

IMPACT OF PERIPROCEDURAL MYOCARDIAL INJURY AFTER SUCCESSFUL RECANALIZATION OF CORONARY ARTERY CHRONIC TOTAL OCCLUSION USING ANTEGRADE VERSUS RETROGRADE APPROACH

By

Amr M. Shaban, Ahmed Rozza and Ashraf Al-Amir

Department of Cardiology, Faculty of Medicine, Al-Azhar University

E-mail: mmomm@live.co.uk

ABSTRACT

Background: The risk of periprocedural myocardial injury (PMI) during percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) may be underestimated because systematic cardiac biomarkers measurement was not performed in published studies.

Objective: To evaluate the incidence, correlations, and clinical implications of periprocedural myocardial injury (PMI) during percutaneous coronary intervention (PCI) of successful chronic total occlusion (CTO) antegrade versus retrograde approach.

Patients and methods: Between February 2018 and November 2019, the study included 80 patients with successful PCI to chronic total occlusion 60 patients with antegrade approach and 20 patients with retrograde approach after exclusion of failed PCI, renal failure, heart failure with moderate and severe reduced ejection fraction: cardiac biomarkers (CKMB) were performed to all patients before PCI and 12 hours after, to assess the periprocedural myocardial injury. PMI was defined as creatine kinase-myocardial band increase $\geq 3 \times$ the upper limit of normal, major adverse cardiac events (MACE) during mid-term follow up were evaluated.

Results: Retrograde approach was used in 25% of all procedures PMI occurred in 9 patients (11.25%). The incidence of PMI was higher in patients treated with retrograde approach than antegrade approach (25%, 6,7% respectively $p=0.039$), during a median follow up of 6 months compared with patients without PMI. Those with PMI had a higher incidence of major adverse cardiac events ($p < 0.001$).

Conclusions: PMI post CTO PCI was associated with the presence of several clinical, angiographic, and procedural factors, and has an adverse effect on 6-months clinical outcomes. These findings could be valuable for improving the quality of care for patients with CTO. The antegrade approach was more safe and effective than retrograde approach.

Keywords: Periprocedural myocardial injury, percutaneous coronary intervention, Chronic total occlusion, Antegrade Approach, Retrograde Approach.

INTRODUCTION

Periprocedural myocardial injury (PMI) is one of the noticed complications of percutaneous coronary intervention (PCI). PMI was defined as the subset of patients who had evidence of prolonged

ischemia as demonstrated by persistent chest pain (>20 minutes), new pathological Q waves seen on the electrocardiogram, or cardiac troponin level elevation using various cutoffs. Higher mortality rates have been associated with this complication, even

when patients do not develop symptoms or electrocardiographic changes (*Thygesen et al., 2012*).

One of the most technically challenging interventions is PCI of chronic total occlusions (CTOs) was documented in nearly 15 % patients undergoing coronary angiography and 10 % of lesions treated by PCI it may require use of advanced crossing techniques, resulting in high rates of PMI. Coronary CTOs were defined as coronary lesions with thrombolysis in myocardial infarction (TIMI) grade 0 flow for duration of at least 3 months (*Brilakis et al., 2012*).

The recanalization of CTO patient remain on of the major challenges for the most interventional cardiologists in current clinical practice, Therefore, a detailed comprehensive assessment for CTO arteries has become very important before PCI revascularization (*Grantham et al., 2010*).

The attempt rates for CTO PCI are significantly lower than attempts rates for PCI for other lesion subsets. The lower-than-normal success rate for CTO PCI indicates that CTO PCI is the most challenging lesion subset to treat in coronary interventional practice. Because of heavy atherosclerotic plaque burden, inability to see the course of the vessel at the site of occlusion, and often longer length of lesions, reliably crossing a CTO with a coronary guide wire is difficult and is the most common reason for failure of CTO PCI. Even with successful wire crossing, delivery of coronary balloons and stents into these fibrotic, calcific lesions can be difficult. In a weighted meta-analysis of patients reporting

complications after CTO PCI, the incidence of PMI was 2.5% (95% CI: 1.9%-3.0%), and the incidence of Q-wave myocardial infarction (MI) was 0.2% (95% CI: 0.1%-0.3%). However, systematic cardiac biomarker measurements were not performed in these studies: Hence, the true incidence of PMI may be underestimated. Furthermore, while in non-CTO PCI PMI is associated with higher immediate and long-term morbidity, the prognostic implications of PMI in CTO PCI remain unclear (*Patel et al., 2013*).

