Resolving Barriers to Intravenous Thrombolysis: Results of the PRACTISE Trial

In The Netherlands, the rates of thrombolysis for ischemic stroke in are not optimal, despite guidelines recommending its use. Diederik W. J. Dippel, MD, PhD, Erasmus Medical Center, Rotterdam, The Netherlands, presented results from the Promoting Acute Thrombolysis for Ischaemic Stroke (PRACTISE: ISRCTN 20405426) trial, which evaluated the effectiveness of an intensive multifaceted implementation strategy aimed at increasing the number of patients who are treated with thrombolysis.

PRACTISE was a cluster-randomized, controlled trial in 12 hospitals in The Netherlands, divided into 2 pairs of 6 (intervention and control), based on academic versus nonacademic setting, size, and previous thrombolysis rate [Dirks et al. *Stroke* 2011. In press]. All patients with a stroke who were admitted within 24 hours of onset of symptoms were registered, and a minimal set of data was collected. Patients who were diagnosed with an ischemic stroke and admitted within 4 hours of symptom onset were registered in more detail. Data acquisition continued for 2 years.

Patients admitted to the 6 hospitals in the intervention group received a high-intensity intervention, based on a recurrent process of measuring, intervention, and feedback. Feedback consisted of training sessions that conformed to an adapted breakthrough model using local teams, SMART goals that were aimed at specific barriers, and 5 training sessions. A tool kit was available on the internet. The primary outcome was treatment with thrombolysis. Multilevel multivariate logistic regression was used with adjustments for cluster effect, academic or nonacademic classification, size of hospital, previous thrombolysis rate, patient's age and gender, and baseline clinical characteristics. At baseline, the mean thrombolysis rate was 5% at the control institutions and 6% at the institutions that received intervention. Of the 5515 patients who were registered (mean age 72 years, ~50% women), 1657 were admitted within 4 hours from onset and 696 were treated with rtPA.

There was a high rate of thrombolysis overall: 12% in the control group and 13% in the intervention group (OR, 1.3; 95% CI, 0.9 to 1.7; p=ns). However, ischemic stroke patients who were admitted within 4 hours were more likely to receive thrombolysis in an intervention center (44%) compared with a control center (39%; OR, 1.6; 95% CI, 1.2 to 2.3). This difference was significant. Although there were more intracranial hemorrhages in the intervention group (n=22; 5.7%) compared with the control group (n=14; 4.6%), the difference was not statistically significant (RR, 1.09; 95% CI, 0.83 to 1.43), and these rates were comparable with those found in other studies and registries. The increased rate of thrombolysis was not explained by the number of admissions, mean onset-to-door time, or mean door-to-needle time, but in the intervention group, unconventional contraindications and contraindications related to "minimal symptoms" and "rapid improvement" were less frequent than in the control group.

Several cultural characteristics of the hospital organization were shown to be related to thrombolysis rate, including an association between thrombolysis and the availability of informal and formal feedback (OR, 1.18; 95% CI, 1.09 to 1.28); a learning culture (OR, 1.12; 95% CI, 1.02 to 1.23); uncompromising, individual clinical leadership (OR, 1.12; 95% CI, 1.03 to 1.23); explicit goals (OR, 1.08; 95% CI, 1.01 to 1.17); and sum score (OR, 1.12; 95% CI, 1.02 to 1.23) [Van Wijngaarden JD et al. *Stroke* 2009].

"Rates of IV thrombolysis should be about 20% of all admitted ischemic stroke patients in general hospitals," Prof. Dippel said. "An intensive multifaceted implementation strategy increases the number of patients treated with thrombolysis, probably due to better application of contraindications for thrombolysis. Implementation of IV thrombolysis for ischemic stroke works and is cost-effective."

