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Short communication

Prognostic implication of thermodilution coronary flow reserve in patients with indeterminate pressure-bounded coronary flow reserve

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ABSTRACT

Background: Recently, the concept of pressure-bounded coronary flow reserve (PB-CFR) has been introduced. However, using pressure-only data, a substantial proportion of patients could not be classified into high or low PB-CFR and remained as indeterminate PB-CFR. The current study evaluated the prognostic implication of thermodilution-based CFR (thermo-CFR) in patients with indeterminate PB-CFR.

Methods: Among 199 patients (211 lesions) with indeterminate PB-CFR, 170 patients (179 lesions) with deferral of revascularization were analyzed for the current study. The rates of patient-oriented composite outcomes (POCO, a composite of all-cause mortality, any myocardial infarction, and any ischemia-driven revascularization) were compared according to thermo-CFR. All patients underwent fractional flow reserve (FFR) and thermo-CFR measurements. Thermo-CFR ≤ 2.0 was classified as low thermo-CFR. The median follow-up duration was 1350.0 (Q1-Q3 1252.0–1468.0) days.

Results: Mean angiographic percent diameter stenosis, FFR, and thermo-CFR were 42.3 ± 13.9, 0.84 ± 0.06, and 3.10 ± 1.15, respectively. Among 170 patients, 36 patients (21.2%) showed low thermo-CFR. Patients with low thermo-CFR showed significantly higher rate of POCO compared to those with high thermo-CFR (30.6% vs. 3.0%, HR 12.117, 95% CI 3.854–38.091, $p < 0.001$). Adding thermo-CFR to a prediction model with FFR significantly increased discrimination and reclassification index for the risk of POCO (c-index 0.545 vs. 0.766, $p = 0.002$, category-free net reclassification index 1.169, $p < 0.001$, relative integrated discrimination index 31.828, $p < 0.001$).

Conclusions: Patients with low thermo-CFR showed a significantly higher risk of POCO compared to those with high thermo-CFR among patients with indeterminate PB-CFR. Thermo-CFR showed additional prognostic implication, in addition to FFR, in patients with indeterminate PB-CFR.

1. Introduction

Coronary physiologic assessment and ischemia-guided percutaneous coronary intervention (PCI) have become a standard practice. Fractional flow reserve (FFR) is the reference standard method to evaluate the functional significance of an epicardial coronary stenosis [1,2]. Coronary flow reserve (CFR) represents the vasodilator capacity of the entire coronary circulation during hyperemia [1,2]. Although these 2 different physiological indices have complementary roles in the evaluation of patients with coronary artery disease, measurement of invasive CFR using thermodilution-technique (thermo-CFR) or Doppler-wire is technically more challenging than FFR [3].

Recently, the method of estimating CFR using pressure data only, pressure-bounded CFR (PB-CFR), has been introduced [4,5]. The concept of PB-CFR is based on the calculation of lowest and highest possible value of CFR using resting and hyperemic ratio of aortic pressure (Pa) and distal coronary pressure (Pd) and PB-CFR classifies the lesions

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into low or high PB-CFR [4,5]. However, many interrogated lesions are categorized into the indeterminate PB-CFR due to its methodological limitation [4]. Therefore, the practical role of PB-CFR might be limited, as the clinical relevance of invasive physiologic assessment is especially important in anatomically or physiologically intermediate stenosis. In this regard, the current study sought to evaluate the prognostic implication of thermo-CFR in lesions with indeterminate PB-CFR.

2. Methods

The study population was selected from the Korean 4-center comprehensive physiologic assessment registry [6]. Briefly, between April 2009 and September 2013, consecutive patients who underwent clinically indicated invasive coronary angiography and FFR, CFR, and index of microcirculatory resistance (IMR) measurements for ≥1 coronary artery were enrolled from 4 university hospitals in Korea. Patients with hemodynamic instability, left ventricular dysfunction, acute myocardial infarction (MI), or a culprit vessel of acute coronary syndrome were excluded. The study protocol was in accordance with the Declaration of Helsinki (clinicaltrials.gov identifier, NCT02186093).

FFR was calculated by mean distal coronary pressure (Pd) / aortic pressure (Pa) during maximal hyperemia induced by continuous infusion of adenosine (140 μg/kg/min), using the pressure-temperature sensor guide wire (Abbott Vascular, Santa Clara, CA, USA). To derive resting and hyperemic mean transit time (Tmn), a thermodilution curve was obtained by using 3 injections of 4 mL of room-temperature saline. Thermo-CFR was calculated by resting Tmn/hyperaemic Tmn. The IMR was calculated by Pd × hyperaemic Tmn.

PB-CFR was calculated as previously published [4]. As the possible CFR value can be bounded from $\sqrt{\frac{1-\text{Hyperemic Pd/Pa}}{1-\text{Resting Pd/Pa}}}$ to $\frac{1-\text{Hyperemic Pd/Pa}}{1-\text{Resting Pd/Pa}}$, lesions with upper-bounded PB-CFR < 2 were classified as low PB-CFR, and those with lower-bounded PB-CFR ≥ 2, as high PB-CFR. When the boundary crossed the value of 2, the lesion was classified to have indeterminate PB-CFR [4]. In our study cohort, a total of 199 patients (211 interrogated vessels) were classified into indeterminate PB-CFR. Among those patients, 170 patients (179 lesions) with deferral of revascularization were included for the current analysis. The clinical outcomes during median follow-up of 1350.0 (IQR 1252.0–1468.0) days were compared, according to thermo-CFR values, in this group. The cut-off values of ≤0.80 or ≤2.0 were used for FFR and thermo-CFR, respectively [6]. The primary outcome was patient-oriented composite outcomes (POCO), including all-cause mortality, any MI, and any ischemia-driven revascularization, defined according to the Academic Research Consortium.

