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Value of Pathological Q Waves and Angiographic Collateral Grade in Patients Undergoing Coronary Chronic Total Occlusion Recanalization: Cardiac Magnetic Resonance Study

Khaled Abdel-Azim Shokry^a, El-Sayed Mohamed Farag^b, Ahmed Mohamed Salem^b,
Ismail Mohamed Ibrahim^b, Mahmoud Abel-Aziz^c, Ahmed El Zayat^{c*}

^a Department of Cardiology, Military Medical Academy, Cairo, Egypt

^b Department of Cardiology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

^c Department of Cardiology, Zagazig University, Zagazig, Egypt

Abstract

Background/aim: Successful coronary chronic total occlusion (CTO) revascularization was found by many studies to be associated with improved left ventricular (LV) systolic function and survival if evidence of viability is present. Little is known about the association of CTO revascularization in patients with electrocardiographic Q waves and improvement in angina burden as a measurement of health-related quality of life (HRQOL) afterwards.

Methods: In this study, 100 patients with single vessel CTO were included. Myocardial viability was tested by late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) and 50 patients showed evidence of viability. Seattle Angina Questionnaire (SAQ) scores were used as a measure of HRQOL.

Results: Pathological Q waves were present in 48 patients (including 19 patients with viable CTO territory) out of 100 patients. Patients with Q waves tended to have worse Seattle Angina Questionnaire (SAQ) scores compared to those with no Q waves (31.2 ± 11.7 vs 45.3 ± 13.9 respectively, $p = 0.002$), worse LV systolic function and wall motion score index (WMSI) on CMR. They also had significantly less prevalence of viability ($p < 0.001$). Patients with Q waves and positive viability had lower SAQ scores (37.2 ± 10.1 vs 52.7 ± 13.2 respectively, $p = 0.02$), higher LVEF and lower WMSI. They also had well developed collateral grade (2.1 ± 1.03 vs 0.7 ± 0.82 respectively, $p < 0.001$). After successful percutaneous coronary intervention (PCI), in the viable LV group, presence of Q waves was not associated with better LV functional recovery, while those with higher collateral grades were more likely to have better LV functional recovery post CTO-PCI. Patients with Q waves and viable CTO territory showed significantly better SAQ scores compared to pre-PCI (87.3 ± 12.2 vs 37.2 ± 10.1 respectively, $p < 0.001$). For angina frequency, post-PCI score was 80.2 ± 7.9 compared to 39.2 ± 7.1 before PCI, $p < 0.001$). Multivariate regression analysis showed that pathological Q waves, Rentrop's collateral grade and the Canadian Cardiovascular Society (CCS) angina class before PCI were the most significant independent predictors of improved HRQOL as reflected by SAQ (OR for Q waves 7.83, 95%CI 1.62–18.91, $p = 0.003$), (OR for Rentrop's collateral grade 8.31, 95% CI 2.21–26.33, $p < 0.001$), (OR for CCS class 8.39, 95%CI 1.21–20.8, $p = 0.01$).

Conclusion: Well-developed collateral circulation could independently predict LV functional recovery after CTO-PCI. Patients with Q waves and viable CTO territory tend to have higher CCS class before revascularization and get significant improvement of HRQOL after PCI. Other predictors of improved HRQOL are Rentrop's collateral grade and worse CCS class before PCI.

Keywords: Chronic total occlusion, Pathological Q waves, Percutaneous coronary intervention, Angina frequency, CMR, Health-related quality of life

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* Corresponding author at: Department of cardiology, Zagazig University, Zagazig, Egypt.
E-mail address: yousefyahia2005@yahoo.com (A. El Zayat).



1. Introduction

Approximately, one in five patients undergoing coronary angiography is found to have a chronic total occlusion (CTO) of one of the epicardial coronaries [1] and CTO is a frequent finding in patients with ischemic cardiomyopathy (ICM) [2].

Successful recanalization of CTO has been found by many studies to be associated with improved left ventricular systolic function and with improved survival as well, provided evidence of viability in the CTO territory is present [3,4].

Revascularization of CTO has a class IIa recommendation in the most recent revascularization guidelines provided that refractory angina is present [5]. However, the effect of percutaneous coronary intervention of chronic total occlusion (CTO-PCI) on health-related quality of life (HRQOL) in patients with pathological Q waves and viable CTO territory remains relatively an unexplored area.

In many cases of CTO, the clinical recognition of myocardial infarction is often challenging [5]. It was found that only 25% of CTO patients (confirmed on angiography) have pathological Q waves on electrocardiograms as an evidence of a previous myocardial infarction compared to 86% on late gadolinium enhancement – cardiac magnetic resonance (LGE-CMR) [6]. This could reflect that the frequency of old myocardial infarction is higher than previously expected in CTO territories. It was also found that the extent of myocardial scarring in the CTO territory is inversely correlated with the degree of the angiographic collaterals [6].

On the other hand, CTO patients remain under-represented regarding enrollment in PCI trials especially those with left ventricular systolic dysfunction [7,8]. Whether CTO-PCI in patients with pathological Q waves and viable CTO territory would be reflected on HRQOL improvement irrespective of the baseline left ventricular (LV) systolic function is unclear.

The aim of this study was to clarify the impact of pathological Q waves and angiographic collateral grade on health-related quality of life in patients undergoing coronary chronic total occlusion recanalization.

