. Left ventricular end-diastolic volume (LVEDV), end-systolic volume (LVESV) and ejection fraction (LVEF) was calculated using the biplane Simpson method in two-dimensional apical four-chamber views. Left ventricular myocardial remodeling (LVR) was defined as >10% increase in LVESV from baseline to 12 months after AMI.

Statistical analysis

All statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA) and GraphPad PRISM version 7.0 (GraphPad Software, La Jolla, CA, USA). Data were expressed as mean $\pm$ standard deviation or number (%). Chi-square tests were used to compare categorical variables such as sex, medical history, Killip classification and culprit vessel. Comparison of ^{68}Ga -FAPI-04 uptake between the LGE and MVO areas was performed by paired samples t-test. Correlations between ^{68}Ga -FAPI-04 UV and LGE volume was analyzed using Pearson correlation coefficient and two-tailed analysis of variance. Univariate and multivariate linear regression was used to analyze the predictability of clinical risk factors and imaging parameters. Comparison of ^{68}Ga -FAPI-04 UV at baseline between patients in the LVR and non-LVR groups was performed using independent samples t-test. Receiver operating characteristic (ROC) analysis was used to assess the predicting accuracy of baseline ^{68}Ga -FAPI-04 UV for late LVR. P-values smaller than 0.05 were considered statistically significant.

Results

Myocardial ^{68}Ga -FAPI-04 uptake intensity and volume at baseline

Baseline clinical characteristics and cardiac functional parameters in all 42 patients are summarized in Tables 1, and detailed in Supplemental Table 1–2. TBR_{max} and TBR_{mean} peaked approximately one week after AMI, whereas the extent of activated myocardial fibroblasts defined by ^{68}Ga -FAPI-04 UV was variable (Fig. 2). ^{68}Ga -FAPI-04 UV was significantly correlated ($r = 0.593$, $p < 0.001$) with LGE volume in 40 of 42 patients undergoing both ^{68}Ga -FAPI-04 PET and LGE MR scan at baseline (Fig. 3A). ^{68}Ga -FAPI-04 UV was greater than LGE volume in most patients; nonetheless, ^{68}Ga -FAPI-04 UV was smaller than LGE volume in 2 of 40 patients probably because of very early scans time (1–2 days) after AMI. In addition, The TBR_{mean} of MVO areas was significantly lower than that of LGE areas in 10 patients with $\geq 1.0\%$ MVO ($p = 0.004$), but was still higher than the ^{68}Ga -FAPI-04 uptake of left ventricular blood pool (Fig. 3B).

Representative PET/MR images showed differences between ^{68}Ga -FAP1-04 UV and LGE volume (Figs. 3C and 3D).

Table 1
Clinical characteristics at baseline in all 42 patients

Patients	
Number	42
Demographic and risk factors	
Age (year)	63.4 ± 9.2
Male (n, %)	39 (92.9)
BMI (kg/m ²)	25.2 ± 3.3
SBP (mmHg)	125.8 ± 18.1
DBP (mmHg)	77.2 ± 12.1
Medical history	
Obesity (n, %)	7 (16.7)
Diabetes (n, %)	9 (21.4)
Hypertension (n, %)	24 (57.1)
CAD (n, %)	10 (23.8)
Killip classification	
I (n, %)	33 (78.6)
II (n, %)	9 (21.4)
III-IV (n, %)	0 (0)
Culprit vessel	
LAD (n, %)	29 (69.0)
LCX (n, %)	4 (9.5)
RCA (n, %)	9 (21.4)
Clinical presentation	
NT-pro-BNP (pg/ml)	1701.9 ± 2094.6
hsCRP (mg/L)	52.9 ± 69.9
LDL-C (mmol/L)	3.0 ± 1.0
HbA1c (%)	6.4 ± 1.7

Data were expressed as mean ± standard deviation, or numbers (%).

	Patients
CK-MB (ng/ml)	218.7 ± 261.6
TnI (ng/ml)	93.8 ± 93.2
LVEDV (ml)	123.9 ± 26.7
LVESV (ml)	52.3 ± 16.9
LVEF (%)	57.8 ± 7.3
Data were expressed as mean ± standard deviation, or numbers (%).	

Both the intensity and extent of myocardial fibroblasts activation decreased from baseline to 12-months follow-up. ^{68}Ga -FAPI-04 UV at 12 months after AMI still showed a significant correlation with LGE volume ($r = 0.534$, $p = 0.019$), but the change rate of ^{68}Ga -FAPI-04 UV from baseline to follow-up was not significantly correlated with that of LGE volume ($r = 0.431$, $p = 0.065$).

