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ARTYKUŁ SPECJALNY / *STATE-OF-THE-ART REVIEW*

TASTE-less endpoint of 30-day mortality (and some other issues with TASTE) in evaluating the effectiveness of thrombus aspiration in STEMI: not the "evidence" to change the current practice of routine consideration of manual thrombus extraction

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INTRODUCTION

The 2012 ST-segment elevation acute myocardial infarction (STEMI) guidelines of the European Society of Cardiology (ESC) state that: "Routine [manual] thrombus aspiration should be considered in STEMI" (Class IIa, level of evidence B) [1].

Consideration of manual thrombus aspiration (TA) is therefore an important part of routine interventional management of STEMI patients [2, 3].

The 2013 ESC Congress presentation of the Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE) study outcome that 30-day all-cause mortality (the primary endpoint) was not significantly affected by manual TA in STEMI [4, 5] made prominent headlines through the ESC press release and internet cardiology services. These headlines indicated that: "*TASTE questions the usefulness of thrombus aspiration as a routine adjunct [to primary PCI]*" [4], "*Thrombectomy a letdown for PCI-treated STEMI patients*" [6], and "*International STEMI guidelines should probably be down-graded*" [4]. Indeed, the official ESC news release of 1 September 2013 indicated that: "*The [TASTE] study results will likely have an immediate impact on clinical practice*" [4]. Even before the TASTE data surfaced, the Heartwire voiced that: "*TASTE most likely will dictate future guidelines*" [7].

As today's physicians (including cardiologists) are becoming increasingly reliant on internet delivery of 'digested' research data [4, 6, 7], a fundamental question that needs to be addressed in the light of TASTE publication and its sensational coverage by cardiology news services is the following: ***Should we indeed, after TASTE, stop our routine consideration of manual thrombus aspiration in STEMI patients?***

Rather than a remote academic question, this is an important practical issue that may affect the long-term clinical outcome of today's STEMI patients [2, 8]. Following the TASTE publication [5] and its sensational coverage [4, 6, 7], in the last quarter of 2013 some primary percutaneous coronary intervention (pPCI) operators have already started abandoning their habit of routine consideration of thrombus aspiration in STEMI. Some others, overwhelmed by the information noise [4, 6, 7], are not sure whether they should stick to the guideline-indicated management and consider offering TA to their patients any longer because the "*guidelines are likely to be down-graded*" [4].

Is there really *any* evidence today that allows the pPCI operator to deliberately fragmentise the clot and send it (parts of it) down to obstruct coronary microcirculation in a STEMI patient — rather than remove the clot (or at least part of it) from the infarct-related artery (IRA) prior to inserting a balloon or implanting, directly, a stent?

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MOST CULPRIT LESIONS IN IRA ARE THROMBOTIC: SOMETHING NEEDS TO 'HAPPEN' WITH THE THROMBUS DURING PRIMARY PCI

Intracoronary thrombosis, resulting from atherosclerotic plaque rupture or erosion, is the leading mechanism of acute coronary syndromes (ACS) [1, 2, 8]. Angiographic thrombus presence and its size are important determinants of the risk of distal macro- and microembolisation and myocardial damage [2, 8]. Stent-assisted pPCI plays a central role in achieving rapid and effective opening of the IRA and elimination of the flow-limiting lesion. Evidence shows a strong association between the presence of IRA thrombus and an increase in myocardial injury with pPCI, leading to adverse clinical outcomes, with the thrombus size being an important negative prognostic marker [2, 8]. It is well-known today that the goal of successful reperfusion strategies in ACS is microcirculatory myocardial perfusion and myocardial salvage rather than 'just' flow re-institution in the IRA [1, 2, 8].

More than a decade ago, the TIMI Group established that myocardial reperfusion resulting in an open microvasculature (manifest as TIMI myocardial perfusion grade [TMPG] 2 or 3) was associated with significantly lower mortality at two years than TMPG 0 or 1 (4.76% vs. 9.07%, p = 0.038) [9]. Consistently, landmark findings from the Cardiovascular Research Foundation investigators demonstrated that in patients in whom epicardial TIMI-3 flow was restored, survival was strongly dependent on the post-angioplasty myocardial perfusion, with one-year cumulative mortality of 6.8% with normal myocardial perfusion, 13.2% with reduced myocardial perfusion, and 18.3% in patients with absence of effective myocardial perfusion (p = 0.004, epicardial IRA flow TIMI-3 in all) [10]. Effective myocardial tissue reperfusion is thus established as a key determinant of left ventricular function and *long-term* (N.B. not: short-term) survival after ACS [2].

IRA thrombus, a major determinant of poor myocardial tissue reperfusion in ACS and a poor long-term clinical outcome, is managed in a pharmacological, a mechanical, or a combined, way [2, 8].

