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Review

Simplifying electrocardiographic assessment in STEMI reperfusion management: Pros and cons

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ABSTRACT

Current guidelines on STEMI reperfusion management do not incorporate further electrocardiographic details over the presence of significant ST elevation. Fibrinolysis is considered an alternative therapy to primary PCI if there is a long PCI-related delay, but the 2 therapies should not be combined. Meanwhile, reperfusion for ischemic stroke has evolved on mechanistic understanding - reperfusion benefit being greatest in the patient with small "core" infarct and large ischemic "penumbra". Fibrinolysis is not regarded as an alternative to mechanical thrombectomy, and the 2 therapies can be combined. In this article describing how reperfusion regimes have evolved along different paths for STEMI and for ischemic stroke, a new concept is made that in STEMI infarct lead Q waves can be the counterpart of the "core" and ST elevation the "penumbra". Suggestions to modify STEMI treatment algorithms are made, exploring further the relative role of (pre-hospital) fibrinolysis versus PCI particularly in younger patients presenting at the onset of their STEMI (no Q waves). In contrast, some patients particularly the older ones with more evolved STEMI (large Q waves present) may be much more suited for PCI despite expecting a long delay. The article finishes by describing potential future alterations in the method of reperfusion. Despite primary PCI being the well-established therapy, there are rooms for further research to optimize STEMI outcomes.

Prompt primary PCI has taken a center stage in the management of STEMI within 12 h of symptoms onset. If timely PCI is not possible, the *alternative therapy* of fibrinolysis should be considered. This simple approach has helped hospital administrators devise the current systems for rapid delivery of *one* of the 2 treatment options – the consensus being that combined fibrinolysis and PCI (facilitated PCI) does not constitute a better therapy.

In the related field of acute ischemic stroke from anterior cerebral circulation occlusion, the American Heart Association/American Stroke Association has released a focused update [1] in June 2015 of the 2013 guidelines incorporating the positive findings of 5 recently published randomized trials (endovascular therapy versus no endovascular therapy) that supported the use of intra-arterial thrombectomy procedures [2–6]. Class I recommendations are given (Level of Evidence: A) for the use of mechanical therapy (specifically the stent retriever) *along with* IV recombinant tPA treatment for eligible patients >18 years of age who have acute ischemic stroke of <6 h duration, large (anterior circulation) vessel occlusion on imaging, NIHSS (National Institutes of Health Stroke Scale) score >6, and ASPECTS (Alberta Stroke Program Early CT Score) >6. Thus fibrinolysis and mechanical therapy are being complementary rather than alternative; and patients are selected – large vessel occlusion with impending major stroke (NIHSS score >6) and limited cerebral infarction evolution (ASPECTS score >6). Of note, these trials have demonstrated not only high efficacy of restoring cerebral arterial flow but also low risk of cerebral hemorrhage. Table 1 compares the recommended reperfusion management for STEMI with that for ischemic stroke.

1. What are the bases for the current STEMI reperfusion recommendations?

The single most important parameter for STEMI reperfusion with the current recommendations is the time duration from symptom onset, despite the well-known fact that symptoms recollection is subjective. Table 2 summarizes the major landmarks in STEMI reperfusion.

While primary PCI was shown to be a superior strategy than in-hospital fibrinolysis, the ASSENT-4 study [7] which was prematurely terminated with 1667 patients (within 6 h of STEMI symptoms) concluded that a strategy of facilitated PCI (full-dose tenecteplase preceding PCI by 1–3 h) was associated with more major adverse events (death and ischemic events) than PCI alone. This forms the basis for having 2 divergent paths for STEMI treatment, either with primary PCI or with fibrinolysis. In the subsequent STREAM trial [8], patients who responded to fibrinolysis (with >50% resolution of ST elevation) could only have angiography >6 h after fibrinolysis, a time point when the main fibrinolytic effect would have dissipated.

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Table 1
Parameters in the recommended reperfusion management for STEMI vs those for ischemic stroke.

	STEMI	Ischemic stroke
Time from symptom onset	<12 h	<6 h
Measure pathological evolution before treatment decision	Nil	Limited infarct evolution based on an ASPECTS score >6
Choice of reperfusion therapy	PCI or fibrinolysis (but not both) as primary therapy	Mechanical thrombectomy with or without fibrinolysis, and vice-versa (for patients within 4.5 h of symptom onset)
Nature of occluded vessel	No specification as long as found suitable for PCI; Irrelevant for fibrinolysis	Large vessel in anterior circulation for mechanical thrombectomy with stent retriever
Measure of potential infarct/ischemic territory	Nil for fibrinolysis except satisfying STEMI criteria with 2 contiguous lead showing ST elevation; Clinical decision upon new angiographic information	Major or impending major stroke as evaluated by an NIHSS score >6

• ASPECT score:
• NIHSS: National Institutes of Health Stroke Scale

2. Why is there no negative (detrimental) effect of the combined lytic and mechanical therapy in stroke reperfusion?

Most hospitalists have witnessed hemorrhagic transformation of an ischemic stroke in patients even without receiving fibrinolysis. This may at least in part explain the low usage of t-PA for treating ischemic stroke despite its approval in 1996 after the NINDS (National Institutes of Neurological Disorders and Strokes) study [9].

