

Clinical and Angiographic Predictors of No-Reflow Phenomenon during Primary Percutaneous Coronary Intervention

K.A.El-Rabat, M.A.Hamouda, A.E.El-Nagar and M.E.Salim
Cardiology Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-Mail: dr_mohamed sami@yahoo.com

Abstract

Foundation: Despite the new advancement in Percutaneous coronary mediation, an extent of patients create epicardial coronary course reperfusion without myocardial reperfusion after essential PCI, a wonder known as no-reflow. The point of this examination was to recognize conceivable clinical, angiographic and procedural indicators of no-reflow in patients with ST-section rise intense myocardial dead tissue after essential percutaneous coronary intercession. **Subjects and strategies:** This investigation included 100 patients who went through essential percutaneous coronary mediation. All patients were treated by uncovered metal stents limited to the guilty party injury just and platelets glycoprotein IIb/IIIa inhibitors were utilized after acknowledgment of coronary life structures as per the blood clot trouble degree and doctor discretion. Patients were characterized into two gatherings as indicated by the post-PCI TIMI stream grade: Group I included 84 patients with angiographically reported TIMI stream grade 3 (reflow) and Group II included 16 patients with angiographically recorded TIMI stream grade ≤ 2 (no-reflow) and were analyzed with respect to clinical, angiographic and procedural information long time from beginning of side effects to reperfusion, lower introductory TIMI stream grade, higher blood clot trouble on benchmark angiography, longer objective sore length and bigger reference luminal width. **Results:** Four investigations were incorporated from 2005 to 2014 with absolute cases 1169 cases 582 in clinical gathering and 587 in fake treatment announced. **Complications after treatment:** There was a measurably huge heterogeneity in the investigations (I2 69%, P 0.02). Utilizing the irregular impacts model, the result results uncovered that fake treatment was unimportantly not the same as clinical with respect to entanglements after treatment. There were three examinations included from 2014 to 2019 with complete cases 362 cases 193 in Surgery with tube inclusion and 169 in without tube detailed Tympanic Membrane Normal after treatment. There was a measurably critical heterogeneity in the examinations (I2 87%, P 0.0005). Utilizing the irregular impacts model, the result results uncovered that Surgery with tube addition was unimportantly not quite the same as without tube with respect to Tympanic Membrane Normal after treatment. **Conclusion:** In the current examination no-reflow happened in 16.0 % of STEMI patients went through essential PCI and was bound to be identified with postponed reperfusion, low starting TIMI stream grade, high clots trouble, enormous reference luminal measurement and long sore length.

Keywords: Angiography, No-Reflow Phenomenon, Primary Percutaneous Coronary Intervention.

1. Introduction

Intense myocardial dead tissue (AMI) is a clinical condition results from impediment of a coronary course with ensuing putrefaction of cardiovascular myocytes in the locale provided by this conduit [1].

The treatment of ST-portion height intense myocardial dead tissue is thought to reestablish antegrade blood stream in the infarct-related corridor (IRA) and limit ischemic harm to the myocardium as ahead of schedule as could be expected [2].

Percutaneous coronary mediation (PCI) limits infarct size, improve forecast in patients with intense myocardial localized necrosis and was discovered to be better than fibrinolytic treatment in prompt reclamation of ordinary coronary stream in the IRA and decrease of intermittent ischemia or reinfarction [3].

Thrombolysis In Myocardial Infarction (TIMI) stream grade 3 following percutaneous coronary mediation is the ideal outcome to limit the impact of ischemic affront on the myocardium and at last improve generally speaking endurance [4].

In spite of the new advancement in essential PCI, an extent of patients create epicardial coronary course reperfusion without myocardial reperfusion after essential PCI, a wonder known as no-reflow [5].

Patients who build up this marvel are at higher danger of left ventricular brokenness, reformist myocardial harm and have higher paces of horribleness and mortality [6].

The point of this investigation was to recognize conceivable clinical, angiographic and procedural indicators of no-reflow in patients with ST-section rise intense myocardial dead tissue after essential percutaneous coronary intercession.

2. Patient and method

This imminent investigation included 100 patients who went through essential percutaneous coronary mediation at the National heart organization (NHI) and cardiology office, Menoufia University medical clinic inside the time frame between January 2016 and June 2016.