Unrecognized Myocardial Infarction Is a Risk Factor for Future Stroke

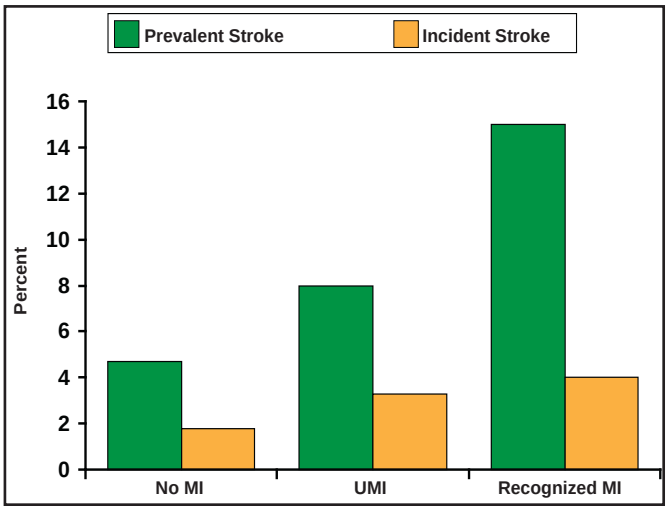
Previous publications from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study examined traditional risk factors for stroke and coronary heart disease among African-Americans and people living in the southeastern United States [Cushman M et al. *Ann Neurol* 2008]. Aaron Anderson, MD, Emory University, Atlanta, Georgia, discussed new data from a substudy of REGARDS that suggested that unrecognized myocardial infarction (UMI) and recognized MI confer a similar risk of stroke and that UMI, in particular, is a risk factor for future stroke in those with prevalent stroke.

Participants in the REGARDS study included 30,239 community-dwelling black and white men and women ≥45 years (50% white, 50% black) who were recruited by phone. In-home examinations, blood collections, ECGs, and anthropometric measurements were performed. Follow-up phone calls were made every 6 months to ascertain a stroke event (defined as a self-reported stroke, transient ischemic attack [TIA], or stroke symptom) or death.

Participants in this substudy were classified as having UMI (n=923), recognized MI (n=1534), or no MI (n=18,055). UMI participants were defined as those individuals who had ECG evidence of MI per Minnesota Code criteria who answered either "no" or "don't know" to the question, "Has a doctor or other health professional ever told you that you had a myocardial infarction or heart attack?" Subjects with self-reported MI were classified as having recognized MI, and those without a self-report of MI or ECG evidence of MI were considered as having no MI. There was a higher percentage of black participants in the UMI group (41.7%) compared with the no-MI (40.9%) and recognized-MI groups (37.5; p=0.028). The recognized-MI group had the highest percentage of men and participants with the traditional risk factors for stroke, such as diabetes, hypertension, and being a current smoker. Level of education and income were highest in the no-MI group and lowest in the recognized-MI group.

The rate of prevalent stroke was higher in both the recognized-MI and the UMI groups compared with the no-MI group. The rate of incident stroke was similar between the UMI and the recognized-MI groups, but both were significantly higher than in the no-MI group (Figure 1).

Figure 1. Proportion of Participants with Prevalent and Incident Stroke



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Time-to-event analyses were performed to determine if prevalent stroke modified the risk between UMI and MI. Those individuals with prevalent stroke had double the risk (RR, 2.69; 1.48, to 4.77) of incident stroke with a UMI. However, participants with a recognized MI and no history of stroke or TIA also had twice the risk (RR, 2.21; 1.56 to 3.12) of stroke. After adjusting these findings for age, race, gender, income, education, age-race interaction, diabetes, hypertension, and smoking, the differences in risk remained. The investigators suggested that the difference may be explained by the potential for subjects with recognized MI to have a cardioembolic stroke compared with subjects with a prevalent stroke and UMI whose stroke may have been the result of underlying atherosclerosis. The differences might also be explained by medication management or the collaborative effort among specialists to treat patients with recognized MI and prevalent stroke that is not provided to UMI participants.

This study may be limited by the possibility that participants may have been previously diagnosed by a physician or health care professional but had poor recollection when questioned or had suffered cognitive decline in the interim.