Relationship Between Baseline Ga-fapi-04 Uv And Late Lvr

In 21 patients who fulfilled 12 months follow-up (Supplemental Table 3–4), both LVESV ($p < 0.001$) and LVEDV ($p < 0.001$) more significantly increased from baseline to 12-months follow-up, and LVEF tended to reduce in the LVR group ($n = 6$) compared with the non-LVR group ($n = 15$) ($p = 0.075$) (Supplemental Fig. 1A-1C).

Univariate linear regression analysis showed that both LAD culprit vessel ($B = -28.264$, $p = 0.005$) and ^{68}Ga -FAPI-04 UV ($B = 0.114$, $p = 0.048$) had a predictive value on the change rate of LVESV during 12 months after STEMI. Multivariate linear regression analysis indicated that besides the LAD culprit vessel, diabetes and hypertension, ^{68}Ga -FAPI-04 UV ($B = 0.083$, $p = 0.023$) was still a significant predictor of the change rate of LVESV (Table 2). As shown in Fig. 4A, the LVR group demonstrated higher baseline ^{68}Ga -FAPI-04 UV compared to the non-LVR group ($p = 0.013$). The area under the curve (AUC) of baseline ^{68}Ga -FAPI-04 UV for predicting the LVR reached 0.833 ($p = 0.019$), with sensitivity of 100.0% and specificity of 60.0% when the cut-off value was 128.15 cm^3 (Fig. 4B). In addition, neither the change rate of ^{68}Ga -FAPI-04 UV nor LGE volume from baseline to follow-up was not significantly correlated with that of LVESV.

Table 2
Predictability of the change in LVESV after AMI by univariate and multivariate analysis

	Univariate linear regression analysis			Multivariate linear regression analysis		
	p	B	95% CI for B	p	B	95% CI for B
Clinical risk factors						
Sex	0.383	-21.315	-71.218 ~ 28.588	0.683	-6.060	-39.016 ~ 26.894
Age (y)	0.427	0.473	-0.747 ~ 1.695	0.969	0.008	-0.448 ~ 0.464
LAD culprit vessel	0.005*	-28.264	-46.85 ~ -9.678	< 0.001*	-24.064	-32.853 ~ -15.274
Hypertension	0.058	19.172	-0.723 ~ 39.067	< 0.001*	26.035	17.322 ~ 34.747
Diabetes	0.136	-19.363	-45.379 ~ 6.652	0.008*	-19.791	-32.755 ~ -6.826
Hyperlipidemia	0.096	-28.682	-62.977 ~ 5.614	0.216	-10.979	-29.848 ~ 7.888
Imaging parameters						
TBR _{max}	0.572	-1.023	-4.743 ~ 2.697	0.362	2.595	-3.594 ~ 8.784
TBR _{mean}	0.491	-1.569	-6.251 ~ 3.113	0.206	-4.743	-12.694 ~ 3.206
UV (cm ³)	0.048*	0.114	0.001 ~ 0.226	0.023*	0.083	0.014 ~ 0.151
LGE volume (ml)	0.778	0.057	-0.366 ~ 0.482	0.612	-0.173	-0.933 ~ 0.585
LGE (%)	0.556	-0.218	-0.981 ~ 0.544	0.114	-0.677	-1.558 ~ 0.203
MVO (%)	0.583	1.282	-3.528 ~ 6.093	0.087	2.982	-0.547 ~ 6.512
*: statistical significance; B: coefficient; CI: confidence interval						

Representative PET/MR images showed that a large extent of myocardial fibroblasts activation may be associated with late LVR in patient No. 7 (Fig. 5). Additionally, ⁶⁸Ga-FAPI-04 uptake was observed at the remote non-LGE area in patient No. 7. Cardiac angiography showed an occlusion of distal branch of right coronary artery (RCA) that dominated this area. In contrast, a small ⁶⁸Ga-FAPI-04 UV in patient No. 4 was associated with a good cardiac functional outcome (Fig. 6).

Discussion

Our initial longitudinal observational study demonstrates that hybrid ^{68}Ga -FAPI-04 PET/MR may be a useful tool to non-invasively quantify activated myocardial fibroblasts and meanwhile assess cardiac morphological changes in patients with STEMI. Baseline ^{68}Ga -FAPI-04 UV detection may have a predictive value for later LVR in STEMI patients.

