Effect of Collateral Circulation on Left Ventricular Systolic Function in Patients with Totally Occluded Artery Undergoing PCI

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ABSTRACT

Background: Over the past three decades, accumulating evidence has documented that pre-existing well-developed CCC at the onset of acute myocardial infarction plays an important role in preserving left ventricular function, reducing infarct size, preventing left ventricular aneurysm formation, and survival.

Objective: The aim of this study is to evaluate the effect of collateral circulation as measured by Rentrop score on left ventricular regional and global systolic function in patients with totally occluded vessel pre and post PCI and the ensuing impact of successful PCI. **Methodology:** Sixty patients have single vessel coronary chronic total occlusion with viable myocardium of CTO related territories, successful revascularization at ERMED and ICS, between June 2017 and December 2018, were considered to participate in this prospective study, The study subjects were divided into three groups according to Rentrop score , each group contain 20 patients : Group (I) Rentrop score 0 , Group (II) Rentrop score 1 and Group (III) Rentrop score 2. **Results:** There was no statistically significant difference between the three groups regarding the incidence of diabetes, smoking and hypertension. There was high statistically significant difference in EF between each group after revascularization, EF was higher in group (III) than group (I) and group (II). There was statistically significant difference in WMSI comparison between each group after revascularization WMSI was lower in group (III) than group (I) and group (II). **Conclusion:** In general increase Rentrop score before revascularization lead to more improvement in WMSI and EF after successful revascularization with improvement of quality of life.

Keywords: Coronary collateral circulation, CTO, PCI.

Abbreviation and acronyms : ATCP =Atypical chest pain, CABG = Coronary artery bypass graft, CAD = Coronary artery disease, CCC = Coronary collateral circulation, CCs = Collateral channels, CMR = Cardiovascular magnetic resonance, CTO = Chronic total occlusion, EF = Ejection fraction, ERMED = Egyptian Railway Medical Center, HTN = Hypertension, ICS = International cardio scan, LAD = Left anterior descending artery, LCX = Left circumflex artery, LV = Left ventricle, MACE = Major adverse cardiac events, OMT = Optimum medical therapy, PCI = Percutaneous coronary intervention, RCA = Right coronary artery, SD = Standard deviation, SOB = Shortness of breath, TIMI = Thrombolysis in Myocardial Infarction, WMSI = Wall motion score index, TCP = Typical chest pain .

INTRODUCTION

Coronary collaterals are potentially present vascular channels, which dilate and supply alternative perfusion to the coronary arteries in case of severe stenosis. Coronary collateral circulation (CCC) usually supplies basal level of perfusion to the ischemic myocardium and maintains the tissue viability **[1].**

Despite shortcomings of the data concerning the relationship between CCC and myocardial viability, CCC does not generally appear to perfuse the nonviable myocardial tissue **[2].**

Despite decades of study, the functional role of coronary collateral circulation remains controversial. A beneficial effect of coronary collaterals on infarct size has been suggested by many clinical investigators but not by others. Although stenotic lesions of between 75% and 90% can produce myocardial ischemia, they are never accompanied by angiographically visible collateral circulation. More severe narrowing or complete obstruction is necessary to stimulate development of angiographically visible collaterals **[3]**.

Over the past three decades, accumulating evidence has documented that pre-existing well-developed CCC at the onset of acute myocardial infarction plays an important role in preserving left ventricular function, reducing infarct size, preventing left ventricular aneurysm formation, and survival **[4].** But there is dispute whether the extent of collaterals is directly related to viability and functional recovery **[5].**

AIM OF THE STUDY

The aim of this study is to evaluate the effect of collateral circulation as measured by Rentrop score on left ventricular regional and global systolic function in patients with totally occluded vessel pre and post PCI and the ensuing impact of successful PCI.

PATIENTS AND METHODS

Patients

Sixty patients have single vessel coronary chronic total occlusion with viable myocardium of CTO related territories, successful revascularization at ERMED and ICS between June 2017 and December 2018 were considered to participate in this prospective study.