Abbreviations

CCS	Canadian Cardiovascular Society
CHF	congestive heart failure
CMR	cardiac magnetic resonance
CTO	chronic total occlusion
HRQOL	health-related quality of life
ICM	ischemic cardiomyopathy
LGE	late gadolinium enhancement
PCI	percutaneous coronary intervention
SAQ	Seattle Angina Questionnaire
WMSI	wall motion score index

2. Methods

2.1. Study population

This single center, prospective study was conducted in Cardiology department, Zagazig University Hospitals and Kobry Al-kobba Hospital, Egypt, in the period from August 2018 to January 2020 on 100 consecutive patients with single vessel CTO in a major epicardial coronary arteries as shown on coronary angiography (CA), provided that CTO lesion was amenable to PCI and has a viable territory. CTO was defined as the presence of Thrombolysis in Myocardial Infarction (TIMI) flow 0 within the occluded vessel with an estimated duration of occlusion of more than 3 months. A major epicardial coronary artery was defined as having a diameter of 2.5 mm or more [9]. We excluded patients with acute coronary syndrome within 90 days, CTO in a non-major epicardial coronary artery, usual contraindications of CMR (implanted pacemakers, cardioverter defibrillators, claustrophobia, and estimated glomerular filtration rate of <30 ml/min), or presence of bundle branch block criteria on ECG.

Written informed consent was obtained from all participants. The study was approved by the institutional review board and local ethical Committee.

2.2. Clinical assessment

Diabetes mellitus was defined as HbA1C > 6.5 g/dL or use of oral hypoglycemic drugs and/or insulin. Hypertension was defined as a systolic blood pressure >140 and/or a diastolic blood pressure >90 during hospitalization or prior use of an antihypertensive medication. Dyslipidemia was defined as fasting total cholesterol >200 mg/dL, low-density

lipoprotein-cholesterol > 130 mg/dL, triglycerides >150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, and/or chronic use of lipid-lowering drugs. Positive family history of premature coronary artery disease (CAD) was defined as documented evidence of CAD in a close relative (men <55 and women <65 years of age). Current smoking was defined as cigarette smoking during the last month. Patients with signs/symptoms of congestive heart failure (CHF), current treatment for CHF, or calculated left ventricular ejection fraction (LVEF) < 40% were considered to have CHF.

2.3. Resting 12-lead ECG

Resting 12-lead ECG: (paper speed of 50 mm/s, sensitivity of 0.1 mV/mm). Q wave were considered pathological if > 30 ms duration involving \geq two contiguous leads [10–13]. This had to be present in 5 consecutive complexes to be considered. ECG analysis was conducted by two investigators and a third investigator was consulted upon disagreement.

2.4. Cardiac magnetic resonance (CMR)

2.4.1. Protocol

CMR was performed within 2 weeks (a median of 4 days) before PCI to assess left ventricular end systolic and end diastolic volumes and ejection fraction by Simpson's method, wall motion score index (WMSI), as well as myocardial viability by late gadolinium enhancement (LGE).

2.4.2. Image acquisition

A 1.5 T scanner (Aera, Syngo MR, Siemens Medical Solutions, Germany) was used. Standard low-resolution localizer scans were performed to define the cardiac long and short axes. Steady state free precession (SSFP) cine images were acquired in the horizontal long axis, vertical long axis and left ventricular outflow tract views. Further SSFP cine images were acquired in 12–10 contiguous, end-expiratory, multiphase short axis slices parallel to the mitral valve annulus covering the whole of the left ventricle (slice thickness 8 mm, interslice gap 1 mm). A total of 0.2 mmol/kg of gadobutrol contrast agent was administered at 4 ml/s via a peripheral venous cannula followed by 30 ml of 0.9% normal saline flush at 4 ml/s. After 10–15 min post-injection of gadolinium-based contrast a breath-hold 2-dimensional segmented inversion recovery sequence, inversion time (TI) 240–300, was acquired in the same orientation as the cine images.

2.4.3. Image analysis

Image analysis was performed on a Siemens' workstation. Left ventricular end diastolic and end systolic volumes were measured allowing the calculation of left ventricular ejection fraction. Each segment of the myocardium was assessed visually and scored by the American College of Cardiology Foundation/American Heart Association 17 segment model with 7 segments for the left anterior descending artery, 5 for the right coronary artery, and 5 for the left circumflex artery. If the left circumflex artery was dominant, 2 inferior segments were reassigned from the right coronary artery to the left circumflex artery. For each segment, wall motion was scored as: 1 (normal/hyperkinetic), 2 (hypokinetic), 3 (akinetic), or 4 (dyskinetic). WMSI was calculated by dividing the sum of all points by the number of segments in the coronary territory (with a WMSI of 1 representing normal function) [14]. All short axis images from the base to the apex of the left ventricle were analyzed and the transmural extent of scar of each myocardial segment was assessed by LGE. Using the same 17-segment model, interpretation of LGE was performed visually with the enhanced area defined as a percentage of the myocardial thickness with each segment scored as 1 (0%), 2 (1–25%), 3 (26–50%), 4 (51–75%), 5 (76–100%). Viable myocardium was identified when most segments in the CTO territory had \leq 50% transmural extent of scar by LGE [15]. Accordingly, patients were divided into 2 groups: viable and non-viable territory group.

