



Editorial

# Age Is Only a Number Also in Hyperacute Stroke Care—But Not an Irrelevant One

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“It is difficult to make predictions, especially about the future.” This we all know, but the phrase is particularly spot-on regarding the prognostication of individual patients. Yet, clinicians are required to make these predictions every day, often with insufficient background data or time to communicate with the patient—let alone contemplate the situation. Since time is brain, modern hyperacute stroke care is perhaps the best example.

The acute care of patients who have experienced ischemic stroke has advanced tremendously in the past two decades. Thrombolysis with tissue plasminogen activator (tPA) has become standard hyperacute therapy. More recently, endovascular thrombectomy (EVT) has become an even more powerful tool that is used in cases when there is an observable large vessel occlusion (LVO) and potentially salvageable brain tissue [1]. However, this therapy is only available in comprehensive stroke centers and requires advanced neurovascular expertise in its provision and patient selection. It is also uncertain whether EVT is better used with or without preceding thrombolysis, and the efficacy of both of these therapies is highly time-dependent [2–6]. Therefore, these advancements have created new challenges in the design of efficient provision strategies regarding acute stroke care services.

Some uncertainty also exists regarding patient selection, as large, controlled trials excluded many (or included very few) patients with situations often encountered in clinical practice. One of these uncertainties concerns patient age. While it is now clear that the elderly can also benefit from both tPA and EVT, they seem to gain less from these treatments than younger patients [7–12]. Additionally, although at least in Finland the elderly are in better shape than has previously been the case, it is also clear that, in general, older patients have a poorer prognosis and, in particular, shorter post-stroke survival times compared to younger patients [13–16]. Therefore, it is even more important to evaluate individual prognoses in elderly patients.

How can this be achieved? While we wait for randomized trials to clarify the situation [17], some clues exist. The SPAN-100 index is perhaps the most obvious one: if patient age + NIHSS score  $\geq 100$ , the outcome is very likely poor [18–20]. On the other hand, as with younger people, some elderly individuals are in better shape than others, so biological age should be considered instead of chronological. One potential biological indicator is frailty, which is a common and important survival predictor in the elderly with or without a stroke [21,22]. Therefore, routine frailty evaluation in acute stroke patients seems to be needed to inform treatment decisions. However, there are many ways to assess frailty, and the suitability of these methods to the hyperacute stroke setting is unclear. Ideally, frail people would be routinely identified by geriatricians and GPs, and this information would be ready and available in the hyperacute setting. As work remains to be done on this, the development and clinical validation of a digital tool utilizing patient record data from previous healthcare encounters could be an intermediate solution [23]. Compared to large, randomized studies evaluating hyperacute interventions, it seems that the investigation and implementation of these assessments can be more easily and swiftly conducted. Therefore, it is likely that targeted interventions to improve knowledge on the signs and risk



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factors of strokes, specifically in elderly populations with lower educational levels, could also be easily and quickly implemented, which might lead to faster admissions and even lower stroke incidences [24]. Interventions are also needed among the younger population to reduce the expected stroke burden in the future elderly population [25,26]. Ultrasound techniques for the pre-hospital identification of LVO in octogenarians should also quickly be evaluated because, in a drip-n-ship setting, these patients might particularly benefit from being transferred directly to an EVT-capable center [6,27]. The strategy of skipping tPA in EVT-eligible LVO patients with a high risk of hemorrhage may also be considered [3].

Acute hospitalization often leads to deterioration in the elderly [28,29]. Fortunately, patients of all ages benefit from care in a stroke unit [30,31], where the first steps can be taken in order to try to achieve their prior functional status. However, no neurological procedure can help a patient achieve a better functional status compared to the one preceding the stroke, and therefore, information on this should be easily available to aid decision making. This highlights the importance of co-operation not only between specialized care providers but also with primary healthcare. User-friendly, comprehensive electronic medical record systems are also needed.

Higher age, prior functional dependence and comorbidities are all related to patients' abilities to benefit from revascularization treatment and need to be taken into account in decision making. Endovascular treatment options may also continue to improve outcomes in the elderly, but more data are needed regarding the optimal treatment pathways [6]. Optimal results can only be achieved with close collaboration using modern equipment and up-to-date scientific and individual patient data.