3. Results

Among the total 487 patients (725 vessels), 199 patients (211 vessels) with indeterminate PB-CFR were selected. After exclusion of 29 patients

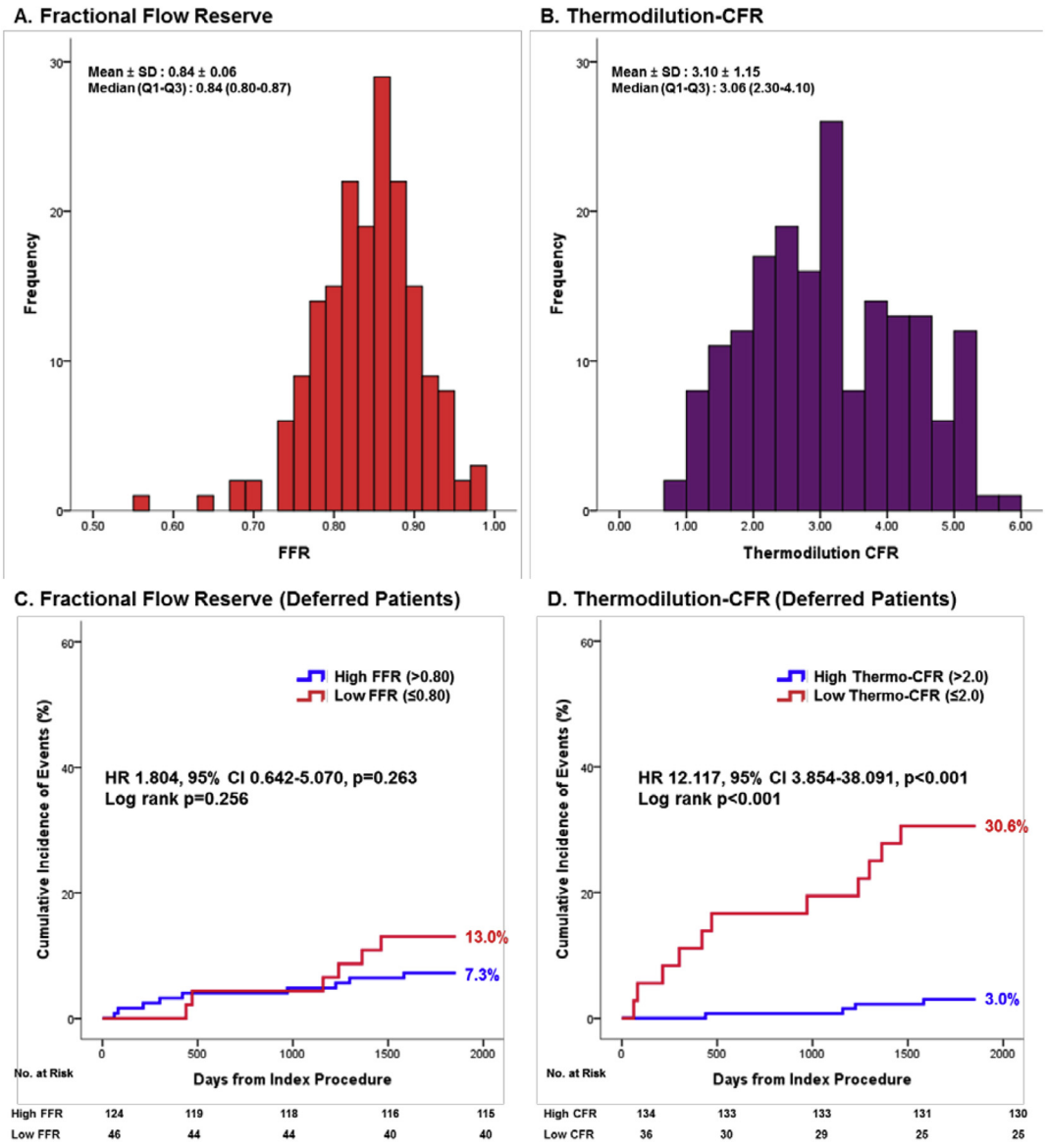

Fig. 1. Distribution of FFR and thermodilution-CFR and comparison of clinical events according to fractional flow reserve and thermodilution-CFR among patients with indeterminate pressure-bounded CFR. Distribution of (A) FFR and (B) thermodilution-CFR among 170 patients with indeterminate PB-CFR are presented. Comparison of rates of POCO (C) between high and low FFR or (D) between high and low thermodilution-CFR among patients with indeterminate PB-CFR are presented. Abbreviations: CFR, coronary flow reserve; FFR, fractional flow reserve; PB-CFR, pressure-bounded CFR.