I. Introduction

In patients with chronic coronary syndrome, chronic total occlusion (CTO) is rather common. Current guidelines recommend CTO percutaneous coronary intervention (PCI) if symptoms are present and myocardial perfusion imaging show significant ischaemia or viable myocardium in the territory supplied by the occluded vessel. It is generally not accepted that retrograde collateralization provides adequate blood flow to reduce ischemia. We reported a case with CTO lesion in RCA who showed symptom relief and improved perfusion after PCI of non-CTO LAD lesion.

II. Case presentation

A 71-year-old male presented in a cardiology outpatient clinic with chest pain, Canadian Cardiovascular Society (CCS) score 2. He had no dyspnoea and no syncope, no clinical signs of heart failure. The patient had medically treated hypertension, otherwise no cardiovascular risk factors. Because the patient was stable at the outpatient visit, the initial potential diagnosis was chronic coronary syndrome, coronary vasospasms, hypertensive heart disease or non-cardiac causes as e.g. reflux.

An electrocardiogram showed sinus rhythm, LV hypertrophy, and no ischemia or arrhythmia. Laboratory tests revealed mild hyperlipidaemia, total cholesterol 5.4mmol/L and LDL-c 3 mmol/L. Other laboratory tests were normal. Baseline Seattle Angina Questionnaire (SAQ) showed minimal physical limitation, moderate angina stability and frequency, fair treatment satisfaction and impaired quality of life (QoL) (Fig. 1).

An echocardiography showed ejection fraction 60% and no sign of valvopathy.

A coronary computed tomography angiography (CTA) was performed revealing a 50–70% LAD stenosis and CTO RCA. An adenosine stress $^{82}$RbPET showed moderate-severe inferoseptal reversible ischemia (Fig. 2) corresponding the RCA territory estimated to cover app. 10% of the left ventricular myocardium. In the anterior/apical myocardium, the perfusion was normal (2.9 ml/g/min). Global stress-flow was 2.4 ml/g/min.

The patient was referred to invasive coronary angiography (ICA) showing a 70% stenosis in the LAD/D1 bifurcation, while a CTO RCA was left untreated. One-year follow-up with Seattle Angina Questionnaire and repeat $^{82}$RbPET revealed symptom relief and improved inferoseptal perfusion likely through LAD collateralization.

KEY WORDS: 82 rubidium positron emission tomography, chronic coronary syndrome, chronic total occlusion, collateral flow, seattle angina questionnaire
double kissing (DK) crush stenting (Resolute Onyx 3.5 × 26 and Resolute Onyx 3.0 × 22, respectively). Control IVUS confirmed complete lesion coverage, stent expansion and apposition. The CTO RCA was left untreated, and the collaterals persisted post-PCI although more diminished (Fig. 3). Optimal medical therapy (OMT) was instituted (clopidogrel® 75mg OD for 6 months, aspirin® 75mg OD, metoprolol® 25mg OD, Atorvastatin® 80 mg OD).

As part of the research protocol, the SAQ and 82RbPET were repeated 1 year after revascularization. The SAQ showed general improvement, especially regarding angina frequency and QoL. 82RbPET revealed markedly improved inferoseptal perfusion as only a discrete reversible perfusion abnormality involving less than 5% of the myocardium remained (Fig. 2). The perfusion in the anteroapical myocardium was normal (2.5 ml/g/min). Global stress-flow was 2.2 ml/g/min.

III. Discussion

Chronic total occlusion of a coronary artery is observed in up to 20% of patients undergoing ICA4). Current guidelines recommend CTO PCI if symptoms are present and myocardial perfusion imaging show significant ischemia or viable myocardium in the territory supplied by the occluded vessel5). Using SAQ, the prospective randomized EuroCTO trial showed improved angina frequency and QoL by CTO PCI compared to OMT alone6). It is generally not accepted that retrograde collateralization provides adequate blood flow to reduce ischemia1, 2). In patients with successfully wired CTOs, Sachdeva et al. reported significant reduced FFR-values irrespective of the angiographic appearance of collaterals7). Moreover, Secemsky et al. showed that revascular-
ization of arteries supplying non-ischemic areas detected by perfusion imaging is common and occurs more frequently in patients undergoing non-CTO PCI compared to CTO PCI patients.

The current case, however, demonstrate that PCI of LAD/D1 supplying the non-ischemic anteroapical myocardium almost normalized the inferoseptal perfusion abnormality and improved symptom burden. It could be argued, though, that the LAD FFR was false positive, hence RCA CTO PCI would normalize LAD FFR and improve the inferoseptal perfusion.

Bucciarelli-Ducci et al. investigated the use of cardiac magnetic resonance imaging (CMR) stress perfusion for CTO PCI guidance. Comparable to the current case, patients were frequently asymptomatic (CCS 1–2: 81%; NYHA1–2: 66%). Following CTO PCI, the CTO region showed significantly improved myocardial perfusion with complete or near-complete resolution of the CTO-related perfusion defect in 90% of patients. The total SAQ score improved from a median of 54 (range 45 to 74) at baseline to 89 (range 77 to 98) after CTO recanalization.