THROMBUS MANAGEMENT CHOICES: REMOVE, DISSOLVE, TRAP AT THE LESION SITE — OR FRAGMENTISE AND SEND DOWN TO OBSTRUCT MICROCIRCULATION

Pharmacologic total thrombus resolution is rare in the absence of fibrinolytic treatment (the latter being associated with a clinically-relevant risk of bleeding complications) [2]. Data prior to the era of routine TA provided evidence that an adverse long-term clinical outcome of pPCI is determined by the magnitude of microcirculatory flow deterioration that occurs with optimisation of stent expansion in a thrombotic lesion through the 'cheese-grater' effect [2, 11]. This led to the concept that thrombus extraction from IRA, as a means to reduce distal vasculature obstruction and myocardial damage, may improve the long-term outcome of pPCI [2, 8, 12].

Multi-centre evidence indicates that manual thrombus extraction through an aspiration catheter, adopted either as a routine strategy or targeted to patients with angiographic evidence of thrombus, leads to improved myocardial perfusion and a reduced infarct size [2, 13–15]. There are theoretical grounds and clinical data that pharmacological and mechanical thrombus burden reduction act synergistically to obtain the best myocardial reperfusion and, in consequence, the best clinical outcome [2, 8]. Pharmacological reduction of thrombus burden is most effective in ACS patients presenting early after symptom onset [1, 2, 16]. Recent data confirm that a strategy that combines manual thrombus extraction with lesion-directed pharmacotherapy translates into maximised infarct size reduction [16]. The INFUSE-AMI trial, using 2 × 2 factorial design in 452 patients presenting with a large anterior myocardial infarction within 4 h of symptom onset (i.e. early presenters) showed that the infarct size by cardiovascular magnetic resonance imaging (cMRI) was smallest when manual thrombus aspiration was combined with abciximab infusion directly at the lesion site via a 'weeping' balloon (median infarct size of 14.7% vs. 17.6%, p = 0.03, comparison of TA + intracoronary abciximab vs. a combined group of no TA/no abciximab + TA/no abciximab + no TA/no abciximab) [16].

The optimal treatment of patients with a thrombus-containing lesion needs to integrate pharmacologic and mechanical approaches to thrombus burden reduction to minimise its impact on myocardial (tissue) reperfusion [2, 8]. Other concepts to reduce the impact of thrombus burden on myocardial loss, discussed in more detail elsewhere [2], include the application of mesh-covered stents to trap the embolic material; the use of these, however, is limited to (for instance) non-bifurcated lesions [2].

MYOCARDIAL SALVAGE WITH THROMBUS EXTRACTION: THE ESTABLISHED SHORT-TERM VS. LONG-TERM ENDPOINTS

Key randomised studies of manual TA, [13–15], registries [17] and meta-analyses [18–21], have consistently demonstrated that TA prior to stent implantation (or balloon use) in pPCI improves *short-term* indices of myocardial salvage such as angiographic measures of myocardial reperfusion (TMPG or myocardial blush grade) or ST segment resolution, and the total infarct size or the size of microvascular obstruction on cMRI [2, 13–21]. In contrast, these studies (and their meta-analyses) have consistently demonstrated that the clinical benefit of TA (mortality reduction or reduction in clinically-significant heart failure [HF]) manifests *not earlier than* 12 months after the index event [18–21].

An increase in time to treatment in STEMI is a major predictor of impaired myocardial reperfusion despite a successful

restoration of the epicardial (IRA) flow [1]. The INFUSE-AMI findings suggest that STEMI patients with short presentation (within 4 h of symptom onset) may receive relatively less benefit from TA when local (intra-lesional) abciximab influsion is on board [16] as the 'early' thrombus is known to be particularly prone to pharmacological management [1, 2]. On the other hand, recent pooled analysis of individual patient data of three prospective randomised trials of manual TA in STEMI showed that TA can attenuate the adverse effect of time-to-treatment prolongation on myocardial reperfusion [22].

In most TA studies and their meta-analyses to-date, TA did not affect the short-term outcome of 30-day mortality in STEMI [13, 17–20]. Nevertheless, long-term data — such as that from INFUSE-AMI — shows that, even in patients with early cathlab presentation in ACS, TA compared to no aspiration was associated with lower rates of new-onset severe HF (0.9% vs. 4.5%; p = 0.02) and of re-hospitalisation for HF by one year (0.9% vs. 5.4%; p = 0.0008) [23]. This is not surprising, because it has been known for a long time that the effect of improved reperfusion on clinical outcome may not become apparent until one–two years after the index ischaemic event [9, 10]. In contrast to the (expected) lack of effect of TA on 30-day mortality, the evidence to date is internally consistent in demonstrating a reduction in 12-month mortality with TA in STEMI [12, 14, 17, 18, 21].

