

## REFERENCES

- Pelliccia A, Sharma S, Gati S, et al. Guía ESC. 2020 sobre cardiología del deporte y el ejercicio en pacientes con enfermedad cardiovascular. *Rev Esp Cardiol.* 2021;74:545e1–545.e73.
- Drezner JA, Sharma S, Baggish A, et al. International criteria for electrocardiographic interpretation in athletes: Consensus statement. *Br J Sports Med.* 2017;51:704–731.
- Malhotra A, Dhutia H, Yeo T, et al. Accuracy of the 2017 international recommendations for clinicians who interpret adolescent athletes' ECGs: a cohort study of 11 168 British white and black soccer players. *Br J Sports Med.* 2020;54:739–745.
- Palermi S, Serio A, Vecchiato M, et al. Potential role of an athlete-focused echocardiogram in sports eligibility. *World J Cardiol.* 2021;13:271–297.
- Malhotra A, Dhutia H, Finocchiaro G, et al. Outcomes of cardiac screening in adolescent soccer players. *N Engl J Med.* 2018;379:524–534.

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## Microvascular dysfunction and invasive absolute coronary flow after percutaneous coronary intervention for a chronic total occlusion. The FLOW-CTO study



### Disfunción microvascular y flujo coronario absoluto invasivo tras intervención coronaria percutánea de oclusión total crónica. Estudio FLOW-CTO

#### To the Editor,

Percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) is a demanding situation. This condition causes abnormalities in the vascular bed distal to the lesion and in the related microvasculature. Percutaneous treatment of CTO improves the patient's quality of life and reduces angina.<sup>1</sup> Positron emission tomography scans have shown an improvement in myocardial blood flow and coronary flow reserve (CFR) after CTO PCI.<sup>2</sup> However, improvement is not immediate and can take weeks or months.<sup>3</sup>

The Microvascular Coronary Resistance and Absolute Coronary Flow in Patients With Percutaneous Intervention of a Chronic Total Occlusion study (FLOW-CTO; NCT05197361) was designed to evaluate the trend over time of microvascular resistance and absolute coronary flow after CTO PCI. The study was conducted at 4 Spanish sites with consecutive patients who underwent a functional study immediately after the procedure and at 6 months and measured the fractional flow reserve (FFR), CFR, and index of microvascular resistance (IMR). Absolute coronary flow and microvascular resistance were determined by continuous thermodilation during maximum hyperemia induced by serum infusion, as previously described.<sup>4</sup> The procedure was performed using the PressureWire X guidewire (Abbott, United States) and the Coroventis program (CoroFlow Cardiovascular System, Sweden). Microvascular dysfunction was defined as  $IMR \geq 25$  or  $CFR < 2.0$  in the presence of  $FFR > 0.80$ . The protocol was approved by the Research Ethics Committee for medications at the coordinating site, and all patients provided written informed consent. The data obtained from the baseline study immediately after CTO PCI are presented for the first 49 patients.

Table 1 lists the clinical, angiographic, and procedure characteristics. Most patients were men, and the mean age was 60 to 69 years. The prevalence of hypertension, dyslipidemia, and diabetes was 71%, 67%, and 41%, respectively. More than half the patients had a history of ischemic heart disease, and 55% had required PCI. The median left ventricular ejection fraction was 55% [interquartile range, 45–60]. A total of 86% of patients had exertional angina, and 14% had a history of heart failure.

The vessel most commonly involved was the right coronary artery (55%), followed by the anterior descending artery (31%). The median Japanese Multicenter CTO Registry (J-CTO) score was 2 points. The most frequently used technique (74%) for PCI was antegrade guidewire upgrade, and the median number of stents

**Table 1**  
Baseline, angiographic, and functional study characteristics

Patients, n	49	P
Age, y	62 [56–69]	
Men	44 (90)	
Hypertension	35 (71)	
Dyslipidemia	33 (67)	
Diabetes mellitus	20 (41)	
Insulin-dependent DM	6 (12)	
History of smoking	24 (49)	
Chronic kidney failure (eGFR < 60 mL/min)	5 (10)	
History of ischemic heart disease	29 (59)	
History of AMI	18 (37)	
History of PCI	27 (55)	
History of CABG	2 (4)	
LVEF, %	55 [45–60]	
Exertional angina	42 (86)	
History of heart failure	7 (14)	
Positive ischemia/viability study	29 (59)	
Stress echocardiography	6 (12)	
SPECT	10 (20)	
Cardiac magnetic resonance	13 (27)	
Normal regional contractility + symptoms of myocardial ischemia	20 (41)	
Vessels with CTO		
Anterior descending artery	15 (31)	
Circumflex artery	7 (14)	
Right coronary artery	27 (55)	
Main collateral vessel		
Anterior descending artery	29 (59)	
Circumflex artery	6 (12)	
Right coronary artery	14 (29)	
J-CTO score	2 [1–2]	
PCI-CTO technique		
Antegrade guidewire upgrade	36 (74)	
Retrograde guidewire upgrade	8 (16)	
Antegrade dissection and re-entry	4 (8)	
Retrograde dissection and re-entry	1 (2)	
Number of stents	2 [1–3]	
Total length of stents, mm	59 ± 25	
Residual stenosis, %	8 ± 4	
Scope time, min	37 [29–45]	
Contrast administered, mL	280 [220–350]	
Collateral persistence after PCI		
Absent	29 (59)	
Present	13 (27)	
Not evaluated	7 (14)	