2.5. Coronary angiography

Assessment of collateral circulation was graded as previously described by the Rentrop score [16]: Grade 0 (no collaterals), Grade 1 (collaterals filling only side branches of the recipient artery), Grade 2 (collaterals partially filling the occluded artery trunk), Grade 3 (collaterals completely filling the occluded vessel trunk). For Data analysis, grade 0 or 1 collaterals were considered a poorly developed collateral group whereas grade 2 or 3 collaterals were considered a well-developed collateral group [16]. Analyses were done by two independent interventionalists who were blinded to all data. In case of inconsistency, the final decision was made by consensus.

2.6. Percutaneous recanalization of CTO

2.6.1. Selection Criteria

Functionally, the CMR criteria of myocardial viability for proceeding to recanalization are

majority of the segments in the CTO territory having $\leq 50\%$ transmural extent of infarction by late gadolinium enhancement (LGE) [14]. 50 patients (viable CTO territory group) had successful CTO-PCI.

2.7. Protocol

The PCI access choice was left to the operator preference either femoral or radial. Each patient received an initial unfractionated heparin bolus (70 u/Kg) and activated clotting time (ACT) was checked every 15 min with ACT target > 250 s. Antegrade approach was the first choice in all cases, with retrograde approach attempted after one unsuccessful antegrade attempt (secondary retrograde approach). Revascularization strategy (contralateral selective injection, wires choice, microcatheter type, lesion crossing techniques) was left to the operator's discretion, depending on his/her own preference and the anatomical setting. Drug-eluting stents were used when feasible. Arterial access closure strategy (manual compression, closure device) was left to operators' preference. Double antiplatelet therapy duration and P2Y12 inhibitor choice was based on current guidelines [17]. Successful technical CTO-PCI was defined as the restoration of TIMI grade 3 flow with residual stenosis of less than 30% [18].

2.8. Assessment of health-related quality of life using Seattle Angina Questionnaire (SAQ)

SAQ was given to patients at the time of their CMR scans (baseline and follow-up). It is a widely used questionnaire to assess health outcome measures in patients with coronary artery disease. It consists of a 9-item scale of physical limitations

(how daily activities are limited by angina), 1-item scale for angina stability (assesses change in frequency of angina at patient most strenuous level of activity), 2-item scale for angina frequency (frequency of symptoms and use of medications), a 3-item for perception scale (effect of angina on quality of life), and a 4-item treatment satisfaction scale quantifies patients' satisfaction with their current treatment. All items use 5 point descriptive scales and scores are calculated summing all the single scores within each group and transforming them to a scale of 0–100, where 0 is the worst and 100 is the best [19,20].

Short term outcome: (6 months follow up)

It was performed 6 months after successful CTO-PCI.

a Assessment of HRQOL: through SAQ.

b CMR follow-up study to assess LV end systolic volume (ESV), LV end diastolic volume (EDV), LVEF and WMSI to detect functional recovery of systolic function and reverse myocardial remodeling. Good LV functional recovery was defined as 5% increase in ejection fraction on follow up study. This definition is concordant with recent large meta-analysis [18].

2.9. Statistical analysis

In the descriptive analysis, categorical variables are presented as number and percentage. Continuous variables are presented as mean \pm SD as normally distributed. Group differences were evaluated using chi-square for categorical variables. Student *t*-test were used for continuous variables. Comparisons between pre- and post-PCI clinical parameters and CMR studies were performed by

Table 1. Baseline characteristics between Q waves & no Q waves groups.

	Q waves (N = 48)	No Q waves (N = 52)	p- value
Age (years), Mean \pm SD	59.2 \pm 8.7	58.1 \pm 5.3	0.79
Male Gender, n (%)	40 (83.3%)	45 (86.5%)	0.89
Diabetes mellitus, n (%)	26 (54.2%)	30 (57.6%)	0.91
Hypertension, n (%)	33 (68.7%)	38 (73.1%)	0.61
Dyslipidemia, n (%)	24 (50%)	28 (46.7%)	0.81
Current smoking, n (%)	33 (68.7%)	39 (75%)	0.31
Family history of premature CAD, n (%)	11 (22.9%)	14 (26.9%)	0.87
SAQ (Total score), (Mean \pm SD)	31.2 \pm 11.7	45.3 \pm 13.9	0.002
CMR measurements			
LVEF (%)	42.3 \pm 12.1	51.2 \pm 10.3	0.01
WMSI (Mean \pm SD)	1.7 \pm 0.42	1.5 \pm 0.5	0.03
Viable myocardium (LGE-CMR), n (%)	19 (39.5%)	31 (59.6%)	<0.001

SAQ Seattle angina questionnaire; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; WMSI: wall motion score index; CMR: cardiovascular magnetic resonance.

Bold values indicate $p < 0.05$.

Table 2. Baseline characteristics between Q waves with viable LV & Q waves with non-viable LV groups.

