Early intervention is critical for stroke care. Delayed time to treatment after onset of stroke symptoms can result in progressive neuron loss and diminished outcome [Lansberg MG et al. *Stroke* 2009; Saver JL. *Stroke* 2006; Saver JL et al. *Stroke* 2004]. The physiological and neuroprotective prowess of magnesium has been amply demonstrated in animal models of stroke. Prehospital administration of magnesium by emergency medical services (EMS) providers can accelerate treatment by nearly 2 hours [Saver JL et al. *JAMA* 2013; Saver JL et al. *Stroke* 2004]. Yet, patient benefits of this 'in-field' treatment are unclear.

The FAST-MAG trial was undertaken to explore whether paramedic administration of magnesium is effective and safe for treatment of acute stroke. The placebo-controlled, double-blind, randomized, Phase 3 trial from January 2005 through March 2013 involved 60 hospitals (952 physicians) and 40 EMS provider agencies (2988 paramedics) throughout Los Angeles and Orange Counties. The 1700 patients received 4 g magnesium sulfate (n=857) or placebo (n=843) within 2 hours of the onset of stroke symptoms. All patients received 16 g maintenance magnesium sulfate within 24 hours. Inclusion criteria were suspected stroke according to the Los Angeles Prehospital Stroke Screen, age 40 to 95 years, last known well time within 2 hours of treatment initiation, and deficit present for ≥15 minutes.

The primary endpoint was the mRS stroke disability score. Secondary endpoints were mRS 0-1 and 0-2, Barthel Index scores of daily living, NIHSS scores, and Stroke Impact Scale scores.

The study arms were comparable in a battery of baseline characteristics and neurological features. There was no difference in the time from onset of symptoms to administration of placebo or magnesium. This shows that the EMS system succeeded in giving drug early after stroke even if the treatment was not effective. The 3-month mRS scores were not significantly different for both arms (Table 1). None of the secondary endpoints differed appreciably between the study arms (Table 2).

Table 1. Global Disability at 3 Months Based on mRS Scores

mRS Scale	Patients (%)	
	Placebo n=843	Magnesium n=857
0	21.7	20.9
1	15.2	15.6
2	15.9	15.9
3	10.8	12.6
4	9.5	10.4
5	11.5	9.3
6	15.4	15.3

Table 2. Secondary Endpoint Data

Endpoint	Placebo n=843	Magnesium n=857	p Value
mRS 0-1	36.9%	36.5%	0.97
mRS 0-2	52.8%	52.4%	0.87
Barthel 95-100	51.6%	49.8%	0.46
Barthel 60-100	66.1%	69.2%	0.17
NIHSS	13.4±17.5	12.4±17.0	0.28
Stroke Impact Scale	65 (range, 5–92)	67 (range, 12–92)	0.32

Subgroup analyses failed to reveal benefits of magnesium depending on use/non-use of tissue plasminogen activator, treatment within 60 or 120 minutes, age, gender, race, and stroke severity. Serious adverse events occurred in 50.1% and 51.2% of patients in the placebo and treatment arm, respectively (p=0.66).

Possible explanations for the disappointing results include slow passage of magnesium across the blood-brain barrier and the inability of magnesium to prevent the ischemic cascade.

New Study Reveals That TCD Is Better Used to Detect PFO Than TEE

Written by **Masha Dowell**

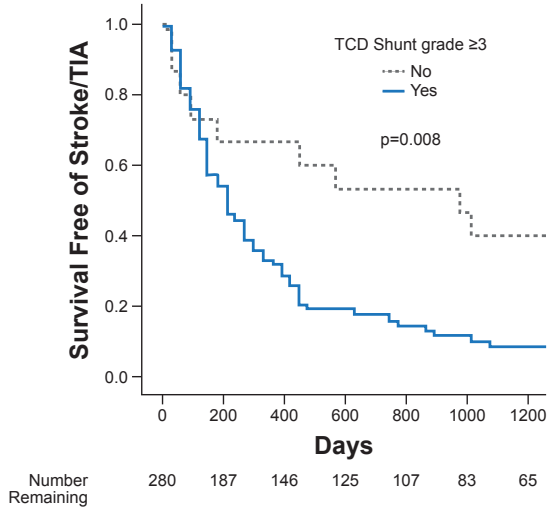
About 25% of the world's population has been reported to have patent foramen ovale (PFO) or symptoms related to it, and they are at a greater risk of paradoxical embolisms [Kent DM, Thaler DE. *Stroke* 2010; Homma S, Sacco RL. *Circulation* 2005]. J. David Spence, MD, Robarts Research Institute of Western University, London, Ontario, Canada, presented new research that revealed that transcranial doppler (TCD) ultrasound is superior to transesophageal echocardiography (TEE) for the detection of PFOs associated with higher stroke risk.

