Pre-hospital Transdermal Glyceryl Trinitrate in Patients With Stroke Mimics: Data From the Right-2 Randomised-controlled Ambulance Trial

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Research article

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Abstract

Background: Prehospital stroke trials will inevitably recruit patients with non-stroke conditions, so called stroke mimics. We undertook a pre-specified analysis to determine outcomes in patients with mimics in the second Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial (RIGHT-2).

Methods: RIGHT-2 was a prospective, multicentre, paramedic-delivered, ambulance-based, sham-controlled, participant-and outcome-blinded, randomised-controlled trial of transdermal glyceryl trinitrate (GTN) in adults with ultra-acute presumed stroke in the UK. Final diagnosis (intracerebral haemorrhage, ischaemic stroke, transient ischaemic attack, mimic) was determined by the hospital investigator. This pre-specified subgroup analysis assessed the safety and efficacy of transdermal GTN (5 mg daily for 4 days) versus sham patch among stroke mimic patients. The primary outcome was the 7-level modified Rankin Scale (mRS) at 90 days.

Results Among 1149 participants in RIGHT-2, 297 (26%) had a final diagnosis of mimic (GTN 134, sham 163). The mimic group were younger, mean age 67 (SD: 18) vs 75 (SD: 13) years, had a longer interval from symptom onset to randomisation, median 75 [95% CI: 47,126] vs 70 [95% CI:45,108] minutes, less atrial fibrillation and a lower systolic blood pressure and Face-Arm-Speech-Time tool score than the stroke group. The three most common mimic diagnoses were seizure (17%), migraine or primary headache disorder (17%) and functional disorders (14%). At 90 days, the GTN group had a better mRS score as compared to the sham group (adjusted common odds ratio 0.54; 95% confidence intervals 0.34, 0.85; p = 0.008), a difference that persisted at 365 days. There was no difference in the proportion of patients who died in hospital, were discharged to a residential care facility, or suffered a serious adverse event.

Conclusions One-quarter of patients suspected by paramedics to have an ultra-acute stroke were subsequently diagnosed with a non-stroke condition. GTN was associated with unexplained improved functional outcome observed at 90 days and one year, a finding that may represent an undetected baseline imbalance, chance, or real efficacy. GTN was not associated with harm.

Trial registration: This trial is registered with International Standard Randomised Controlled Trials Number ISRCTN 26986053.

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Full Text

This preprint is available for download as a PDF.