	Q waves with viable LV (n = 19)	Q waves with Non-viable LV (n = 29)	p- value
Age (years), Mean ± SD	58.3 ± 7.2	56.7 ± 6.9	0.42
Male Gender, n (%)	14 (73.6%)	22 (75.8%)	0.91
Diabetes mellitus, n (%)	8 (42.1%)	13 (44.8%)	0.84
Hypertension, n (%)	12 (63.1%)	20 (68.9%)	0.77
Dyslipidemia, n (%)	10 (52.6%)	17 (58.6%)	0.32
Current smoking, n (%)	12 (63.1%)	17 (58.6%)	0.45
Family history of premature CAD, n (%)	4 (21.1%)	6 (20.7%)	0.88
SAQ (Total score), (Mean ± SD)	37.2 ± 10.1	52.7 ± 13.2	0.02
CCS (3 or 4), n (%)	14 (73.6%)	2 (6.8%)	<0.001
CHF, n (%)	7 (36.8%)	20 (68.9%)	0.01
CMR measurements (Mean ± SD)			
LVEF %	46.3 ± 10.1	41.7 ± 9.8	0.008
WMSI	1.5 ± 0.4	1.8 ± 0.2	0.02
Angiographic Data			
Site of CTO, n (%)			
LAD	14 (73.7%)	16 (55.2%)	0.12
LCX	3 (15.7%)	7 (24.1%)	
RCA	2 (10.5%)	6 (20.7%)	
Rentrop grade			
grade 0, n (%)	2 (10.5%)	13 (44.8%)	<0.001
grade 1, n (%)	4 (21.1%)	9 (31.03%)	
grade 2, n (%)	6 (31.5%)	3 (10.3%)	
grade 3, n (%)	7 (36.8%)	4 (13.7%)	

CAD: coronary artery disease; SAQ Seattle angina questionnaire; CCS: Canadian Cardiovascular Society; CHF: congestive heart failure; CHF congestive heart failure. CMR: cardiovascular magnetic resonance; CTO: chronic total occlusion; LAD: left anterior descending; LCX; left circumflex; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; RCA: right coronary artery; WMSI: wall motion score index.

Bold values indicate p < 0.05.

Table 3. Comparison between patients with good functional recovery post CTO-PCI versus those with poor functional recovery.

	Good Functional Recovery (n = 34)	Poor Functional Recovery (n = 16)	p- value
Age (years), Mean± SD	56 ± 7	57 ± 9	0.783
Male Gender, n (%)	32 (94.1%)	15 (93.8%)	0.959
Diabetes mellitus, n (%)	17 (50%)	6 (37.5%)	0.408
Hypertension, n (%)	22 (64.7%)	7 (43.8%)	0.161
Dyslipidemia, n (%)	15 (44.1%)	10 (62.5%)	0.225
Current smoking, n (%)	24 (70.6%)	12 (75%)	0.746
Family history, n (%)	9 (26.5%)	1 (6.3%)	0.095
SAQ (at follow up)	90 ± 4.4	88 ± 3.8	0.417
Mean ±SD			
Pathological Q, n (%)	15 (44.1%)	4 (25%)	0.194
Type of CTO vessel, n (%)			
LAD	20 (58.8%)	16 (100%)	
LCX	7 (20.6%)	0 (0%)	
RCA	7 (20.6%)	0 (0%)	0.01
Collateral grade,			
Grade 0, n (%)	1 (2.9%)	5 (31.3%)	0.001
Grade 1, n (%)	2 (5.9%)	6 (37.5%)	
Grade 2, n (%)	14 (41.2%)	1 (6.3%)	
Grade 3, n (%)	17 (50%)	4 (25%)	
Collateral state			
Well-developed, n (%)	31 (91.2%)	5 (31.3%)	0.001
Poor, n (%)	3 (8.8%)	11 (68.8%)	
Viability score			
Score 1, n (%)	12 (35.2%)	4 (25%)	0.056
Score 2, n (%)	11 (32.4%)	4 (25%)	
Score 3, n (%)	11 (32.4%)	8 (50%)	

SAQ Seattle angina questionnaire, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, CTO chronic total occlusion, well developed collaterals refer to Rentrop grade.

Bold values indicate p < 0.05.

Table 4. Comparison between before and after CTO-PCI in patients with Q waves and viability.

	Q waves with viable LV Before CTO PCI (N = 19)	Q waves with viable LV After CTO PCI (N = 19)	p-value
SAQ			
Total score	37.2 ± 10.1	87.3 ± 12.2	<0.001
physical Limitation	58.3 ± 13.7	90.2 ± 13.7	<0.001
Treatment satisfaction	52.4 ± 7.8	88.9 ± 11.3	<0.001
Angina stability	32.9 ± 5.9	79.3 ± 8.3	<0.001
Angina frequency	39.2 ± 7.1	80.2 ± 7.9	<0.001
Disease Perception	35.2 ± 6.4	87.4 ± 9.3	<0.001
CMR			
LVEF %	46.3 ± 10.1	52.3 ± 6.3	0.002
WMSI	1.5 ± 0.4	1.2 ± 0.2	0.01

SAQ Seattle angina questionnaire, EF ejection fraction, WMSI wall motion score index, CMR cardiac magnetic resonance, CTO chronic total occlusion.

Bold values indicate $p < 0.05$.

paired t-tests. Subgroup analysis was performed based on mean difference of LVEF by CMR 5% to evaluate LV functional recovery and reverse remodeling [18].

Univariate logistic regression analysis was performed for the identification of possible significant predictors of functional recovery and improved HRQOL. Multivariate regression analysis was performed for the significant variables in the univariate logistic analysis. A two tailed $p < 0.05$ was considered significant. Data were imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis.

3. Results

This study included 100 patients with single vessel CTO and no other significant CAD. Forty-eight patients (48%) had Q waves on their 12-lead surface ECG and compared with those with no Q waves (52 patients), they tended to have worse SAQ scores, lower LVEF and WMSI on CMR. Q waves patients were found to have significantly less viability as shown by LGE-CMR ($p < 0.001$), (Table 1).