Systematic evaluation of cardiac biomarkers after CTO PCI was done in few studies which showed that PMI occurs more commonly than previously reported after CTO PCI. PMI is also more frequent when the retrograde approach is used and is associated with worse subsequent clinical outcomes (*Nathan et al., 2014*).

In the present study, we aimed to compare the incidence of both symptomatic and asymptomatic PMI in CTO PCI using serial cardiac biomarker measurements, and assess the association of PMI with various CTO PCI techniques as well as determine the impact of PMI antegrade versus retrograde approach.

PATIENTS AND METHODS

This prospective randomized study was conducted between February 2018 and November 2019. The study included 80 patients with successful PCI to chronic total occlusion: 60 patients with antegrade approach and 20 patients with retrograde approach, Cardiac biomarkers were performed to all patients, and their medical records, electrocardiograms,

echocardiographs, and coronary angiograms were reviewed.

Inclusion Criteria:

Patients presented by IHD and referred on elective bases for PCI with either of the following clinical presentation: stable angina and chronic total occlusion. All CTO lesions included in the study were successfully reanalyzed through one of the approved PCI techniques.

Exclusion Criteria:

1. Heart failure with moderate, or severe reduced ejection fraction (EF).
2. Renal insufficiency with creatinine above 2 mg/dl.
3. Diseases that limit life expectancy, e.g. malignancy.

Exclusion of failed PCI trials to recanalize CTO included failure due to:

1. Failure attempts to wire CTO lesions.
2. Acute complications as coronary perforation, tamponade, acute stent thrombosis, no reflow, MI and death.
3. Emergency bypass graft surgery required for side-branch occlusion, trauma to non-diseased vessels (such as the left main), guide wire fracture with entrapment and perforation.

All patients were subjected to:

1. Complete history taking.
2. Thorough physical examination.
3. Routine laboratory investigation.
4. ECG analysis.
5. Echocardiography: to assess EF.
6. Estimation of J-CTO score.

Statistical analysis:

The collected data were revised, coded, tabulated and computed by using Statistical package for the Social Sciences (SPSS) version 23.0 for windows (SPSS Inc, Chicago, IL, USA). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Descriptive statistics; Mean and Standard deviation (\pm SD) for numerical data, percentage of non-numerical data. Unpaired Student t test was used to compare continuous variables between 2 independent groups, ensuring first that the data was approximately normally distributed for the unadjusted analysis. Non-parametric Mann-Whitney U-test was used to compare the differences in infarct size and cardiac biomarkers between groups which were not normally distributed. Linear regression was used for comparing left ventricular ejection in relation to infarct size. For all analyses, a value of $p \leq 0.05$ was considered as statistically significant.

RESULTS

In our study of total 80 patients 9 patients, had PMI about (11.25%) sixty patients undergoing antegrade approach of them 4 Patients had PMI (6.7%) and 20 patients undergoing retrograde approach 5 of them had PMI (25%).

Regarding different parameters, 33 (46.5%) and 8 (88.9%) patients had length >20 in patients without PMI and patients with PMI respectively. 44 (62%) and 9 (100%) patients had calcification in patients without PMI and patients with PMI respectively. 19 (26.8%) and 2 (22.2%) patients had Bending > 45 in patients without PMI and patients with PMI respectively. 28 (39.4%) and 6 (66.7%) patients had had PX stump blunt in patients without PMI and patients with PMI respectively. 6 (8.5%) and 4 (44.4%) patients had had re-trial in patients without PMI and patients with PMI respectively. The Mean \pm SD of J CTO

score was 1.83 ± 1.01 and 3.22 ± 1.09 in patients without PMI and patients with PMI respectively. There was statistically significant difference between both groups regarding J CTO score.

Regarding different parameters, The Mean \pm SD of number of wires was 4.11 ± 1.47 and 6.78 ± 2.44 in patients without PMI and patients with PMI respectively. The Mean \pm SD of number of balloons was 3.15 ± 1.01 and 4.11 ± 1.27 in patients without PMI and patients with PMI respectively. The Mean \pm SD of number of stents was 1.73 ± 0.86 and 1.89 ± 0.78 in patients without PMI and patients with PMI respectively. There was statistically significant difference between both groups regarding number of wires and balloons while there was no statistically significant difference regarding number of stents (**Table 1**).

