Systemic Inflammatory Response Syndrome in Tissue-Type Plasminogen Activator–Treated Patients is Associated With Worse Short-term Functional Outcome

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Background and Purpose—Systemic inflammatory response syndrome (SIRS) is a generalized inflammatory state. The primary goal of the study was to determine whether differences exist in outcomes in SIRS and non-SIRS intravenous tissue-type plasminogen activator–treated patients.

Methods—Consecutive patients were retrospectively reviewed for the evidence of SIRS during their admission. SIRS was defined as the presence of ≥2 of the following: body temperature <36°C or >38°C, heart rate >90, respiratory rate >20, and white blood cells <4000/mm or >12000 mm, or >10% bands. Patients diagnosed with infection (via positive culture) were excluded.

Results—Of the 241 patients, 44 had evidence of SIRS (18%). Adjusting for pre–tissue-type plasminogen activator National Institutes of Health Stroke Scale, age, and race, SIRS remained a predictor of poor functional outcome at discharge (odds ratio [OR], 2.58; 95% confidence interval [CI], 1.16–5.73; P=0.0197).

Conclusions—In our sample of tissue-type plasminogen activator–treated (tPA) patients, ~1 in 5 patients developed SIRS. Furthermore, we found the presence of SIRS to be associated with poor short-term functional outcomes and prolonged length of stay. (Stroke. 2013;44:2321-2323.)

Key Words: inflammation ■ ischemic stroke ■ stroke care ■ tPA

Systemic inflammatory response syndrome (SIRS) is a generalized whole body reaction to a stimulus (ie, trauma and surgery) characterized by the absence of infection and the presence of ≥2 of the following: body temperature <36°C or >38°C, leukocytosis or leucopenia, elevated heart rate or elevated respiratory rate. Stroke itself can produce an inflammatory response, with inflammation playing a role in the pathophysiology of tissue damage through ischemia–reperfusion injury. Previous research has shown that patients with acute ischemic stroke with more severe strokes are at higher odds of having SIRS, but successful thrombolytic therapy with intravenous tissue-type plasminogen activator (tPA) has been shown to attenuate this process. We investigated the differences in outcomes in tPA-treated patients with SIRS and without SIRS.

Methods

Study Population and Variable Definition

We retrospectively identified consecutive tPA-treated patients who presented to our center from 2008 to 2011 using our stroke registry. Patients who developed SIRS during their hospital stay were identified via chart review. SIRS was defined as the presence of ≥2 of the following: (1) body temperature <36°C or >38°C, (2) heart rate >90, (3) respiratory rate >20, or (4) white blood cells <4000/mm or >12000/mm or >10% bands for >24 hours. The focus of our study was SIRS, not sepsis or other detected infection; thus, patients who were diagnosed with an infection were excluded.

Three outcomes were examined. Poor functional outcome, defined as a modified Rankin Scale of 4 to 6 at discharge, poor discharge disposition (being discharged somewhere other than home or an inpatient rehabilitation center), and death.

Statistics

Patients with SIRS were compared with those without SIRS using χ² and t tests with nonparametric equivalents when appropriate. Logistic regression analyses were conducted to assess the relationship between SIRS and outcomes of interest. As this was an exploratory analysis, no adjustments were made for multiple comparisons. An α of 0.05 was set as the level of significance. This study was approved by the institutional review board at the University of Alabama at Birmingham.
Results

Baseline Information

Of the 241 tPA-treated patients included in this study, 44 had evidence of SIRS (18.2%). The Table demonstrates the differences in baseline characteristics between patients with SIRS and patients without SIRS. Patients with SIRS were more likely to be black (48 versus 25%; \( P = 0.0117 \)) and had lower median total cholesterol at baseline (143 versus 168 mg/dL; \( P = 0.0207 \)).

Outcome Assessment

Patients with SIRS were more likely to have a longer length of stay than those without SIRS (5 versus 3 days; \( P < 0.0001 \)). Although patients with SIRS had higher odds of poor functional outcome at discharge (OR, 2.82; 95% CI, 1.36–5.87; \( P = 0.0054 \)), there was no association between SIRS and discharge disposition (OR, 1.26; 95% CI, 0.56–2.80; \( P = 0.5770 \)) or death (OR, 1.98; 95% CI, 0.77–5.06; \( P = 0.1545 \)). Even after adjusting for National Institutes of Health Stroke Scale on admission, age, black race, and evidence of prior stroke, SIRS remained predictive of poor functional outcome (OR, 3.55; 95% CI, 1.47–8.58; \( P = 0.0049 \)).

Discussion

Our study showed that \( \approx 1 \) in 5 of our tPA-treated patients developed SIRS. Given that prior studies have shown that...
successful tPA therapy diminishes the risk of adverse outcomes associated with SIRS, we sought to assess the differences in outcomes in patients with SIRS treated with tPA. Patients who developed SIRS were at greater odds of being discharged with poor functional outcomes, even after adjusting for covariates previously shown to influence outcome. Yoshimoto et al demonstrated that SIRS was associated with clinical worsening and poor outcomes after subarachnoid hemorrhage. Despite the increased odds of poor functional outcome, SIRS was not a predictor of poor discharge disposition or in-hospital mortality in our sample. Although infection after stroke remains a significant predictor of poor outcome, there has been little research on SIRS in the absence of infection as a predictor of outcome. Because individual components of the SIRS classification were linked to poor outcomes (eg, leukocytosis, elevated body temperature), it is plausible that the combined effects of the components within SIRS are related to poor outcomes, despite attenuation from thrombolytic therapy.

Our study is limited by a small sample size involving only 1 academic center, which may limit its generalizability. We are further limited by the retrospective nature of this study. Although our outcomes were not blinded, all data on SIRS criteria were collected separately from the stroke outcome data. We examined only short-term outcomes because long-term data were not available. Furthermore, levels of inflammatory markers such as high-sensitivity C-reactive protein or various interleukins were not available. Prospective studies that include the measurement of inflammatory markers to determine whether there is an elevated inflammatory response in patients who develop SIRS and to determine whether levels correlate with clinical outcome are needed.

Conclusion

Despite its influence on functional outcome and its prevalence, SIRS is often overlooked in the ischemic stroke population. Larger prospective studies are needed to determine whether early identification of patients at risk of SIRS could serve to mitigate the risk of poor functional outcome in this vulnerable group.

Disclosures

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References

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/content/44/10/e141.full.pdf
The version of the article, “Systemic Inflammatory Response Syndrome in Tissue-Type Plasminogen Activator–Treated Patients is Associated With Worse Short-term Functional Outcome” by Boehme et al (Stroke. 2013;44:2321–2323) that published online ahead-of-print on May 23, 2013 contained an error in the author byline. Dr Reza Bavarsad Shahripour’s abbreviated name appeared as, “Shahripour RB”. This has been corrected in final online version as, Bavarsad Shahripour R.