Nineteen patients (19%) had evidence of significant viability on LGE-CMR and pathological Q

waves on 12-lead ECG. On the other hand, 29 patients had no evidence of viability and had pathological Q waves. Patients with Q waves and viability evidence by CMR showed significantly lower SAQ scores, lower LVEF and higher WMSI on CMR. They also showed evidence of more well-developed coronary collateral circulation on angiography as shown by Rentrop collaterals grade ($p < 0.001$). Higher CCS angina class III and IV were more frequently encountered in patients with pathological Q waves and viable myocardium, while congestive heart failure symptoms were more encountered in those with pathological Q waves and non-viable territories, as shown in Table 2.

On comparing patients with good LV functional recovery after CTO-PCI (34 patients) with those with poor LV functional recovery (16 patients), we found that the presence of Q waves was not significantly associated with functional recovery after CTO-PCI. On the other hand, patients with well-developed coronary collateral circulation in CTO segments, as evidenced by higher Rentrop collateral grades, were more likely to have good functional recovery after CTO-PCI, as shown in Table 3.

After successful CTO-PCI, patients with Q waves and evidence of viability (19 patients) showed a

Table 5. Binary logistic regression analysis to determine predictors of improvement of LV systolic function after single CTO-PCI.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Diabetes Mellitus	1.6 (0.4–56)	0.41	–	–
Pathological Q	2.3 (0.6–8.8)	0.21	–	–
LVEF% (CMR)	5.2 (0.5–43.2)	0.005	–	–
WMSI (CMR)	0.3 (0.1–1.8)	0.25	–	–
Well-developed Collaterals	22.7 (4.6–111.2)	0.0001	41.5 (51–336.3)	0.0001

LVEF left ventricle ejection fraction, WMSI wall motion score index, CMR cardiac magnetic resonance, well developed collaterals refer to Rentrop grade 2 or 3.

Bold values indicate $p < 0.05$.

Table 6. Binary logistic regression analysis to determine predictors of improvement of HRQOL after single vessel CTO-PCI.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Diabetes Mellitus	0.82 (0.17–0.89)	0.03	0.41 (0.11–2.1)	0.08
Hypertension	0.63 (0.18–0.97)	0.041	0.19 (0.01–1.92)	0.12
CCS (before PCI)	0.16 (0.03–0.51)	0.004	0.39 (1.21–20.8)	0.01
CHF (before PCI)	1.06 (1.02–1.30)	0.003	0.32 (0.11–2.39)	0.32
Pathological Q wave	6.22 (1.28–33.17)	<0.001	7.83 (1.62–18.91)	0.003
LVEF% (CMR) (after PCI)	0.87 (0.29–1.33)	0.03	7.29 (1.23–18.22)	0.06
Well-developed Collaterals	6.52 (2.11–28.22)	0.001	8.3 (2.21–26.33)	<0.001

CCS Canadian cardiovascular score, CHF congestive heart failure, LVEF left ventricle ejection fraction, PCI percutaneous coronary intervention, CMR cardiac magnetic resonance, well developed collaterals refer to Rentrop grade 2 or 3.

Bold values indicate $p < 0.05$.

highly significant statistical difference regarding SAQ total score and SAQ items scores compared to pre-PCI scores ($p < 0.001$). On CMR follow up study after CTO-PCI, patients with Q waves and positive viability had significant improvement in both LV systolic function and WMSI (p value = 0.002 and 0.01 respectively), as shown in Table 4.

By using binary logistic regression analysis to detect predictors of LV functional recovery after CTO-PCI, only well-developed collateral circulation (Rentrop grade 2 or 3) was a significant independent predictor on multivariate analysis, as shown in Table 5.

Table 6 shows that pathological Q waves, well-developed collateral circulation, CCS angina class before PCI and LVEF were the independent predictors of HRQOL improvement as shown by SAQ scores on multivariate regression analysis.

4. Discussion

To the best of our knowledge, this is the first study to address the relationship of pathological Q waves and angiographic collaterals with LV functional recovery and HRQOL assessed by SAQ after single vessel CTO-PCI. Only single vessel CTO with no other significant CAD cases were included in this study. This greatly identifies patients' symptoms to be due to the single CTO territory.

Different ECG criteria were tested to predict myocardial viability and recovery of systolic function as QT dispersion and T wave normalization [21,22]. Moreover, a QRS score (Silvester score) was established to predict infarction size and LV function after MI [23,24].

CTO-PCI can lead to recovery of regional LV function and may even improve survival [25] if viable territory is present (as should have been shown by viability tests before attempting revascularization).

We found that cases with no pathological Q waves were more likely to have viable CTO territory

compared to those with Q waves. Surber et al. reported that absence of Q-waves in pre-PCI ECG significantly predicted improved LV regional function in the reperfused territory, whereas their presence predicted lack of recovery [26]. They found that wall motion severity index improved from -2.92 ± 0.28 at baseline to -1.34 ± 0.61 on post-PCI echocardiographic assessment ($p < 0.001$) in cases of absent Q waves, compared to $(-3.01 \pm 0.3$ and $-2.81 \pm 0.32)$ ($p = 0.11$) in cases of presence of Q waves on the pre-PCI ECG.

They concluded that absence of Q waves predicted recovery of CTO territory regional function with 89% sensitivity, 67% specificity and 68% positive predictive value [26].

Surber et al. showed that on multivariate logistic regression analysis, only absence of Q wave in the CTO territory (among all other set variables) predicted functional recovery of the LV [26].

