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Assessing gait speed in acutely ill older patients admitted to an acute care elders hospital unit.

Ostir G, Berges I, Yong-Fang K *et al. Arch Intern Med.* 2012; **172(4):** 358-9.

The aims of this study were to assess whether there were any associations between gait speed and length of stay and home discharge. The study concluded that gait speed could be used to complement the information obtained by self-reporting activities, as gait speed was found to be a clinically relevant indicator of functional status and health outcomes including length of stay and home discharge.

This was a prospective study of 322 patients 65 years or older admitted to hospital acutely. Patients were excluded if they were not orientated in time and place on admission, admitted from palliative care or transferred from a nursing home or intensive care.

206 patients completed the gait speed walk (personal assistance devices were permitted) with a mean gait speed of 0.53m/s, 116 did not complete the walk. Those patients who could not complete the walk or had gait speeds of less than 0.4m/s had significantly longer lengths of stay (increased by 1.9 and 1.4 days respectively). Patients unable to complete the walk (odds ratio, 0.03; 95% CI, 0.003-0.21) and patients having gait speeds of less than 0.4m/s had significantly decreased likelihood of home discharge compared with patients having gait speeds of at least 0.60m/s(odds ratio, 0.07 CI, 0.0001-0.63).

The exclusion of patients with cognitive impairment suggests that this is an area where further work could be done.

Prehospital epinephrine use and survival among patients with out of hospital cardiac arrest

Hagihara A, Hasegawa M, Abe T *et al. JAMA.* 2012; **307(11):** 1161-8.

Epinephrine is used widely in the treatment of cardiopulmonary resuscitation but the effectiveness of epinephrine use before hospital has not been established. Epinephrine has been associated with increased myocardial demand and disturbed cerebral microcirculation post arrest but animal studies have supported the beneficial short term effects of epinephrine.

The aim of this study was to evaluate the association between epinephrine use before hospital arrival and short and long term mortality in patients with cardiac arrest.

This was a prospective, non-randomised, observational analysis of data from 417,188 out of hospital cardiac arrests (OHCA) occurring between 2005-2008 in Japan in those over the age of 18. The main outcome measures were return of spontaneous circulation (ROSC) before hospital arrival, survival at 1 month after cardiac arrest, survival with good or moderate cerebral performance or survival with no mild or moderate cerebral neurological disability.

2786 of the 15,030 (18.5%) patients in the epinephrine group and 23,042 of 403,158 (5.7%) of the non-epinephrine group had ROSC pre-hospital. The patients who received pre-hospital epinephrine were observed to have a higher likelihood of ROSC before arriving at hospital (OR 2.36; 95% CI 2.22-2.50; P <.001). There were negative associations observed between pre-hospital epinephrine and long term outcome measures at 1 month.

The study concluded that the use of pre-hospital epinephrine in OHCA increased the chance of ROSC before hospital arrival but there was a decreased chance of survival and good functional outcome at I month. One confounding issue in this study is that although a patient may not have received epinephrine prior to arrival, they may have received it in hospital. The differences in long term survival may not be attributed to the drug itself but to the care after hospital arrival. The study did not include any data on in house CPR after arrival to hospital and any techniques used, which may be a study for the future.

A randomised trial of tenecteplase versus alteplase for acute ischaemic stroke

Parsons M, Spratt N, Bivard A *et al. N Engl J Med.* 2012; **366(12):** 1099-1107.

Currently, alteplase is the thrombolytic drug of choice in acute ischaemic stroke in accordance

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with the most recent NICE guidelines. This study has examined the use of tenecteplase, a genetically engineered mutant tissue plasminogen activator, as an alternative thrombolytic agent.