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The study subjects were divided into three groups according to Rentrop score:

- **Group I Rentrop score 0:** n=20 no filling of any collateral vessels.
- **Group II Rentrop score 1:** n=20 filling of side branches of the artery to be perfused by collateral vessels without visualization of the epicardial segment.
- **Group III Rentrop score 2:** n=20 partial filling of the epicardial vessel by collateral circulation.

The primary end point of the study was the change in regional wall motion as assessed by wall motion score index pre and post PCI at least two weeks after PCI.

Inclusion criteria

Patients referred for PCI to totally occluded lesion who fulfill the

(1) TIMI 0 coronary flow before PCI

(2) Presence of TIMI III flow after recanalization of totally occluded vessel.

(3) Viable myocardium.

Exclusion criteria

- Refusal of the patient to participate in the study.
- Acute myocardial infarction
- Patients with bad echo window or when complete echo study cannot be completed.
- Hyper/Hypothyroidism.
- Hypertrophic cardiomyopathy.
- TIMI score <III after recanalization of totally occluded artery.
- Multiple totally occluded coronary arteries.
- Other significant coronary artery lesions.

All patients were subjected to the following:

• Informed consent

• Evaluation of patients:

o History taking:

- Personal history
- History of present illness.
- Past medical history.

o Clinical evaluation

All patients were assessed clinically with full cardiological examination.

• Electrocardiographic (ECG) evaluation:

Resting 12 leads electrocardiography was done to all patients for assessment of:

1. Chamber enlargement
2. ST segment shift.
3. Reversal of T wave polarity.
4. Pathological Q wave
5. Arrhythmias.

•Transthoracic Echocardiography:

All the patients were examined in the left lateral decubitus position. Echocardiographic images were acquired from the standard views (parasternal long-axis, parasternal short axis at level of the great vessels, apical four–chambers, apical five–chambers and apical two-chambers). Recordings and calculations of different cardiac chambers, regional left ventricular myocardial function using LV wall motion score index and left ventricular global systolic function using LV ejection fraction were made according to the recommendations of the American Society of Echocardiography [(6)].

• Viability study

Viability study was done by dobutamine stress echocardiogram and myocardial perfusion imaging for detection of viable myocardium.

• Coronary Angiography

Angiographic evaluations were done by experienced cardiologists, who were blinded to the study. Coronary angiography was performed by the femoral approach and multiple views was obtained. Images were recorded on a digital system. The Rentrop classification to grade the filling of collateral channels: 0, no visible collateral channel filling; I, faintly visible collaterals with filling of branches but no filling of the distal stenotic (culprit) artery; II, collaterals partially filling the branches of the stenosed artery; III, complete collateral filling of the stenosed artery [(7)].

All patients received aspirin (300 mg) and a loading dose of clopidogrel (600 mg) prior to or at the time of PCI. All patients received anticoagulation during the procedure. Following PCI, all patients received aspirin 100 mg daily (indefinitely), clopidogrel 75 mg daily for at least 1 year. Each groups was followed up clinically and for MACE for 6 months.

Statistical Methods

Data were coded and entered using the statistical package SPSS version 25.

Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables.

Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test or unpaired t test in normally distributed quantitative variables while non-parametric Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a).

For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b).

P-values less than 0.05 were considered as statistically significant.

