Acute Basilar Artery Occlusion in the Basilar Artery International Cooperation Study
Does Gender Matter?

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Background and Purpose—Randomized trials suggested a different benefit of intravenous thrombolysis (IVT) and intra-arterial thrombolysis (IAT) between men and women with anterior circulation stroke because of a worse outcome of women in the control group.

Methods—We compared outcome and recanalization in men and women with basilar artery occlusion treated with antithrombotic treatment alone, IVT or combined IVT–IAT, or IAT in the Basilar Artery International Cooperation Study.

Results—Overall, 389 male and 226 female patients were analyzed. In the antithrombotic treatment group, 68 of 111 (61%) men and 47 of 70 (67%) women had a poor outcome defined as a modified Rankin Scale score of 4 to 6 (adjusted risk ratio [aRR], 0.96; 95% CI, 0.75 to 1.24), in the IVT/combined IVT–IAT group, 47 of 77 (61%) men and 24 of 43 (56%) women (aRR, 1.19; 95% CI, 0.89 to 1.60), and in the IAT group, 142 of 185 (77%) men and 71 of 102 (70%) women (aRR, 1.01; 95% CI, 0.88 to 1.17). Mortality was not different between men and women in the antithrombotic treatment group (aRR, 0.80; 95% CI, 0.55 to 1.16), the IVT/combined IVT–IAT group (aRR, 1.11; 95% CI, 0.72 to 1.73), or in the IAT group (aRR, 1.01; 95% CI, 0.75 to 1.36). Insufficient recanalization after combined IVT–IAT or IAT was similar in men and women (23% versus 22%; aRR, 0.92; 95% CI, 0.58 to 1.46).

Conclusions—In patients with acute basilar artery occlusion, no significant gender differences for outcome and recanalization were observed, regardless of treatment modality. (Stroke. 2010;41:2693-2696.)

Key Words: gender ■ acute stroke ■ basilar artery occlusion ■ thrombolysis

In previous studies on patients with acute stroke, gender-based differences have been observed with respect to clinical presentation, management, and outcomes.1 Studies on patients with ischemic stroke not treated with thrombolysis reported less favorable outcomes for women than for men.2 Further, it has been reported that women benefited more from intravenous thrombolysis (IVT) and intra-arterial thrombolysis (IAT) than men.3,4 The main reason for this difference in favor of women was that nonthrombolysed women in the control group had a worse outcome than nonthrombolysed men, whereas in patients undergoing IAT or IVT, outcome was similar in men and women.3,4

Large studies on differences between men and women with acute basilar artery occlusion (BAO) are lacking. The Basilar Artery International Cooperation Study (BASICS) is the largest observational study of consecutive patients with acute BAO and provides multicenter data for secondary analyses.5,6

The aim of this study was to determine the association between gender and outcome in patients from the BASICS registry.

Methods

BASICS was a prospective, observational, international registry of consecutive patients presenting with an acute symptomatic and radiologically confirmed BAO. Details of the protocol have been published previously.5,6

For the analyses of gender differences in outcome and mortality, patients were divided into 3 groups: (1) antithrombotic treatment (AT; antiplatelets or systemic anticoagulation) alone, (2) IVT or combined IVT–IAT (cIVT-IAT), and (3) IAT (including thrombolysis, mechanical thrombectomy, stenting, and a combina-
Unadjusted risk ratios and aRRs for poor outcome at 1 month according to gender for each treatment group are shown in Table 2. In the AT group, 68 of 111 (61%) men and 47 of 70 (67%) women had a poor outcome (aRR, 0.96; 95% CI, 0.75 to 1.24), in the IVT/cIVT-IAT group, 47 of 77 (61%) men and 24 of 43 (56%) women (aRR, 1.19; 95% CI, 0.89 to 1.60), and in the IAT group, 142 of 185 (77%) men and 71 of 102 (70%) women (aRR, 1.01; 95% CI, 0.88 to 1.17). The Figure shows detailed clinical outcomes in men and women.

Mortality did not differ between men and women in any group (AT group [aRR, 0.80; 95% CI, 0.55 to 1.16]; IVT/cIVT-IAT group [aRR, 1.11; 95% CI, 0.72 to 1.73]; IAT group [aRR, 1.01; 95% CI, 0.75 to 1.36]).

Recanalization was investigated in 37 of 44 (91%) patients after cIVT-IAT and in 252 of 287 (88%) patients after IAT. Insufficient recanalization (Thrombolysis in Myocardial Infarction score of 0 or 1) after cIVT-IAT or IAT was similar in men and women (23% versus 22%; aRR, 0.92; 95% CI, 0.58 to 1.46). The rate of symptomatic intracranial hemorrhage was equal in men (30 of 343; 8%) and women (17 of 215; 8%).

