



## EDITORIAL

### Time and training: Keys to success in the treatment of acute ischemic stroke<sup>☆</sup>

### Tiempo y entrenamiento: claves del éxito en el tratamiento del ictus isquémico agudo

F. Murillo-Cabezas

*U.G.C. Cuidados Críticos y Urgencias, H.U. Virgen del Rocío, Sevilla, Spain*

The introduction of intravenous cerebral thrombolysis (ICT) with recombinant tissue plasminogen activator (rt-PA) has constituted a milestone in the management of acute ischemic stroke, since both a randomized, controlled clinical trial and posterior studies conducted in the routine clinical practice setting have shown it to improve patient functional prognosis.<sup>1,2</sup> ICT is moreover cost-effective and is maintained over time; as a result, all the clinical guides currently recommend its administration in indicated patients. However, despite its benefits and recommendations, the use of ICT remains limited. According to most series, ICT is used in less than 5% of all candidate patients,<sup>3</sup> when theoretically it could be used in about 25% of the cases.<sup>4</sup> The greatest barriers against a more widespread use of the technique include patient arrival outside the therapeutic window, and the recommendation of some guides and clinical practices to transfer the patients from hospitals where ICT could be performed to more or less distant reference centers equipped with stroke units—this in some cases leading to a loss of treatment opportunities, and in all cases to a loss of recoverable brain tissue.

A useful collateral effect of ICT has been increased physician interest in a hitherto rather neglected disorder. This in some cases has given rise to futile discussions as to where ICT should be performed and by whom. The evidence sustaining the recommendation to treat ischemic stroke patients

in reference centers equipped with stroke units is based on studies that have demonstrated lesser mortality and dependency when patients are treated in such units, in the acute phase of the process.<sup>5,6</sup> The better results obtained in these units are explained by the adequate monitoring and prevention, and faster management of cardiac and respiratory complications, infections, metabolic disorders, etc., as well as by an earlier secondary prevention of further stroke episodes and start of rehabilitation.<sup>7</sup> It might be expected that any other disease condition likewise would yield better results if dealt with in the acute phase in monitored areas equipped with the same human and technological resources, compared with the care provided in a general hospital ward. However, as in other disease conditions, ischemic stroke is characterized by the presence of what some authors aptly refer to as a "hyperacute phase",<sup>8</sup> comprising the short time window open for the use of ICT—currently extended to four and a half hours.<sup>9</sup> Nevertheless, it must be taken into account that the results are better and the bleeding complications less important when rt-PA is administered early after stroke onset. In fact, the guides recommend a door-to-needle time of no more than 60 min.<sup>10</sup> This hyperacute phase in turn is followed by the acute and subacute phases which can be dealt with in reference centers if so advised by the patient condition, following the application of fibrinolytic therapy is soon as possible.

Many experiences both within and outside Spain warrant the effectiveness and safety of ICT in district or general hospitals lacking a stroke unit, with specialized unit support and supervision via telemedicine technology,<sup>11</sup> telephone contact, or simply activation of the stroke code, involving written protocols developed by well trained,

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E-mail address: [francisco.murillo.sspa@juntadeandalucia.es](mailto:francisco.murillo.sspa@juntadeandalucia.es)

multidisciplinary stroke teams coordinated with their reference hospitals with a view to referring the patient and continuing therapy in the acute phase with the prescription of rescue interventions where needed.<sup>12</sup> This approach has recently and aptly been suggested by Rodríguez-Martín et al.<sup>13</sup> Although these authors define fibrinolysis in the first hospital as being useful in late detection of ischemic stroke, the same concept is applicable to any case of stroke detected in the hyperacute phase, for improving the results obtained. Studies such as those of Varela et al.<sup>14</sup> in Spain, or Charipar et al.<sup>15</sup> in the United States show that ICT with rt-PA can be administered safely and effectively in rural or basic hospital centers. It is interesting to note that in the series published by Charipar, the rate of ICT performed by general practitioners, emergency care specialists and internists reached 16.2% of the global eligible patients—this figure being higher than the average described in the literature in specialized centers.

Using a validated and sensitive technique (Monte Carlo simulation), Latour et al.,<sup>16</sup> in this issue of the journal, contribute new evidence for the conduction of ICT in non-specialized centers. They concluded that the neurological outcome, evaluated with the modified Rankin scale, is better in 77.2% of the cases when thrombolysis is performed *in situ* versus thrombolysis performed in reference centers—even after assuming a 30% loss of effectiveness when ICT is performed in the former type of center. These observations come as no surprise, when considering that the existing data indicate that the sooner thrombolysis is applied, the more effective it becomes. Logically, these results would only be expectable under the conditions defined by the authors, when a delay in treatment is expected because of patient transfer to the center equipped with a stroke unit—a situation which on the other hand is common in our routine practice and in countries such as the United States.<sup>17</sup>

As underscored by Latour et al.,<sup>16</sup> the ischemic stroke plans and guides used in some Spanish Autonomous Communities, lacking the support of the best available evidence, recommend patient transfer to hospitals with stroke units for performing ICT. In contrast, in Andalusia, development of the integrated process for the management of stroke,<sup>18</sup> and the PLACA project created with the same purpose,<sup>19</sup> has placed emphasis not so much on the specialty or physical location where ICT is performed but more on the intervening stroke team—the latter being conceived as a multidisciplinary and motivated team trained in the management of stroke patients. A stroke team with such multidisciplinary and training characteristics, coordinated with the corresponding reference centers, and with the support of neurologists, is easier to establish in any hospital in our country with a view to dealing with the hyperacute phase of ischemic stroke—thereby improving equity and accessibility for stroke patients, as elements central to healthcare ethics. Lastly, it also must be stressed that we still spend a lot of time and energy debating where ICT should be carried out and by whom, and in contrast, as we have recently described,<sup>20</sup> we dedicate very little attention to citizen and healthcare professional awareness-enhancing campaigns designed to get the message across that stroke is an emergency—characterized by signs and symptoms that must be quickly recognized, with immediate patient transfer

to a hospital offering a well trained medical team,<sup>21</sup> since in these situations “time is brain”.

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