RESULTS

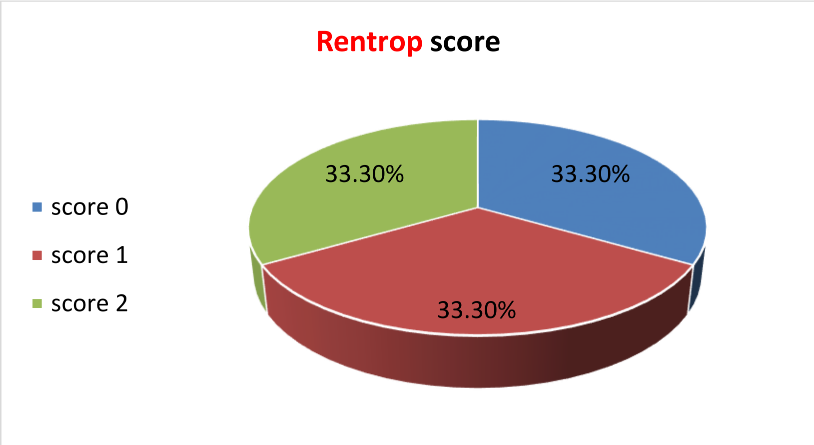

Figure (1): Three groups according to Rentrop score.

1 - Demographic characteristics and risk factors for CAD:

Group I:

Age: Their age ranged from 45 to 91 years with mean age ± SD was 57.05 ± 11.63 years.
Sex: 19 patients (95%) were males and 1 patient (5%) was female.

Risk Factors: 7 patients (35%) were diabetic, 10 patients (50%) were hypertensive, 8 patients (40%) were dyslipidemic, 16 patients (80%) were smokers, 5 patients (25%) had positive family history for CAD and 9 patient (45 %) had past history with CAD.

Group II:

Age: Their age ranged from 42 to 71 years with mean age ± SD was 56.90 ± 8.25 years.
Sex: 19 patients (95%) were males and 1 patient (5%) was female.

Risk Factors: 12 patients (60%) were diabetic, 13 patients (65%) were hypertensive, 8 patients (40%) were dyslipidemic, 13 patients (65%) were smokers, 2 patient (10%) had positive family history for CAD and 9 patients (45 %) had past history with CAD

Group III:

- **Age:** Their age ranges from 40 to 67 years with mean age ± SD was 56.60 ± 6.96 years.
- **Sex:** 16 patients (80%) were males and 4 patients (20%) were females.
- **Risk Factors:** 9 patients (45%) were diabetic, 12 patients (60%) were hypertensive, 8 patients (40%) were dyslipidemic, 11 patients (55%) were smokers, 6 patient (30%) had positive family history for CAD and 9 patient (45 %) had past history with CAD.

Comparison between the three groups according to demographic characteristics and risk factors (Age, Sex, diabetes, hypertension dyslipidemia, smoking, family history and past history of CAD) :

There was no significant difference between the three groups as regard age **(P-value =0.988)**. As shown in table (1)

Table (1): Three groups according to Rentrop score

		Rentrop score			P value
		Score 0	Score 1	Score 2	
Age	Mean	57.05	56.90	56.60	0.988
	Standard Deviation	11.63	8.25	6.96	
	Median	55.50	55.50	58.50	
	Minimum	45.00	42.00	40.00	
	Maximum	91.00	71.00	67.00	

There was no significant difference between the three groups as regard Sex **(P-value =0.344)**, diabetes **(P-value =0.28)**, hypertension **(P-value =0.619),** dyslipidemia **(P-value =1)**, smoking **(P-value =0.241)**, family history **(P-value =0.381)** and past history of CAD **(P-value =1)**. As shown in table (2).

Table (2): Comparison between the three groups according to demographic characteristics and risk factors

		Rentrop score						
		Score 0		Score 1		Score 2		P value
		Count	%	Count	%	Count	%	
Sex	Male	19	95.0%	19	95.0%	16	80.0%	0.344
	Female	1	5.0%	1	5.0%	4	20.0%	
Diabetic	Yes	7	35.0%	12	60.0%	9	45.0%	0.280
	No	13	65.0%	8	40.0%	11	55.0%	
Hypertension	Yes	10	50.0%	13	65.0%	12	60.0%	0.619
	No	10	50.0%	7	35.0%	8	40.0%	
Dyslipidemic	Yes	8	40.0%	8	40.0%	8	40.0%	1
	No	12	60.0%	12	60.0%	12	60.0%	
Smoking	Yes	16	80.0%	13	65.0%	11	55.0%	0.241
	No	4	20.0%	7	35.0%	9	45.0%	
Family history	Yes	5	25.0%	2	10.0%	6	30.0%	0.381
	No	15	75.0%	18	90.0%	14	70.0%	
Past history	Yes	9	45.0%	9	45.0%	9	45.0%	1
	No	11	55.0%	11	55.0%	11	55.0%	