Thus a consistent body of evidence indicates that the short-term (such as 30-day) effectiveness of TA is reflected by myocardial perfusion and infarct size parameters. In contrast, the clinical effect of TA, as manifested by a reduction in new-onset HF and HF hospitalisations or mortality reduction, does not become detectable until some 12 months after STEMI.

TASTE SHOWS DISSOCIATION BETWEEN THE STUDY HYPOTHESIS AND CHOICE OF THE ENDPOINT

When evaluating the applicability of a study to clinical practice, two fundamental questions need to be addressed: (i) is this study aim/hypothesis valid?; and (ii) do the findings from the study support the hypothesis? (N.B. the third question is whether the findings are applicable to a particular ('my') patient) [2, 3].

TASTE was conducted to test the hypothesis that manual TA, as an adjunct to standard PCI, "*confers a better outcome* compared to PCI alone in patients with STEMI" [24]. The TASTE study was undertaken because, in view of its Investigators, "additional evidence needed to be established" [24] since "thrombus aspiration [in STEMI] either saves lives or is a killer, we don't know" [7]. To test the hypothesis of a potentially better outcome with TA in STEMI patients, TASTE selected the primary endpoint of all-cause mortality at 30 days [5, 24]. Here comes the principal problem with TASTE: its choice of 30-day mortality as the study endpoint [5, 24] is against the wealth of published evidence (in an overall patient population similar to that in TASTE) that TA is highly unlikely to affect 30-day mortality [13, 14, 17, 18]. No explanation for this unfounded *early* mortality primary endpoint choice has been provided [5, 24]. It is also surprising that the TASTE power calculations [5, 24] were based on the 30-day mortality in the TAPAS study in which (in contrast to the significant 12-month mortality reduction in a study of 1,071 STEMI patients [12]), the 30-day mortality was unaffected by manual TA [13]. Moreover, the seemingly firm conclusion from TASTE is based, in fact, on only half of the originally scheduled events in this study [5, 24].

Thus the principal hypothesis of TASTE, that the reduction in myocardial injury/infarct size with TA (if it occurred) would be *large enough* to affect mortality 'already' at 30 days is not founded by pathophysiology or data from other studies. The totality of pre-TASTE evidence (in an overall group of ca. 4,000 patients) [13, 14, 17, 18] shows that, in present patient populations, the endpoint of early (such as 30-day) mortality is highly unlikely to be sensitive enough as the demonstration of clinical effect of TA on myocardial salvage.

In essence, while undertaking a study that aims to evaluate whether manual TA reduces mortality is (with Ethics Committee approval) acceptable for investigators who do not find the totality of prior evidence sufficient, the choice of 30-day mortality as the primary study endpoint of a TA study is unfounded.

TASTE: MISSING ROUTINE BIOMARKER INFARCT SIZE AND ST-SEGMENT RESOLUTION DATA

With the scheduled study population of 5,000 STEMI patients [24] and 7,244 actually randomised [5], TASTE had the potential to detect an effect TA on, for instance, ST segment resolution and biomarker infarct size reduction. In view of the effect on these routine short-term endpoints in prior studies of manual TA in STEMI [13, 17, 18, 20], it is unclear why the TASTE protocol, focused on a short-term outcome [5], did not include ST segment resolution at (for instance) 90 min after reperfusion. It is also unclear why routinely available infarct size data (e.g. peak CK-MB or peak troponin value that is known to correlate with infarct size on MRI [2, 25]) were not collected in TASTE. These could have served as important secondary endpoints.

Unfortunately, the impact of TA on routine short-term indices of myocardial salvage remains, in the TASTE study, unknown, and it is unclear why this important data was not captured.

SOME OTHER ISSUES WITH TASTE — SUCH AS EXCLUSION OF PATIENTS IN WHOM THROMBUS ASPIRATION WAS CONSIDERED TO BE INDICATED

There is no doubt that TASTE Investigators are to be commended for their pioneering concept of a randomised trial

within a national registry [24], and the effort they have made to gather and analyse data from a large patient population, including data capture in those not randomised. While long-term clinical results from TASTE are awaited (i.e. the endpoints that TA, in light of prior evidence, might actually have an effect on [12, 14, 17, 18, 21]), several points other than the unfounded choice of 30-day mortality as a primary TASTE endpoint need to be made.

In TASTE, 40% of patients presenting with STEMI and referred to pPCI were excluded from randomisation [5]. The principle of randomisation is uncertainty to the treatment effect [2], and randomisation in TASTE was performed after obtaining the angiogram [5, 24]. Therefore one would expect that at least some TASTE operators would have decided, on a purely ethical basis, to exclude from randomisation patients with a substantial thrombus burden in their IRA. Is there any evidence that this subject selection bias did actually occur?

