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Review

Use of thrombectomy devices in primary percutaneous coronary intervention: A systematic review and meta-analysis

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ABSTRACT

Aims: Primary percutaneous coronary intervention (PPCI) has become the treatment of choice in patients with ST-elevation myocardial infarction (STEMI) over the recent years. A number of studies have demonstrated a morbidity and mortality benefit over thrombolysis, which has been attributed to better coronary perfusion in patients undergoing PPCI. However although PPCI usually achieves normal flow in the affected epicardial vessel, myocardial reperfusion is not fully restored in a significant percentage of patients. This is commonly the result of distal thrombus embolization with subsequent impairment of myocardial microcirculation. Recognition of this has led to the development of a number of devices with different mechanisms of action that aim to reduce such distal embolization and therefore improve end myocardial perfusion. Recent studies indeed demonstrate that the use of such devices offer additional clinical advantage in patients undergoing PPCI compared to the current practice. This report focuses on thrombectomy devices and reviews the evidence that advocates their routine use in PPCI patients.

Methods and results: We have performed a systematic review of currently available thrombectomy devices. We also performed a literature search, using the terms "thrombectomy" and "thrombus aspiration" in PubMed and EMBASE. Thrombectomy devices were divided in "manual" and "non-manual" groups. We performed a meta-analysis of the available randomized control trials that compared adjunctive thrombectomy in PPCI to standard PPCI. The use of manual thrombectomy devices is associated with significant improvements in ST-segment resolution (STR) ($p<0.00001$), Myocardial Blush Grade (MBG) 3 ($p<0.00001$), Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow ($p=0.01$) as well as clinical parameters (43% reduction in mortality, $p=0.04$) in patients undergoing PPCI.

Conclusion: Current evidence advocates the routine use of manual thrombectomy devices in PPCI. Non-manual (mechanical) thrombectomy may have a role in selected PPCI patients with large caliber vessels and heavy thrombus burden although their routine use is not presently supported.

1. Introduction

PPCI has become the treatment of choice for STEMI in the developed world as studies have demonstrated its superiority over conventional thrombolytic treatment [1]. STEMI usually results from the rupture of non-flow limiting coronary plaques with thin fibrous caps [2,3]. These are characterized by a lipid-laden necrotic core in which macrophage infiltration leads to the release of matrix metalloproteinases and inflammatory cytokines. This initiates a vicious inflammatory process that culminates in plaque rupture with subsequent vessel occlusion [4,5]. PPCI aims to restore coronary flow to thrombolysis in myocardial infarction (TIMI) grade 3 and although successful in most cases, up to 40% of patients do not achieve adequate myocardial reperfusion despite successful treatment of the culprit lesion as evidenced by failure of ST-segment resolution (STR) and poor myocardial blush grade (MBG) [6]. This phenomenon, known as no- or slow-reflow, has been associated with adverse clinical outcomes and has been attributed to a combination of distal embolization of plaque debris, vasoconstriction and reperfusion injury [7,8]. Microembolization can lead to the occlusion of arterioles in the microcirculation thus impairing end myocardial perfusion whereas embolization of larger atherosclerotic particles can lead to the occlusion of pre-arterioles and side branches [9,10]. The resulting capillary edema along with endothelial dysfunction and leukocyte activation leads to impaired oxygen delivery and eventually to myocardial cell necrosis [11]. It is therefore not surprising that in patients with no-reflow infarct size is larger, early post-infarction complications are more common and longer-term outcomes such as left ventricular function and survival are worse [12–15]. The use of glycoprotein

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(GP) IIb/IIIa inhibitors, either peripherally or intra-coronary, and that of coronary vasodilators such as verapamil and adenosine has been shown to be effective in reducing such events [16]. The need however to reduce such phenomena further and the fact that distal embolization seems to occur predominantly at the time of first balloon inflation and stent deployment has led to the development of devices whose efficacy has been examined in clinical trials [10]. Such devices broadly fall into two categories: distal or proximal protection and thrombectomy devices. Studies to date have failed to demonstrate a benefit for distal protection devices in the setting of PPCI although their use in Bypass Graft PPCI has not been evaluated by randomized control trials. Evidence to date appears to be more promising for thrombectomy devices as recognized by recent international guidelines [17].

2. Thrombectomy devices

Thrombectomy devices currently in use vary in design and mechanism of action but can be broadly divided in two groups depending on the presence or absence of a motorized system. Manual thrombectomy devices (Fig. 2.) include the Export (Medtronic), Diver CE (Invatec), Pronto (Vascular Solutions), QuickCat (Spectranetics), Fetch (Possis Medical Inc.), Thrombuster (Kaneka), Hunter (IHT Cordynamic), Fast Funnel (Genesis Medical Interventional), Xtract (Lumen Biomedical), Eliminate (TERUMO, VMax (Astron Medical) and Fetch2 (MEDRAD), aspiration catheters whereas non-manual thrombectomy devices (Fig. 1.) include the Angiojet (Possis Medical Inc.), X-Sizer (ev3 Inc.), Rinspirator (EV3 Inc.), Rescue (Boston Scientific) and TVAC (Nipro) catheters (Tables 1 and 3).

The excimer laser coronary angioplasty system (ELCA) can also be considered as a form of thrombectomy as thrombus is highly susceptible to laser energy and the device has already been used as an adjunct therapy in PPCI.