There was no significant difference between the three groups as regard symptomatology **(P-value =0.06)**. As shown in table (3).

Table (3): Comparison between the three groups according to symptoms

		Rentrop score						
		Score 0		Score 1		Score 2		P value
		Count	%	Count	%	Count	%	
Complaint	TCP	18	90.0%	15	75.0%	12	60.0%	0.060
	SOB	0	0.0%	3	15.0%	3	15.0%	
	Both	0	0.0%	2	10.0%	1	5.0%	
	ATCP	2	10.0%	0	0.0%	4	20.0%	

There was no significant difference between the three groups as regard Chamber enlargement **(P-value =0.059)**, ST segment deviation **(P-value =0.162)**, Reversal of T wave **(P-value =0.812)**, Pathological Q wave **(P-value =0.117)** and Arrhythmia **(P-value =0.367)**. As shown in table (4).

Table (4): Comparison between the three groups according to ECG changes

		Rentrop score						
		Score 0		Score 1		Score 2		P value
		Count	%	Count	%	Count	%	
Chamber enlargement	yes	7	35.0%	1	5.0%	6	30.0%	0.059
	no	13	65.0%	19	95.0%	14	70.0%	
ST segment deviation	yes	12	60.0%	6	30.0%	9	45.0%	0.162
	no	8	40.0%	14	70.0%	11	55.0%	
Reversal of T wave	yes	7	35.0%	9	45.0%	8	40.0%	0.812
	no	13	65.0%	11	55.0%	12	60.0%	
Pathological Q wave	yes	9	45.0%	6	30.0%	3	15.0%	0.117
	no	11	55.0%	14	70.0%	17	85.0%	
Arrhythmia	yes	8	40.0%	4	20.0%	7	35.0%	0.367
	no	12	60.0%	16	80.0%	13	65.0%	

There was significant difference between the three groups as regard CTO vessel **(P-value =0.025)**. As shown in table (5).

Table (5): Comparison between the three groups according to CTO vessel

		Rentrop score						
		Score 0		Score 1		Score 2		P value
		Count	%	Count	%	Count	%	
CTO vessel	LAD	18	90.0%	10	50.0%	12	60.0%	0.025
	LCX	2	10.0%	3	15.0%	3	15.0%	
	RCA	0	0.0%	7	35.0%	5	25.0%	

There was statistically significant difference in EF before and after revascularization in each group. As shown in table (6). EF in group I (score 0) before revascularization was (45.7±5.55) and after revascularization was (46.9±4.96) and (p<0.001). EF in group II (score 1) before revascularization was (50.6±8.41) and after revascularization was (53.2±7.77) and (p<0.001).EF in group III (score 2) before revascularization was (47.7±7.77) and after revascularization was (52.15±6.84) and (p<0.001).

There was high statistically significant difference in EF between each group after revascularization (p=<0.001) Table (7), EF was higher in group III than groups I and II by Post Hoc comparison **Table (8)**

Table (6): EF pre and post revascularization and EF % changes in each group

		Rentrop score			P value
		Score 0	Score 1	Score 2	
LV EF before evascularization	Mean	45.70	50.60	47.70	0.115
	Standard Deviation	5.55	8.41	7.77	
	Median	48.00	49.00	47.00	
	Minimum	34.00	30.00	34.00	
	Maximum	53.00	73.00	63.00	
Post-revascularization EF	Mean	46.90	53.20	52.15	0.009
	Standard Deviation	4.96	7.77	6.84	
	Median	48.00	52.50	51.00	
	Minimum	38.00	35.00	40.00	
	Maximum	54.00	73.00	68.00	
EF % change	Mean	2.90	5.53	9.90	< 0.001
	Standard Deviation	4.37	3.33	4.33	
	Median	2.02	4.26	8.70	
	Minimum	-2.44-	0.00	-1.61-	
	Maximum	14.71	16.67	17.65	