Longitudinal ^{68}Ga -FAPI-04 PET imaging allowed observing dynamic changes of activated myocardial fibroblasts after STEMI. As early as 1–2 days after AMI, ^{68}Ga -FAPI-04 uptake was smaller than that of LGE signal, suggesting the fact that inflammatory edema occurs earlier than myocardial fibroblasts activation in the infarcted area. Infarct healing has two phases: inflammatory (0–4 days), characterized by robust immune cell infiltration and tissue digestion, and reparative (lasting 10–14 days), manifested by myofibroblast conversion and proliferation and tissue repair [14]. Increased extracellular interstitial volume caused by edema in the inflammatory phase is rapidly demonstrated as increased signal on LGE images [15], while the activation of myocardial fibroblasts, which are generally originated from fibroblasts in response to TGF- β and other growth factors including platelet-derived growth factor along with the impact of neutrophils [16], peaked after inflammatory phase following AMI. Subsequently, different from ^{68}Ga -FAPI-04 uptake in the animal model of myocardial infarction declined to background levels within 2 weeks due to decreased number of activated myofibroblasts and increased apoptosis of myofibroblasts during the healing phase (14 days to several months after AMI), ^{68}Ga -FAPI-04 uptake of infarcted myocardium in all patients of our study could be observed as long as one year after AMI, suggesting that activated myocardial fibroblasts involved in human cardiac repair or LVR exist much longer than that in the animal model.

LGE MR imaging is currently the preferred technique for evaluating myocardial fibrosis. Unlike the principle of cardiac LGE MR imaging which is based on the widening of the extracellular gap in the infarcted area resulting in the retention of gadolinium, PET imaging with ^{68}Ga -FAPI-04 tracer as a new technique reflects the state of myocardial fibroblasts activation. The different principles of these two imaging techniques make their imaging characteristics show differences. First, ^{68}Ga -FAPI-04 UV was significantly correlated with LGE volume, but the extent of activated myocardial fibroblasts was larger than LGE volume in most patients, which may be due to the recruitment of activated fibroblasts on the edge of AMI area [8]. Second, the LGE signal confounded effects of edema and myocardial fibrosis throughout the inflammatory and repair period after AMI, while ^{68}Ga -FAPI-04 PET more specifically showed the distribution and intensity of myocardial fibroblasts activation. Third, in line with a previous study [9], ^{68}Ga -FAPI-04 uptake could be observed in the remote non-LGE myocardium. It might be related to microscopic myocardial infarction due to the occlusion of distal small branch of culprit vessel, which is sensitively detected by ^{68}Ga -FAPI-04 PET but not by LGE MR imaging.

Furthermore, compared to LGE volume, ^{68}Ga -FAPI-04 UV at baseline demonstrated better prediction of late LVR including increased LVESV and LVEDV accompanied with reduced LVEF, although infarct size on LGE MR strongly correlated with cardiac outcomes [17, 18]. Previous studies showed uncertain predictive power of infarct size for late LVR because of high individual variability, i.e., a portion of patients with large

infarct size might not incur late LVR on follow-up, while those with a limited infarct size might unexpectedly suffer late LVR [17, 19]. Persistent and dysregulated inflammation response may be one of important participants in the development of late LVR [19]. Since myocardial fibroblast is activated by inflammatory factors, ^{68}Ga -FAPI-04 UV might not only correlate with infarct size as shown in our study, but also indirectly reflect the intensity of cardiac inflammatory response, which may be the reason why ^{68}Ga -FAPI-04 UV demonstrated better predictive value for late LVR than conventional LGE volume. However, it should be noted that though ^{68}Ga -FAPI-04 UV was a significant predictor of late LVR, there was partial overlap in ^{68}Ga -FAPI-04 UV between the LVR and non-LVR groups. Our results showed that LAD culprit vessel, diabetes and hypertension might be also attributable in the late LVR. In fact, previous studies have indicated that late LVR occurrence was also associated with other factors such as neurohormonal activations [20], humoral factors including cytokines and associated growth factors [21, 22], and chronic systemic inflammation due to metabolic causes including diabetes and hyperlipidemia [22] suggesting the complexity of mechanisms underlying the development of late LVR. Nevertheless, ^{68}Ga -FAPI-04 UV at approximately one week after AMI may be a promising predictive imaging indicator for late LVR, which will likely make ^{68}Ga -FAPI-04 PET/MR an important workflow in the future for monitoring the efficacy of related drugs that act directing on the myocardial fibrosis process [23] or combat ongoing dysregulated inflammation [24].

The present study has the following limitations: (1) Only patients with relatively mild symptoms (Killip class I and II) who could tolerate long scan time of PET/MR were enrolled in the present study; therefore, data on patients with severe symptoms (Killip III and IV [25]), who are more likely to have serious LVR and poor cardiac functional outcomes, were limited; (2) Only 21 of 42 patients had 12-months follow-up data, which could imply a risk of selection bias. However, we compared baseline clinical characteristics of 21 patients who fulfilled 12-months follow-up to all enrolled 42 patients. No significant difference was observed between these two cohorts (Supplemental Table 5); (3) Although ^{68}Ga -FAPI UV have shown to be very valuable in predicting LVR, strong conclusions still require larger samples to be obtained.

Conclusions

Overall, ^{68}Ga -FAPI-04 PET/MR is a useful tool to non-invasively quantify myocardial fibroblasts activation, and baseline ^{68}Ga -FAPI-04 UV in the early stage of STEMI may have predictive value for the late LVR.

