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Impact of right atrial pressure on fractional flow reserve calculation in the presence of a chronic total occlusion☆,☆☆,★

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ABSTRACT

Background: The aim of this study was to assess the impact of right atrial pressure (Pra) on non-CTO vessels FFR measurements in patients with a chronic total occlusion.
Methods: Consecutive patients who underwent PCI for a CTO of the right coronary artery (RCA) were included. Prior to RCA recanalization, FFR and FFR_{myo} were measured in non-CTO vessels. FFR was calculated using the Pd/Pa equation during maximum hyperaemia and also accounting for right atrial pressure (Pd-Pra/Pa-Pra). Non-CTO vessels were characterised as major or minor donors based on angiographic assessment of provided collaterals.
Results: FFR and FFR_{myo} were measured in 68 arteries (34 LAD and 34 Cx) in 34 consecutive patients with successful RCA CTO PCI. Patients' mean age was 62 ± 10 years old and 88% were male. Mean left ventricular ejection fraction was 51% ± 20. During maximum hyperaemia, mean Pra, Pa, and Pd were 4.1 ± 3.8 mm Hg, 82.6 ± 12.2 mm Hg, and 63.8 ± 14.3 mm Hg, respectively. In the major donor vessel, FFR_{myo} showed a difference of 0.007 to FFR (0.760 ± 0.113 vs. 0.767 ± 0.112, $p = 0.004$). In the minor donor vessel the difference was 0.004 (0.895 ± 0.067 vs. 0.899 ± 0.065, $p < 0.001$). There was a strong positive correlation between the FFR and FFRmyo in both the major and minor donor vessel groups ($r = 0.993$, $p < 0.001$ and $r = 0.996$, $p < 0.001$ respectively).
Conclusion: In the presence of a CTO, RA pressure adjustment of FFR in the non-CTO vessels leads to trivial numerical changes, which are statistically significant but clinically negligible.

1. Introduction

Fractional flow reserve is the current gold standard for invasive physiological assessment of intermediate coronary lesion severity in patients with stable coronary artery disease [1]. It is defined as the ratio of maximal achievable blood flow in the stenotic coronary artery to the maximal achievable blood flow if the same artery was normal [2]. In the original description of the FFR, the initial mathematical equation incorporated the right atrial pressure (Pra) into the computation as follows: FFRmyo = Pd-Pra/Pa-Pra (where Pd is the distal to the lesion pressure, Pa is the proximal arterial pressure and Pra is the venous or right atrial pressure) [2,3]. In daily clinical practice the right atrial pressure (Pra) is considered to have minimal impact and is omitted from the equation, which has been simplified in its current form: FFR = Pd/Pa during hyperaemia [4]. This is supported by a large retrospective study on a cohort of patients who underwent right and left heart catheterisation for clinical reasons [5].

Coronary chronic total occlusions (CTOs) are often encountered in patients with coronary artery disease undergoing coronary angiography [6]. Although, historically, the frequency of CTO PCI has been low [7], recent progress in techniques and equipment has led to significantly improved procedural and clinical outcomes [8,9]. Hence, interventional cardiologists more frequently tackle these complex lesions nowadays. CTOs are commonly found in the context of multi-vessel disease, making the use of FFR in this population important as it can delineate stenosis severity in the non-CTO vessels and guide clinical decision-making and subsequent management. There are a very limited number of studies that have specifically reported FFR measurements in the presence of a CTO in the non-CTO vessels. Indeed, whether the incorporation of Pra

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would significantly affect FFR and alter the clinical decisions has not previously been investigated.

The aim of this study was to assess the impact of right atrial pressure (Pra) on FFR measurements in the non-CTO vessels in patients with a chronic total occlusion.

2. Material and methods

This was a prospective observational study, part of a research project on coronary CTO physiology ("The physiological impact of coronary chronic total occlusion percutaneous coronary intervention on coronary pressure-derived measurements and the influence of collateral circulation"/IMPACT-CTO study, NCT 02643940).

2.1. Study patients

Consecutive patients with symptomatic stable angina scheduled for elective RCA CTO PCI in a tertiary centre with a dedicated CTO programme were recruited from October 2015 to November 2016. All patients had an RCA total occlusion with duration ≥3 months, evidence of viability and/or ischaemia in the CTO territory as shown by non-invasive cardiac imaging and spontaneously visible collaterals from a contralateral donor artery. Patients with previous CABG, >1 CTO and significant LMS disease were excluded. The study was approved by the local ethics committee (15/EE/0269) and all patients provided written informed consent prior to the procedure.

2.2. Fractional flow reserve measurements

The FFR and FFR_{myo} were measured and calculated for the non-CTO vessels (LAD and Cx) before attempting PCI to the CTO. Measurements were performed simultaneously in both vessels using 2 pressure wires (Philips Volcano Corporation, San Diego, California). Three hundred (300) mcg of intra-coronary nitro-glycerine was administered prior to each measurement. The pressure wire was normalised at the tip of the guide catheter and advanced to the distal vessel. Hyperaemia was achieved with intravenous adenosine infusion administered centrally through a femoral vein at a dose of 140 mcg/kg/min. Right atrial pressure (Pra) was measured with a 5-F pigtail catheter placed at the level of the right atrium via the femoral vein. The FFR was calculated as follows:

$$FFR = Pd/Pa,$$

where Pd is the mean arterial pressure at the distal vessel and Pa the mean aortic pressure at the tip of the guide catheter under maximum steady state hyperaemia.