This small 2B trial studied 75 patients who presented with acute ischaemic stroke to three large stroke centres in Australia between 2008-2011. In addition to standard thrombolysis criteria (including baseline NIHSS score), CT perfusion and angiographic imaging was used to select patients who would most benefit from early reperfusion (ie. patients with large vessel occlusion and large perfusion lesion without large infarct core). The patients were randomly assigned to receive alteplase (0.9mg/kg), tenecteplase (0.1mg/kg) or tenecteplase (0.25mg/kg) within 6 hours of presentation. MRI and repeat clinical assessment were performed at 24 hours and 90 days post treatment to assess efficacy. Imaging efficacy outcomes assessed lesion reperfusion, extent of infarct growth and vessel recanalization. Clinical efficacy outcomes assessed neurological recovery using change from baseline in NIHSS score and modified Rankin scale.

The tenecteplase groups showed a significant benefit in both imaging and clinical efficacy outcomes compared to the alteplase group. Reperfusion at 24 hours in the tenecteplase groups was 79.3% compared to 55.4% in the alteplase group (P<0.004). Improvement from baseline in NIHSS score after 24 hours was 8.0 points in the tenecteplase groups compared to 3.0 points in the alteplase group (P<0.001). In addition the higher dose of tenecteplase was superior to all other groups for all efficacy outcomes. This was associated with no significant increase in risk of intracranial bleeding or other serious adverse events.

These positive findings are encouraging but preliminary owing to the small size of the study. It is also important to note that the 75 patients studied were carefully selected as most likely to benefit from early reperfusion. Therefore the results, particularly risk of intracranial bleeding or other serious adverse events, cannot be extrapolated to the majority of patients eligible for thrombolysis; the group plan to perform a phase 3 study to determine this.

Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism

The EINSTEIN-PE Investigators. *N Engl J Med* 2012; **366:** 1287-97.

The current standard treatment for patients with venous thrombo-embolism (VTE) is administration of low molecular weight heparin or unfractionated heparin alongside warfarin until a required therapeutic target is achieved and further continuation of warfarin along with monitoring of international normalised ratio (INR). However, recently there have been studies that showed simplification of such therapy with oral factor Xa inhibitor rivaroxaban. There is evidence to suggest that rivoroxaban is effective and safe for the prevention of VTE after major orthopaedic surgery and for the prevention of stroke in patients with atrial fibrillation. EINSTEIN PE investigators evaluated the efficacy and safety of rivaroxaban alone as therapeutic anticoagulant when compared to standard therapy in patients who had acute symptomatic pulmonary embolism (PE) with or without deep vein thrombosis.

This study was a randomised, open label, event driven, non inferiority trial and involved 4832 patients who had acute symptomatic PE. The patients were randomised to either rivaroxaban group or to standard therapy by a computerised voice response system. The rivaroxaban group were given 15mg twice daily for 3 weeks, followed by 20 mg once daily. The duration of treatment was determined by the treating physician (3, 6 or 12 months).

Fifty events of symptomatic recurrent venous thromboembolism occurred in the rivaroxaban group compared to 44 events in the standard therapy group (primary efficacy outcome), that corresponded to a hazard ratio of 1.12 (95%CI, 0.75-1.68). The principal safety outcome was the composite of major bleeding or clinically relevant non-major bleeding. There was a non-significant reduction in the composite safety outcome events among the rivaroxaban group (10.3%) compared to the standard therapy group (11.4%) (Hazard ratio 0.90; 95%CI 0.76-1.07; p=0.23). However there was a significant reduction in the number of patients who developed major bleeding among the rivoroxaban group compared to standard therapy group (1.1% versus 2.2% respectively. Hazard ratio, 0.49; 95% CI 0.31 to 0.79; p=0.003).

The study showed that rivaroxaban, when used alone for PE was not inferior to the standard therapy. This simplified drug regimen may help to achieve compliance and reduce use of resources associated with monitoring. However the safety profile appears less convincing with concerns relating to the difficulties in reversal of anticoagulant effect and the absence of long-term safety data. The study was funded by Bayer Health care and Janssen Pharmaceuticals.

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