Body Weight, Not Thrombus-Burden Tissue Plasminogen Activator Dosing
But Still

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After studies in cardiology that used body weight dosing, intravenous tissue plasminogen activator (tPA) dose for stroke (0.9 mg/kg alteplase, maximum 90 mg) emerged from small dose-escalation studies that started with doses far less than those for myocardial infarction.1 These studies were conducted before tests like CT angiography became readily available to determine thrombus location and extent in acute ischemic stroke. Current guidelines endorse this body weight-based dose as standard of care after pivotal randomized trials showed a significant benefit from systemic thrombolysis.2,3 During clinical trials and in daily practice, clinicians have to obtain body weight (actual or estimate) urgently when special beds equipped with calibrated scales are generally not available in emergency departments. Weighing the patient without a stretcher with built-in bed scales would require a Hoyer lift scale, and because tPA should be given as soon as possible, this could delay care. As a result, dosing errors could be frequent. These errors were documented by many across different patient populations.4,5

Bruer et al provide a useful account that details body weight estimation and resulting tPA dosing errors at a busy single stroke center.6 Their data offer a preliminary look into the clinical significance of over- and underdosing. To begin with, half of the patients were unable to provide body weight to treating physicians, most likely due to stroke symptoms, and only 20% had relatives able to provide this information. Every fifth patient incorrectly stated their own body weight, whereas 38% to 42% of health professionals estimated it erroneously. These results are in parallel with the study conducted at our own center and elsewhere.7,8

As a potential solution, Bruer et al looked for more objective ways to estimate body weight rather than eyeballing. The use of anthropometric measurements produced fewer errors, including overestimation in almost 18% and underestimation in only 2% of subjects.

What were the risks of overestimation body weight and overdosing tPA? In the study by Bruer et al, tPA overdosing did not increase the risk of symptomatic intracerebral hemorrhage (sICH). This is counterintuitive because results of the European Cooperative Acute Stroke Study (ECASS) trial indicate a greater sICH risk with the 1.1-mg/kg dose of tPA.9 However, this finding needs to be placed in perspective. As our cumulative experience with tPA grows, the rate of sICH decreases presumably due to better patient selection, adherence to protocol, and blood pressure management. It is reassuring to see that inadvertent overdosing of tPA in experienced hands at a busy stroke center did not lead (or at least did not show a trend given relatively small numbers) to increasing risk of sICH. Of note, only 8% of study subjects exceeded 100 kg necessitating a maximum 90-mg dose. At centers with a greater proportion of obese patients, weight overestimation may pose even less problems. Finally, it should be kept in mind that the relatively small sample size (n=109) and the limited number of sICHs (n=3) may account for the lack of significant association between overdosing and risk of sICH (Type I error).

Underdosing on the other hand was associated with worse outcomes in terms of dependency and death (modified Rankin Scale score of 3 to 6), and this indeed deserves further investigation in the settings of an independent, prospective, multicenter study. Patients with underestimated body weight tended to have more severe pretreatment neurological deficits, a finding that makes one wonder if a thrombus burden was also larger, tPA dose could have been even further insufficient. Unfortunately, the authors provide no data regarding the potential association of underdosing with the likelihood of recanalization that might have provided some answers to the former question. Less tPA means less thrombolytic activity. Although no tPA trial that has been conducted so far actually weighed patients, the benefit of tPA could be even greater if weight underestimation could have been avoided. However, it should be noted that the monocenter nature of the study in addition to the limited sample size leaves the question whether these findings are due to local aspects depending on the specific setting of the hospital, personal influences and experience of the staff as well as specific emergency room settings. Therefore, they may only serve for preliminary data generation to conduct formal sample size estimation for a future multicenter study that should also be properly powered to detect a potential relationship between overdosing and increased risk of sICH.

Use of anthropometric measurements could have reduced the weight underestimation; however, the authors noted that obtaining measurements such as height, waist and hip circumference along with body mass index were often logistically difficult to obtain. This in itself could delay tPA...
administration. Perhaps, simpler measurements such as mid-darm circumference and knee height may offer a faster solution worth investigating in patients with acute stroke in the future. On the other hand, practically all patients with stroke are being placed on a CT scan gantry in emergency departments and lie still long enough to complete head scanning. Why not equip this sophisticated moving console with calibrated scales? Weigh the patient precisely and have this information by the time CT scanning is completed. It could be a quick and practical solution to tackle the issue of correct tPA dosing in acute stroke care if an association between incorrect dosing and unfavorable outcomes after thrombolysis is firmly established in future, prospective multicenter studies.

Disclosures

None.

References


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