Figures

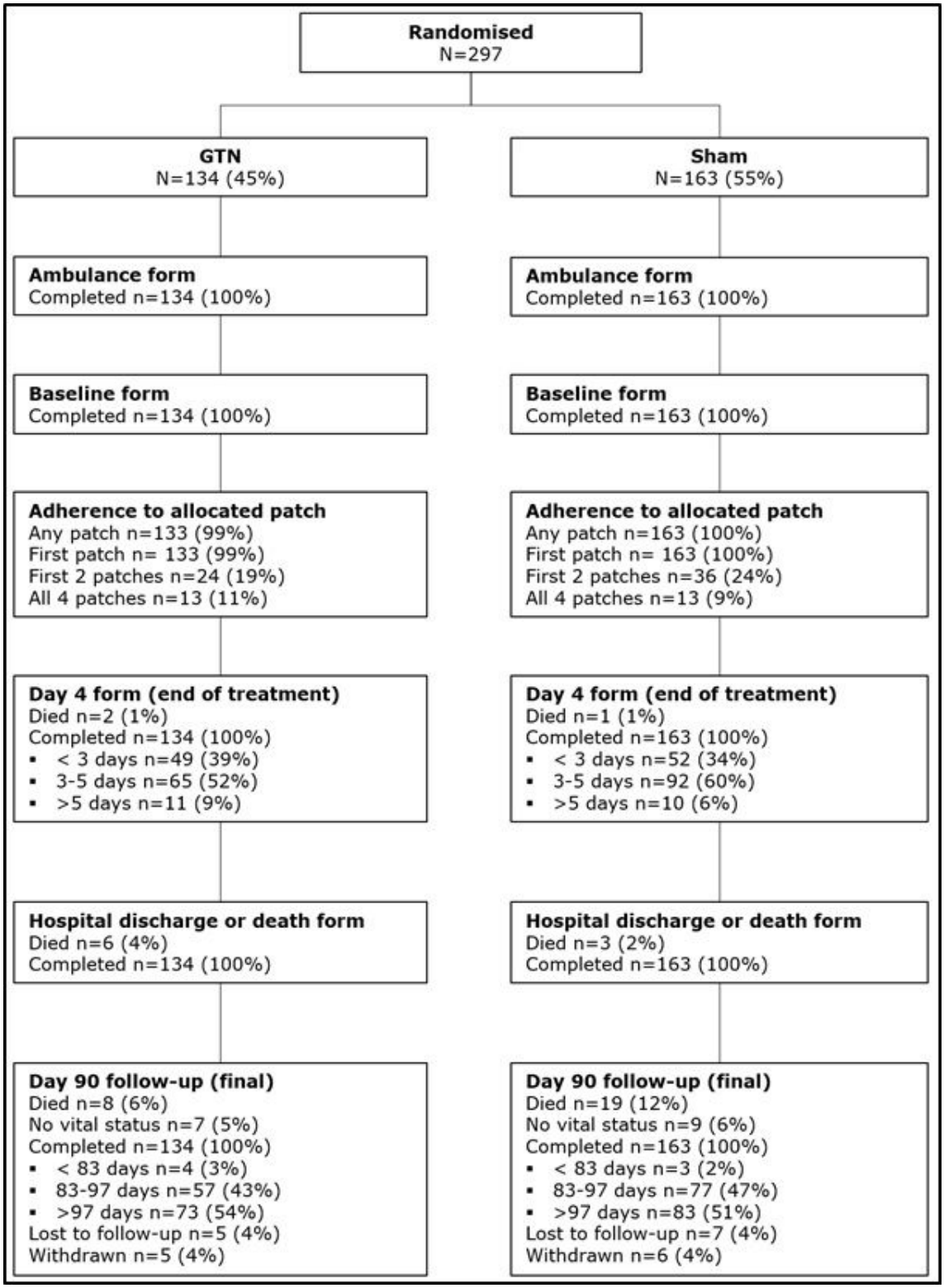

Figure 1

Trial profile for mimic group.

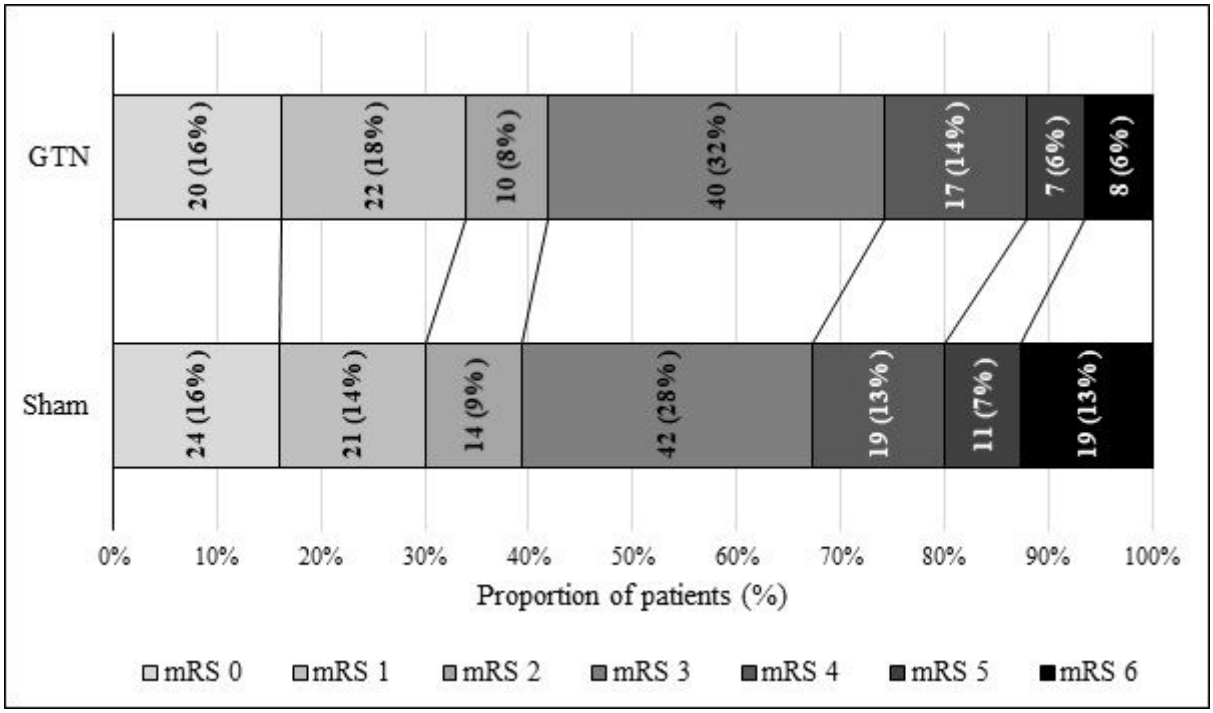

Figure 2

Distribution of mRS scores at day 90 for GTN versus sham among 274 stroke mimic participants. Comparison of GTN versus sham, adjusted common odds ratio 0.54 (0.34, 0.85), p=0.008, by ordinal logistic regression, with adjustment for age, sex, pre-morbid modified Rankin Scale, face-arms-speech-time test, pre-treatment SBP, final diagnosis (stroke mimic) and time to randomisation. The effect of treatment for GTN versus sham is shown as adjusted common odds ratio (acOR).

