Parachutes to prevent death and disability from gravitational challenge.
The basis for parachute use is purely observational.
Apparent efficacy could be explained by a healthy cohort effect.
Individuals who insist that all interventions need to be validated by a RCT need to come down to earth with a bump.7

Basilar artery thrombosis (BAT) is a rare but most severe subtype of ischemic stroke often presenting with progressive or hyperacute brain stem symptoms, tetraplegia, and loss of consciousness ranging from somnolence to frank coma. It is associated with a mortality between 50% and 90% in patients treated conventionally (antiplatelets or heparin) or not at all.2,3 If survived, the consequence thinkable. Different patterns include caudal vertebrobasilar, mid-basilar and top-of-the-basilar thrombosis, the former mostly being of atherothrombotic and the latter of embolic origin.4 Multiple case series mostly addressing intraarterial (IA) and less frequently intravenous5 thrombolytic therapy for BAT have been published in the last 20 years, the first report by Zeumer et al dating back to 1982.6,7 Most studies suffered from small numbers: <10 patients with only a few in the range of 40 to 50 patients.2,8,9 All had an open, retrospective or partly prospective design with differing treatment regimens, mostly IA thrombolytic drugs formally rendering level III evidence at best.

Whereas some studies only used presence or absence of recanalization induced by a thrombolytic as a surrogate outcome, in all but 1 series it was shown that overall survival and an independent outcome was associated with successful partial or complete recanalization of the occluded basilar artery (BAO).2,8,9 Recanalization rates ranged from 40% to 100%, on average =50% to 60% in line with the results from the Prolyse in Acute Cerebral Thromboembolism II (PROACT II) trial.10 Survival in patients without recanalization ranged from 0% to 20% as opposed to 40% to 80% in those with recanalization. A recent meta-analysis by Lindberg analyzed systematically published case series of ≥10 patients reporting the outcome of BAO after IA or IV thrombolysis within 12 hours.11 In 420 BAO patients treated with IV thrombolysis (n=76) and IA thrombolysis (n=344), death or dependency were equally common: 78% (59 of 76) and 76% (260 of 344), respectively (P=0.82). Recanalization was achieved more frequently with IA thrombolysis (225 of 344; 65%) than with IV thrombolysis (40 of 76; 53%; P=0.05), but survival rates after IV thrombolysis (38 of 76; 50%) and IA thrombolysis (154 of 344; 45%) were similar (P=0.48). A total of 24% of patients treated with IA thrombolysis and 22% treated with IV thrombolysis reached good outcomes (P=0.82). Without at least partial recanalization, the likelihood of a good outcome was close to zero (2% versus 38%).

An Australian group ventured to perform a randomized trial (Australasian Urokinase Stroke Study)12 after a pilot trial (Australasian Urokinase Stroke Trial [AUST]) published in 1997.13 The pilot study included 15 patients within 31 hours (mean 18 hours) in an uncontrolled observational design. Eleven of 15 patients recanlalized, 10 of these survived (only 1/4 nonrecanalizers). The AUS study was designed as an open-label, multicenter, randomized controlled trial with a blinded end point assessment and launched in 1996.12 Inclusion criteria were an acute posterior circulation stroke syndrome ≤24 hours time from symptom onset, age 18 to 85, and no hemorrhage on CT. Patients underwent digital subtraction angiography and, if a lysable lesion was identified, were randomized to either heparin (unfractionated, partial thromboplastin time [PTT] 60 to 80 s, 5000 IU bolus) or heparin plus IA urokinase (increments of 100 000 IU up to a maximum of 1 000 000 IU) followed by warfarin (international normalized ratio, 1.5 to 2.5) for 6 months. Clinical outcomes (modified Rankin Scale, National Institutes of Health Stroke Scale, Barthel Index) were independently assessed by a nurse or neurologist blinded for treatment. The
study was terminated because of low recruitment (20 patients screened, 16 randomized). There were only 4 deaths in each group, 7/8 in the placebo group were disabled or dead, only 4 in the treatment group (ie, all survivors had an independent outcome). The early termination is disappointing because the total sample size would have been 65 patients (absolute effect size of 35%, 2-sided α, power 0.8) to answer this question once and for all with IA thrombolysis for vertebrobasilar stroke becoming a level A recommendation.

Taking into account recent recommendations a new randomized study could screen with CT angiography, randomize 2:1 (active IA):1 (placebo), and have a consistent protocol regarding the therapeutic strategies such as concomitant treatment with abciximab, use of devices and other interventions.

We believe such a study would be desirable but it will never happen. The condition itself is rare, and we doubt that logistical problems can be overcome, and investigators at the expert centers with the largest experience will hesitate to randomize their patients. On the other hand, do we really need a new trial? Recanalization and reperfusion whether in anterior or posterior territory stroke is the strongest predictor and just let go. Let go!16

Therefore, although we advocate randomized studies to answer several questions in acute and secondary prophylactic treatment of stroke we find it ethically unacceptable to randomize a patient to placebo versus conventional treatment thereby precluding him the chance of ≈50% for surviving an otherwise almost always deadly stroke and a ≈35% chance for being an independent survivor. We doubt that critics of IA thrombolysis for BAT would consent to inclusion in such a placebo-controlled study for themselves or their next of kin, like we doubt they would enter the above-mentioned parachute trial. At a certain point, patients with an infrequent disease with such a grim prognosis should be treated despite lack of level I evidence data. “Stop trying to control everything and just let go. Let go!”16

References

Intra-Arterial Thrombolysis Is the Treatment of Choice for Basilar Thrombosis: Pro
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