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Letters

TO THE EDITOR

The Risk for Stroke With Aspiration Thrombectomy: Procedure or Patient Related?

Insights From a Meta-Analysis

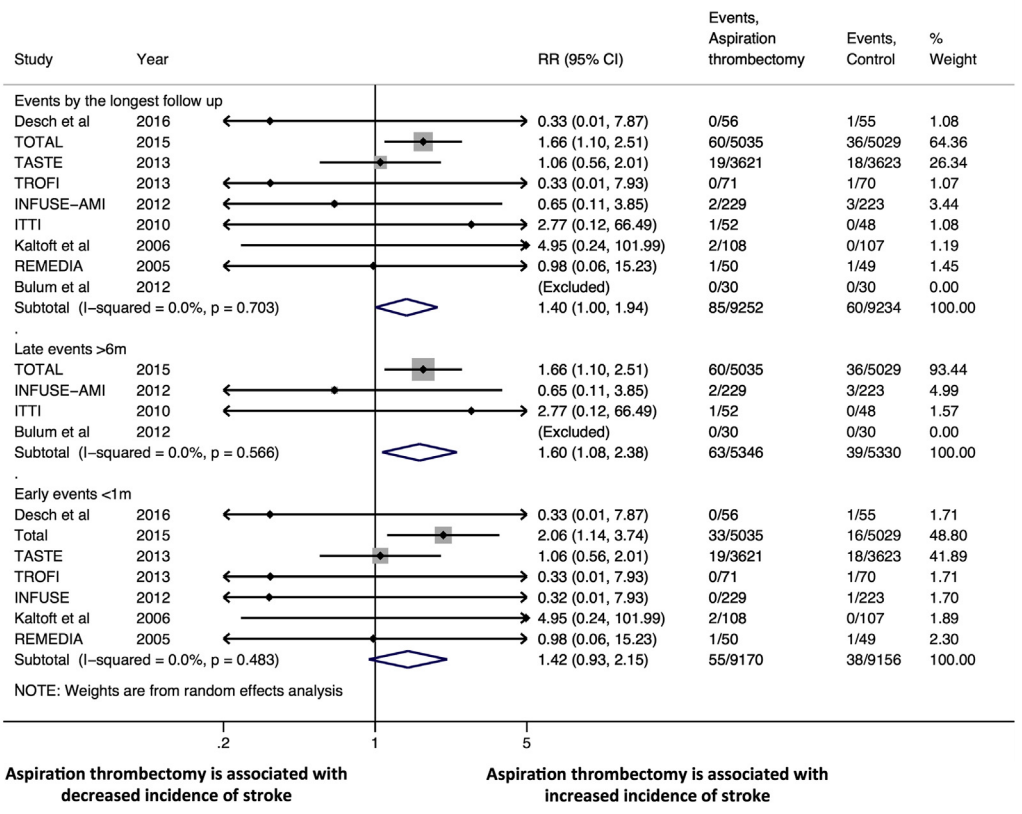
Although earlier studies suggested that aspiration thrombectomy might reduce the risk for adverse events (1), recent randomized trials and meta-analyses have demonstrated a lack of any benefit on clinical endpoints with routine aspiration thrombectomy and suggested that it might increase the risk for stroke (2,3). Therefore, we aimed to conduct a meta-analysis of randomized trials with a focus on stroke to explore some potential explanations for this finding.

Electronic databases were searched for randomized trials that compared aspiration thrombectomy prior to primary percutaneous coronary intervention with conventional percutaneous coronary intervention. Trials that did not report the incidence of stroke were excluded. Summary risk ratios (RRs) were constructed with a DerSimonian and Laird model. If a trial reported the outcome of stroke at different time points, we preferentially used the longer follow-up period in the overall analysis. Subgroup analysis was conducted according to follow-up period: an early follow-up (i.e., ≤1 month) and a late follow-up period (i.e., ≥6 months). A sensitivity analysis was constructed, excluding the largest trial to determine its magnitude on the overall effect size. Random-effects meta-regression analyses were pre-specified for the overall analysis with age, female sex, diabetes mellitus, and hypertension.