Previous studies have focused on which PFO patients were most likely to have paradoxical embolisms. Clinical clues to paradoxical embolism have included pulmonic surges, dyspnea, tachycardia at onset, extended travel or sitting, previous deep vein thrombosis, and others. Small studies suggest that patients with paradoxical embolism had larger shunts, septal mobility [De Castro S et al. Stroke 2000], and atrial septal aneurysm [Mas J-L et al. *N Engl J Med* 2001]. More recent studies (the Northern Manhattan study and the ROPE study) have documented that neither septal aneurysm nor mobility predict strokes, however [Di Tullio MR et al. *J Am Coll Cardiol* 2013; Wesseler B et al. *Circ Cardiovasc Imaging* 2013].

In this trial, the research team studied the performance of TCD, in comparison with TEE, as it relates to the detection of high risk PFO. Of those patients (n=340) included in the research, 61.5% were women with a mean age of 53 years.

All patients were confirmed to have had a cryptogenic stroke or were suspected of having a paradoxical embolism and were referred to the Urgent Transient Ischemic Attack (TIA) Clinic between the years of 2000 to 2013. Median follow-up was 420 days. At that time, the researchers discovered that 85 patients had a recurrent ischemic stroke or TIA. Occurrence of recurrent stroke or TIA was predicted by TCD shunt of Grade 3 or more (p=0.008; Figure 1), but not by TEE (p=0.6; Figure 2) [Spencer MP et al. *J Neuroimaging* 2004].

Figure 1. Survival Free of Stroke/TIA by TCD Shunt Grade



TCD=transcranial Doppler; TIA=transient ischemic attack.

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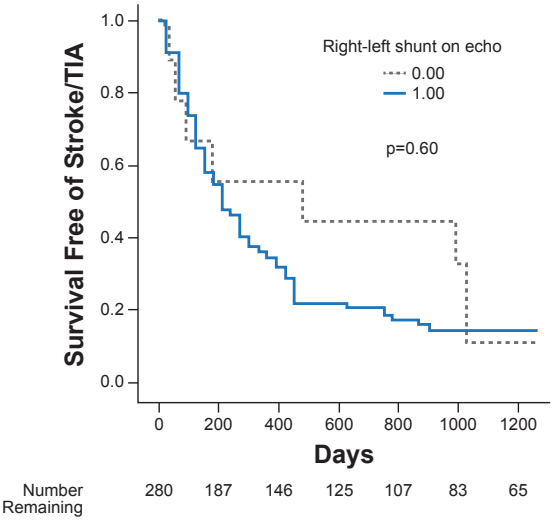
Figure 2. Survival Free of Stroke/TIA by Right-Left Shunt on TEE



TEE=transesophageal echocardiography; TIA=transient ischemic attack.

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In conclusion, because it was more sensitive for the diagnosis of PFO, TCD ultrasound was determined to be the better choice compared with TEE. The study additionally revealed that although TCD is superior to TEE for the ultimate detection of PFO.

Rapid Reperfusion Therapy in Acute Ischemic Stroke Reduces Complications and Improves Outcomes

Written by **Masha Dowell**

The American Heart Association (AHA)/American Stroke Association (ASA) guidelines recommend a door-to-needle (DTN) time of ≤60 minutes for reperfusion therapy for acute ischemic stroke patients [Jauch EC et al. *Stroke* 2013]. The rapid treatment is important for improving stroke outcome, but many studies have concluded that this time frame has been met by <30% of intravenous tissue plasminogen activator (t-PA)-treated stroke patients.

Gregg C. Fonarow, MD, University of California Los Angeles, Los Angeles, California, USA, presented the principal results from the Target: Stroke Initiative, a national program organized by the AHA/ASA, which addresses this timing dilemma by increasing the proportion of stroke patients with DTN time frames of <60 minutes. The primary goal of the study was to treat at least 50% of acute ischemic stroke patients at Get With The Guidelines (GWTG)-Stroke participating hospitals and see that they were treated within 60 minutes of their arrival to the hospital [Fonarow GC et al. *Stroke* 2011]. In performing this assessment, 10 key evidence-based strategies were utilized to meet the goal (Table 1).

Table 1. Evidence-Based Strategies to Reduce DTN Time

1. Hospital prenotification by Emergency Medical Services
2. Rapid triage protocol and stroke team notification
3. Single call/paging activation system for entire stroke team
4. Use of a stroke tool kit containing clinical decision support, stroke-specific order sets, guidelines, hospital-specific algorithms, critical pathways, NIHSS, and other stroke tools
5. Rapid acquisition and interpretation of brain imaging
6. Rapid laboratory testing (including point-of-care testing) if indicated
7. Premixing t-PA medication ahead of time for high likelihood candidates
8. Rapid access to intravenous t-PA in the ED/brain imaging area
9. Team-based approach
10. Rapid data feedback to stroke team on each patient's DTN time and other performance data.

DTN=door-to-needle; ED=emergency department; t-PA= tissue plasminogen activator.

This study included various ongoing adjustments as they related to assessing the variables of patients and characteristics. Assessments were made of in-hospital mortality, discharge destination, ambulatory status, and symptomatic intracranial hemorrhage ≤36 hours following t-PA administration. Patient