This examination was carried on 100 patients gave ST-fragment rise intense myocardial dead tissue characterized as average chest torment and either ST-section height in two coterminous leads ≥ 2 mm in guys and ≥ 1.5 mm in females in V2-3 and/or ≥ 1 mm in different leads or the new beginning of left group branch block with 2-overlap rise of creatine kinase (CK) and creatine kinase-MB (CK-MB) part (156) who were qualified for essential PCI.

Incorporation models was Patients went through essential PCI inside 12 hours after beginning of indications and Patients with ongiong chest torment for over 12 hours who went through essential PCI inside 24 hours after beginning of manifestations.

Avoidances rules was Patients who were dealt with moderately for coronary course fit or $<$ half width stenosis of the offender injury with ordinary coronary blood stream, Patient required emanant careful revascularization for huge

left principle coronary conduit sickness or progressed multivessel infections not manageable for PCI, Patients with saphenous vein unites or left inward mammary corridor sores, Patients didn't accomplished coronary supply route patency and Presence of mechanical confusions, for example, analyzation or angiographically obvious distal embolization after consummation of the system.

2.1 Signs of heart failure were classified with estimation of Killip classification degree as follow:

- No signs of heart failure.
- Mild heart failure: rales at bases, S3 gallop or elevated JVP.
- Heart failure: acute pulmonary edema.
- Cardiogenic shock (SBP < 90 mmHg, cyanosis, oliguria, sweating).

12-Lead ECG documented either ST-segment elevation of >1mm in 2 consecutive leads or new onset left bundle-branch block.

Cardiac biomarkers including cardiac troponin, CK and CK-MB and serum creatinine. All patients received oral aspirin (300 mg) and clopidogrel (600 mg). Standard coronary angiogram was carried. Arterial puncture was done through femoral approach according to physician discretion using Seldinger puncture needle after giving local anesthesia with subcutaneous infiltration of lidocaine 2 % at the puncture site. After placement of the arterial sheath, intravenous unfractionated heparin (8.000-10.000 IU) was given, baseline coronary angiogram was obtained with assesment and Identification of the IRA, initial TIMI flow grade as follow:

- TIMI 3: Flow rate equal to that in non-infarct arteries.
- TIMI 2: Distal flow in the artery less than non-infarct arteries.
- TIMI 1: Some contrast filling beyond the culprit lesion but no antegrade flow.
- TIMI 0: No flow beyond the total occlusion [7].

All patients were treated by bare metal stents according to the insurance policy. Stenting was restricted to the culprit lesion only according to the insurance policy. Platelets glycoprotein IIb/IIIa inhibitors (Tirofiban or Eptifibatide)

were used on downstream basis according to the thrombus burden degree and physician discretion. Manual aspiration thrombectomy device was used according to the thrombus burden degree and physician discretion.

The whole study group was classified into two groups according to the post-PCI TIMI flow grade: Group I with angiographically documented TIMI flow 3 (reflow) and Group II with angiographically documented TIMI flow ≤ 2 (no-reflow). The patient was considered to exhibit a no-reflow phenomenon if TIMI flow grade in the IRA was ≤ 2 despite successful dilatation and absence of mechanical complications such as dissection or angiographically evident distal embolization after completion of the procedure. Then comparative analysis between both groups was carried out to detect clinical, angiographic and procedural predictors of no-reflow.

3. Results

The whole study group was classified into two groups according to the post-PCI TIMI flow grade: Group I included 84 patients with angiographically documented TIMI flow 3 (reflow) and Group II included 16 patients with angiographically documented TIMI flow ≤ 2 (no-reflow).

Both study groups were compared regarding the angiographic data such as infarction location (anterior, inferior or others), infarct related artery (LAD, LCX or RCA), target lesion location (proximal, mid or distal), thrombus burden (mild, moderate or high), total occlusion morphology (tapered or cut-off), subtotal occlusion morphology (eccentric or concentric) and initial TIMI flow with statistically significant higher thrombus burden (≥ 4) and lower initial TIMI flow (0-1) in the No-reflow group Table (1) , Fig (1) and Fig (2).

Both study groups were compared regarding the procedural data such as direct stenting, stenting after predilatation and single or multiple stents used to cover the culprit lesion, target lesion length, reference luminal diameter, manual aspiration device use and Platelets glycoprotein IIb/IIIa inhibitors use with statistically significant larger reference luminal diameter and longer lesion length in the No-reflow group Table (2) , Table (3) and Fig (3).

Table (1) The angiographic categorical data of both study groups.

