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Research Letter

Comparison of intracoronary physiological assessment for the non-left anterior descending artery in patients with non-obstructive coronary artery disease: Insight from ^{13}N-ammonia positron emission tomography findings

1. Introduction

Intracoronary physiological assessment (IPA) via thermodilution is commonly used to interrogate the left anterior descending artery (LAD) to evaluate coronary microvascular dysfunction (CMD) in patients with non-obstructive coronary artery disease (CAD). However, the inter-territorial agreement and whether non-LAD interrogation provides representative global information remain unclear. This study evaluated the inter-territorial agreement of invasive physiological parameters in patients with suspected CMD compared with myocardial perfusion positron emission tomography (PET) findings.

2. Methods

We identified 34 patients with angina and non-obstructive CAD confirmed by coronary computed tomography angiography (<50% diameter stenosis) who underwent an IPA for two major coronary arteries [LAD plus left circumflex (LCX) or right coronary artery (RCA)] simultaneously, and ^{13}N-ammonia perfusion PET within 3 months of the IPA between 2022 and 2025 (Online Fig. 1). During the invasive diagnostic procedures, coronary flow reserve (CFR), index of microcirculatory resistance (IMR), and microvascular resistance reserve (MRR) [1] were measured via bolus thermodilution using the CoroVentis CoroFlow System (Abbott Vascular, Abbott Park, IL, USA); and a stepwise dose-escalating acetylcholine spasm provocation testing was performed before the IPA in all patients [2]. Perfusion PET provided quantitative measurements of myocardial flow reserve (MFR) globally and by territories. The study was approved by our Institutional Review Board (No. 20216). Differences and correlations were assessed using Wilcoxon rank-sum, McNemar, and Pearson correlation tests.

3. Results

The study patients (median 72 years; 50% male) underwent the IPA for the LAD and non-LAD (LCX: 12, RCA: 22). Detailed clinical and PET findings are shown in Online Tables 1 and 2. Correlations between the LAD and non-LAD were moderate for CFR ($r = 0.55$, $p < 0.001$), IMR ($r = 0.42$, $p = 0.01$), and MRR ($r = 0.55$, $p < 0.001$) (Fig. 1). In contrast, strong correlations were observed in MFR between the LAD and non-LAD ($r = 0.84$, $p < 0.0001$) and between global and LAD-MFR ($r = 0.98$, $p < 0.0001$). Additionally, correlations of LAD-CFR with global MFR ($r = 0.46$, $p = 0.006$) and LAD-MFR ($r = 0.48$, $p = 0.004$) were moderate. Notably, in 29 patients with vessel-FFR ≥0.80, correlations remained consistent (LAD-CFR vs. non-LAD-CFR: $r = 0.53$, $p = 0.003$) (Online Fig. 2). Spasm provocation testing was positive in 23 patients (68%) (either epicardial or microvascular spasm), with no significant differences in physiological parameters between spasm-positive and spasm-negative patients (Online Table 3). Non-negligible diagnostic disagreements occurred between the LAD and non-LAD for CFR (24%), IMR (35%), and MRR (29%) based on standard cut-offs (i.e. CFR <2.0, IMR ≥25, and MRR ≤3.0 for abnormality) [1,2], highlighting the potential reclassification of CMD when moving from global MFR to vessel-specific invasive indices.

4. Discussion

This study found strong correlations in MFR between the LAD and non-LAD, indicating relatively small inter-territorial variation in PET-derived MFR in this cohort. In contrast, invasively measured CFR, IMR, and MRR showed only moderate correlations, with non-negligible diagnostic discordance between territories. Additionally, the presence of potential epicardial disease or coronary spasm did not significantly alter these inter-territorial relationships. Therefore, the exact mechanisms underlying this discrepancy remain uncertain and may involve both methodological factors inherent to bolus thermodilution (e.g. manual injection technique) and potential, localized physiological heterogeneity that was not captured by PET.

Based on PET findings, a single-vessel approach using the LAD aligns with current guidelines [2] and appears relevant for most cases. However, a multi-vessel approach should be considered in selected cases, such as those with inconclusive findings or anatomically unsuitable LADs (e.g. severe tortuosity, small vessel diameter, or significant myocardial bridging). Importantly, PET and IPA are not theoretically interchangeable; PET assesses tissue-level perfusion, whereas IPA evaluates vessel-specific physiology. Thus, high correlations between CFR and MFR may not be expected [3]. While our PET findings might suggest the potential utility of prior PET imaging or a single-vessel approach using the LAD, these implications remain speculative and warrant further investigation in larger cohorts.

Limitations include individual variability in coronary dominance affecting regional MFR and the inclusion of patients with near-normal physiological values, which may have influenced the observed correlations.

5. Conclusions

Invasively measured CFR showed non-negligible inter-territorial discordance despite relatively small inter-territorial variation in MFR. Localized physiological indices should be interpreted with caution, since the underlying mechanisms of this discrepancy remain uncertain and may include both procedural variability and true physiological heterogeneity.