The TASTE publication indicates clearly that when TA was considered indicated it was performed, and the patient was not part of the randomised study [5]. Thus the patients who were considered to benefit most from TA became, paradoxically, removed from the study of the effect of TA in STEMI [5]. While this is certainly right in terms of ethics, such a study is no longer able to test the effect of TA in a "STEMI population". Therefore what TASTE, in fact, tested was the effect of TA in patients in whom TA was *not* considered to be indicated, with an obvious impact of this patient selection bias also on the long-term study endpoints. Lack of an appropriate statement (with an appropriate weight — such as in the title or abstract) confuses the recipient of the study message. Large patient numbers cannot (and thus will not) make up for the (possible) design and (definite) study data communication flaws.

The TASTE data shows that among those non-randomised to TASTE (n = 4,697), TA was actually performed in 1,162 (25%) patients, including those in whom TA was *a priori* considered to be indicated [5]. This calls for at least an additional per-treatment analysis of outcomes including those patients in whom TA was *a priori* considered to be indicated. This bias is likely to be significant because TASTE (although it claims that its "patients were treated according to international guidelines" [5]) did continue to recruit patients after publication of the 2012 ESC STEMI guidelines (October 2012) where TA consideration is a class IIa recommendation. In fact, 2,442 (33.7%) TASTE patients were recruited after the interim data analysis that occurred in August 2012 [5].

TASTE data has not been centrally adjudicated. It is unclear why a very large proportion of non-randomised STEMI patients (38%) [5] were the patients flagged as "unable to provide informed oral consent" to undergo randomisation to TA–assisted pPCI vs. pPCI without TA. This 'main' flag is likely to hide a proportion of non-randomised patients in whom TA was actually performed [5].

Another important limitation of TASTE is that its protocol restricted TA to the use of 6 F aspiration catheters while the aspiration capacity of 7 F catheter is known to be ≈50% higher than that of a 6 F aspiration catheter [2, 3]. This limitation goes against the current practice of TA with the use of 7 F catheters in larger arteries and larger thrombus burdens [2, 3] (examples in Figs. 1, 2) and it might have significantly confounded TASTE data by leading to suboptimal thrombus extraction in patients with large arteries and large thrombus burden (i.e. those likely to gain most benefit from thrombus extraction) [2, 3].

POST-TASTE LANDSCAPE: NO EVIDENCE TO CHANGE THE CURRENT PRACTICE

A large body of consistent data shows, in aggregate, that TA in STEMI patients is associated with an improved myocardial perfusion and reduced infarct size while the clinical benefit of TA (manifest as a reduction in new onset HF, reduction in HF hospitalisations, or reduction in mortality) does not occur until 12–24 months after the index ACS [12, 14, 17, 18, 21].

TASTE, a randomised registry trial [24], aimed to evaluate the hypothesis that TA "confers a better outcome" compared to PCI alone [5, 24]. This hypothesis was tested by assessing 30-day mortality as the primary endpoint of the study; the endpoint known *not* to be affected by TA in prior studies and their meta-analyses [13, 14, 17, 18].

Importantly, TASTE excluded from randomisation patients in whom TA was considered to be indicated [5], and TA was performed in 25% of those excluded from randomisation [5]. Routine exclusion, from a study of TA, of the patients expected to benefit from TA, is likely to affect also the long-term outcome from the study. Irrespective of whether this patient proportion is 10% or 25%, these are likely to be the patients who might have driven the outcome of the study. Therefore, even if future 12-months TASTE data shows no apparent effect of mortality, this will not form any evidence that TA is not overall effective in today's STEMI patients.

What TASTE demonstrated is that, in the randomised patients (i.e. having excluded those in whom TA was considered to be indicated), the 30-day mortality was not significantly affected by TA (2.8% TA vs. 3.0% PCI-only group; p = 0.63) [5]. This finding is not unexpected as it is entirely consistent with prior evidence that myocardial salvage with TA translated into reduction of long-term clinical endpoints (including mortality) but not of 30-day mortality [13, 17, 18, 24]. For these reasons, TASTE provides no grounds to change the current (evidence-based and guideline-indicated) strategy of routine TA consideration in STEMI patients [1].

It needs to be noted that manual TA is not the management for all STEMI patients and all culprit lesions in STEMI; several limitations to its use are discussed elsewhere [2, 3]. It is also known that, in inexperienced hands in particular, TA can be associated with an increased risk of coronary and extracar-