Variables	Post-PCI TIMI flow				Chi-square	
	Reflow (84)		No-reflow (16)		X ²	P-value
	N	%	N	%		
Infarction location	anterior	55	65.5%	10	62.5%	0.231
	inferior	26	31.0%	5	31.3%	
	others	3	3.6%	1	6.3%	
	LAD	55	65.5%	10	62.5%	
	LCX	10	11.9%	2	12.5%	
	RCA	19	22.6%	4	25.0%	0.209
IRA	Proximal	31	36.9%	7	43.8%	0.794

Table (1) Continue

Target lesion location	Mid	45	53.6%	7	43.8%	0.264	0.608
	distal	8	9.5%	2	12.5%		
	High	45	53.6%	7	43.8%		
Thrombus burden	Moderate	33	39.3%	9	56.3%	4.98	0.047*
	High	21	25.0%	4	25.0%	4	
	Low	30	35.7%	3	18.8%		
Total occlusion morphology	Cut-off	33	39.3%	8	50.0%	0.529	0.487
	Tapered	27	32.1%	4	25.0%	0.097	0.755
Subtotal occlusion morphology	Concentric	11	13.1%	2	12.5%		
	Eccentric	13	15.5%	2	12.5%		
Initial TIMI flow	T2/3	31	36.9%	3	18.8%	5	0.794
	T0/1	53	63.1%	13	81.2%		

IRA: Infarct related artery LAD: Left anterior descending LCX: Left circumflex RCA: Right coronary artery
 TIMI: Thrombolysis in myocardial infarction

Table (2) The procedural categorical data of both study groups.

Variables	Post-PCI TIMI flow				Chi-square	
	Reflow (84)		No-reflow (16)		χ ²	P-value
	N	%	N	%		
Stenting After Predilatation	34	40.5%	7	43.8%	0.059	0.808
Direct Stenting	50	59.5%	9	56.3%	0.059	0.808
Single Stent	67	79.8%	12	75.0%	0.177	0.674
Multiple Stents	17	20.2%	4	25.0%	0.177	0.674
Aspiration Device	4	58.3%	10	62.5%	0.097	0.755
Use GP Iib/Iiia Inhibitors use	95	65.5%	11	68.8%	0.065	0.799

Table (3) The procedural continuous data of both study groups.

Variables	Post-PCI TIMI flow						T-test	
	Reflow (84)			No-reflow (16)			t	P-value
	Mean	±	SD	Mean	±	SD		
Reference Diameter Mm	3.247	±	0.361	3.500	±	0.365	-2.565	0.012*
Target Lesion Length Mm	22.583	±	5.811	25.625	±	4.646	-1.974	0.05*

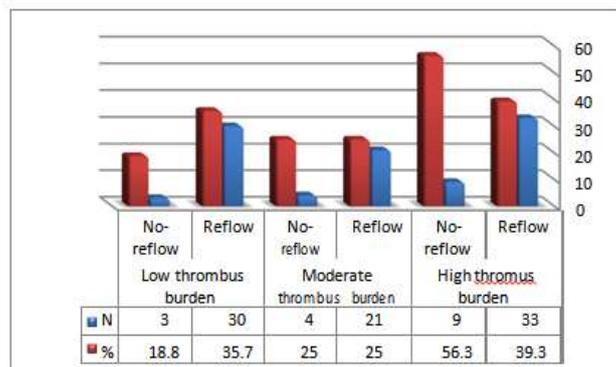


Fig (1) The thrombus burden of both study groups

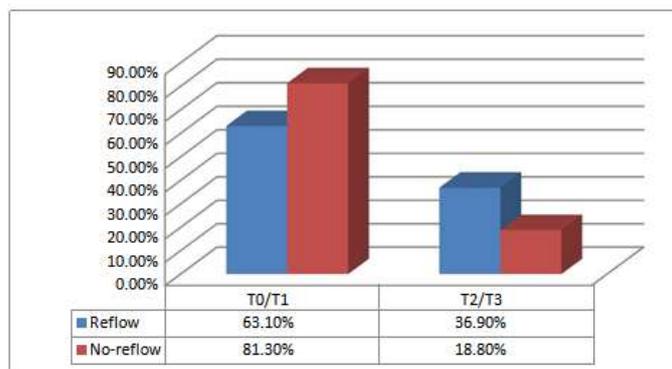


Fig (2) The initial TIMI flow of both study groups.