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## References

1. Wassélius, J.; Arnberg, F.; von Euler, M.; Wester, P.; Ullberg, T. Endovascular thrombectomy for acute ischemic stroke. *J. Intern. Med.* **2022**, *291*, 303–316. [[CrossRef](#)] [[PubMed](#)]
2. Krajičková, D.; Krajina, A.; Herzig, R.; Vyšata, O.; Šimůnek, L.; Vališ, M. Acute Recanalization of Large Vessel Occlusion in the Anterior Circulation Stroke: Is Mechanical Thrombectomy Alone Better in Patients over 80 Years of Age? Findings from a Retrospective Observational Study. *J. Clin. Med.* **2021**, *10*, 4266. [[CrossRef](#)] [[PubMed](#)]
3. Honig, A.; Hallevi, H.; Simaan, N.; Sacaggi, T.; Seyman, E.; Filioglo, A.; Gomori, M.J.; Rotschild, O.; Jonas-Kimchi, T.; Sadeh, U.; et al. Safety and Efficacy of Intravenous Alteplase before Endovascular Thrombectomy: A Pooled Analysis with Focus on the Elderly. *J. Clin. Med.* **2022**, *11*, 3681. [[CrossRef](#)] [[PubMed](#)]
4. Smith, E.E.; Zerna, C.; Solomon, N.; Matsouaka, R.; Mac Grory, B.; Saver, J.L.; Hill, M.D.; Fonarow, G.C.; Schwamm, L.H.; Messé, S.R.; et al. Outcomes After Endovascular Thrombectomy With or Without Alteplase in Routine Clinical Practice. *JAMA Neurol.* **2022**, *79*, 768–776. [[CrossRef](#)]
5. Katsanos, A.H.; Turc, G.; Psychogios, M.; Kaesmacher, J.; Palaiodimou, L.; Stefanou, M.I.; Magoufis, G.; Shoamanesh, A.; Themistocleous, M.; Sacco, S.; et al. Utility of Intravenous Alteplase Prior to Endovascular Stroke Treatment: A Systematic Review and Meta-analysis of RCTs. *Neurology* **2021**, *97*, e777–e784. [[CrossRef](#)]
6. Sipilä, J.O.T. Anterior circulation large vessel occlusion outcomes in patients transferred from a peripheral primary stroke centre. *Neurol Res.* **2022**, *44*, 554–559. [[CrossRef](#)]
7. Bluhmki, E.; Danays, T.; Biegert, G.; Hacke, W.; Lees, K.R. Alteplase for Acute Ischemic Stroke in Patients Aged > 80 Years: Pooled Analyses of Individual Patient Data. *Stroke* **2020**, *51*, 2322–2331. [[CrossRef](#)]
8. Emberson, J.; Lees, K.R.; Lyden, P.; Blackwell, L.; Albers, G.; Bluhmki, E.; Brott, T.; Cohen, G.; Davis, S.; Donnan, G.; et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials. *Lancet* **2014**, *384*, 1929–1935. [[CrossRef](#)]
9. Adcock, A.K.; Schwamm, L.H.; Smith, E.E.; Fonarow, G.C.; Reeves, M.J.; Xu, H.; Matsouaka, R.A.; Xian, Y.; Saver, J.L. Trends in Use, Outcomes, and Disparities in Endovascular Thrombectomy in US Patients With Stroke Aged 80 Years and Older Compared With Younger Patients. *JAMA Netw. Open.* **2022**, *5*, e2215869. [[CrossRef](#)]
10. Zhao, W.; Ma, P.; Zhang, P.; Yue, X. Mechanical Thrombectomy for Acute Ischemic Stroke in Octogenarians: A Systematic Review and Meta-Analysis. *Front. Neurol.* **2020**, *10*, 1355. [[CrossRef](#)]