Table (1): Relation between PMI and different parameters (n= 80)

Parameters \ PMI	No (N=71)		YES (N=9)		P
	No.	%	No.	%	
Length >20	33	46.5	8	88.9	^{FE} p=0.029
Calcification	44	62.0	9	100.0	^{FE} p=0.025
Bending > 45	19	26.8	2	22.2	^{FE} p=1.000
Px stump blunt	28	39.4	6	66.7	^{FE} p=0.159
Re-trial	6	8.5	4	44.4	^{FE} p=0.012
J CTO score					
Min. – Max.	0.0 – 4.0		2.0 – 5.0		0.002
Mean \pm SD.	1.83 ± 1.01		3.22 ± 1.09		
Number of wires					
Min. – Max.	2.0 – 8.0		3.0 – 10.0		0.002
Mean \pm SD.	4.11 ± 1.47		6.78 ± 2.44		
Number of balloons					
Min. – Max.	1.0 – 5.0		2.0 – 6.0		0.029
Mean \pm SD.	3.15 ± 1.01		4.11 ± 1.27		
Number of Stents					
Min. – Max.	0.0 – 4.0		1.0 – 3.0		0.538
Mean \pm SD.	1.73 ± 0.86		1.89 ± 0.78		

χ^2 : Chi square test, FE: Fisher Exact test, U: Mann Whitney test.

p: p value for association between different categories.

Regarding flouro time and procedure time, the mean ± SD was 60.54 ± 22.84 and 104.7 ± 27.59 minute in patients without PMI and patients with PMI respectively while procedure time was 125.9 ± 45.44 and 224.2 ± 68.41 minute respectively. There was statistically significant difference between both groups regarding flouro time and procedure time. Regarding contrast amount, mean ± SD was 257.8 ± 132.7 ml and 538.9 ± 147.4 ml in patients without PMI and patients

with PMI respectively. There was statistically significant difference between both groups regarding contrast amount. Regarding MACE within 6 months, 1 (1.4%) patient had MACE within 6 months in patients without PMI while in patients with PMI 5 (55.6%) patients had MACE within 6 months. There was statistically significant difference between both groups regarding MACE within 6 months (**Table 2**).

Table (2): Relation between PMI and flouro time, procedure time, contrast amount and MACE within 6 months (n= 80)

Parameters	PMI		P		
	No (n = 71)	Yes (n = 9)			
Flouro time					
Min. – Max.	20.0 – 110.0	50.0 – 140.0	<0.001		
Mean ± SD.	60.54 ± 22.84	104.7 ± 27.59			
Procedure time					
Min. – Max.	45.0 – 250.0	120.0 – 310.0	<0.001		
Mean ± SD.	125.9 ± 45.44	224.2 ± 68.41			
Contrast amount (ml)					
Min. – Max.	50.0 – 600.0	250.0 – 700.0	<0.001		
Mean ± SD.	257.8 ± 132.7	538.9 ± 147.4			
MACE within 6 months					
No	70	98.6	4	44.4	FE p<0.001
Yes	1	1.4	5	55.6	

χ²: Chi square test, FE: Fisher Exact test, U: Mann Whitney test
 p: p value for association between different categories

Regarding flouro time and procedure time, the mean ± SD was 59.70 ± 24.25 and 82.90 ± 28.44 minute in antegrade and retrograde group respectively while procedure time was 122.48 ± 47.41 and 180.25 ± 63.50 minute respectively. There was statistically significant difference between both groups regarding flouro time and procedure time. Regarding contrast amount, mean ± SD was 263.33 ± 144.64 ml and 367.50 ± 183.73 ml in antegrade and retrograde group respectively. There was statistically significant difference between both groups regarding contrast amount.

Regarding MACE within 6 months, 2 (3.3%) patients had MACE within 6 months in antegrade group while in retrograde group 4 (20%) patients had MACE within 6 months. There was statistically significant difference between both groups regarding MACE within 6 months.

Regarding PMI, 4 (6.7%) patients had PMI in antegrade group while in retrograde group 5 (25%) patients had PMI. There was statistically significant difference between both groups regarding PMI (**Table 3**).