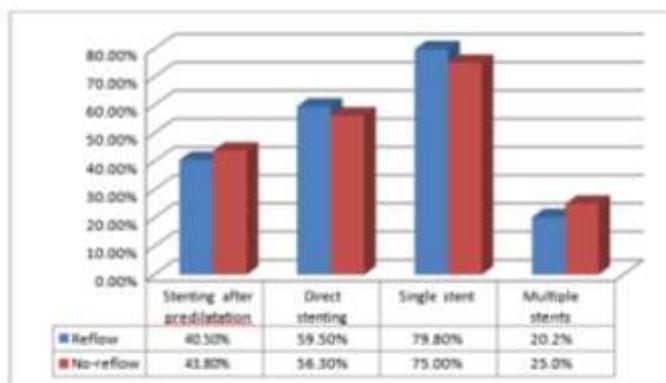


Fig (3) The procedural data of both study groups.

4. Discussion

Coronary angiography is the most straightforward strategy to analyze no-reflow in the catheterization research center. Numerous straightforward and complex angiographic calculations have been utilized however practically speaking, TIMI stream evaluation and MBG are the most regularly utilized. TIMI stream alludes to the force and degree of representation of IRA and the speed of stream of color. TIMI stream is reviewed 0–3. MBG alludes to the power of radio-murkiness of the myocardial tissue and the speed with which the upgrade clears. MBG is likewise evaluated as 0–3 [7].

In the current investigation, no-reflow happens in 16.0% of study populace. This rate was lower than that revealed by Watanabe et al., 2003 [8] (26.0%), Chen et al., 2012 [9] (25.3%), Mazhar et al., 2016 (10) (25.0%), Morishima et al., 2000 [11] (25.0%) and Kirma et al., 2008 [4] (24.3%), near that announced by Zhou et al., 2014 [12] (17.3%) and higher than that detailed by Tanaka et al., 2002 [13] (13.0%).

The rate of no-reflow marvel was at first discussed, notwithstanding, a lot of test and clinical information have unmistakably indicated that it happens with variable predominance going from 5% up to 25%, as per the techniques used to survey the wonder and to the populace under examination [5].

As of late, it was recorded to be 10-30 % as per touchy techniques for surveying no-reflow and microcirculatory brokenness including myocardial difference

echocardiography (MCE) and cardiovascular attractive reverberation imaging (CMRI) [14].

At that point the two examination bunches were analyzed in regards to segment and clinical information, for example, age, sex, hazard components of coronary conduit sickness, earlier PCI, earlier MI, Killip class, HR, Systolic and diastolic blood pressures, top CK-MB and reperfusion time with measurably huge longer reperfusion time in the No-reflow gathering (8.0 ± 4.0 versus 5.8 ± 3.0 hours for no-reflow and reflow, separately).

Critical longer reperfusion time in patients with no-reflow was concordant to that exhibited by Mazhar et al., 2016 [10], Zhou et al., 2014 [12] and Kirma et al., 2008 [4] yet grating to that showed by Chen et al., 2012 [9], Watanabe et al., 2003 [8], Tanaka et al., 2002 [13] and Morishima et al., 2000 [11].

Deferred introduction is a conceivably preventable factor and connected with more prominent ischemic injury which prompts edema of slender bed, growing of myocardial cells and neutrophil stopping. It is notable from creature contemplates that more drawn out term of impediment of coronary conduit is related with no-reflow in the wake of resuming the supply route [15].

Measures to teach people in general in acknowledgment of cardiovascular failure side effects and early introduction by rescue vehicle to the clinic might be useful. Proceeded with endeavors to limit delay inside the wellbeing framework because of conclusion, move and

mediation in STEMI patients may likewise decrease the general danger of no-reflow [16].

In the beginning phases of AMI, the clots is wealthy in thrombocytes and generally simpler to lysis. With a more drawn out reperfusion time, the clots takes on more erythrocytes and turns out to be more inflexible. Such thrombi will in general part with expand dilatation which can prompt distal coronary embolization during essential PCI and diminish the probability of accomplishing TIMI 3 stream after the method [17].

Howl et al., 2002 [18] showed that in patients with AMI who had a high clots trouble, the pace of no-reflow was lower in those with reperfusion under 4 hours. This shows the conceivable relationship between's blood clot weight and span of reperfusion.