Declarations

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Disclosures

The authors have declared that no competing interest exists.

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Ethical approval

All procedures involving human participants were conducted in accordance with the ethical guidelines of the Declaration of Helsinki and national regulations. The study was approved by the Research Ethics Committee of Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine (2020CER152) and was registered at ClinicalTrials.gov (NCT04723953).

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Figures

Figure 1

Study Flow Chart

Flow chart showing selection and attrition of patients through the study.

Figure 2

Myocardial ^{68}Ga -FAPI-04 uptake intensity and volume at baseline

TBR_{max} (green triangle) and TBR_{mean} (red square) of ^{68}Ga -FAPI-04 uptake in the myocardium increased from days 1-3 to days 4-8 after AMI. There was interpatient variability in ^{68}Ga -FAPI-04 UV (blue circles).

Figure 3

Comparison between $^{68}\text{Ga-FAPI-04}$ UV and LGE volume at baseline

(A) $^{68}\text{Ga-FAPI-04}$ UV on PET images was significantly correlated ($r = 0.593, p < 0.001$) with LGE volume at baseline. $^{68}\text{Ga-FAPI-04}$ UV was larger than LGE volume in most patients, but was smaller than LGE volume in only two patients (the dot at the bottom right of the dashed line). Representative PET/MR

images showed differences between ^{68}Ga -FAPI-04 UV and LGE volume. (B) The TBR_{mean} of MVO areas was significantly lower than that of LGE areas in 10 patients with $\geq 1.0\%$ MVO ($p = 0.004$), but was still higher than the ^{68}Ga -FAPI-04 uptake of blood pool. (C) Patient No. 2 (male, 55 years old, with LAD occlusion) presented a ^{68}Ga -FAPI-04 UV (241.18 cm^3) greater than LGE volume (115.10 ml) on the front, septum, and lower wall of the left ventricle (white arrow) 8 days after AMI. The MVO area (red dashed line) showed much lower ^{68}Ga -FAPI-04 uptake ($\text{TBR}_{\text{mean}} = 2.27$) than those without MVO ($\text{TBR}_{\text{mean}} = 3.59$). (D) ^{68}Ga -FAPI-04 UV (4.70 cm^3) in patient No. 3 (male, 66 years old, with LAD occlusion) was much smaller than LGE volume (38.9 ml) on the left ventricular septum probably because of very early scan (2 days) after AMI.

Figure 4

Relationship between baseline ^{68}Ga -FAPI-04 UV and late LVR

(A) In 21 patients with follow-up, the LVR group ($n = 6$) demonstrated higher ^{68}Ga -FAPI-04 UV at baseline than the non-LVR group ($n = 15$) ($p = 0.013$). (B) The AUC of ^{68}Ga -FAPI-04 UV at baseline for predicting the LVR reached 0.833 ($p = 0.019$), with sensitivity of 100.0 % and specificity of 60.0 % when the cut-off value was 128.15 cm^3 .

Figure 5

Representative ^{68}Ga -FAPI-04 PET/MR images in a patient with late LVR

LGE MR scan (upper line) and ^{68}Ga -FAPI-04 PET/T2 STIR scan (lower line) on Day 5 (A), and Day 332 (B) after AMI were performed in patient No. 7 (male, 66 years old, with RCA occlusion). Large ^{68}Ga -FAPI-04 UV (small red arrow) was observed at both baseline (251.3 cm³) and follow-up scan (229.3 cm³). More importantly, NT-pro-BNP levels from baseline to follow-up only decreased by 35.8%. LVEDV and LVESV increased by 36.4% and 56.2%, respectively, and LVEF decreased by 11.8%, indicating adverse LVR. Additionally, ^{68}Ga -FAPI-04 uptake was observed in the remote non-infarcted LV myocardium (big red arrow). Cardiac angiography showed an occlusion (C) and a recanalization (D) of a distal branch of RCA (red arrow) before and after PCI. Poor contrast enhancement in the remote non-LGE myocardium might be associated with microscopic myocardial infarction. However, myocardial fibroblasts activation in the microscopic infarcted area was detected by ^{68}Ga -FAPI-04 PET.

Figure 6

Representative ^{68}Ga -FAPI-04 PET/MR images in a patient with good cardiac functional outcomes

Patient No. 4 (male, 64 years old, with LAD occlusion) underwent LGE MR (upper line) and ^{68}Ga -FAPI-04 PET/T2 STIR MR (lower line) on Day 4 (A) and Day 370 (B) after AMI. The ^{68}Ga -FAPI-04 UV (red arrow) at baseline and follow-up was 82.8 cm³ and 15.4 cm³, respectively. LVEDV and LVESV decreased by 5.6% and 5.7%, respectively with stable LVEF (67%) indicating good cardiac functional outcomes.

Supplementary Files

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- [SupplementalMaterials.docx](#)