3. Non-manual thrombectomy devices

Non-manual thrombectomy devices vary in their working mechanism depending on their ability to actively fragment atherosclerotic thrombus material prior to aspiration. The Angiojet, X-sizer and Rinspirator System catheters are capable of such active thrombus fragmentation.

3.1. The Angiojet rheolytic thrombectomy system

The mechanism in the Angiojet rheolytic thrombectomy system (MEDRAD Interventional/Possis) involves the delivery of pressurized heparinized saline from the catheter where saline jets travel backwards creating a low pressure zone and thus a powerful vacuum effect. Thrombus as a result is drawn back into the catheter where it is fragmented by the saline jets prior to being evacuated from the body. The use of the Angiojet system as an adjunct in PPCI has been tested in three randomized trials. The first study demonstrated a benefit in its use as compared to standard PPCI in terms of infarct size as assessed by Tc-99 m sestamibi scintigraphy and STR [18]. The larger, multi-center, randomized AiMI trial however failed to reproduce such results [19]. Inclusion criteria were an anterior or a large inferior STEMI irrespective of angiographic evidence of thrombus. The primary end-point was infarct size at 14–28 days with secondary end-points being STR, post-procedure TIMI flow, corrected TIMI frame count, MBG, MACE (death, new Q wave MI, stroke, target lesion revascularization), ejection fraction and procedural complications. Importantly MACE was higher in the thrombectomy group as a result of more death at 30 days. The discrepancy between the two studies could be explained to some extent by the complexity of the device and therefore the importance of operator experience in its use. This may explain the higher rate of coronary perforation

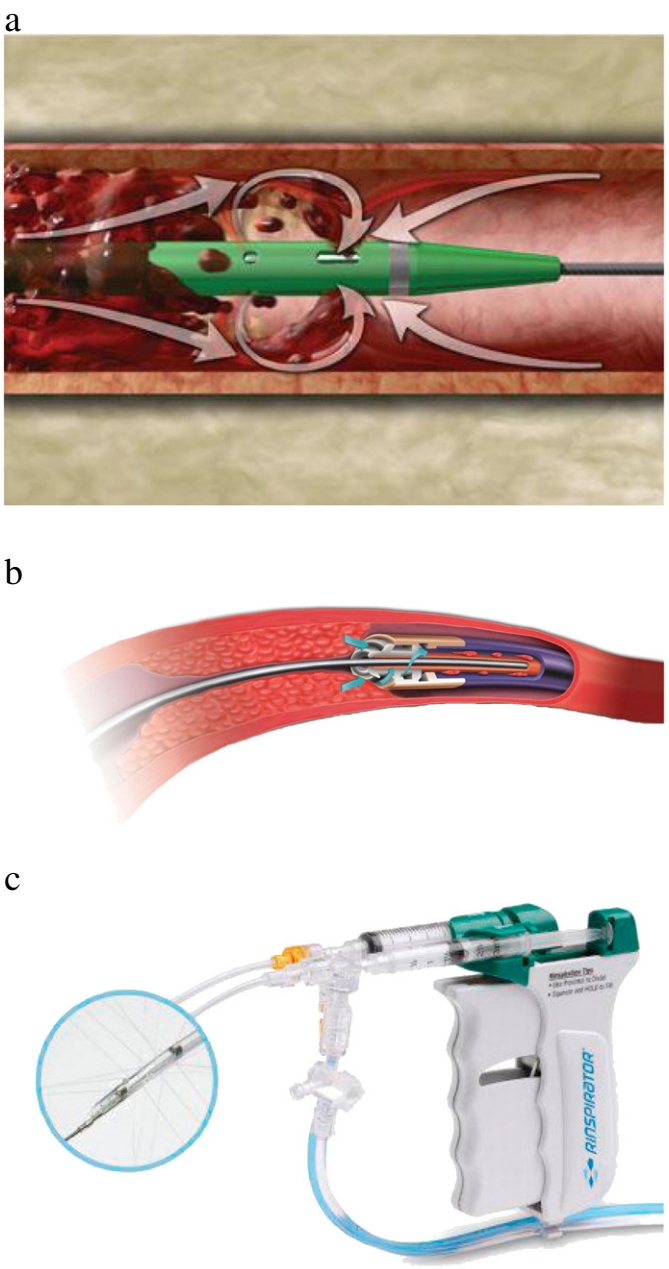

Fig. 1. Mechanical thrombectomy devices. a. The Angiojet System. b. The X-sizer system. c. The Rinspirator system.

observed in the AiMI trial. In addition, TIMI 3 flow prior to intervention was encountered significantly more often in the standard PPCI than in the thrombectomy group, which could explain the differences in infarct size between the two groups. Furthermore, a retrograde thrombectomy technique was used without activation of the device prior to crossing the lesion, which could have promoted distal embolization. Finally, angiographic evidence of thrombus was absent in a large percentage of both groups (25%) suggesting that the Angiojet device is perhaps best suited in cases with high thrombus burden. In agreement with this, a recent meta-analysis comparing Angiojet thrombectomy to standard PPCI showed that both clinical (MACE) and angiographic end-points (TIMI flow) were similar in both groups despite the fact that in the Angiojet group patients had a larger thrombus burden and longer symptom duration compared to the