Endovascular therapy in acute stroke: directly to the catheter lab!

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Abstract

The recent compelling evidence of intra-arterial therapies in acute ischemic stroke have urged the revision of local algorithms in stroke units across the globe. In fact, in the presence of a proximal intracranial occlusion endovascular treatments reached unprecedented hemodynamic and functional efficacy in an otherwise problematic clinical scenario. Up until recently, the attempt to reperfuse the symptomatic area was limited to the “old” intravenous infusion of alteplase (IVtPA). Albeit its merits, the clinical impact caused is significantly impaired due to its narrow therapeutic window, extensive list of contra-indications and limited efficacy in large vessel occlusions.

In acute ischemic stroke with salvageable cerebral tissue a simplistic and pragmatic approach could define three main clinical scenarios: patients with contra-indication to IVtPA, patients with and those without large-vessel occlusions. For the first clinical scenario the answer is straightforward: to the catheter lab in all those with proximal occlusions. The answer is more troublesome in the advent of a large vessel occlusion without contra-indication to IVtPA. In this setting IVtPA has a reported recanalization rate of 10-20% with very limited clinical impact. On the other hand, it is not without side effects in the ischemic area, in remote cerebral areas as well as other organs susceptible to bleeding, not rarely in uncompressible locations. Ultimately, it may represent exposing the patient to potentially severe risks for minimal impact in the ischemic brain. For patients without proximal intracranial occlusions IVtPA is highly efficacious, rendering intra-arterial therapies as unnecessary.

In conclusion, IVtPA will remain the mainstay of acute stroke treatment for all those with clear clinical indications. However, the advent of intra-arterial therapies has had a dramatic impact on stroke algorithms worldwide. Particularly, in the subset of patients with large vessel occlusions the option of going straight to the catheter laboratory is appealing as it would prevent the use of a marginally effective therapy with rare but potentially severe complications, promoting the need for urgent intra-arterial recanalization.

Keywords: Acute stroke, Fibrinolysis, Neurosonology
Therapies in acute ischemic stroke have been a matter of clinical and investigational interest in the previous years. The introduction of alteplase (tPA) as a possible acute phase treatment allowed a dramatic improvement in stroke outcomes [1]. However, notwithstanding its merits, the clinical impact caused is significantly impaired due to its narrow therapeutic window, extensive list of contra-indications and limited efficacy in large vessel occlusions.

Up until recently intravenous tPA (IVtPA) was the only option to reperfuse the symptomatic area. Recent work have suggested that endovascular therapies have a role in acute stroke, enhancing the number of patients that may have access to acute phase treatment. Moreover, intra-arterial therapies achieve high levels of hemodynamic and functional efficacy in proximal intracranial occlusions—one of the major limitations of IVtPA [2-6]. This change in paradigms has urged the revision of local algorithms in stroke units across the globe.

Beholding an acute phase stroke patient with salvageable cerebral tissue, a pragmatic and simplistic approach would present three main clinical scenarios for reperfusion therapies: patients without proximal occlusions of intracranial arteries, and among those with proximal occlusions, patients with and without contra-indication to IVtPA (Figure 1). For the first clinical scenario IVtPA is highly efficacious, rendering intra-arterial therapies as unnecessary. Moreover, in patients with proximal occlusions and contra-indication to intravenous thrombolysis the answer is straightforward: straight to the catheter lab.

The answer is more troublesome in the presence of a large vessel occlusion without contra-indication to IVtPA. In this scenario IVtPA has reported recanalization rates of 10-30%, depending of clot location and very limited clinical impact [7]. Moreover, in larger thrombus (particularly when longer than 8mm in length) recanalization in the acute phase is almost nonexisting [8]. This has been expressed in all treatment guidelines, recognizing that in this setting all patients should proceed as soon as possible to endovascular treatment and that IVtPA should not delay this procedure [9, 10]. Furthermore, IVtPA has some potentially severe side effects, not only in the ischemic area, but also in remote cerebral areas as well as other organs susceptible to bleeding, frequently in uncompressible locations. There are even reports of higher rates of hemorrhagic complications in patients with proximal occlusions [11].

It is therefore reasonable to reconsider the role of IVtPA in acute ischemic stroke in the setting of a large vessel occlusion with the increasing availability of endovascular treatments. Recent retrospective data on this subject confirmed the absence of any therapeutic effect in pre-treatment with IVtPA and inconsistent data of hemodynamic outcome. Observational data from 93 patients who presented with an occlusion of the middle cerebral artery suggested a higher rate of successful recanalizations in those treated with concomitant IVtPA and endovascular treatments, as opposed to intra-arterial treatments alone (89.4% vs. 66.7% respectively), suggesting that IVtPA may facilitate mechanical recanalization, however it did not have any significance on early clinical outcome [12]. Other retrospective study described similar rates of good outcome and revascularization of endovascular therapy with and without associated IVtPA [13, 14]. In a recent study with matched pair analysis of patients receiving direct endovascular therapy vs. bridging thrombolysis, similar reperfusion and recanalization rates were observed with lower asymptomatic intracerebral hemorrhage and mortality rates in the direct endovascular therapy group [15].

A parallel evaluation can be made with another leading cause of death worldwide: ST-segment-elevation myocardial infarction (STEMI). Treatment options have been suffering an evolution similar to acute stroke. Initially, in the 1970-1990s, there was only one therapy approved: intravenous fibrinolysis [16]. However, standard fibrinolytic regimens suffered from several limitations – slow recanalization, low rates of complete recanalization and considerable rates of bleeding complications (much like cerebrovascular events) [17]. In the 2000s, percutaneous coronary intervention (PCI) became an optional therapy for STEMI, with primary PCI showing benefits in recanalization, residual ventricular function and hemorrhagic risk, when performed in the first 120 minutes. Facilitated PCI, i.e. pharmacological reperfusion therapy delivered prior to a PCI showed no clinical benefit in several studies [18]. Nowadays, primary PCI is the preferred strategy if the procedure can be performed by an experienced team and within the first 120 minutes of a STEMI. Only when the delay to PCI is expected to be longer than 120 minutes, fibrinolytic therapies become an option, maintaining however the urgent need of delivering the patient to a PCI capable centre [19]. Naturally, this analogy should be read with caution, considering the significant pathological differences between cardiac and cerebral ischemic events. Nonetheless, it is tempting and reasonable to wonder if there might also be a time frame in which if prompt endo-

Figure 1: Pragmatic flow chart of reperfusion options for patients with acute ischemic stroke and salvageable brain tissue. IVtPA = intravenous thrombolysis.
vascular treatment is deliverable to patients with proximal occlusions, no IVtPA is needed, as opposed to situations where endovascular therapy is not readily accessible and IVtPA should be administered as soon as possible.

All arguments considered, there is in fact the need of randomized clinical trials to reassess the real role of IVtPA in the presence of large vessel occlusion, with endovascular therapies progressively assuming a more central role.

In conclusion, IVtPA will remain the mainstay of acute stroke treatment for all those with clear clinical indications. However, the advent of intra-arterial therapies has had a massive impact on stroke algorithms worldwide. Moreover, the option of going straight to the catheter laboratory with a highly efficient therapy is appealing in the subset of patients with large vessel occlusions and readily accessible neurointervention team, as it would prevent the use of a marginally effective therapy with rare but potentially severe complications.

Abbreviations
IVtPA: intravenous alteplase; PCI: Percutaneous coronary intervention; STEMI: ST-segment-elevation myocardial infarction; tPA: alteplase

Competing interests
The authors declare no conflict of interest.

References