Based on positron emission tomography (PET) nuclear studies and dobutamine stress echocardiography (DSE), about 60% of Q waves areas show viability [27–29]. On the other hand, only 50–80% of viable myocardial tissue as shown by different viability testing modalities assumed functional recovery after revascularization [30].

Histologically, severely ischemic hibernating myocardium shows advanced structural changes that eventually lead to lack of functional recovery after reperfusion [31]. Such changes could be very pronounced in Q waves territories of CTO with eventually lack of recovery after reperfusion.

We found that patients with Q waves and evidence of viability, as assessed by LGE-CMR, had more CCS class III and IV before PCI. This agrees with Chen Seak Park et al. study where CTO patients with CCS III or IV symptoms before revascularization were more encountered in those with Q waves. On the other hand, they showed that 64% of CTO patients with Q waves had RWMA compared to 24% of those without Q waves [32].

In contrast to our study, health-related quality of life was assessed by OAT trial investigators [33] and found that CTO PCI was associated with a marginal and un-sustained advantage in cardiac physical function at 4 months' follow-up. Furthermore, no difference in the psychological well-being aspect of quality of life was found. However, these results cannot be widely applied to patients with CTO (occlusion duration of ≥ 3 months) because the OAT patient cohort presented with an occluded infarct related coronary artery 3–28 days after acute myocardial infarction (MI), and PCI was not guided by the presence of residual myocardial viability and ischemia [34].

We found that well-developed collaterals (Rentrop grade 2–3) were independent predictors of functional recovery and improvement of regional and global systolic function. This was concordant with Choi et al. [35] who reported that successful PCI for CTO lesions in patients with well-developed collaterals was associated with reduced incidence of the composite of death or MI, improved LV function, especially in certain subgroups of patients compared with optimal medical therapy (OMT) alone despite increased incidence of repeat mechanical revascularization for target CTO segments.

A recent study by Shaikh et al. [36] found that Q-waves associated with postinfarct chronic total occlusion arteries predicted non-viable myocardium even in the presence of good collaterals. In their study, viability was assessed by PET scan in 75 patients with a history of STEMI. In our study, although many patients gave a history suggestive of a myocardial infarction with admission to other local hospitals, the exact MI subtype (STEMI or NSTEMI) was not clear in many cases due to unavailable data and hence 'previous STEMI' was not part of the comparison between viable and non-viable Q-waves groups in our statistical analysis. Moreover, Shaikh et al. study was a single-center retrospective study with a small sample size. To conclusively state that prior MI with Q-waves on the ECG preclude viability even in the presence of grade 3 collaterals, larger sample size, prospective studies are needed.

We found that the independent predictors for improved HRQOL as assessed by SAQ after CTO-PCI were pathological Q waves, collateral grade, and CCS class before PCI. ECG, as an inexpensive, readily available, noninvasive, and easy to use tool compared to other sophisticated, expensive, time consuming imaging modalities, could have an integral role regarding prediction of improvement of HRQOL following reperfusion in single vessel CTO patients.

4.1. Limitations of the study

A major limitation of this study was the small number of patients and that it was a single center study. Larger caliber multi-center studies recruiting larger sample sizes are required to consolidate our findings. Another limitation was that we did not conduct a post-PCI (follow up) coronary angiography to assess stent patency. Re-occlusion or in-stent stenosis, if present, could have affected reperfused territory regional function and quality of life. Another limitation was that we did not perform a follow up LGE-CMR or stress CMR at 6 months after PCI in any of the patients. We rather assessed LV function by non-contrast CMR in the follow up study.

5. Conclusion

Well-developed collateral circulation could independently predict LV functional recovery after CTO-PCI. Patients with Q waves and viable CTO territory tend to have higher CCS class before revascularization and get significant improvement of HRQOL after PCI.

Author's contribution

Khaled Abdel-Azim Shokry: Conception and design of Study, Literature review, Research coordination and management, El-Sayed Mohamed Farag: Conception and design of Study, Acquisition of data, Revising and editing the manuscript critically for important intellectual contents, Supervision of the research, Research coordination and management, Ahmed Mohamed Salem: Literature review, Acquisition of data, Analysis and interpretation of data, Research investigation and analysis, Data collection, Revising and editing the manuscript critically for important intellectual contents, Supervision of the research, Research coordination and management, Ismail Mohamed Ibrahim: Acquisition of data, Analysis and interpretation of data, Research investigation and analysis, Data collection, Drafting of manuscript, Revising and editing the manuscript critically for important intellectual contents, Data preparation and presentation, Data preparation and presentation, Research coordination and management, Mahmoud Abel-Aziz: Analysis and interpretation of data, Data collection, Drafting of manuscript, Revising and editing the manuscript critically for important intellectual contents, Data preparation and presentation, Supervision of the research, Research coordination and management, Ahmed El

Zayat: Research investigation and analysis, Data collection, Drafting of manuscript, Data preparation and presentation, Supervision of the research.

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Conflict of interest

None to disclose.

