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Case report

STEMI with high thrombus burden – two different therapeutic approaches?

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Abstract

Introduction: High thrombus burden (HTB) in patients presenting with acute ST segment elevation myocardial infarction (STEMI) is related to post-operative complications, adverse effects and worse prognosis.

Case reports: We present two similar patients presenting with STEMI, in whom we used two different strategies to cope with HTB after failed manual thrombus aspirations: in the first case we did immediate stenting of infarct related artery (IRA); in the second case, after persisting of no-reflow phenomenon, despite implantation of two stents, we decided to intracoronary administer low-dose alteplase.

Conclusion: Aldo still controversial, evidence suggest that low-dose intracoronary fibrinolytic therapy could be useful in patients presenting with HTB, especially when manual thrombus aspiration have failed. The experience from our center confirms those statements.

Key words intracoronary fibrinolytics, high thrombus burden, ST segment elevation myocardial infarction.

Introduction

Acute ST elevation myocardial infarction (STEMI) most often occurs in the set of atherosclerotic plaque disruption, with the consequent formation of a thrombus that occludes the epicardial coronary artery.[1] According to literature, presence of thrombus can be angiographicaly verified in 91.6% STEMI patients,[2] while the presence of high thrombus burden (HTB) has been reported in 16.4% of cases.[3] While percutaneous coronary interventions (PCI) have revolutionized the treatment of STEMI and have become the standard of care,[4] preforming percutaneous revascularization in the setting of HTB remains challenging.[5]

Quantification of thrombus burden is usually based on Thrombolysis in Myocardial Infarction Risk Scores (TIMI Risk Scores or TS), according to which TS 0 indicates no thrombus is present, and TS 5 indicates definite thrombus, with the largest dimension ≥4 vessel diameters. HTB is defined as TS ≥ 4.[6] However, since there is a high incidence of coronary occlusion in STEMI, in which thrombus burden cannot be adequately assessed due to the absence of antegrade flow distal to occlusion site, *Sianosand colleagues* have proposed a new classification, in which TS 5 is reclassified after wire crossing and/or small balloon (≤ 1.5 mm) is used to recanalize the infarct related artery (IRA).[7]

Presence of HTB in acute myocardial infarction (AMI) patients is related to larger infarction area, left ventricle (LV) function deterioration, greater incidence of post-operative complications and adverse effects, including malignant arrhythmia and heart failure, and worse prognosis in general. [5,8]

This is particularly due to thrombus shifting and distal (micro)embolization, with consequent severe microvasculature obstruction (MVO) causing the no-reflow phenomenon.[9] While angiographic signs of distal embolization occur in 6–18% of cases of primary PCI in STEMI, the true incidence may be much higher. This is demonstrated by retrieval of visible debris in up to 73% patients in studies such as the Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris (EMERALD) trial.[10]

No-reflow phenomenon is associated with worsen LV function, adverse clinical effects and death, and is estimated to occur in at least 10% of STEMI patients.[9,11,12] HTB is considered to be one of the major predictors of the no-reflow phenomenon.[13]

Therefore, several strategies in the setting of HTB have been proposed, including thrombectomy devices, with manual thrombus aspiration as the most commonly used, as well as pharmacological pretreatment. Recently, intracoronary-targeted thrombolysis has become popular and efficient in handling coronary thrombotic lesions.[1,14]

Case report 1

A 55-year-old male was referred to emergency room department due to anginal chest pain, which lasted for 5 hours before admission. ECG showed ST segment elevation > 2 mm in inferior leads with contralateral ST