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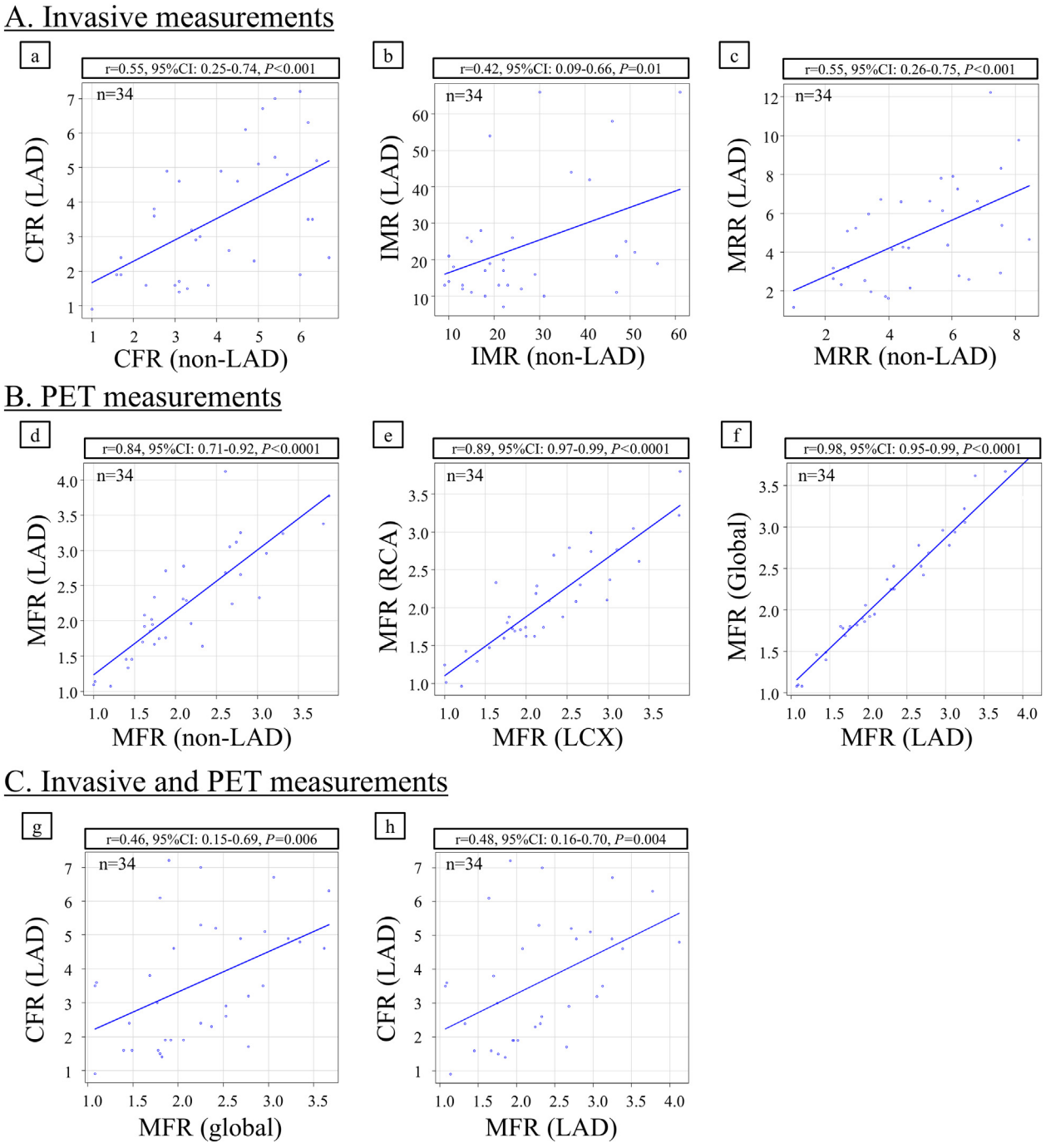

Fig. 1. Correlations observed in the study. (A) Correlations of bolus thermodilution-derived CFR, IMR, and MRR between the LAD and non-LAD. (B) Correlations of PET-derived MFR among territories. (C) Correlations of LAD-CFR with global MFR and LAD-MFR.
CFR, coronary flow reserve; IMR, index of microcirculatory resistance; LAD, left anterior descending artery; MFR, myocardial flow reserve; MRR, microvascular resistance reserve; PET, positron emission tomography.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jjcc.2026.07.007.

References

[1] Hoshino M, Hoek R, Jukema RA, Dahdal J, van Diemen P, Raijmakers P, et al. Homogeneity of the coronary microcirculation in angina with non-obstructive coronary artery disease. Eur Heart J Cardiovasc Imaging 2025;26:1120–7.
[2] Hokimoto S, Kaikita K, Yasuda S, Tsujita K, Ishihara M, Matoba T, et al. JCS/CVIT/JCC 2023 guideline focused update on diagnosis and treatment of vasospastic angina (coronary spastic angina) and coronary microvascular dysfunction. Circ J 2023;87:879–936.

[3] Everaars H, de Waard GA, Driessen RS, Danad I, van de Ven PM, Raijmakers PG, et al. Doppler flow velocity and thermodilution to assess coronary flow reserve: a head-to-head comparison with [(15)O]H(2)O PET. JACC Cardiovasc Interv 2018;11:2044–54.

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