Compared to non-CTO PCI, CTO PCI complication rates are higher. The OPEN CTO was a single-arm, multicentre registry of 1,000 consecutive patients undergoing CTO PCI. The technical success was 86%, and 48 patients (4.8%) had perforations requiring treatment. Periprocedural myocardial infarction was observed in 26 patients (2.6%), and 7 patients (0.7%) were referred for emergent surgery. However, the complication rates of CTO PCI are reported to be decreasing and more similar to non-CTO PCI. In this case, we follow our current CTO program. We treat non-CTO lesions first and repeat quantification of reversible ischemia and evaluate residual symptoms. Improving collateral circulation to the RCA CTO may be responsible for the reduction of ischemia and angina. Other factors rather than PCI-improved collateral flow, however, could explain our findings. First, OMT is both anti-ischemic and event preventing with class 1c and 1a recommendations in the recent European guidelines on chronic coronary syndrome, respectively. OMT improves QoL in CTO patients, whereas addition of CTO recanalization further reduces symptom burden. Moreover, OMT itself improves myocardial perfusion. Second, it is possible that natural collaterals were developed during the follow-up period. The ongoing "International Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy of Chronic Total Coronary Occlusions With Myocardial Ischemia" (NCT03563417) will reveal the prognostic and symptomatic effect of CTO-PCI.

Non-invasive perfusion examinations depict the integrated myocardial perfusion comprising of flow through epicardial arteries, the small vessels and microcirculation as well as the collateral circulation. Especially the latter is a pitfall when myocardial perfusion in specific areas is assigned to a coronary territory as algorithms in the software rely on pre-specified coronary territories which vary considerably between patients. Using coronary CTA to adjust the coronary territories and ICA as reference, Thomassen et al. showed that individually defined territories deviate from standard territories in 52% of patients. However, MBF in the three coronary territories defined by standard and individualized models did not differ, and per-patient sensitivity was higher compared to per-vessel sensitivity. Furthermore, disagreements between regional myocardial perfusion and ICA findings in the corresponding artery may partly or completely be explained by a sufficient collateral perfusion.

IV. Conclusions

Improving myocardial perfusion and symptoms, this clinical case illustrates that non-CTO PCI is an alternative to CTO PCI in patients with sufficient collateralization.

Learning objectives

1. Collateralization explains some cases of mis-match between myocardial perfusion examination and FFR.

2. The report from a myocardial perfusion study must clearly describe the localization, reversibility, extent and severity of
ischemia. Exact descriptions on which artery is causing ischemia should be given with caution.

Statement of consent
The patient has accepted this case for blinded publication.

Sources of funding
The study was supported by Aarhus University and Health Research Fund of Central Denmark Region.

Disclosure
All authors have nothing to declare.

Units and abbreviations

$^{82}$RbPET: Rubidium-82 Positron Emission Tomography
CCS: Canadian Cardiovascular Society
CTA: Computed tomography angiography
CTO: Chronic total occlusion
DK: Double kissing
FFR: Fractional flow reserve
ICA: Invasive coronary angiography
LAD: Left anterior descending
OMT: Optimal medical therapy
PCI: Percutaneous coronary intervention
QoL: Quality of life
RCA: Right coronary artery
SAQ: Seattle Angina Questionnaire

References
1) Werner GS, Surber R, Ferrari M, et al: The functional reserve of collaterals supplying long-term chronic total coronary occlusions in patients without prior myocardial infarction. Eur Heart J 2006; 27: 2406–2412
2) Werner GS. The role of coronary collaterals in chronic total occlusions. Curr Cardiol Rev 2014; 10: 57–64
3) Rasmussen LD, Winther S, Westra J, et al: Danish study of Non-Invasive testing in Coronary Artery Disease 2 (Dan-NICAD 2): Study design for a controlled study of diagnostic accuracy. Am Heart J 2019; 215: 114–128
4) Grantham JA, Marso SP, Spertus J, et al: Chronic total occlusion angioplasty in the United States. JACC Cardiovasc Interv 2009; 2: 479–486
5) Neumann FJ, Sousa-Uva M, Ahlsson A, et al: 2018 ESC/EACTS guidelines on myocardial revascularization. EuroIntervention 2019; 14: 1435–1534
6) 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
7) Sachdeva R, Agrawal M, Flynn SE, et al: The myocardium supplied by a chronic total occlusion is a persistently ischemic zone. Catheter Cardiovasc Interv 2014; 83: 9–16
8) Secemsky EA, Gallagher R, Harkness J, et al: Target vessel revascularization and territory of myocardial ischemia in patients with chronic total occlusions. J Am Coll Cardiol 2017; 70: 1196–1197
9) Bucciarelli-Ducci C, Auger D, Di Mario C, et al: CMR guidance for recanalization of coronary chronic total occlusion. JACC Cardiovasc Imaging 2016; 9: 547–556
10) Sapontis J, Salisbury AC, Yeh RW, et al: Early procedural and health status outcomes after chronic total occlusion angioplasty: a report from the OPEN-CTO registry (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures). JACC Cardiovasc Interv 2017; 10: 1523–1534
11) Patel VG, Brayton KM, Tamayo A, et al: Angiographic success and procedural complications in patients undergoing percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 18,061 patients from 65 studies. JACC Cardiovasc Interv 2013; 6: 128–136
12) Knuuti J, Wijns W, Saraste A, et al: 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020; 41: 407–477
13) Zoghbi GJ, Dorfman TA, Iskandrian AE: The effects of medications on myocardial perfusion. J Am Coll Cardiol 2008; 52: 401–416
14) Thomassen A, Petersen H, Johansen A, et al: Quantitative myocardial perfusion by O-15-water PET: individualized vs. standardized vascular territories. Eur Heart J Cardiovasc Imaging 2015; 16: 970–976