Table (7): Comparison between the three groups according EF % change

	P value
Score 0 vs score 1	0.085
Score 0 vs score 2	< 0.001
Score 1 vs score 2	0.013

Table (8): Post Hoc comparison of EF after revascularization

		Retrop score		
		score 0	score 1	score 2
Post EF	score 0		0.012	0.045
	score 1	0.012		1.000
	score 2	0.045	1.000	

There was statistically significant difference in WMSI before and after revascularization in each group. As shown in table (9). WMSI in group I (score 0) before revascularization was (1.48±0.27) and after revascularization was (1.33±0.22) and (p=0.005). WMSI in group II (score 1) before revascularization was (1.38±0.17) and after revascularization was (1.21±0.14) and (p=0.005). WMSI in group III (score 2) before revascularization was (1.53±0.33) and after revascularization was (1.28±0.24) and (p=0.005). There was statistically significant difference in WMSI comparison between each group after revascularization (p=0.005) WMSI was lower in group III than group I and II Table (9)

Table (9): WMSI before and after revascularization and WMSI change in both groups

		Rentrop score			P value
		Score 0	Score 1	Score 2	
Pre WMSI	Mean	1.48	1.38	1.53	0.192
	Standard Deviation	0.27	0.17	0.33	
	Median	1.44	1.31	1.50	
	Minimum	1.18	1.16	1.00	
	Maximum	2.06	1.75	2.38	
Post WMSI	Mean	1.33	1.21	1.28	0.178
	Standard Deviation	0.22	0.14	0.24	
	Median	1.28	1.18	1.25	
	Minimum	1.06	1.06	1.00	
	Maximum	1.88	1.50	1.87	
WMSI change	Mean	-9.39-	-11.78-	-15.30-	0.005
	Standard Deviation	5.58	3.77	7.26	
	Median	-9.51-	-10.51-	-16.67-	
	Minimum	-21.43-	-21.71-	-28.21-	

	Maximum	-1.69-	-6.25-	0.00	

Patients of each group were followed up for detection of MACE and there were no MACE complications noted in each group.

DISCUSSION

A CTO is defined as a 100% obstructive coronary lesion present for at least 3 months, with less than, or equal to thrombosis in myocardial infarction grade 0 flow [8]**.** It is reported to occur in 15% to 23% of patients who undergo coronary angiograms and is the most common feature leading to coronary bypass surgery as a treatment recommendation for revascularization [9]**.**

Collateral channels (CCs) originate as arterioles connecting the vascular beds of visible coronary arteries. With increased chronicity of an occlusion, these small arteriole collaterals undergo remodeling to become muscular arteries known as arteriogenesis [10]**.**

PCI in CTO is indicated for improvement of quality of life and angina relief in patients with high-risk non-invasive functional studies or persistent angina despite OMT with acceptable procedural complication risk. Appropriateness use criteria for CTO PCI have been described and adopted by many organizations [11]**.**

Quality of life measures including angina, dyspnea, and depression are significantly improved after CTO recanalization [12]**.**

Successful CTO recanalization has been associated with improvement in cardiopulmonary exercise capacity in a cohort of patients with normal ejection fraction [13]**.** In observational studies, it was associated with improved clinical outcomes, including lower residual angina, risk of death, stroke, or need for CABG [14]**.** Because percutaneous coronary intervention (PCI) success rates with CTOs are less than with no occluded lesions, CTOs impact decision making in different clinical scenarios. Significant improvements in technique and development of novel dedicated PCI strategies have recently emerged. In parallel, industry has been investing large efforts in advancing device and wire technologies [15]**.**

