Prevalence of OCT-defined high-risk plaque in relation to physiological characteristics by fractional flow reserve and coronary flow reserve

Prevalencia de placas de alto riesgo definidas por OCT y su relación con la reserva fraccional de flujo y la reserva de flujo coronario

To the Editor,

Fractional flow reserve (FFR) has firmly proven clinical value in randomized clinical trials.[1] Coronary flow impairment can alternatively be assessed by coronary flow reserve (CFR), which has also been shown to provide significant prognostic information of adverse outcomes when reduced, regardless of the presence or absence of epicardial stenosis.[2,3] Patients with preserved FFR with reduced CFR have been reported to exhibit worse outcomes than those with preserved FFR and CFR. Conversely, compared with patients with concordantly ischemic FFR and CFR, those with ischemic FFR with preserved CFR showed better outcomes.[4] Although we previously reported that lower FFR and microvascular dysfunction were independent predictors of the presence of optical coherence tomography (OCT)-defined thin-cap fibroatheroma (TCFA),[5] no comparisons have been reported on the basis of FFR/CFR quadrants regarding OCT-derived high-risk plaque features.

We retrospectively investigated 473 de novo intermediate coronary artery lesions (30%-80% visual stenosis) from 419 patients who underwent OCT and physiological assessments during the same procedure. OCT images were acquired with the frequency domain OCT systems (ILUMIEN, Abbott Vascular, Santa Clara, California, United States; or LUNAWAVE, Terumo, Tokyo, Japan). Physiological assessments were performed using a Pressure Wire Certus as previously described.[2] The prevalence of TCFA and plaque rupture (PR) were evaluated. Established cutoff values of pressure-derived physiologic indices (FFR $\leq$ 0.80 and CFR $\leq$ 2.0) were used to divide FFR/CFR into quadrants in 2 concordantly classified [FFR+/CFR + (173 vessels) and FFR-/CFR- (103 vessels)] and 2 discordantly classified [FFR + /CFR- (171 vessels) and FFR-/CFR + (26 vessels)] groups. OCT-derived plaque characteristics were compared among FFR/CFR quadrants.

CFR was correlated to FFR (r = 0.454, $P < .001$) and FFR-based decision making disagreed with that of CFR in 41.7% (197 vessels). TCFAs and PRs were detected in 66 vessels (14.0%) and 73 vessels (15.4%) in the total cohort. The patient and lesion characteristics of the FFR/CFR quadrants are summarized in table 1. Compared with the FFR-/CFR + group, patients in the FFR + /CFR- group were significantly younger. There were no significant differences in the prevalence of nonculprit lesions of acute coronary syndrome among the 4 quadrants. The prevalence of TCFAs and PRs were significantly different among the 4 quadrants (figure 1A,B). Compared with

Table 1
Patient and lesion characteristics

	Total	FFR + /CFR + 4	FFR + /CFR-2	FFR-/CFR + 3	FFR-/CFR-1	*P*
Vessels, No.	473	173	171	26	103	
Patients, No.	419	136	161	26	96	
Baseline characteristics						
Age, y	68.0 [61.0-74.0]	69.0 [61.0-75.5]	66.0 [60.0-72.0]	72.5 [66.0-77.5]	69.0 [60.0-74.3]	.004[a]
Female	82 (19.6)	29 (21.5)	25 (15.4)	8 (30.8)	20 (20.8)	.236
Hypertension	294 (70.2)	95 (70.4)	113 (69.8)	19 (73.1)	67 (69.8)	.988
Diabetes mellitus	162 (38.7)	63 (46.7)	58 (35.8)	12 (46.2)	29 (30.2)	.052
Dyslipidemia	283 (67.5)	84 (62.2)	108 (66.7)	18 (69.2)	73 (76.0)	.172
Current smoker	125 (29.8)	35 (25.9)	48 (29.6)	9 (34.6)	33 (34.4)	.528
Ejection fraction, %	64.0 [58.0-69.0]	63.0 [55.5-68.5]	64.5 [59.0-69.0]	64.0 [57.3-68.5]	65.0 [60.0-69.3]	.288
eGFR, mL/min/1.73 m^2	69.7 [58.4-82.6]	68.0 [55.4-80.7]	70.1 [60.0-84.0]	70.0 [55.4-78.3]	71.0 [59.4-82.0]	.367
ACS, nonculprit lesion	56 (13.4)	21 (15.6)	17 (10.5)	5 (19.2)	13 (13.5)	.478
Angiographic findings						
Diameter stenosis	57.3 [50.3-65.8]	63.4 [55.5-73.1]	56.3 [49.6-62.7]	59.4 [53.3-67.3]	52.4 [46.3-57.5]	< .001[b,c,d,e]
Reference diameter	2.68 [2.27-3.06]	2.65 [2.19-3.05]	2.54 [2.25-2.90]	2.97 [2.45-3.26]	2.95 [2.53-3.22]	< .001[d]
Minimum lumen diameter	1.11 [0.88-1.37]	0.95 [0.68-1.20]	1.11 [0.91-1.32]	1.12 [0.94-1.41]	1.36 [1.15-1.58]	< .001[b,c,d,e]
Lesion length	11.7 [8.5-16.2]	13.1 [9.0-18.6]	10.9 [8.0-15.8]	11.1 [9.5-15.8]	10.4 [8.2-13.5]	< .001[b,c]
OCT findings						
Minimal lumen area, mm^2	1.28 [0.91-1.9]	0.97 [0.72-1.28]	1.33 [1.03-1.72]	1.62 [1.06-1.90]	1.98 [1.40-2.45]	< .001[b,c,d,f]
Fibroatheroma	328 (69.3)	125 (72.3)	112 (65.5)	19 (73.1)	72 (69.9)	.559
Calcification	205 (43.4)	81 (46.8)	82 (48.0)	11 (42.3)	31 (30.1)	.021[c,d]
TCFA	66 (14.0)	38 (22.0)	14 (8.2)	6 (23.1)	8 (7.8)	< .001[b,c]
Plaque rupture	73 (15.4)	39 (22.5)	11 (6.4)	6 (23.1)	17 (16.5)	< .001[b]