Table (3): Comparison between the two studied groups according to flouro time, procedure time, contrast amount, MACE within 6 months and PMI

Parameters \ Groups	Antegrade (n = 60)		Retrograde (n = 20)		P
Flouro time (min)					
Min. – Max.	20.0 – 120.0		30.0 – 140.0		0.001
Mean ± SD.	59.70 ± 24.25		82.90 ± 28.44		
Procedure time					
Min. – Max.	45.0 – 264.0		75.0 – 310.0		<0.001
Mean ± SD.	122.48 ± 47.41		180.25 ± 63.50		
Contrast amount (ml)					
Min. – Max.	50.0 – 700.0		100.0 – 700.0		0.025
Mean ± SD.	263.33 ± 144.64		367.50 ± 183.73		
MACE within 6 months					
No	58	96.7	16	80.0	^{FE} p= 0.032
Yes	2	3.3	4	20.0	
PMI					
No	56	93.3	15	75.0	^{FE} p= 0.039
Yes	4	6.7	5	25.0	

χ^2 : Chi square test, FE: Fisher Exact test, U: Mann Whitney test
p: p value for association between different categories

DISCUSSION

In the current study, 11% of patients developed PMI. This came in agreement with *Dautov et al. (2018)* who found that CTO PCI patients, a considerable proportion of otherwise successful procedures with satisfactory angiographic results show significant post-procedural cardiac myonecrosis. This is attributable partly to microembolization of thrombotic or atherosclerotic material that is undetectable by coronary angiography but can be traced using high-intensity transient Doppler ultrasound signals during balloon and stent dilatation and visualized using cardiac magnetic resonance (*Karpaliotis et al., 2012*).

Lo et al. (2014) found that PMI occurred in 8.6% of patients post CTO-PCI by systematic measurement of cardiac biomarkers, and the occurrence of PMI post CTO-PCI was associated with worse

mid-term clinical outcomes. In our study, the prevalence of PMI (11%) was much higher than those previously reported, which may be explained by that serum levels of cardiac enzyme (CK-MB) was systematically measured before and after PCI, which could detect more patients with silent myocardial injury post PCI.

In the current study, patients without PMI were 71.8% males and 28.2% females. Their ages ranged from 37 - 73 years. Patients with PMI were 88.9% males and 11.1% females. Their ages ranged from 48 – 74 years. There was no statistically significant difference between both groups regarding age and sex. This came in agreement with *Zhang et al. (2016)* who found that there were no significant differences with respect to age and sex.

In the present study, regarding risk factors of studied cases, 50.7% and 55.6%

patients presented with diabetes in patients without PMI and patients with PMI respectively. 56.3% and 55.6% patients presented with hypertension in patients without PMI and patients with PMI respectively. 52.1% and 77.8% patients were smokers in patients without PMI and patients with PMI respectively. 59.2% and 88.9% patients presented had dyslipidemia in patients without PMI and patients with PMI respectively. 32.4% and 22.2% patients had MI in patients without PMI and patients with PMI respectively. 2.8% underwent CABG in patients without PMI, while none in patients with PMI underwent CABG. There was no statistically significant difference between both groups regarding risk factors.

In a study done by *Goliasch et al. (2019)*, they found that regarding risk factors of studied cases, 29% and 27% patients presented with diabetes in patients without PMI and patients with PMI respectively. 82% and 85% patients presented with hypertension in patients without PMI and patients with PMI respectively. 20% and 17% of patients were smokers in patients without PMI and patients with PMI respectively. 86% and 81% patients presented had dyslipidemia in patients without PMI and patients with PMI respectively. 29% and 35% patients had previous MI in patients without PMI and patients with PMI respectively. 14% underwent CABG in patients without PMI while 20% underwent CABG in patients with PMI. They found that there was no statistically significant difference between both groups regarding smoking, diabetes, dyslipidemia while there was statistically significant difference regarding hypertension, previous MI and previous CABG surgery.

In the present study, the Mean \pm SD of J CTO score was 1.83 ± 1.01 and 3.22 ± 1.09 in patients without PMI and patients with PMI respectively with statistically significant difference between both groups. In agreement with our study, *Goliasch et al. (2019)* found that the Mean \pm SD of J CTO score was 2.0 and 3.0 in patients without PMI and patients with PMI respectively with statistically significant difference between both groups.

