

## Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke

Jeffrey L. Saver, M.D., John D. Carroll, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D. for the RESPECT Investigators\*

### Abstract

#### BACKGROUND

Whether closure of a patent foramen ovale reduces the risk of recurrence of ischemic stroke in patients who have had a cryptogenic ischemic stroke is unknown.

#### METHODS

In a multicenter, randomized, open-label trial, with blinded adjudication of end-point events, we randomly assigned patients 18 to 60 years of age who had a patent foramen ovale (PFO) and had had a cryptogenic ischemic stroke to undergo closure of the PFO (PFO closure group) or to receive medical therapy alone (aspirin, warfarin, clopidogrel, or aspirin combined with extended-release dipyridamole; medical-therapy group). The primary efficacy end point was a composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization. The results of the analysis of the primary outcome from the original trial period have been reported previously; the current analysis of data from the extended follow-up period was considered to be exploratory.

#### RESULTS

We enrolled 980 patients (mean age, 45.9 years) at 69 sites. Patients were followed for a median of 5.9 years. Treatment exposure in the two groups was unequal (3141 patient-years in the PFO closure group vs. 2669 patient-years in the medical-therapy group), owing to a higher dropout rate in the medical-therapy group. In the intention-to-treat population, recurrent ischemic stroke occurred in 18 patients in the PFO closure group and in 28 patients in the medical-therapy group, resulting in rates of 0.58 events per 100 patient-years and 1.07 events per 100 patient-years, respectively (hazard ratio with PFO closure vs. medical therapy, 0.55; 95% confidence interval [CI], 0.31 to 0.999;  $P=0.046$  by the log-rank test). Recurrent ischemic stroke of undetermined cause occurred in 10 patients in the PFO closure group and in 23 patients in the medical-therapy group (hazard ratio, 0.38; 95% CI, 0.18 to 0.79;  $P=0.007$ ). Venous thromboembolism (which comprised events of pulmonary embolism and deep-vein thrombosis) was more common in the PFO closure group than in the medical-therapy group.

#### CONCLUSIONS

Among adults who had had a cryptogenic ischemic stroke, closure of a PFO was associated with a lower rate of recurrent ischemic strokes than medical therapy alone during extended follow-up. (Funded by St. Jude Medical; RESPECT ClinicalTrials.gov number, NCT00465270. opens in new tab.)

## Author Affiliations

From the University of California, Los Angeles (UCLA), Ronald Reagan UCLA Medical Center, Los Angeles (J.L.S.); University of Colorado, Denver, and University of Colorado Hospital, Aurora (J.D.C.), and South Denver Cardiology, Swedish Medical Center, Littleton (L.A.M.) — all in Colorado; Tufts University, Tufts Medical Center, Boston (D.E.T.); University of Texas, Memorial Hermann Heart and Vascular Institute, Houston (R.W.S.); Medical College of Wisconsin, Milwaukee (D.S.M.); and University of Washington, Seattle (D.L.T.).

Address reprint requests to Dr. Saver at UCLA, Neurology Department, 710 Westwood Plaza, Los Angeles, CA 90095, or at [jsaver@mednet.ucla.edu](mailto:jsaver@mednet.ucla.edu).

A complete list of investigators in the Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT) trial is provided in the Supplementary Appendix, available at [NEJM.org](http://NEJM.org).