ACS, acute coronary syndrome; CFR, coronary flow reserve; eGFR, estimated glomerular filtration rate; FFR, fractional flow reserve; OCT, optical coherence tomography; TCFA, thin-cap fibroatheroma.
Unless otherwise indicated, values are expressed as No. (%) or median [interquartile range].
[a] $P < .05$ FFR + /CFR- vs FFR-/CFR + .
[b] $P < .05$ FFR + /CFR + vs FFR + /CFR-.
[c] $P < .05$ FFR + /CFR + vs FFR-/CFR-.
[d] $P < .05$ FFR + /CFR- vs FFR-/CFR-.
[e] $P < .05$ FFR-/CFR + vs FFR-/CFR-.
[f] $P < .05$ FFR + /CFR + vs FFR-/CFR + .

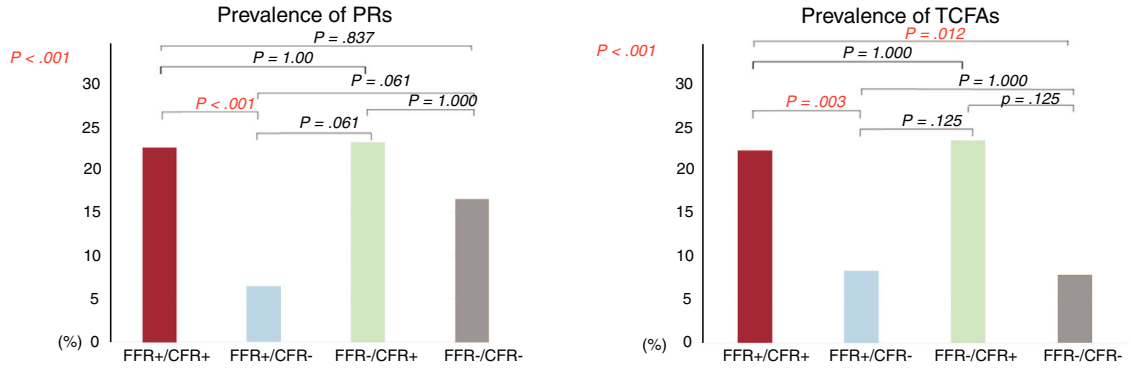

Figure 1. Prevalence of PRs and TCFAs. A: the prevalence of PRs according to FFR/CFR quadrants. B: the prevalence of TCFAs according to FFR/CFR quadrants. CFR, coronary flow reserve; FFR, fractional flow reserve; PR, plaque rupture; TCFA, thin-cap fibroatheroma.

FFR + /CFR-, the prevalence of both TCFAs and PRs tended to be higher, although, in the post hoc analysis, this difference was not significant in the FFR-/CFR + group. The net reclassification index and integrated discrimination improvement index were both significantly improved when CFR was added to the FFR-based classification for predicting PR and TCFA (PR; net reclassification index 0.462, $P < .001$, integrated discrimination improvement 0.031, $P < .001$, TCFA; net reclassification index 0.320, $P = .012$, integrated discrimination improvement 0.017, $P = .002$).

Our results indicate that physiological classifications of coronary stenosis evaluated by FFR and CFR are associated with the difference in plaque instability. Even in patients with lesions showing preserved FFR, CFR may add incremental information on plaque instability, which might be associated with worse outcomes. In the present study, we would like to address the importance of CFR in addition to FFR for evaluating plaque vulnerability. This differs from our previous report5 in which we evaluated the significance of microvascular dysfunction in addition to FFR. Further studies are needed to test the hypothesis of the possible link between physiological lesion assessment and lesion instability, and its impact on subsequent adverse cardiac events.

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Differences between cardiologists' perceptions and clinical reality of the quality of anticoagulation with vitamin K antagonists in Spain

Diferencias entre la percepción de los cardiólogos y la realidad sobre la calidad de la anticoagulación con antagonistas de la vitamina K en España

To the Editor,

Evidence from clinical trials and 'real-world' studies has demonstrated that direct oral anticoagulants (DOAC) are as safe or safer than vitamin K antagonists (VKA) and at least as effective at preventing embolic events; DOACs are therefore now recommended as the first-line anticoagulation therapy in clinical guidelines.[1] Nevertheless, use of DOACs in Spain is limited and lower than that of comparable countries.[2] While this situation may be related to restrictions imposed by the Spanish health care system,[2] there is also evidence that VKA prescription is influenced by physicians' perceptions and attitudes.[3] Our aim in the present study was to analyze Spanish cardiologists' perceptions of the quality of anticoagulation with VKAs and to compare this perception with real-world evidence.

The cardiology services of all hospitals within the Spanish national health system were invited to participate in the study. In total, 171 centers agreed, and the heads of service at each hospital selected members of their teams to participate. A total of 588 cardiologists were interviewed by an external company between April and May 2018. The study participants were not forewarned of the study objectives. Each participant was asked to access his or her center's records and retrieve the medical history of a patient with nonvalvular atrial fibrillation (NVAF) who had attended the clinic that same day; the cardiologist was asked to assess the patient's international normalized ratio (INR) and time