In the current study, there was no statistically significant difference between both groups regarding blunt stump and calcification. This came in agreement with *Zhang et al. (2016)* who found the same results.

In the present study, regarding flouro time and procedure time, the mean \pm SD was 60.54 ± 22.84 and 104.7 ± 27.59 in patients without PMI and patients with PMI respectively while procedure time was 125.9 ± 45.44 and 224.2 ± 68.41 respectively. There was a statistically significant difference between both groups regarding flouro time and procedure time. In disagreement with our study, *Zhang et al. (2016)* found that there was no statistically significant difference between both groups regarding flouro time and procedure time.

In the current study, regarding contrast amount, mean \pm SD was 257.8 ± 132.7 and 538.9 ± 147.4 in patients without PMI and patients with PMI respectively with statistically significant difference between both groups. This came in agreement with *Goliasch et al. (2019)* who found that mean \pm SD was 280 and 380 in patients without PMI and patients with PMI

respectively with statistically significant difference between both groups.

In disagreement with our study, *Zhang et al. (2016)* found that there was no statistically significant difference between both groups regarding contrast amount. As our study showed statistically significant difference between groups regarding contrast amount, may thte they have more expert operators, AND more qualified centers.

Our study demonstrated a favorable overall MACE rate of 7.5% at 6 months discharge. This came in agreement with *Maeremans et al. (2018)* who found that overall MACE rate of 8.7% at post discharge.

In the present study, there was statistically significant difference between both groups regarding MACE within 6 months. This came in agreement with *Zhang et al. (2016)* who found that the overall occurrence of MACE was a significantly higher for patients with PMI.

In the present study, patients undergoing antegrade approach were 73.3% males and 26.7% females. Their ages ranged from 38 – 74 years. Patient undergoing retrograde approach were 75% males and 25% females. Their age ranged from 37 – 71 years. There was no statistically significant difference between both groups regarding age and sex. This came in agreement with *Michael et al. (2014)* who found that there was no statistically significant difference between both groups regarding age and sex.

In the current study, regarding culprit vessel, RCA was the most common one in antegrade group (45%), followed by LAD (33.3%), LCX (11.7%), OM (8.3%) and

PDA (1.7%). In retrograde group, RCA was the most common one (60%) followed by LAD (30%) then LCX (10%), while no patients had OM or PDA culprit lesion. There was no statistically significant difference between both groups regarding type of culprit vessel. This came in agreement with *Lee et al. (2017)* who found that RCA was the most common one in antegrade group (40.7%) followed by LAD (33.5%) then LCX (25.6%). In retrograde group, RCA was the most common one (55.6%) followed by LAD (37.2%) then LCX (5.9%). There was a statistically significant difference between both groups regarding type of culprit vessel. Also, *Michael et al. (2014)* found the same results.

In the present study, the Mean \pm SD of J CTO score was 1.85 ± 1.13 and 2.40 ± 0.94 in antegrade and retrograde group respectively with a statistically significant difference between both groups. The J-CTO score has been used as a useful predictor for antegrade guidewire crossing within defined procedure time. This came in agreement with *Lee et al. (2017)* who found that the Mean \pm SD of J CTO score was 2.3 ± 1.5 and 4.2 ± 0.9 in antegrade and retrograde group respectively with a statistically significant difference between both groups.

In the current study, regarding flouro time, the mean \pm SD was 59.70 ± 24.25 and 82.90 ± 28.44 in antegrade and retrograde group respectively, while procedure time was 122.48 ± 47.41 and 180.25 ± 63.50 respectively. There was statistically significant difference between both groups regarding flouro time and procedure time. In agreement with our study, *Lee et al. (2017)* found that

regarding flouro time, was 33.1 ± 16.7 and 50.0 ± 18.2 in antegrade and retrograde group respectively, while procedure time was 85.3 ± 35.0 and 122.5 ± 39.7 respectively. There was a statistically significant difference between both groups regarding flouro time and procedure time. Also, *Michael et al. (2014)* and *Zivelonghi et al. (2019)* found the same results.

In the present study, regarding PMI, 6.7% patients had PMI in antegrade group, while in retrograde group 25% patients had PMI with statistically significant difference between both group. This came in agreement with *Lo et al. (2014)* who found that the retrograde approach may be associated with higher rates of periprocedural myocardial injury.