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segment depressions, as well as ST segment elevation > 1 mm in V4R lead.
On physical examination, patient was eupnoeic, normotensive. After administering 300 mg of acetylsalicylic acid and 60 mg of Prasugrel, in a hemodynamically stable state, patient was transferred to catheterization lab.
Coronary angiography showed proximally occluded right coronary artery (RCA). (Fig. 1A) After passing the guide wire (GW), TIMI II flow occurred with large residual thrombus burden – TS 4. (Fig. 1B) After several unsuccessful manual thrombus aspirations, DES XiencePro 3,5x38 mm (Boston Scientific, Massachusetts, USA) was primo-implanted in medial RCA at 12 atmospheres (atm), after which DES ResoluteOnyx (Boston Scientific, Massachusetts, USA) 4,5x30 mm was primo-implanted in proxo-medial segment at 12 atm, with overlap. Coronary angiography performed after stent implantations showed migrations of thrombus masses in proximal and distal segment. (Fig. 1C) After implantation of DES Resolute Onyx 4,5x15 mm in ostio-proximal segment at 12 atm and intracoronary administering of nitroglycerin, coronary angiography showed entrapped thrombus masses. (Fig. 1D)
After several postdilations using non-compliant balloons and repeated intracoronary administration of nitroglycerin, final coronary angiogram showed optimal result with TIMI III flow in RCA. (Figure 1E)
In a hemodynamically stable state patient was transferred to Intensive care unit for further treatment. Control coronary angiography, planned 6 months after the procedure, is yet to be conducted.

Case report 2

A 45-year-old male was referred to emergency room department due to chest pain which lasted for 5 hours before admission.ECG showed ST segment elevation > 2 mm in inferior leads with contralateral ST segment depressions. On physical examination, patient was upset, eupnoeic, normotensive. After administering 300 mg of acetylsalicylic acid and 180 mg of Ticagrelor, in a hemodynamically stable state, patient was transferred to catheterization lab.
Coronary angiography showed proximally occluded RCA. After passing the GW, TIMI II flow occurred with large residual thrombus burden – TS gr 4. (Fig. 2-A)
After several unsuccessful manual thrombus aspirations, POBA was performed using the semi-compliant balloon.Control angiogram showed no-reflow phenomenon from medial part of RCA, with presisting thrombus masses in proximal segment. (Fig. 2-B) Procedure was continoued by implanting DES Resolute Onyx3,0x26 mm (Boston Scientific, Massachusetts, USA) in proximal segment, which resulted only in shifting of the starting point of the no-reflow bellow the distal edge of the stent. (Fig. 2-C) We implanted DES Orsiro 3,0x26 (Biotronik, Switzerland)distal segment, after which no-reflow persisted below the crux. (Fig. 2-D) At that point, considering the persisting no-reflow, we decided to intracoronary administer 10 mg of alpteplase in a slow manual infusion over 10 minutes. After restoration of coronary flow and resolution of initial ST segment elevations, we finished the procedure by implanting DES Orsiro 2,5x18 mm (Biotronik, Switzerland) in PL branch. Final angiogram showed optimal result with TIMI III flow. (Fig. 2-E)
In a hemodynamically stable state patient was transferred to Intensive care unit for further treatment. Control coronary angiography, planned 6 months after the procedure, is yet to be conducted.

Discussion

Aldo HTB is recognized to be associated with greater incidence of post-operative complications and adverse effects,[5,8]there are currently no proven recommendations for intervention in this setting. Several strategies have been advocated, including utilization of pharmacological agents and interventional strategies.[1,14] One of the most commonly used interventional strategy is manual thrombus aspiration. However, due to its failure in randomized clinical trials (RCT), the current European Society of Cardiology (ESC) guidelines recommend against the routine use of thrombus aspiration in percutaneous interventions, with consideration in specific cases where there is a HTB and risk of embolization.[4] In both patients, due to significant thrombus burden, we have performed several manual tromboaspirations, but they were without success.
In the first case, after failed thrombus aspirations, we went for immediate stenting of IRA. After implantation of two stents, we witnessed shifting of thrombus masses in both proximal and distal direction, as well as entrapped thrombus masses. This could indicate distal embolization and, possibly, a significant MVO, causing further myocardial injury.[9] Another therapeutic approach in this setting could be deffered stenting, which has showed beneficial effect in several single center experiences and non-randomized trials,[15] as well as in DEFER-STEMI trial (A Randomized Trial of Deferred Stenting Versus Immediate Stenting to Prevent No- or Slow-Reflow in Acute ST-Segment Elevation Myocardial Infarction).[16] However, the largest RCT, the DANAMI 3-DEFER trial (The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: DEFERred stent implantation in connection with primary PCI) failed to show any benefit of deferred stenting on clinical outcomes.[17] Possible alteration that could lead to more beneficial results when deffering the stent implantation could be dosing and duration of GP IIb/IIIa inhibitors, as well as the time period of stenting delay.[15]
In the second case, after failed thrombus aspirations, we have again went for immediate stenting of IRA. After POBA and DES implantation of proximal RCA segment, we witnessed no-reflow phenomenon bellow the distal edge of the stent. In further course of the procedure, and implanting stent in distal segment, no-reflow persisted, only with shifting the starting point of the no-reflow to the lower edge of the distal stent. At that point, we decided to intracoronary administer alteplase in a total dose od 20 mg. Intracoronary thrombolysis has gained some popularity over the past decade, but is still controversial. The