Nine trials were included. Seven trials reported early stroke events (all at 1 month except for 1 that reported events during the hospitalization), and 4 trials reported late events (2 reported events at 6 months and 2 at 12 months). Two trials reported events at early and late follow-up. The mean follow-up for the overall analysis was 11 ± 2 months. There was a modest increased risk for stroke in the aspiration thrombectomy arm compared with the conventional arm (0.92% vs. 0.69%; RR: 1.40; 95% confidence interval [CI]: 1.00 to 1.94; $p = 0.048$). Subgroup analysis according to follow-up period demonstrated that the risk for stroke was increased at late follow-up (RR: 1.60; 95% CI: 1.09 to 2.37; $p = 0.02$) but not at early follow-up (RR: 1.42; 95% CI: 0.93 to 2.15; $p = 0.10$) (**Figure 1**). Sensitivity analysis excluding the TOTAL (A Randomized Trial of Routine Aspiration Thrombectomy With PCI Versus PCI Alone in Patients With STEMI Undergoing Primary PCI) trial illustrated that the risk for stroke was similar in both groups in the overall analysis (RR: 1.02; 95% CI: 0.58 to 1.76; $p = 0.96$) and the early follow-up period (RR: 0.99; 95% CI: 0.55 to 1.77; $p = 0.98$). Meta-regression analyses did not identify a difference in treatment effect on the basis of age, female sex, diabetes mellitus, and hypertension ($p = 0.31$, $p = 0.51$, $p = 0.78$, and $p = 0.95$, respectively).

This meta-analysis of 9 randomized trials demonstrated that routine aspiration thrombectomy might be associated with an increased risk for stroke. This effect was driven mainly by the effect of the TOTAL trial. Subgroup analysis suggested that the risk for stroke was not observed in the early follow-up period. It would be expected that the risk for stroke would increase in the periprocedural period (i.e., during the early follow-up period) if the stroke events were due to embolization from the procedure. However, we observed that the risk for stroke was increased at late follow-up. The number of trials reporting stroke events over the longer follow-up period was less than those reporting stroke events during the early follow-up period, which could have magnified the effect size of the TOTAL trial in the late follow-up period. Although the risk for stroke was increased within 48 h of the procedure in the TOTAL trial (4), we noted a higher incidence of stroke events in the aspiration thrombectomy arm in the TOTAL trial beyond 30 days (27 vs. 20 events). A post hoc analysis of the TOTAL trial demonstrated that older age, peripheral vascular disease, history of prior stroke, and hypertension were all independent predictors of stroke (4). In the TOTAL trial, these variables were numerically higher in the aspiration thrombectomy group at baseline, which might explain the higher incidence of stroke at late follow-up in the aspiration thrombectomy arm. Although we demonstrated in a previous

FIGURE 1 Summary Plot for Stroke and Subgroup Analysis According to Follow-Up Period



The relative sizes of the data markers indicate the weights of the sample sizes from each study. CI = confidence interval; INFUSE-AMI = Intracoronary Abciximab and Aspiration Thrombectomy in Patients With Large Anterior Myocardial Infarction; ITTI = Initial Thrombosuction and Tirofiban Infusion; REMEDIA = Reduction of Distal Embolization by Thrombus Aspiration in Primary and Rescue Angioplasty; RR = risk ratio; TASTE = Thrombus Aspiration in ST-Elevation myocardial Infarction in Scandinavia; TOTAL = A Randomized Trial of Routine Aspiration Thrombectomy With PCI Versus PCI Alone in Patients With STEMI Undergoing Primary PCI; TROFI = Thrombus Aspiration on Flow Area in Patients With ST-Elevation Myocardial Infarction.