11. Lasek-Bal, A.; Binek, Ł.; Żak, A.; Student, S.; Krzan, A.; Puz, P.; Bal, W.; Uchwat, U. Clinical and Non-Clinical Determinants of the Effect of Mechanical Thrombectomy and Post-Stroke Functional Status of Patients in Short and Long-Term Follow-Up. *J. Clin. Med.* **2021**, *10*, 5084. [[CrossRef](#)] [[PubMed](#)]
12. Merlino, G.; Smeralda, C.; Lorenzut, S.; Gigli, G.L.; Surcinelli, A.; Valente, M. To Treat or Not to Treat: Importance of Functional Dependence in Deciding Intravenous Thrombolysis of “Mild Stroke” Patients. *J. Clin. Med.* **2020**, *9*, 768. [[CrossRef](#)] [[PubMed](#)]
13. Romain, G.; Mariet, A.-S.; Jooste, V.; Duloquin, G.; Thomas, Q.; Durier, J.; Giroud, M.; Quantin, C.; Bèjot, Y. Long-Term Relative Survival after Stroke: The Dijon Stroke Registry. *Neuroepidemiology* **2020**, *54*, 498–505. [[CrossRef](#)] [[PubMed](#)]
14. Sennfält, S.; Norrving, B.; Petersson, J.; Ullberg, T. Long-Term Survival and Function After Stroke. *Stroke* **2019**, *50*, 53–61. [[CrossRef](#)]
15. Munukka, M.; Koivunen, K.; von Bonsdorff, M.; Sipilä, S.; Portegijs, E.; Ruoppila, I.; Rantanen, T. Birth cohort differences in cognitive performance in 75- and 80-Year-Olds—A comparison of two cohorts over 28 years. *Aging Clin. Exp. Res.* **2021**, *33*, 57–65. [[CrossRef](#)] [[PubMed](#)]
16. Koivunen, K.; Sillanpää, E.; Munukka, M.; Portegijs, E.; Rantanen, T. Cohort differences in maximal physical performance: A comparison of 75- and 80-year-old men and women born 28 years apart. *J. Gerontol. A Biol. Sci. Med. Sci.* **2021**, *76*, 1251–1259. [[CrossRef](#)]
17. Creutzfeldt, C.J.; Levitt, M.R.; Leslie-Mazwi, T.M. Is Endovascular Thrombectomy for the Very Elderly? *Stroke* **2022**, *53*, 2227–2229. [[CrossRef](#)]
18. Saposnik, G.; Guzik, A.K.; Reeves, M.; Ovbiagele, B.; Johnston, S.C. Stroke Prognostication using Age and NIH Stroke Scale: SPAN-100. *Neurology* **2013**, *80*, 21–28. [[CrossRef](#)]
19. Möbius, C.; Blinzler, C.; Schwab, S.; Köhrmann, M.; Breuer, L. Re-evaluation of the stroke prognostication using age and NIH Stroke Scale index (SPAN-100 index) in IVT patients—The-SPAN 10065 index. *BMC Neurol.* **2018**, *18*, 129. [[CrossRef](#)]
20. Elsaid, N.; Bigliardi, G.; Dell’Acqua, M.L.; Vandelli, L.; Ciolli, L.; Picchetto, L.; Borzi, G.; Ricceri, R.; Pentore, R.; Vallone, S.; et al. Evaluation of stroke prognostication using age and NIH Stroke Scale index (SPAN-100 index) in delayed intravenous thrombolysis patients (beyond 4.5 hours). *J. Stroke Cerebrovasc. Dis.* **2022**, *31*, 106384. [[CrossRef](#)]
21. Burton, J.K.; Stewart, J.; Blair, M.; Oxley, S.; Wass, A.; Taylor-Rowan, M.; Quinn, T.J. Prevalence and implications of frailty in acute stroke: Systematic review & meta-analysis. *Age Ageing* **2022**, *51*, afac064. [[PubMed](#)]
22. Shamliyan, T.; Talley, K.M.; Ramakrishnan, R.; Kane, R.L. Association of frailty with survival: A systematic literature review. *Aging Res. Rev.* **2013**, *12*, 719–736. [[CrossRef](#)] [[PubMed](#)]
23. Schnieder, M.; Bähr, M.; Kirsch, M.; Maier, I.; Behme, D.; Riedel, C.; Psychogios, M.-N.; Brehm, A.; Liman, J.; von Arnim, C. Analysis of Frailty in Geriatric Patients as a Prognostic Factor in Endovascular Treated Patients with Large Vessel Occlusion Strokes. *J. Clin. Med.* **2021**, *10*, 2171. [[CrossRef](#)] [[PubMed](#)]
24. Soto-Cámara, R.; González-Bernal, J.J.; González-Santos, J.; Aguilar-Parra, J.M.; Trigueros, R.; López-Liria, R. Knowledge on Signs and Risk Factors in Stroke Patients. *J. Clin. Med.* **2020**, *9*, 2557. [[CrossRef](#)] [[PubMed](#)]
25. Soto-Cámara, R.; González-Bernal, J.J.; González-Santos, J.; Aguilar-Parra, J.M.; Trigueros, R.; López-Liria, R. Age-Related Risk Factors at the First Stroke Event. *J. Clin. Med.* **2020**, *9*, 2233. [[CrossRef](#)]
26. Owolabi, M.O.; Thrift, A.G.; Mahal, A.; Ishida, M.; Martins, S.; Johnson, W.D.; Pandian, J.; Abd-Allah, F.; Yaria, J.; Phan, H.T.; et al. Primary stroke prevention worldwide: Translating evidence into action. *Lancet Public Health* **2022**, *7*, e74–e85. [[CrossRef](#)]
27. Eyding, J.; Fung, C.; Niesen, W. Twenty Years of Cerebral Ultrasound Perfusion Imaging—Is the Best yet to Come? *J. Clin. Med.* **2020**, *9*, 816. [[CrossRef](#)]
28. Winkelman, C. Bed rest in health and critical illness: A body systems approach. *AACN Adv. Crit. Care* **2009**, *20*, 254–266. [[CrossRef](#)]
29. Brown, J.D.; Sato, R.; Morley, J.E. Association between Pneumonia, Fracture, Stroke, Heart Attack and Other Hospitalizations with Changes in Mobility Disability and Gait Speed in Older Adults. *J. Clin. Med.* **2021**, *10*, 3802. [[CrossRef](#)]
30. Fisher, S.R.; Kuo, Y.F.; Graham, J.E.; Ottenbacher, K.J.; Ostir, G.V. Early Ambulation and Length of Stay in Older Adults Hospitalized for Acute Illness. *Arch. Intern. Med.* **2010**, *170*, 1942–1943. [[CrossRef](#)]
31. Langhorne, P. The Stroke Unit Story: Where Have We Been and Where Are We Going? *Cerebrovasc. Dis.* **2021**, *50*, 636–643. [[CrossRef](#)] [[PubMed](#)]