Be that as it may, the no-reflow wonder can happen even in patients with AMI who have a low clots trouble and long reperfusion time. Regardless of whether the material potential to embolize is little, drawn out ischemia can upset the microvascular bed and the level of this disturbance is known to be a vital factor in the pathogenesis of no-reflow which is the reason an expanded pace of no-reflow is found in instances of delayed reperfusion [19].

Patients with no-reflow were more seasoned in the current examination however measurably not huge (57.3 ± 9.4 versus 53.3 ± 10.2 years for no-reflow and reflow, separately), this was concordant to that shown by Chen et al., 2012 [9], Watanabe et al., 2003 [8], Tanaka et al., 2002 [13] and Morishima et al., 2000 (161) however conflicting to that exhibited by Mazhar et al., 2016 [10], Zhou et al., 2014 [12] and Kirma et al., 2008 [4] as they showed genuinely critical more established patients in the no-reflow gathering.

It is realized that old patients have a higher plaque trouble with high necrotic center as shown by IVUS which may prompt distal embolization during essential PCI bringing about no-reflow, notwithstanding microcirculatory brokenness and adjusted neurohormonal and autonomic impacts [20].

Ongoing meta-examination was against routine clots goal use, yet in instances of huge leftover clots trouble subsequent to opening the vessel with a guide-wire or inflatable, clots goal might be thought of [21].

Isaaz et al., 2006 [22] prompted treatment with low-portion thrombolytic medications or Platelet GP IIb/IIIa receptor inhibitors and delaying of PCI if sufficient antegrade stream is accomplished by starting predilatation in patients with high blood clot trouble or long objective sore to keep away from or limit injury to the vessel divider to diminish the danger of no-reflow creating during essential PCI. It is imperative to stay away from redundant inflatable dilatations and utilize the briefest stent if conceivable.

Kirma et al., 2008 [4] exhibited that accomplishment of TIMI 3 stream in the IRA after predilatation didn't forestall advancement of no-reflow marvel following stent implantation. Antonucci et al., 2001 [23] showed that coronary stent implantation without predilatation is

practical and can be performed securely in those patients with AMI.

Dudek et al., [24] have exhibited that immediate stenting following clots goal (PIHRATE) Trial bringing about better microvascular perfusion evaluated by MBG. By and by, for direct stenting, a specific degree of basal antegrade TIMI stream and appropriate injury highlights (i.e., subtotal impediment without over the top angulations or serious calcification) are required. The absence of predilatation prior to stenting may diminish the probability of clots as well as plaque content dislodgement and ensuing distal embolization. The total and direct framework of a painting blood clot might be another clarification of the preventive impact of direct stenting. Notwithstanding, the presence of basal TIMI stream as well as effectively open sore highlights in the IRA before the system is itself a free indicator of expanded achievement rate. Subsequently the speculations that direct stenting can diminish no-reflow stays a sketchy issue.

5. Conclusion

In the current examination no-reflow happened in 16.0 % of STEMI patients went through essential PCI and was bound to be identified with deferred reperfusion, low beginning TIMI stream grade, high clots trouble, huge reference luminal breadth and long sore length.

References

- [1] H. Ting, E.H. Yang, C.S. Rihal, Reperfusion strategies for ST-segment elevation myocardial infarction. *Ann Intern Med*, Vol.145, PP.610-617,2006.
- [2] G.W. Stone, C.L. Grines, K.F. Browne, Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: the Primary Angioplasty in Myocardial Infarction (PAMI) trial. *J Am Coll Cardiol*, Vol.25, PP.370-377,1995.
- [3] K .Nagao, N .Hayashi, K. Kanmatsuse, An early and complete reperfusion strategy for acute myocardial infarction using fibrinolysis and subsequent transluminal therapy: The FAST trial. *Circ J*, Vol.66, PP.576 – 582,2002.
- [4] C. Kirma, Akin Izgi, Cihan Dundar, Clinical and Procedural Predictors of no-Reflow Phenomenon after Primary Percutaneous Coronary Interventions. *Circ J*, Vol.72, PP.716 – 721,2008.
- [5] T .Reffemann , R.A.Kloner, The no-reflow phenomenon: Basic science and clinical correlates. *Heart*, Vol.87, PP.162– 168,2002.
- [6] F. Cura, P. L'Allier, S.R. Kapadia, Predictors and prognosis of suboptimal coronary blood flow after primary coronary angioplasty in patients with acute myocardial infarction. *Am J Cardiol*, Vol.88, PP.124– 128,2001.
- [7] J.P.S. Henriques , F. Zijlstra , A.W.J. van't Hof , Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade. *Circulation*, Vol.107, PP.2115–2119,2003.
- [8] T .Watanabe, S. Nanto, M .Uematsu, Prediction of No-Reflow Phenomenon after Successful Percutaneous Coronary Intervention in Patients With Acute