meta-analysis that aspiration thrombectomy might increase the risk for stroke at a mean of 3 months (2), some of the trials included in the present meta-analysis were not included in the earlier one. In addition, the longer follow-up duration of the TOTAL trial was not available at the time of the previous meta-analysis. Although the updated American College of Cardiology and American Heart Association guidelines downgraded the routine use of aspiration thrombectomy prior to primary percutaneous coronary intervention to class III, selective use of aspiration thrombectomy (e.g., for high thrombus burden) remains a reasonable approach (5). The findings of this meta-analysis provide some insight that the marginal increased risk for stroke with aspiration thrombectomy might be attributed to the patient risk profile rather than the procedure.

In conclusion, aspiration thrombectomy might be associated with an increased risk for stroke. This risk was influenced mainly by the longer follow-up duration of the TOTAL trial and was not observed in the earlier follow-up period.

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High-Risk Percutaneous Coronary Interventions

First, Do No Harm

We read with great interest the paper by Atkinson et al. (1) regarding an algorithm for percutaneous mechanical circulatory support (MCS) selection in patients undergoing high-risk percutaneous coronary intervention (HRPCI). Although the stated objective of the paper is for selection of MCS, the investigators left out the important consideration that not all HRPCI patients require MCS, and MCS may remain an option for standby when performing HRPCI. The algorithm essentially calls for Impella (Abiomed, Danvers, Massachusetts) use for all patients being treated with HRPCI, whenever technically anatomically feasible.

There is a clear role for protected percutaneous coronary intervention, yet we must proceed with caution. Although hemodynamic support devices, including the Impella percutaneous left ventricular assist device (PLVAD) or intra-aortic balloon pumps, may provide support during HRPCI, we must keep in mind the limitations. PROTECT II (A Prospective, Multi-center, Randomized Controlled Trial of the IMPELLA RECOVER LP 2.5 System Versus Intra Aortic Balloon Pump [IABP] in Patients Undergoing Non Emergent High Risk PCI) was stopped early and failed to meet its primary endpoint (reduction in 30-day composite major adverse events). It showed significant reduction in a composite of 10 endpoints at 90-day follow-up, driven by a difference in revascularization, with no significant differences in mortality and myocardial infarction (2). PROTECT II compared the Impella with an intra-aortic balloon pump, a support device that has historically failed to show any significant benefit in HRPCI.

The hemodynamic benefits of PLVAD are not without risk. In a real-world Impella database, the vascular complication rate was 17%, with need for amputation in 4.4% (3). The composite of major bleeding, hemolysis, and pericardial tamponade occurred in 37.8% of patients in the Impella-EUROSHOCK registry (4). Eleven percent of patients treated in the USpella registry required blood transfusions. Vascular complications requiring surgery occurred in 2.5% of USpella registry patients (5). In PROTECT II, there was a 68.8% composite of adverse events in patients treated with rotational atherectomy with Impella support.

MCS can improve hemodynamic status, but it has not been shown to improve any periprocedural outcomes in this complex higher-risk indicated patient cohort. The use of PLVAD is on the rise, as we work to optimize management of high-risk patients, but this is based largely not on randomized controlled data but on registry experience. We must be mindful that the benefits of PLVAD come with a cost, in the form of both procedural complications for patients and significant financial costs.

Although there is a role for protected percutaneous coronary intervention in appropriate patients, overuse should be avoided until there are additional data. Patients undergoing elective HRPCI should be referred to high-volume centers with operators specializing in treatment of complex higher-risk indicated patients. The algorithm is an excellent start once MCS has been selected, but there should be emphasis on assessing each individual patient's need for MCS when undergoing HRPCI. Rather than indicating that the Impella should be used whenever technically feasible for all HRPCI patients, perhaps the guidance should recommend that MCS be considered. MCS shows great promise in advancing the field, but it is not without risk, and we must proceed with caution, remembering that with each patient encounter, "first, do no harm."

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