References

- [1] Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. *Am J Cardiol* 2005;95: 1088–91. <https://doi.org/10.1016/j.amjcard.2004.12.065>.
- [2] Tajstra M, Pyka L, Gorol J, et al. Impact of chronic total occlusion of the coronary artery on long-term prognosis in patients with ischemic systolic heart failure: insights from the COMMIT-HF registry. *JACC Cardiovasc Interv* 2016;9: 1790–7. <https://doi.org/10.1016/j.jcin.2016.06.007>.
- [3] Jones DA, Weerackody R, Rathod K, et al. Successful recanalization of chronic total occlusions is associated with improved long-term survival. *JACC Cardiovasc Interv* 2012; 5:380–8. <https://doi.org/10.1016/j.jcin.2012.01.012>.
- [4] Olivari Z, Rubartelli P, Piscione F, et al. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions. *JACC (J Am Coll Cardiol)* 2003;41:1672–8. [https://doi.org/10.1016/s0735-1097\(03\)00312-7](https://doi.org/10.1016/s0735-1097(03)00312-7).
- [5] Galassi AR, Brilakis ES, Boukhris M, et al. Appropriateness of percutaneous revascularization of coronary chronic total occlusions: an overview. *Eur Heart J* 2016;37:2692–700. <https://doi.org/10.1093/eurheartj/ehv391>.
- [6] Choi JH, Chang SA, Choi JO, et al. Frequency of myocardial infarction and its relationship to angiographic collateral flow in territories supplied by chronically occluded coronary arteries. *Circulation* 2013;127:703–9. <https://doi.org/10.1161/CIRCULATIONAHA.112.092353>.
- [7] Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503–16. <https://doi.org/10.1056/NEJMoa070829>.
- [8] Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360: 961–72. <https://doi.org/10.1056/NEJMoa0804626>.
- [9] Sapontis J, Marso SP, Cohen DJ, et al. The outcomes, patient health status, and efficiency in chronic total occlusion hybrid procedures registry: rationale and design. *Coron Artery Dis* 2017;28:110–9. <https://doi.org/10.1097/MCA.0000000000000439>.
- [10] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Niemenen MS, Gheorghiu M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S. Joint ESC/ACCF/AHA/WHF task force for the universal definition of myocardial infarction. Third universal definition of myocardial infarction. *Circulation* 2012;126:2020–35. <https://doi.org/10.1093/eurheartj/ehs184>. Epub 2012 Aug 24.
- [11] Fefer P, Knudtson ML, Cheema AN, Galbraith PD, Osheroov AB, Yalonetsky S, Gannot S, Samuel M, Weisbrod M, Bierstone D, Sparkes JD, Wright GA, Strauss BH. Current perspectives on coronary chronic total occlusions: the Canadian multicenter chronic total occlusions registry. *J Am Coll Cardiol* 2012;59:991–7. <https://doi.org/10.1016/j.jacc.2011.12.007>.
- [12] Canto JG, Rogers WJ, Goldberg RJ, Peterson ED, Wenger NK, Vaccarino V, Kiefe CI, Frederick PD, Sopko G, Zheng ZJ, NRCMI Investigators. Association of age and sex with myocardial infarction symptom presentation and in-hospital mortality. *J Am Med Assoc* 2012;307:813–22. <https://doi.org/10.1001/jama.2012.199>.
- [13] Kwong RY, Sattar H, Wu H, Vorobiof G, Gandla V, Steel K, Siu S, Brown KA. Incidence and prognostic implication of unrecognized myocardial scar characterized by cardiac magnetic resonance in diabetic patients without clinical evidence of myocardial infarction. *Circulation* 2008;118: 1011–20. <https://doi.org/10.1161/CIRCULATIONAHA.107.727826>.
- [14] Kramer DG, Trikalinos TA, Kent DM, Antonopoulos GV, Konstam MA, Udelson JE. Quantitative evaluation of drug or device effects on ventricular remodeling as predictors of therapeutic effects on mortality in patients with heart failure and reduced ejection fraction: a Meta-Analytic approach. *J Am Coll Cardiol* 2010;56(5):392–406. <https://doi.org/10.1016/j.jacc.2010.05.011>.
- [15] Wang N, Fulcher J, Abeyesuriya N, Adams M, Lal S. Predictors of successful chronic total occlusion percutaneous coronary interventions: a systematic review and meta-analysis. *Heart* 2018;104:517–24. <https://doi.org/10.1136/heartjnl-2017-311986>.
- [16] Rentrop KP, Cohen M, Blanke H, Phillips RA. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol* 1985;5:587–92. [https://doi.org/10.1016/s0735-1097\(85\)80380-6](https://doi.org/10.1016/s0735-1097(85)80380-6).
- [17] Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. ESC Scientific Document Group; ESC Committee for Practice Guidelines (CPG); ESC National Cardiac Societies. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018 Jan 14;39(3):213–60. <https://doi.org/10.1093/eurheartj/ehx419>.
- [18] Megaly M, Saad M, Tajti P, Burke M, Chavez J, Gössl M, et al. Meta-analysis of the impact of successful chronic total occlusion percutaneous coronary intervention on left ventricular systolic function and reverse remodeling. *J Interv Cardiol* 2018 Oct;31(5):562–71. <https://doi.org/10.1111/joic.12538>.
- [19] Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonell M, Fihn SD. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol* 1995;25: 333–41. [https://doi.org/10.1016/0735-1097\(94\)00397-9](https://doi.org/10.1016/0735-1097(94)00397-9).
- [20] Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. *Circulation* 2002;106:43–9. <https://doi.org/10.1161/01.cir.0000020688.24874.90>.
- [21] Schneider CA, Voth E, Baer FM, Horst M, Wagner R, Sechtem U. QT dispersion is determined by the extent of viable myocardium in patients with chronic Q-wave myocardial infarction. *Circulation* 1997;96:3913–20. <https://doi.org/10.1161/01.CIR.96.11.3913>.
- [22] Mobilia G, Zanco P, Desideri A, Neri G, Alitto F, Suzzi G, Chierichetti F, Celegon L, Ferlin G, Buchberger R. T wave normalization in infarct-related electrocardiographic leads during exercise testing for detection of residual viability: comparison with positron emission tomography. *J Am Coll*