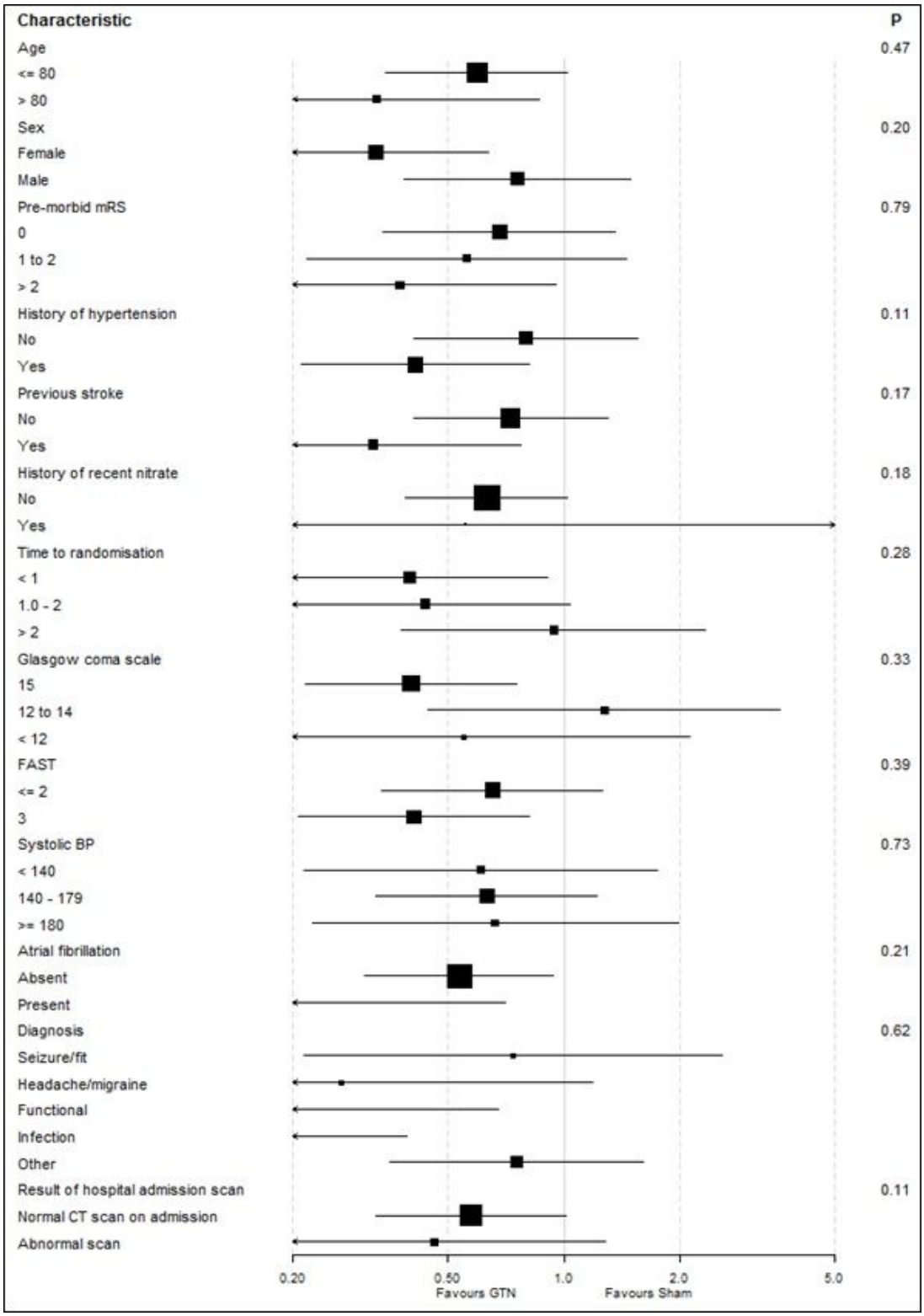

Figure 3

Forest plot showing modified Rankin Scale, analysed as adjusted ordinal outcome, in subgroup of participants with stroke mimics, with p-value for interaction. Heterogeneity of the treatment effect on the primary outcome was assessed in by adding an interaction term to an ordinal logistic regression model with adjustment for age, sex, pre-morbid modified Rankin Scale (mRS), face-arm-speech time test, pre-treatment systolic blood pressure (SBP), final diagnosis (stroke mimic) and time to randomisation.