largest meta-analysis about the issue, conducted by S. Agrawal, showed that low-dose intracoronary fibrinolytic therapy is, in general, safe and effective, with a reference that it could be used in the setting of HTB and failed thrombus aspiration.[18] Contrary to that, a RCT - *Effect of Low-Dose Intracoronary Alteplase During Primary Percutaneous Coronary Intervention on Microvascular Obstruction in Patients With Acute Myocardial Infarction*, in which intracoronary alteplase was administered after reperfusion and before stent implantation, showed that adjunctive low-dose intracoronary alteplase given early during the PCI did not reduce MVO.[19] The study included all STEMI patients with impaired blood flow and evidence of thrombus (TS ≥ 2). Therefore, in the authors opinion, the methodology of the study was not adequately set to examine the true clinical use of intracoronary fibrinolytic therapy, for it is reserved, and should be examined, in the setting of HTB and failure of other recommended approaches. In this manner, adequate patient selection and the time point of administering intracoronary fibrinolytic should be defined. Currently, there are two ongoing RCT to evaluate intracoronary low-dose alteplase: the "*Adjunctive Low-dose tPA in Primary PCI for STEMI*" (STRIVE, NCT03335839) study, and "*the Restoring Microcirculatory Perfusion in STEMI"* (RESTORE-MI; ACTRN 12618000778280) trial. Finally, the utility of low-dose intracoronary fibrinolytic was recognized by the actual 2019 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Guidelines on the Acute Management of ST-Elevation Myocardial Infarction.[20]

Conclusion

HTB in STEMI patients is challenging, and there is still no strong recommendations to help us safely and effectively lead these procedures.

Manual thrombus aspiration has been downgraded in the actual ESC guidelines and is now not routinely recommended, but reserved to be considered in STEMI patients with HTB. Still, at least in our clinical experience, thrombus aspiration is usually not effective.

Aldo still controversial, evidence suggest that low-dose intracoronary fibrinolytic therapy could be useful in patients presenting with HTB, especially when manual thrombus aspiration have failed. The adequate patient selection and the time point of administering intracoronary fibrinolytic should be defined.

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Sažetak

STEMI sa velikim trombom – dva različita dijagnostička pristupa

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***Uvod**: Kod pacijenata koji se prezentuju infarktom miokarda sa elevacijom ST segmenta (STEMI), veliko trombotsko opterećenje se dovodi u vezu sa post-opreativnim komplikacijama, neželjenim događajima i gorom prognozom.*
***Prikaz slučaja**: Prezentujemo dva pacijenta sa infarktom miokarda sa ST elevacijom, a kod kojih smo koristili dve različite strategije u cilju rešavanja problema velikog trombotskog opterećenja nakon neuspešne trombo-aspiracije: kod prvog pacijenta odlučili smo se za neposredno stentiranje infarkne arterije; kod drugog pacijent, nakon perzistiranja no-reflow fenomena, čak i nakon implantacije dva stenta, odlučili smo se za intrakoronarnu aplikaciju niske doze alteplaze.*
***Zaključak**: Iako još uvek kontroverzno, dokazi ukazuju na to da bi niske doze intrakoronarno ordiniranih fibrinolitika mogle biti korisne kod pacijenata sa velikim trombotskim opterećenjem, naročito nakon neuspešne trombo-aspiracije. Iskustvo iz našeg centra saglasno je sa tim tvrdnjama.*

***Ključne reči:** intrakoronarna fibrinoliza, veliko trombotsko opterećenje, infarkt miokarda sa ST elevacijom.*