- Cardiol 1998;32:75–82. [https://doi.org/10.1016/s0735-1097\(98\)00205-8](https://doi.org/10.1016/s0735-1097(98)00205-8).
- [23] Palmeri ST, Harrison DG, Cobb FR, Morris KG, Harrell FE, Ideker RE, Selvester RH, Wagner GS. A QRS scoring system for assessing left ventricular function after myocardial infarction. *N Engl J Med* 1982;306:4–9. <https://doi.org/10.1056/NEJM198201073060102>.
- [24] Selvester RH, Wagner GS, Hindman NB. The Selvester QRS scoring system for estimating myocardial infarct size. The development and application of the system. *Arch Intern Med* 1985;145:1877–81. <https://doi.org/10.1001/archinte.1985.00360100147024>.
- [25] Suero JA, Marso SP, Jones PG, Laster SB, Huber KC, Giorgi LV, Johnson WL, Rutherford BD. Procedural outcomes and long-term survival among patients undergoing percutaneous coronary intervention of a chronic total occlusion in native coronary arteries: a 20-year experience. *J Am Coll Cardiol* 2001;38:409–14. [https://doi.org/10.1016/s0735-1097\(01\)01349-3](https://doi.org/10.1016/s0735-1097(01)01349-3).
- [26] Surber R, Schwarz G, Figulla HR, Werner GS. Resting 12-lead electrocardiogram as a reliable predictor of functional recovery after recanalization of chronic total coronary occlusions. *Clin Cardiol* 2005;28:293–7. <https://doi.org/10.1002/clc.4960280608>.
- [27] Haque T, Furukawa T, Takahashi M, Kinoshita M. Identification of hibernating myocardium by dobutamine stress echocardiography: comparison with thallium-201 reinjection imaging. *Am Heart J* 1995;130:552–63. [https://doi.org/10.1016/0002-8703\(95\)90366-6](https://doi.org/10.1016/0002-8703(95)90366-6).
- [28] Schinkel AF, Bax JJ, Elhendy A, Boersma E, Vourvouri EC, Sozzi FB, Valkema R, Roelandt JRTC, Poldermans D. Assessment of viable tissue in Q-wave regions by metabolic imaging using single-photon emission computed tomography in ischemic cardiomyopathy. *Am J Cardiol* 2002;89:1171–5. [https://doi.org/10.1016/S0002-9149\(02\)02299-3](https://doi.org/10.1016/S0002-9149(02)02299-3).
- [29] Shivalkar B, Maes A, Borgers M, Ausma J, Scheys I, Nuyts J, Mortelmans L, Flameng W. Only hibernating myocardium invariably shows early recovery after coronary revascularization. *Circulation* 1996;94:308–15. <https://doi.org/10.1161/01.CIR.94.3.308>.
- [30] Schinkel AF, Bax JJ, Geleijnse ML, Boersma E, Elhendy A, Roelandt JRTC, Poldermans D. Noninvasive evaluation of ischaemic heart disease: myocardial perfusion imaging or stress echocardiography? *Eur Heart J* 2003;24:789–800. [https://doi.org/10.1016/s0195-668x\(02\)00634-6](https://doi.org/10.1016/s0195-668x(02)00634-6).
- [31] Pagano D, Townend JN, Parums DV, Bonser RS, Camici PG. Hibernating myocardium: morphological correlates of inotropic stimulation and glucose uptake. *Heart* 2000;83:456–61. <https://doi.org/10.1136/heart.83.4.456>.
- [32] Park CS, Kim HY, Park HJ, et al. Clinical, electrocardiographic, and procedural characteristics of patients with coronary chronic total occlusions. *Korean Circ J* 2009;39:111–5. <https://doi.org/10.4070/kcj.2009.39.3.111>.
- [33] Mark DB, Pan W, Clapp-Channing NE, Anstrom KJ, Ross JR, Fox RS, et al. Quality of life after late invasive therapy for occluded arteries. *N Engl J Med* 2009;360:774–83. <https://doi.org/10.1016/j.ahj.2010.09.009>.
- [34] Bondarenko O, Beek AM, Twisk JW, Visser CA, van Rossum AC. Time course of functional recovery after revascularization of hibernating myocardium: a contrast-enhanced cardiovascular magnetic resonance study. *Eur Heart J* 2008;29:2000–5. <https://doi.org/10.1093/eurheartj/ehn266>.
- [35] Choi SY, Choi BG, Rha SW, Baek MJ, Ryu YG, Park Y, et al. Percutaneous coronary intervention versus optimal medical therapy for chronic total coronary occlusion with well-developed collaterals. *J Am Heart Assoc: Cardiovasc Cerebrovasc Dis* 2017 Sep;6(9). <https://doi.org/10.1161/jaha.117.006357>.
- [36] Shaikh MM, Sadiq MA, Nadar SK. Q-waves associated with postinfarct chronic total occlusion arteries predict non-viable myocardium even in the presence of collaterals. *J Invasive Cardiol* 2020 Aug;32(8):E213–5. Epub 2020 Jul 22. PMID: 32694225.