In the earlier trials with thrombectomy devices, the mechanical embolus removal in cerebral ischemia (MERCI) device (tested in 164 patients within 8 h of an ischemic stroke) resulted in recanalization in ~50% and intracranial hemorrhage rate in ~10% [10]. The Penumbra Stroke system, another mechanical thrombo-aspiration device for occluded intracranial vessels, was applied to 125 patients with NIHSS scores ≥8 presenting within 8 h of symptom onset, and resulted in successful recanalization in ~80% and intracranial hemorrhage in ~11% [11].

Why were the intracranial hemorrhage rates lower in the 5 recent mechanical thrombectomy [2–6] trials despite higher rates of arterial recanalization? Hemorrhagic transformation may be related to blood pressure control and the use of antiplatelet medications, but one fundamental factor is whether the ischemic damage is reversible (with salvageable tissue) or irreversible (with necrotic tissue that becomes exposed to higher perfusion pressure after the infract-related artery is recanalized). Many of the recent trials employed direct imaging techniques to identify patients with predominantly reversible cerebral ischemia like having a small "core" on CT or MRI imaging [3–6].

"Small core and large penumbra" reflects an early phase of cerebral infarction when the major part of the jeopardized area remains salvageable with prompt reperfusion. Indirect method identifying patients with abundant arterial collateral networks [3] has similar implications. As in the current 2015 guideline, an ASPECTS score >6 (indicating relatively small territories with ischemic changes on a plain CT scan) also helps identify those with a relatively early stage of ischemic stroke [1].

3. "Small core and large penumbra" in ischemic stroke: are there counterparts in STEMI?

Unlike the sophisticated imaging techniques used in evaluating cerebral infarct evolution, the evolution of STEMI towards an irreversible stage (the counterpart of the "core" in ischemic stroke) is reflected by simple and easily accessible surface ECG changes, classically the evolution of pathological Q waves in the infarct leads.

The potential territory of STEMI (the counterpart of the penumbra) is semi-quantitatively described by the extent of ST elevation. With the primary PCI approach, an estimation of STEMI size can be made from the angiographic infarct-related arterial distribution but there is little information on the extent of STEMI evolution. These 2 parameters (STEMI potential size and STEMI evolution) interact with the inherent PCI-related delay in impacting outcome, and will be further discussed in later sections.

Table 2
Major landmarks in STEMI reperfusion.

	Patient number	Comparators	Time from symptoms	Treatment benefit (potential)	Treatment risk (potential)
FTT Lancet 1994 [12]	58,600	Fibrinolysis vs placebo	Within 24 h	Among patients presenting with ST elevation or BBB there was highly significant absolute mortality reductions of about 30 per 1000 for those presenting within 0–6 h and of about 20 per 1000 for those presenting 7–12 h from onset, and a statistically uncertain benefit of about 10 per 1000 for those presenting at 13–18 h	2 extra non-fatal strokes per 1000 during days 0–1
ASSENT-IV Lancet 2006 [7]	1667	Tenecteplase 1–3 h before PCI (Facilitated PCI) vs primary PCI	Within 6 h	Nil, early termination recommended by DSMB because of risks	Higher in-hospital mortality in the facilitated than in the standard PCI group (6% vs 3%, $P = 0.0105$), composite primary endpoint of death or congestive heart failure or shock within 90 days (19% vs 13%; $P = 0.0045$), and strokes during hospital stay (1.8% vs 0, $P < 0.0001$).
STREAM NEJM 2013 [8]	1892	Tenecteplase (with timely angiography 6–24 h OR rescue PCI for failed lysis at 90 min) vs primary PCI	Within 3 h and PCI not feasible within next hour	The primary end point (composite of death, shock, congestive heart failure, or reinfarction up to 30 days) was 12.4% vs 14.3%; $P = 0.21$	More intracranial hemorrhages occurred in the fibrinolysis group than in the primary PCI group (1.0% vs. 0.2%, $P = 0.04$ before and 0.5% vs. 0.3%, $P = 0.45$ after protocol amendment)