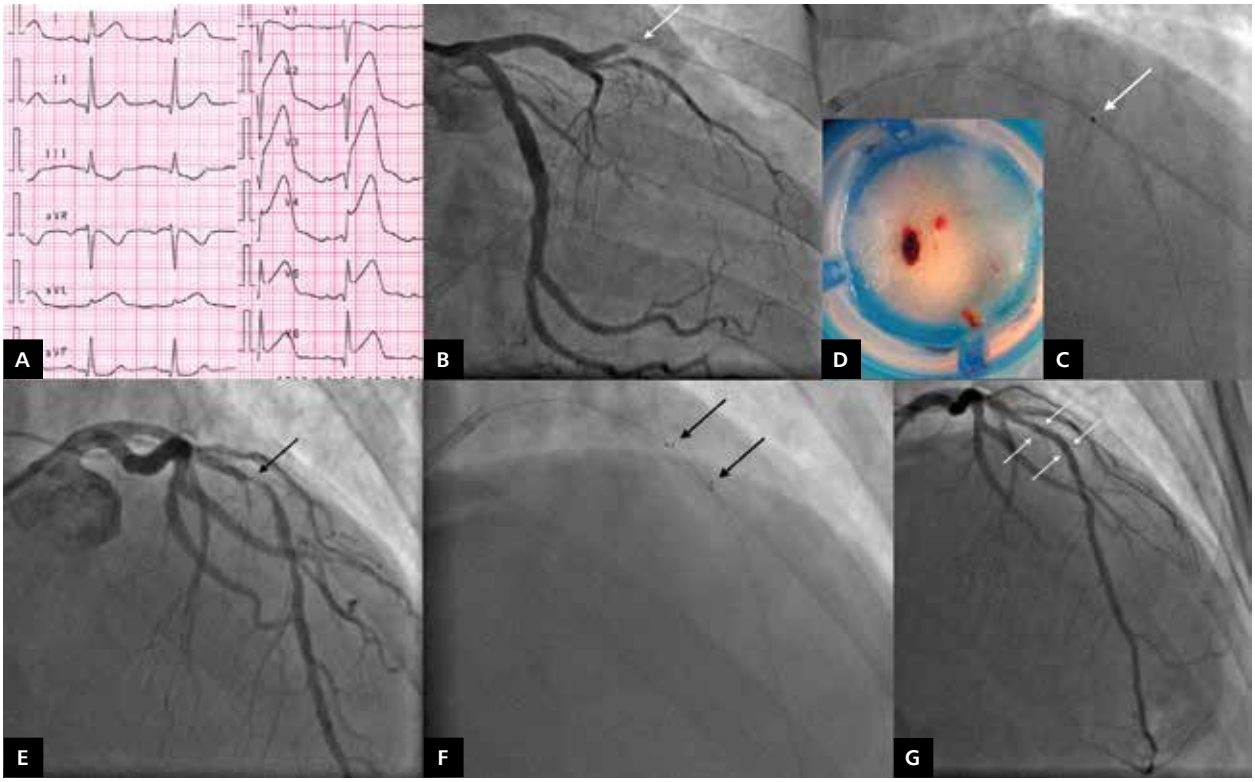
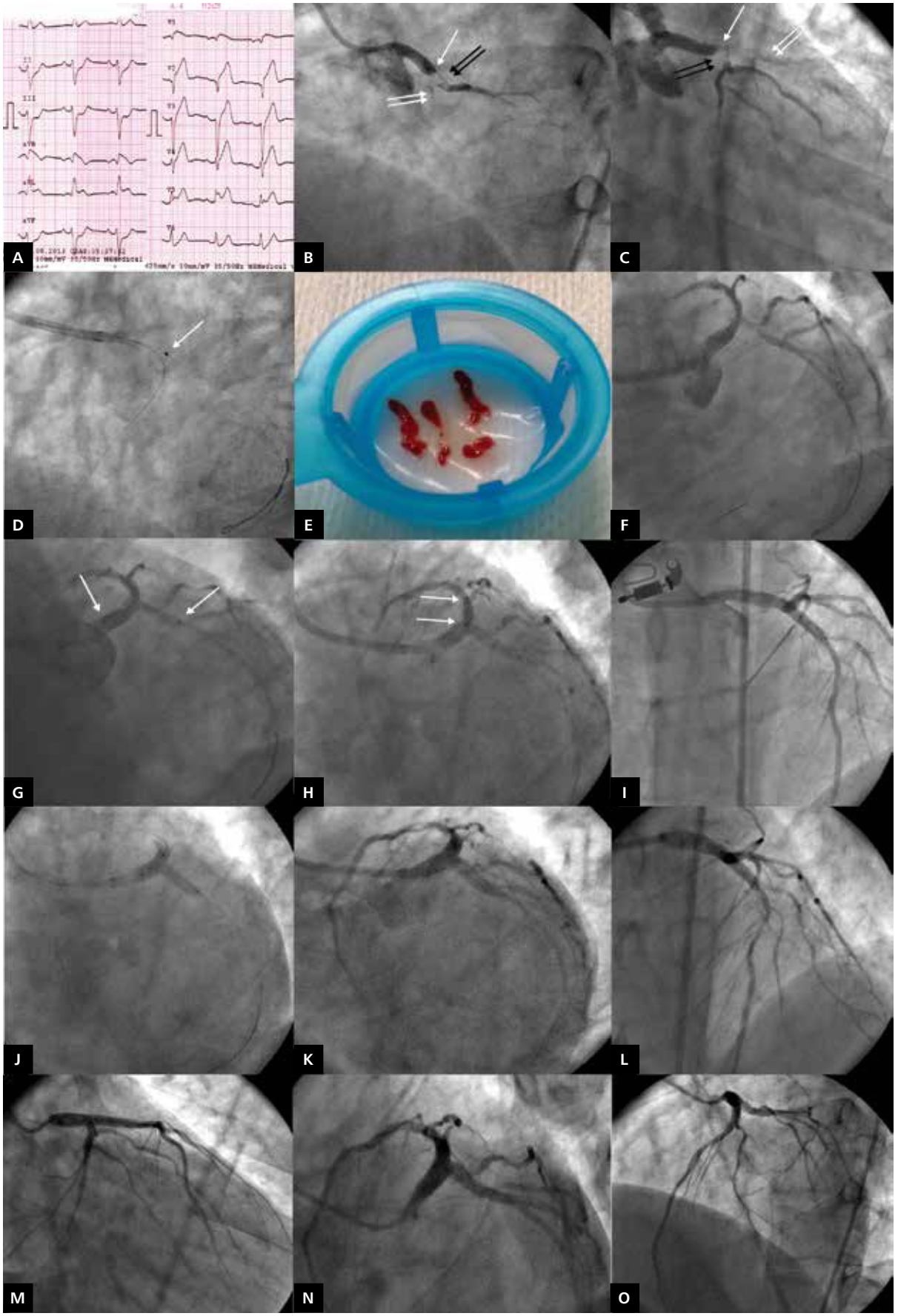