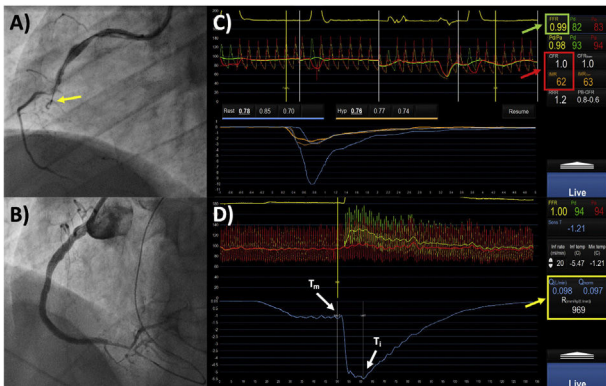
**Table 1** (Continued)

Baseline, angiographic, and functional study characteristics

Patients, n	49	P
FFR	0.91 [0.83-0.3]	
FFR ≤ 0.80	10 (20)	
IMR	12 [8-19]	
IMR ≥ 25 (only if FFR > 0.80)	5/37 (14)	
CFR	2 [1.1-2.5]	
CFR < 2.0 (only if FFR > 0.80)	19/37 (51)	
Microvascular dysfunction	20/37 (54)	
Invasive absolute coronary flow, mL/min	170 [124-239]	.9119
CTO in anterior descending artery	168 [127-263]	
CTO in circumflex artery	169 [112-257]	
CTO in right coronary artery	205 [116-239]	
Microvascular resistance, mmHg/L/min	453 [322-642]	.7605
CTO in anterior descending artery	460 [246-704]	
CTO in circumflex artery	366 [255-642]	
CTO in right coronary artery	433 [326-625]	

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CFR, coronary flow reserve; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; FFR, fractional flow reserve; IMR, index of microvascular resistance; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SPECT, single-photon emission computed tomography.

Data are expressed as No. (%), mean ± standard deviation, or median [interquartile range].



**Figure 1.** 58-year-old man with diabetes mellitus. Exertional angina with inducible inferior ischemia. A, coronary angiography revealed chronic total occlusion (CTO) of the middle segment of the right coronary (yellow arrow). B, post-PCI angiographic follow-up, with excellent outcome. C, the pressure guidewire study showed an insignificant fractional flow reserve (FFR) (0.99) (green box); the microcirculation study revealed signs of microvascular dysfunction, with a reduced (< 2) coronary flow reserve (CFR) and high index of microvascular resistance (IMR > 25) (red box). D, calculation of absolute coronary flow (Q) and microvascular resistance (R) (yellow box). Ti, temperature at saline infusion site; Tm, temperature of homogeneous mixture of serum and blood.

implanted was 2 (1-3), with a total length of the devices of  $59 \pm 25$  mm. Angiographic outcome was good, with a mean residual stenosis of  $8\% \pm 4\%$ .

Despite good angiographic outcome, the post-PCI functional study revealed 20% of lesions with  $\text{FFR} \leq 0.80$ . Among patients with an insignificant FFR value ( $> 0.80$ ), 54% had signs of microvascular dysfunction. Compared with patients with normal IMR, patients with high IMR ( $\geq 25$ ) showed an insignificant tendency to lower absolute coronary flow ( $143 \pm 79$  vs  $192 \pm 59$  mL/min;  $P = .1043$ ), with significantly more elevated microvascular resistance ( $694 \pm 206$  vs  $471 \pm 166$  mmHg/L/min;

$P = .0328$ ). However, compared with patients with normal CFR, patients with reduced CFR ( $< 2.0$ ) had lower absolute coronary flow ( $166 \pm 57$  vs  $207 \pm 64$  mL/min;  $P = .0460$ ) and an insignificant tendency toward higher microvascular resistance ( $535 \pm 240$  vs  $466 \pm 195$  mmHg/L/min;  $P = .3419$ ). Diabetes mellitus was the only predictor found to be related to high IMR (odds ratio [OR] = 6.3; 95% confidence interval [95%CI], 1.1-13;  $P = .046$ ) or reduced CFR (OR = 5.7; 95%CI, 1.4-22;  $P = .013$ ) immediately after CTO PCI. Figure 1 provides an example of the study protocol.

This prospective study analyzed microcirculation parameters in patients after CTO PCI, finding that more than half the patients exhibited signs of microvascular dysfunction immediately after revascularization. Furthermore, despite an optimal angiographic outcome, a fifth of patients had a functional study showing significant abnormalities in parameters related to epicardial circulation, such as FFR. Microvascular dysfunction was seen more often in the invasive functional study when diabetes mellitus was present. Data analysis during follow-up of this patient cohort will allow us to evaluate whether or not these functional abnormalities improve after CTO PCI.