A growing number of studies reporting procedural results and/or assessing functional effects and long-term clinical outcomes of CTO PCI are now available. We therefore sought to review and critically appraise the evidence base for procedural outcomes and potential clinical benefits of CTO PCI [16]**.**

In this study we found that:

There was no statistically significant difference between the frequencies of gender in the three groups. These results are concordant with the results of **Sanguineti *et al.*** [17]**.**There was no significant statistical difference between the three groups regarding the age. These results are concordant with the results of **Takeshita** [18] (323 patients, P value =0.73) but not in agreement with **Sanguineti *et al.*** [17]**.** in which there was significant statistical difference between age of groups where the ages of successful CTO revascularization were significantly lower then failed group (P=0.02). This disagreement may be due to:

(1) Limited number in our study, 60 patients while **Sanguineti *et al.*** [17] study population was 1343 patients.

(2) Sanguineti *et al.* [17]**,** age group (mean age 64) was older than this study age group (mean age 56.86)

There was no statistically significant difference between the three groups regarding the incidence of diabetes **(P-value =0.280)**, smoking **(P-value =0.241)**. These results are concordant with the results of **Sanguineti *et al.*** [17].

There was no statistically significant difference between the three groups regarding the incidence of hypertension **(P-value =0.619).** These results are not in agreement with the results of **Sanguineti *et al.*** [17]**.** This disagreement may be due to previous mentioned reasons.

There was high statistically significant difference in EF between each groups after revascularization, EF was higher in group III than group I and II. These results are concordant with the results of **Dongen *et al.*** [19] and **Elias *et al.*** [20]**.**

There was statistically significant difference in WMSI comparison between each groups after revascularization. WMSI was lower in group III than groups I and II**.**

MACE complications for Six months follow up in both groups:

Patients of the three groups were followed up six months for detection of MACE and there were no MACE complications noted in each group. These results are not in agreement with **Sanguineti *et al.***[17]**.** In which there was significant statistical difference between two groups where MACE complications were lower with successful CTO (P=0.0235). This disagreement may be due to:

(1) Limited number in our study, 60 patients while **Sanguineti *et al.*** [17] study population was 1343 patients.

(2) We followed our patients for six months while **Sanguineti *et al.*** [17] study followed the patients for 4.1 years

MACE complications in our study are concordant with the results of **Takeshita *et al.*** [18]**.**

Takeshita *et al.* [18] study showed that no survival changes between two groups in short term follow up (500 days) while at long term follow up (1500 days) there was an improvement of cardiac survival in patients with total revascularization and successful PCI to CTO (P=0.011).

Statistical correlation between Rentrop score and EF before revascularization and after revascularization in each groups:

The EF before and after revascularization correlated positively with Rentrop score. The higher Rentrop score before revascularization the higher is EF improvement after revascularization, (P < 0.001). These results are concordant with the results of **Dongen *et al.* [19] and Elias *et al.* [20].**

Statistical correlation between Rentrop score and WMSI changes before and after revascularization in each groups:

The WMSI before and after revascularization correlated positively with Rentrop score. The higher Rentrop score before revascularization is the higher WMSI improvement after revascularization, (P 0.005). These results are concordant with the results of **Gibson and Korjian [4] and Choi *et al.* [21]** but not in agreement with **Ripley *et al.* [22] study** in which there was no relationship between collateral circulation supply and wall motion score index (WMSI) .This disagreement may be due to :

(1) Ripley *et al.* [22] did study with CMR while our study was by ECHO

(2) Ripley *et al.* [22] had retrospective nature so some clinical information was not available from the case notes.

CONCLUSION

So finally, according to this study we can conclude that:

In general, increase Rentrop score before revascularization lead to more improvement in WMSI and EF after successful revascularization with improvement of quality of life.

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