Figure 1. Coronary thrombus extraction in current state-of-the-art management of a STEMI patient. A 45-year-old man was admitted following 20-min severe retrosternal pain and ventricular fibrillation on paramedics' arrival. Cathlab direct admission ECG (**A**) was consistent with anterior STEMI, and coronary angiogram demonstrated left anterior descending coronary artery abrupt occlusion (**B**, white arrow; N.B. the right coronary artery was normal and is not shown). The patient was loaded orally with prasugrel (initial intravenous heparin and oral aspirin had been given by the paramedics). In the operator's judgment, the clinical presentation and image in **B** were consistent with a thrombotic occlusion of the IRA; thus thrombus extraction was performed with a 7 F Export aspiration catheter whose aspiration capacity is ≈50% higher than that of a 6 F aspiration catheter [2, 3] (**C**, white arrow indicates the marker at the tip of aspiration catheter, **D** shows the thrombi extracted from IRA in this patient). With thrombus extraction (considered by the operator, in this scenario, routine) the IRA flow was re-established (**E**). This enabled direct stenting, which was performed with a bioabsorbable sirolimus-eluting Absorb 3.5 × 12 mm scaffold implanted at 4–12 atm over 70 s and post-dilated with a non-compliant 3.5 × 9 mm balloon at 16 atm (image **F** was taken immediately after the stent-implantation balloon deflation, black arrows point to the platinum markers of the stent which itself, made of poly-L--lactide, is completely invisible on angiogram; the external markers along the angioplasty wire are the deflated balloon markers). Final angiographic result is shown in **G** (arrows indicate the position of the stent that will undergo complete biodegradation over ≈2 years; vascular reparative/restoration therapy — VRT). The patient was discharged home on day 4, with normal anterior wall thickness on echocardiogram, and only moderate anterior hypokinesia with an early left ventricular ejection fraction of 50%. [*Procedure performed by the Author.*]
Note that while the IRA thrombus extraction by itself cannot be reasonably expected to reduce the risk of 30-day death in this patient (provided that any pPCI effective in IRA opening is performed), this manoeuvre removed a significant part of the thrombotic burden that would have otherwise embolised IRA microcirculation, extending the myocardial injury (i.e. the infarct size — a well-established predictor of long-term STEMI outcome [1]). Randomisation of such a patient to TASTE would have been dependent on whether or not the operator believed that thrombus aspiration was indicated (in the latter case, TA would have been performed and the patient would have not contributed to the TASTE randomised cohort; if randomised to TASTE, however, this patient would have a 50% chance of a 6 F-only aspiration catheter thrombus extraction attempt). While the TASTE data was not centrally adjudicated, according to TASTE report [5], TA in TASTE was considered "indicated" in a minority of all-comer STEMI patients, suggesting that patients like this one (a 'typical' STEMI patient with an average thrombus burden) contributed to TASTE. It is unreasonable to expect that TA, in such patients, would reduce the risk of death at 30 days.
A likely TASTE trial-represented patient with respect to TA use.

diac embolisation with the IRA thrombotic material through the drag-and-drop effect [2, 3, 19]. In this respect, the TASTE data showing no stroke excess with TA [5, 19] is reassuring.

