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CE - LETTER TO THE EDITOR

Primary stroke centers: are they worthy of an upgrade?

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Dear Editor,

The recently published PRISMS trial [1] shows that intravenous alteplase is not effective in treating mild nondisabling acute ischemic stroke compared with aspirin. Although addressed to a limited number of stroke patients, the trial might have an unintended impact on the acute care of mild ischemic stroke and on the role of primary stroke centers.

Intravenous alteplase is an established safe and effective treatment for acute ischemic stroke whose indication has been extended to patients with mild but disabling stroke symptoms [2]. In the PRISMS trial [1], patients with mild nondisabling ischemic stroke were randomized to intravenous alteplase within 3 h from stroke onset or oral single-dose aspirin 325 mg within 24 h. The trial was stopped early by a unilateral sponsor decision claiming slow recruitment. Results show no difference between the two treatments in the proportion of patients with modified Rankin Scale (mRS) score 0–1 at 90 days from enrolment in the presence of a higher proportion of patients with symptomatic intracranial hemorrhage within 36 h from symptom onset in the alteplase group (3.2%) compared with the aspirin group (0%).

Difficulties in identifying patients with a mild nondisabling stroke might have contributed to slow recruitment. Indeed, in our opinion, the adopted definition of nondisabling stroke is somehow contradictory, as stroke is disabling by definition, while transient ischemic attack is temporarily and mildly disabling. Besides, the trial compared two treatments (alteplase and aspirin) with different time windows (3 and 24 h), routes of administration (i.v. and oral), pharmacokinetics, and targets (clots and platelets). Moreover, about 40% of the enrolled patients were under premorbid treatment with antiplatelets. More detailed information on the clinical course of ischemic cerebral events is not provided, and fortuitous randomization of some TIA patients cannot be excluded.

In our opinion, study results referring to patients with 'mild nondisabling acute ischemic stroke' might have a negative impact on the management of patients with low NIHSS score (0–5), excluding several of them from appropriate treatment because of the over conceptualization of the divide between 'mild nondisabling stroke' and 'mild but disabling stroke'. Without such a divide, the results of the PRISMS study, following the GRADE system, might gain a B-R level of evidence.

On the opposite side, we should consider that the results of the DAWN and DEFUSE-3 trials [3, 4] are expanding the therapeutic window for mechanical thrombectomy in severely disabled stroke patients with large vessel occlusion up to 6–16 and 6–24 h from last-known-normal. The quantification of salvageable brain tissue with advanced neuroimaging techniques is fundamental for the implementation of mechanical thrombectomy.

The stroke care revolution [5] prompted by several recent trials should rely on comprehensive stroke centers, which can rapidly and safely treat patients with large vessel occlusion. However, as recently underlined [5], the crucial points of this ongoing revolution are the availability of perfusion imaging techniques, and expertise and specialists trained in the care of patients with stroke including interventional radiologists. The availability of those resources in primary stroke centers might be cost-effective, contributing to better patient selection and preventing the overload of comprehensive stroke centers.

Excluding patients from treatment with i.v. alteplase on the basis of a subjective evaluation of nondisabling symptoms might inadvertently reduce the role model of primary stroke centers. These centers should instead prepare themselves to become the protagonists for a new organization of acute ischemic stroke care, including the possibility of performing endovascular treatments together with the current treatment with i.v. alteplase.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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