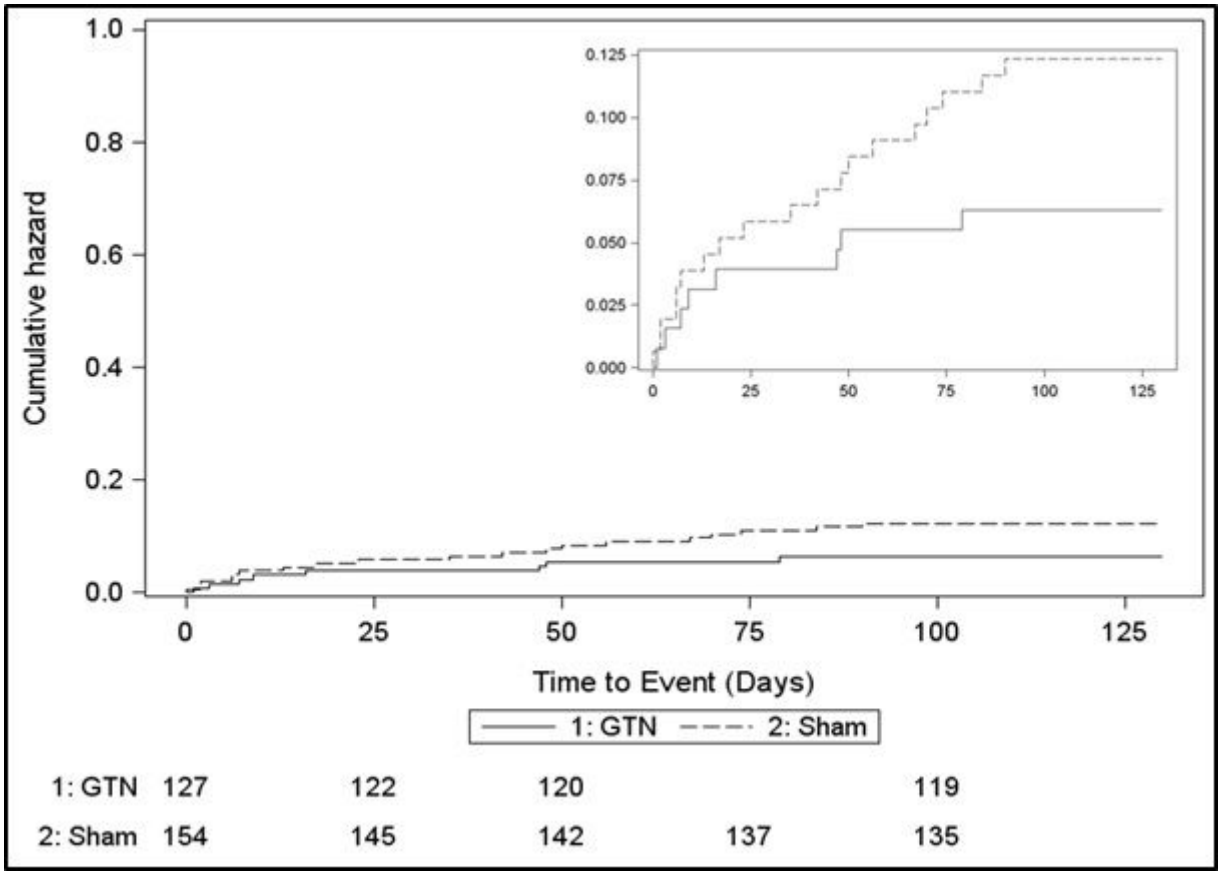

Figure 4

Kaplan-Meier curve for time to death in participants with a stroke mimic, by assigned treatment group. Comparison of GTN versus sham, adjusted hazard ratio 0.49 (95% confidence intervals 0.20, 1.19), p=0.11, by Cox proportional hazards regression with adjustment for age, sex, pre-morbid modified Rankin Scale, face-arms-speech time test, pre-treatment SBP, final diagnosis (stroke mimic) and time to randomisation.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- RIGHT2MimicCONSORTChecklist.doc
- Right2MimicAdditionalFiles.pdf