It can be debated whether manual TA should be offered to all STEMI patients undergoing primary PCI (i.e. irrespective of angiographic evidence/absence of thrombus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presence [12, 13]) or whether it should be limited to those ACS patients whose angiogram shows evidence of thrombus presence [2, 26]. Recent meta-analysis of 4,514 TA patients in 21 randomised studies indicated a relationship between the magnitude of ST-segment resolution and the presence of thrombus at baseline angiography ($p = 0.0016$), indicating that TA (rather than applied routinely) should be used, first of all, when the angiogram suggests intracoronary thrombus presence [20]. Indeed, strategies of selective use of TA are becoming crystallised [2, 3, 26].

Another important issue is whether TA should be limited to those ACS that manifest with electrocardiographic (ECG) ST-segment elevation. It is well known, for instance, that angiographic evidence of the occluded culprit artery is seen in 20–25% of non-ST segment elevation myocardial infarction (NSTEMI) patients [27, 28]. This is particularly relevant for left circumflex coronary artery occlusions which may not manifest as ST segment elevation due to the standard ECG lead location (poorly reflecting the lateral wall phenomena) and the late depolarisation of the lateral wall [27]. The use of manual TA in NSTEMI is accepted by the current ESC NSTEMI guidelines [28] and it should be considered in NSTEMI patients with angiographic thrombus evidence undergoing pPCI [2, 3].

CONCLUSIONS

Current 30-day mortality in STEMI, ranging from ≈3% in clinical studies [1, 5, 14, 16, 29] to ≈5% in out-of-study patients [1, 5, 29], is low and likely to be very close to the 'bottom' of what can be achieved today with a reduction of the symptom-to-treatment window and timely implementation of the pharmaco-invasive strategy in present patient populations. Any further significant mortality reduction may not be feasible, due to the STEMI population and patient presentation factors such as, for instance, the proportion of patients with extensive coronary artery disease or severe pre-pPCI cardiac damage including cardiogenic shock, the proportion of those at risk of early post-hospital arrhythmic death or due to stent thrombosis by 30 days, or the proportion of patients with severe co-morbidities that affect short-term prognosis [1].

Therefore, manual TA (similar to any other, present or hypothetical, pharmacological or mechanical intervention in STEMI) should not be reasonably expected to be the intervention powerful enough to further reduce the early (i.e. in-hospital or 30-day) STEMI mortality in a statistically significant and clinically meaningful manner. The principal finding from TASTE (i.e. lack of effect of TA on 30-day mortality in the *TASTE-randomised* STEMI population) is thus fully expected

Figure 2. Coronary thrombus extraction as an essential live-saving manoeuvre in a STEMI patient. This STEMI patient is a 52-year-old man who was woken up by crushing retrosternal pain. ECG on paramedics' arrival is shown in **A**; the patient was given oral aspirin (300 mg) and clopidogrel (600 mg), and unfractionated heparin (5000 IU) intravenously. While in the ambulance (transport time to a primary PCI centre 40 min), the patient developed cardiogenic shock and arrested several times. He arrived directly to the cathlab in profound cardiogenic shock, on pharmacologic inotropic support, intubated and artificially ventilated. Coronary angiogram (7 F right femoral access) demonstrated non-critically diseased right coronary artery (not shown) and a thrombotic occlusion of the left main (LM) coronary artery (single white arrow, **B** and **C**) extending to the left anterior descending coronary artery (LAD, double white arrow, **B** and **C**) and the circumflex artery (Cx, double black arrow, **B** and **C**); note the low-cardiac-output-related contrast stagnation in the aorta in **B** and **C**. An immediate thrombus extraction was performed with a 7 F Export aspiration catheter from LM/LAD and from LM/Cx (**D**; N.B. had this first-line strategy been not sufficiently effective, the mother-and-child, i.e. long 6 F catheter in an 8 F guiding [2, 3], or guiding catheter direct thrombus aspiration would have been employed). This was a live-saving procedure that led to flow re-institution in LAD and Cx (**F**; the thrombi extracted are shown in **E**). Intra-aortic balloon counterpulsation was inserted via the left groin as no other means of mechanical circulatory support was available on site, and an intracoronary bolus of abciximab was administered and followed by an intravenous abciximab infusion; unfractionated heparin was supplemented. LM/Cx/LAD stenting was then performed. First, a drug-eluting stent (Xience 3.5 × 23 mm) was implanted in the LM-Cx (stent positioning, arrows, is shown in **G**, the non-diseased proximal LM portion was deliberately not covered with the stent). Following expansion of the 1st stent, LAD was re-wired and a 2nd stent (Xience 3.5 × 18 mm) was implanted from LAD ostium to proximal LAD, with a small, intentional, proximal protrusion to the LM (stent positioning in **H**, arrows, whereas **I** is the image immediately after LAD stent implantation; T-and-protrusion technique — TAP). Final kissing balloon inflation is shown in **J**, whereas **K** and **L** are the index procedure final angiographic images. The patient, without any neurological deficit, was discharged to a cardiac rehabilitation centre on day 6, with an overall left ventricular ejection fraction (LVEF) of 40%. Control coronary angiogram, performed 4 months later (**M**, **N**, **O**), confirmed an optimal result of the index procedure (optimal stents expansion with no angiographic in-stent restenosis); echocardiogram showed LVEF of 45–50%. With the large thrombotic burden seen in **B** and **C**, it is unlikely that any reasonable operator would have included any similar patient in the TASTE randomised study. Note that, as something has to 'happen' with the thrombus during pPCI, theoretical randomisation of such a patient to no-thrombus extraction (i.e. deliberate thrombus fragmentation and IRA microcirculation obstruction) pPCI vs. thrombus extraction–assisted pPCI, although hard to accept ethically, could well lead to the demonstration of an early mortality benefit with thrombus extraction in STEMI.
Not a trial-represented patient.
[*Index procedure by the Author and Dr Marek Andres as 2nd operator; follow-up angiogram courtesy of Dr Marek Skura, Szpital św. Łukasza, Tarnów*].

