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Impact of Percutaneous Revascularization on Exercise Hemodynamics in Patients With Stable Coronary Disease

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ABSTRACT

BACKGROUND Recently, the therapeutic benefits of percutaneous coronary intervention (PCI) have been challenged in patients with stable coronary artery disease (SCD).

OBJECTIVES The authors examined the impact of PCI on exercise responses in the coronary circulation, the microcirculation, and systemic hemodynamics in patients with SCD.

METHODS A total of 21 patients (mean age 60.3 $\pm$ 8.4 years) with SCD and single-vessel coronary stenosis underwent cardiac catheterization. Pre-PCI, patients exercised on a supine ergometer until rate-limiting angina or exhaustion. Simultaneous trans-stenotic coronary pressure-flow measurements were made throughout exercise. Post-PCI, this process was repeated. Physiological parameters, rate-limiting symptoms, and exercise performance were compared between pre-PCI and post-PCI exercise cycles.

RESULTS PCI reduced ischemia as documented by fractional flow reserve value (pre-PCI 0.59 $\pm$ 0.18 to post-PCI 0.91 $\pm$ 0.07), instantaneous wave-free ratio value (pre-PCI 0.61 $\pm$ 0.27 to post-PCI 0.96 $\pm$ 0.05) and coronary flow reserve value (pre-PCI 1.7 $\pm$ 0.7 to post-PCI 3.1 $\pm$ 1.0; $p < 0.001$ for all). PCI increased peak-exercise average peak coronary flow velocity ($p < 0.0001$), coronary perfusion pressure (distal coronary pressure; $p < 0.0001$), systolic blood pressure ($p = 0.01$), accelerating wave energy ($p < 0.001$), and myocardial workload (rate-pressure product; $p < 0.01$). These changes observed immediately following PCI resulted from the abolition of stenosis resistance ($p < 0.0001$). PCI was also associated with an immediate improvement in exercise time (+67 s; 95% confidence interval: 31 to 102 s; $p < 0.0001$) and a reduction in rate-limiting angina symptoms (81% reduction in rate-limiting angina symptoms post-PCI; $p < 0.001$).

CONCLUSIONS In patients with SCD and severe single-vessel stenosis, objective physiological responses to exercise immediately normalize following PCI. This is seen in the coronary circulation, the microcirculation, and systemic hemodynamics. (J Am Coll Cardiol 2018;72:970–83) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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In patients with stable coronary artery disease (SCD), the primary treatment goal of percutaneous coronary intervention (PCI) is the relief of angina and improvement in functional capacity. However, the first double-blind, placebo-controlled trial of PCI for stable angina, the ORBITA trial (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) (1), found a far smaller effect on exercise tolerance and symptoms than found in unblinded research (2-4) and in everyday clinical practice. This finding has refocused attention on the need to comprehensively define the therapeutic mechanisms of PCI in SCD.

SEE PAGE 984

Cardiac catheter laboratory protocols have recently been described that enable invasive measurements of coronary and systemic hemodynamics to be performed during supine exercise. Application of these protocols have yielded important mechanistic insight into a variety of anginal conditions. These include the physiological mechanisms underlying the warm-up angina phenomenon (5), the mechanisms of angina in severe aortic stenosis (6), and the alleviation of angina on exertion by sublingual nitroglycerin (7).

In this study, we exercised patients on the coronary catheter laboratory table during cardiac catheterization, immediately before and after PCI. Our hypothesis was that in patients with stable angina and hemodynamically significant single-vessel disease, PCI would immediately improve objectively documented exercise responses in the coronary circulation, the microcirculation, and systemic hemodynamics.

METHODS

STUDY POPULATION. Patients with exertional angina and single-vessel coronary artery disease were recruited from elective PCI waiting lists at both the Hammersmith Hospital and the Essex Cardiothoracic Centre. Inclusion criteria were left ventricular ejection fraction >50% and hemodynamic significance of the target vessel (defined as either fractional flow reserve [FFR] ≤0.80 or instantaneous wave-free ratio [iFR] ≤0.89). All patients were on maximally tolerated antianginal medical therapy. Exclusion criteria were hemodynamically significant multivessel disease, left main stem or ostial stenosis, moderate/severe valvular disease, chronotropic incompetence with pacemaker, severe airways disease, or physical inability to exercise. Patients continued all usual medications and were loaded with dual antiplatelet agents as per routine practice of the recruiting center. All subjects gave written informed consent in accordance with the protocol approved by the regional ethics committee (16/LO/1928).

CATHETERIZATION PROTOCOL. The patient was positioned on the catheterization laboratory table and secured to a pre-mounted supine cycle ergometer (Lode Angio, Lode, Groningen, the Netherlands). The ergometer was connected to a laptop computer with software (Lode Export Manager 10, V 10.5.1, Lode) to initiate the exercise protocol and acquire performance data. The target vessel was intubated with a standard 6-F guide catheter from the right radial artery. Intra-arterial unfractionated heparin (70 to 100 U/kg) and intracoronary nitroglycerin (300 μg) were given before coronary angiography and physiological measurements.

The optimal working view was determined, and a standard coronary guidewire was advanced distally to secure the target vessel. A dual pressure and velocity sensor 0.014-inch intracoronary wire (Combowire XT, Volcano Corporation, San Diego, California) was then advanced to the tip of the guiding catheter, and the pressure signals normalized. The Combowire tip-mounted sensor was advanced distal to the stenosis by a minimum of 15 mm, and its position recorded cineographically. Therefore, 2 wires were positioned in the target vessel for all study measurements. An optimal Doppler velocity trace was obtained by rotational manipulation of the Combowire. Continuous pressure-flow measurements were performed under resting conditions, during a 2-min intravenous infusion of adenosine and during an incremental exercise protocol. The order of adenosine and exercise was randomly assigned. A return to baseline hemodynamic conditions was mandated between each stage of the experimental protocol.

ABBREVIATIONS AND ACRONYMS

BEW = backward expansion wave
CCS = Canadian Cardiovascular Score
CFR = coronary flow reserve
DMR = diastolic microvascular resistance
DTF = diastolic time fraction
DTI = diastolic time index
FCW = forward compression wave
FFR = fractional flow reserve
iFR = instantaneous wave-free ratio
LAD = left anterior descending coronary artery
PCI = percutaneous coronary intervention
PP = pulse pressure
RPP = rate-pressure product
SCD = stable coronary disease
TTI = tension-time index
WIA = wave-intensity analysis

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