CONCLUSION

PMI post CTO PCI was associated with the presence of several clinical, angiographic, and procedural factors and has an adverse effect on 6-months clinical outcomes. These findings are valuable for improving the quality of care for patients with CTO. The antegrade approach more safe and effective than retrograde approach.

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التأثير على إصابة عضلة القلب في ما حول عمليات القسطرة التداخلية الناجحة لمرضى الانسداد المزمن للشرايين التاجية باستخدام الاتجاه الأمامي و مقارنته بالاتجاه الخلفي

عمرو محمد شعبان مهدي، أحمد عبدالحميد رزة، أشرف الأمير عبد الفتاح

قسم أمراض القلب والأوعية الدموية، كلية الطب، جامعة الأزهر

خلفية البحث: خطورة إصابة القلب في ما حول عمليات القسطرة التداخلية لمرضى الانسداد المزمن للشرايين التاجية من الممكن ان تكون غير مقدرة وغير محسوبة بمعرفة حيث أن عمليات سحب إنزيمات القلب للمرضى المصابين بانسداد مزمن في أحد شرايين القلب ما قبل القسطرة وما بعدها لم تكن مفعلة في الدراسات السابقة.

الهدف من البحث: الكشف عن إصابة عضلة القلب خلال عملية القسطرة التداخلية للشرايين التاجية المسدودة انسداداً مزمناً ومقارنة فتح تلك الشرايين عن طريق الإتجاه الأمامي أو الإتجاه الخلفي.

المرضى وطرق البحث: شملت هذه الدراسة جميع المرضى المرشحين للقسطرة التداخلية للانسداد الكلي المزمن لأحد الشرايين التاجية واستوفت معايير الاشتمال في دراستنا. وتم ذلك في مراكز القسطرة بمستشفى جامعة الأزهر ومعهد القلب القومي بمصر. وقمنا في هذه الدراسة بتقييم 80 مريضاً نجحت القسطرة في فتح الشريان لهم 60 مريضاً عن طريق الاتجاه الامامي و 20 مريضاً عن طريق الاتجاه الخلفي، مع استبعاد المرضى الذين فشلنا لهم القسطرة التداخلية، والمرضى الذين يعانون من فشل كلوي، والمرضى الذين يعانون من ضعف شديد او متوسط بعضلة القلب. وقد تم سحب انزيمات القلب الفوسفوكيناز كرياتين القلبي ما قبل القسطرة وما بعدها باثنتا عشر ساعة، وتم التعرف علي إصابة القلب في ما حول عمليات القسطرة التداخلية بإرتفاع في إنزيمات القلب أكثر من 3 أضعاف القيمة في ما قبل القسطرة التداخلية مع متابعة جميع المرضى لمدة 6 شهور ومدى الإصابة بالأعراض القلبية الضائرة الكبرى.

نتائج البحث: استخدم الإتجاه الخلفي في حوالي 25 % من المرضى البالغ عددهم 80 مريضاً. وقد حدث إصابه في عضلة القلب في 9 مرضى في ما حول عمليات القسطرة التداخلية : 5 مرضى من الاتجاه الخلفي و 4 مرضى من الأتجاه الأمامي ووجد فرق معتد به إحصائياً. ومع متابعة المرضى للاحداث القلبية الضائرة الكبرى في خلال 6 شهور تبين انها اعلي في المرضى الذين حدثت لهم إصابة في عضلة القلب في ما حول عملية القسطرة التداخليه عنها في المرضى الذين لم يحدث لهم إصابة ووجود فرق معتد به إحصائياً.

الإستنتاج: يرتبط إصابة عضلة القلب في ما حول عمليات القسطره التداخلية الناتج عن القسطرة التداخلية للشرايين التاجية المسدودة بشكل مزمن بوجود عدة عوامل سريرية ووعائية وإجرائية له تأثير سلبي على النتائج السريرية لمدة 6 أشهر. وهذه النتائج ذات قيمة لتحسين جودة رعاية المرضى الذين يعانون من الشرايين التاجية المسدودة بشكل مزمن، الإتجاه الامامي لإعادة التروية في الشريان المزمّن أفضل وأكثر أماناً من الإتجاه الخلفي .