on the basis of the aggregate of data from prior randomised studies of TA in STEMI [13, 14, 17, 18]. Interpretation of this TASTE finding, however, as "evidence" for the "lack of effectiveness" [4–6] of thrombus aspiration is fundamentally wrong. Not only because no evidence (irrespective of TASTE) indicates that TA could affect early mortality in STEMI, but also because *TASTE excluded from randomisation patients in whom TA was considered to be indicated* [5].

In essence, the (expected) "lack of evidence" for a significant reduction in 30-day mortality with TA in TASTE that excluded from randomisation patients with expected benefit from TA (2.8% TA vs. 3.0% no TA; p = NS) is clearly not "evidence for lack" of an effect of TA in STEMI patients on myocardial injury and infarct size reduction. Nor can it be taken as "evidence for lack" of a long-term effect on HF development or hospitalisations for HF exacerbations, or its potential long-term mortality benefit. Indeed, it is well known that a modest reduction in infarct size with TA-associated improved myocardial perfusion in STEMI [13–15, 17–20] may translate to a reduction in mortality at one–two years but not at 30 days [12, 14, 17, 18]. Unfortunately, the important patient selection bias in TASTE is likely to have an effect also on the long-term study outcome.

Although practicing medicine (and interventional cardiology in particular) is becoming more and more the work of highly-skilled craftsmen, it will always remain an art of selecting the best available treatment strategy for a particular patient. While correct manual TA has a clear learning curve [30] that includes appropriate training and clear understanding of procedural steps [2, 3], primary PCI operators should adhere to current guidelines [1] and continue to provide acute myocardial infarction patients with manual TA from IRA, particularly when the thrombus presence is evident on angiography [2, 20].

Manual TA, an adjunct to pPCI, does not "need" to further reduce 30-day mortality in present STEMI patients to "work". Pivotal therapies in STEMI, such as aspirin or thrombolysis, required over 17,000 study patients to demonstrate mortality reduction at five weeks [32]. Current data indicates that by reducing myocardial injury, particularly in patients with a substantial thrombus burden amenable to manual TA [2], TA leads to evidence-based improvement in clinical outcomes such as reduction in HF or reduction in mortality at 12–24 months [12, 14, 17, 18].

Therefore, when it comes to the applicability of thrombus removal from IRA in STEMI patients today, do not get misled by the increasing noise of some medical headlines' "tabloidism" [4, 6, 7, 31]. Publication of controversial data in a major journal will no doubt contribute to the journal's citations, and TASTE Investigators stated that they *"have been continuously contacted by […] two leading scientific journals wishing to publish"* [7]. On the other hand, however, the losers — due to inaccurate interpretation of biased data — may be your patients.

Physicians have the right, and the duty, to evaluate the validity of published data. Therefore, for your STEMI and NSTEMI patients in 2014, stay with the guidelines in *considering* thrombus extraction (the guidelines, by the way, do not tell you what to *do* in every patient but help by indicating what one should *consider* in the trial-represented patients (Fig. 1) while a significant proportion of the all-comer population you treat may be not be trial-represented (Fig. 2) [2, 33].

Data from TASTE are neither surprising nor disappointing. Until (and unless) proved otherwise, the body of consistent evidence that TA saves myocardium which translates into improved *long-term* clinical outcomes cannot be discarded.

Conflict of interest: *The author prepared an interactive educational session on manual thrombus extraction for the 2011 EuroPCR; this, however, was not associated with any honoraria. He declares no other conflict of interest.*

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