- Myocardial Infarction Circulation Journal , Vol.67, PP.16-12, 2003.
- [9] Y. Chen, C .Wang, Xinchun, Independent no-reflow predictors in female patients with ST-elevation acute myocardial infarction treated with primary percutaneous coronary intervention Heart Vessels , Vol.27, PP.243–249,2012.
- [10] J .Mazhar, M. Maschicharan , A.Farshid, Predictors and outcome of no-reflow post primary percutaneous coronary intervention for ST-elevation myocardial infarction. IJC Heart Vasc, Vol.10, PP.8–12,2016.
- [11] I .Morishima, T. Sone , K.Okumura ,Angiographic No-Reflow Phenomenon as a Predictor of Adverse Long-Term Outcome in Patients Treated With Percutaneous Transluminal Coronary Angioplasty for First Acute Myocardial Infarction. JACC , Vol.36(4), PP.1202–9,2000.
- [12] Zhou, Xiao-yan He, Shao-wei, Clinical and procedural predictors of no-reflow in patients with acute myocardial infarction after primary percutaneous coronary intervention. Department of Cardiology, East Hospital, Tongji University School of Medicine, Shanghai 200120, China. World J Emerg Med, Vol. 5(2), PP.5-3, 2014.
- [13] A. Tanaka, T. Kawarabayashi, Yoshiharu , No-Reflow Phenomenon and Lesion Morphology in Patients with Acute Myocardial Infarction Circulation, Vol.105, PP.2148-2152,2002.
- [14] R.W. Harrison, A. Aggarwal, F.S. Ou, Incidence and outcomes of no-reflow phenomenon during percutaneous coronary intervention among patients with acute myocardial infarction. Am J Cardiol, Vol.111(2), PP.178–184,2013.
- [15] B.G. Schwartz , R.A. Kloner, Coronary no-reflow, J. Mol. Cell. Cardiol, Vol.52 (4), PP.873-882,2012.
- [16] P.T. O’Gara, F.G. Kushner, D.D. Ascheim, 2013 ACCF/AHA guidelines for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol, Vol.61, PP.485–510,2013.
- [17] Y. Nagata, K. Usuda, A .Uchiyama, Characteristics of the pathological images of coronary artery thrombi according to the infarct-related coronary artery in acute myocardial infarction. Circ J, Vol.68, PP.308–314,2004.
- [18] H.K. Yip, M.C. Chen, H.W. Chang, Angiographic morphologic features of infarct-related arteries and timely reperfusion in acute myocardial infarction: predictors of slow-flow and no-reflow phenomenon. Chest, Vol.122, PP.1322–32,2002.
- [19] G .De Luca, H .Suryapranata, F. Zijlstra, Symptom onset to balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol, Vol.42, PP.991 – 997,2003.
- [20] A.Ruiz-Garcia, G.Lerman, Weisz, Age and gender related changes in plaque composition in patients with acute coronary syndrome: the PROSPECT study, EuroIntervention , Vol.8(8) , PP.929–938,2012.
- [21] S.S. Jolly, S. James, V. Dzavik, Thrombus aspiration in ST-segment elevation myocardial infarction. An individual patientmeta-analysis: Thrombectomy Trialists Collaboration. Circulation, Vol.135 (2), PP.143–152,2017.
- [22] K .Isaaz, C. Robin, A .Cerisier, A new approach of primary angioplasty for ST-elevation acute myocardial infarction based on minimalist immediate mechanical intervention. Coron Artery Dis, Vol.17, PP.261 – 269,2006.
- [23] D .Antoniucci, R. Valenti, A. Migliorini, Direct infarct artery stenting without predilatation and no-reflow in patients with acute myocardial infarction. Am Heart J, Vol.142, PP.684 –690,2001.
- [24] D. Dudek, W .Mielecki, F .Burzotta, Thrombus aspiration followed by direct stenting: a novel strategy of primary percutaneous coronary intervention in ST-segment elevation myocardial infarction. Results of the Polish–Italian–HungarianRandomized ThrombEctomy (PIHRATE Trial). Am Heart J, Vol.160 (5), PP.966–972,2010.