The FFR_{myo} was calculated offline as:

$$FFR_{myo} = (Pd - Pra)/(Pa - Pra),$$

where Pra is the mean atrial pressure.

Once measurements were completed, the pressure guide wire was pulled back to the guide catheter and assessed for drift of the Pd/Pa recording. In the presence of drift (>±0.02), measurements were repeated; otherwise the operator would proceed to CTO PCI.

2.3. Angiographic assessment of CTO and collateral circulation

J-CTO score [10] and donor vessel collateral contribution to the occluded artery using the Rentrop [11] and collateral connections (CC) grading systems [12] were assessed by two experienced CTO operators. For the purpose of the study non-CTO vessels were differentiated into major and minor collateral donors. The major collateral donor vessel was defined as the artery making the largest collateral contribution to the CTO. QCA analysis was performed in optimal projections using quantitative coronary angiography software (Philips Allura, The Netherlands).

2.4. Statistical analysis

All quantitative variables were tested for normal distribution according to the Kolmogorov-Smirnov test. Continuous variables are reported as mean and standard deviation values. Categorical variables are expressed as frequency and proportion. The paired *t*-test was used for the primary analysis to compare FFR with FFRmyo values. Scatter plots and Pearson's correlation coefficients or Spearman's correlation coefficients were used to assess the relationship between two variables as appropriate. The level of statistical significance was set at $p = 0.05$ with two tails. Statistical analysis was carried out using SPSS 20 software (SPSS Inc., Chicago, Illinois).

3. Results

Forty consecutive patients were recruited and 34 of them had successful CTO PCI. FFR and FFR_{myo} were measured in 68 coronary arteries. Baseline demographics and angiographic details are outlined in Table 1. Overall, the mean age was 62 ± 10 years and 88% of the patients were male. Average LVEF was 51% and the area of ischemia measured by CMR was 13.6 ± 5%. The LAD was the predominant donor vessel in 88% of the cases with a mean maximum stenosis of 41 ± 12.6%.

The baseline mean Pra was 4.6 ± 3.8 mm Hg. The hyperaemic mean Pra was 4.1 ± 3.6 mm Hg with normal distribution across a range of measurements (minimum: −2 mm Hg and maximum: 15 mm Hg) (Fig. 1A). There was no statistically significant difference between the baseline and the hyperaemic Pra ($p = 0.09$). During hyperaemia, the mean Pa was 82.6 ± 12.2 mm Hg, and the mean Pd 63.8 ± 14.3 mm Hg.

The mean FFR and FFR_{myo} in the major donor vessels were 0.767 and 0.760 ($p = 0.004$) respectively, showing a mean difference of 0.007 ± 0.013. In the minor donor vessels mean FFR was 0.899 and mean FFR_{myo}

Table 1
Baseline demographics, angiographic and procedural details.

	n (%) or mean ± SD
Demographic ($n = 34$)	
Male	30 (88.2)
Age (years)	61.76 ± 10.53
Previous MI	21 (61.8)
Previous PCI	14 (41.2)
Hypertension	22 (64.7)
Hypercholesterolaemia	24 (70.6)
Diabetes mellitus	9 (26.5)
Current smoker	7 (20.6)
Angina Duration (months)	39.88 ± 65.58
Estimated duration of CTO (weeks)	221.38 ± 397.30
Angina CCS Class (1/2/3/4)	4(11.8)/12(35.3)/17(50.0)/1 (2.9)
LVEF on CMR (%)	51.26 ± 19.61
RVEF on CMR (%)	51.76 ± 23.37
Ischaemia in RCA territory on CMR (%)	13.65 ± 5.00
Angiographic characteristics	
CTO Vessel (RCA)	34 (100)
CTO length (mm)	34.59 ± 25.70
J-CTO Score (0/1/2/3/4)	7(20.6)/5(14.7)/8(23.5)/10 (29.4)/4(11.8)
Predominant donor vessel (LAD/LCx)	30 (88)/4 (12)
Predominant donor vessel stenosis on QCA (%)	41.43 ± 12.59
Minor donor vessel stenosis on QCA (%)	35.06 ± 13.72
Overall Rentrop Classification grading (0/1/2/3)	0(0.0)/0(0.0)/2(5.9)/32(94.1)
Overall Collateral Connection Classification grading (0/1/2/3)	0 (0.0)/3(8.8)/22(64.7)/9(26.5)

MI = myocardial infarction; PCI = percutaneous coronary intervention; CTO = chronic total occlusion; CCS = Canadian cardiovascular society; LVEF = left ventricular ejection fraction; CMR = cardiac magnetic resonance imaging; RVEF = right ventricular ejection fraction; RCA = right coronary artery; LAD = left anterior descending artery; LCx = left circumflex artery; QCA = Quantitative coronary angiography.

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