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## AUTHORS' CONTRIBUTIONS

M. García-Guimarães, lead and corresponding author, designed the study, analyzed the data, and wrote the first version of the manuscript. M. García-Guimarães, A. Gutiérrez-Barrios, J. Gómez-Lara, N. Salvatella, and F. Rivero performed the coronary angiography studies. A. Aparisi participated in the data collection. All authors participated in the final version of the manuscript.

## CONFLICTS OF INTEREST

No conflicts of interest related to this project.

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## REFERENCES

1. Werner GS, Martin-Yuste V, Hildick-Smith D, et al. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions. *Eur Heart J*. 2018;39:2484–2493.
2. Schumacher SP, Driessen RS, Stuijzand WJ, et al. Recovery of myocardial perfusion after percutaneous coronary intervention of chronic total occlusions is comparable to hemodynamically significant non-occlusive lesions. *Catheter Cardiovasc Interv*. 2019;93:1059–1066.
3. Keulards DCJ, Vlaar PJ, Wijnbergen I, Pijls NHJ, Teeuwen K. Coronary physiology before and after chronic total occlusion treatment: what does it tell us? *Neth Heart J*. 2021;29:22–29.
4. van't Veer M, Geven MCF, Rutten MCM, et al. Continuous infusion thermodilution for assessment of coronary flow: theoretical background and in vitro validation. *Med Eng Phys*. 2009;31:688–694.

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## Introduction of the Ozaki technique in Spain. A new procedure for congenital aortic valve plasty?



### Experiencia inicial con la técnica de Ozaki en España. ¿Una nueva alternativa en el tratamiento de la valvulopatía aórtica congénita?

#### To the Editor,

Congenital aortic valve disease accounts for 3% to 6% of congenital heart diseases, and in many cases requires surgical

treatment. The options are limited by the child's weight and development. Percutaneous procedures (balloon valvuloplasty) and surgical interventions (surgical valvuloplasty or aortic valve replacement [AVR]) are both available. The initial approach varies depending on the underlying lesion and the policies of each center, and is a subject of international debate. When surgical repair is unfeasible, the alternative is AVR, and the options depend on the size of the aortic ring. Three techniques predominate in children: prosthesis implantation, Ross surgery, and homograft implantation. They are all known to have certain difficulties and problems.

**Table 1**

Demographic, surgical, and postoperative variables

	Total (n = 11)	Younger than 18 y (n = 6)	Older than 18 y (n = 5)	P
Age, y	15.77 [8.46-29.07]	9.28 [7.32-10.96]	29.07 [26.67-32.95]	.006
Males	5 (45)	3 (50)	2 (40)	1
Weight, kg	48 [29-67]	32 [23-48]	67 [65-78]	.006
Previous surgery	1 (9)	1 (17)	0	1
Previous balloon valvuloplasty	6 (4.6)	4 (66.7)	2 (40)	1
Asymptomatic	7 (64)	4 (67)	3 (60)	1
Aortic valve morphology				1
Tricuspid	0	0	0	
Bicuspid	8 (73)	4 (67)	4 (80)	
Unicuspid	3 (27)	2 (33)	1 (20)	
Mean peak gradient, mmHg	70.5 [46-95]	58 [35-71]	88 [75.5-99.5]	.16
Mean gradient, mmHg	42 [35-50]	35 [21-45]	46 [41.5-57]	.22
AR ≥ moderate	9 (82)	6 (100)	3 (60)	.18
Aortic ring, mm	20 [18-24]	18 [17-20]	24 [23-27]	.01
Associated procedure	3 (27)	3 (50)	0	.18
CPB time, min	150 [143-184]	169.5 [149-203]	148 [140-150]	.1
Ischemia time, min	134 [120-148]	142 [125-160]	129 [120-134]	.27
Conversion	0	0	0	1
Re-entry in CPB	1 (9)	1 (17)	0	1
OTI time, h	3 [2-7]	3.5 [2-16]	3 [2-3]	.45
ICU stay, d	3 [2-4]	3.5 [2-4]	3 [3-3]	.44
Hospital stay, d	7 [7-8]	7.5 [7-10]	7 [7-8]	.57
Mortality	0	0	0	1
Peak gradient at discharge, mmHg	24 [18-38]	22 [20-35]	36 [12-38]	1
Mean gradient at discharge, mmHg	16 [8-22]	14 [10-19.5]	20 [7-22]	.81
AR ≥ moderate-severe	0	0	0	1
Reintervention (percutaneous or surgical)	0	0	0	1
Peak gradient at follow-up, mmHg	24 [19-30]	24 [19-45]	23.5 [14.5-28]	.67
Mean gradient at follow-up, mmHg	16 [12-21]	21.5 [21-22]	12 [11-16]	.083
AR ≥ 3 at follow-up	1 (9)	1 (17)	0	1

AR, aortic regurgitation; CPB, cardiopulmonary bypass; ICU, intensive care unit; OTI, orotracheal intubation. Values are expressed as No. (%) or median [interquartile range].