### Discussion

In this secondary analysis of BASICS, no significant gender differences in clinical outcome were observed, regardless of treatment modalities. Recanalization rates after IAT and cIVT-IAT were similar for men and women.

The lack of an association between gender and outcome for patients treated with IVT, IAT, or cIVT-IAT is in line with the results of previous studies. However, the similar outcome of men and women with BAO in the AT group is in contrast with previous studies performed on patients with mainly or exclusively anterior circulation stroke. In a pooled analysis of randomized trials of acute stroke patients, women treated with IV recombinant tissue plasminogen activator derived a greater benefit than men independently of other variables. This effect of gender on outcome was caused primarily by a worse outcome of women among the control patients who were not treated with thrombolysis.

Similar results were reported in patients treated with intra-arterial pro-urokinase for acute ischemic stroke resulting from M1 or M2 segment occlusion of the middle cerebral artery. In a secondary analysis of the PROACT-2 study, an association between gender and treatment effect was demonstrated, with women showing a larger benefit (20% absolute risk reduction for achieving a modified Rankin Scale score ≥2) compared with men (10% absolute risk reduction). Again, the reason for this difference was that in the control group, women had a worse outcome than men, whereas in the thrombolytic group, outcome was similar in men and women. This gender-based effect in the PROACT-2 trial was not attributable to differences in vessel recanalization rates between women and men, and the reasons for these differences remained unexplained. An observational study including patients with middle cerebral artery or internal carotid artery occlusion showed no difference between men and women of recanalization rate and clinical outcome after IAT with urokinase and is in line with the PROACT-2 data. In contrast, a smaller observational study showed higher recanal-

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**Table 1. Baseline Characteristics of Patients According to Gender**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Female (n=215)</th>
<th>Male (n=337)</th>
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</thead>
<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>64 (17)</td>
<td>63 (13)</td>
</tr>
<tr>
<td>Age ≥50 y</td>
<td>53 (25%)</td>
<td>61 (16%)</td>
</tr>
<tr>
<td>Age &lt;70 y</td>
<td>102 (47%)</td>
<td>114 (31%)</td>
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<tr>
<td>Hypertension</td>
<td>125 (58%)</td>
<td>237 (64%)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>39 (18%)</td>
<td>86 (23%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>48 (22%)</td>
<td>113 (30%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>50 (23%)</td>
<td>74 (20%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>23 (11%)</td>
<td>83 (22%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>23 (11%)</td>
<td>78 (21%)</td>
</tr>
<tr>
<td>Prodromal minor stroke</td>
<td>36 (17%)</td>
<td>73 (20%)</td>
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<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Diabetes mellitus</strong></td>
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<td><strong>Hyperlipidemia</strong></td>
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<td><strong>Atrial fibrillation</strong></td>
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<td><strong>Smoking</strong></td>
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**Data are mean (SD), No. (%), or median (interquartile range).**

NIHSS indicates National Institutes of Health Stroke Scale.

*Coma, locked-in state, or tetraplegia.*

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A total of 619 patients from 48 centers were included in BASICS. Four patients were not included because of missing data for gender, and 27 were excluded for further analysis because they did not receive any AT, IVT, or IAT. Of these 27 patients, 26 died and 1 survived, with a modified Rankin Scale score of 5. Of the remaining 588 patients (373 [63%] men; 215 [37%] women), 181 received AT alone, 120 IVT (n=79) or cIVT-IAT (n=41), and 287 IAT. Table 1 shows baseline characteristics of men and women.
alization rates and more frequent early clinical neurological improvements after intravenous recombinant tissue plasminogen activator among women than men.10

The Canadian Alteplase for Stroke Effectiveness Study reported similar clinical outcome and mortality for men and women treated with IVT.11

The reasons for the differences between the gender-based analyses of BASICS with regard to treatment effect of AT therapy and those of previous studies are difficult to explain. Differences in coagulation and endogenous fibrinolysis between men and women were reported previously and might contribute to different outcomes according to gender in patients with acute stroke treated with AT.12,13 Higher factor VII:C levels in women than men have been described in healthy persons and in patients with noninsulin-dependent diabetes mellitus.14,15 Moreover, plasminogen activator inhibitor-1 levels were shown to be higher in women than men with diabetes mellitus.15 However, it is difficult to understand why such gender differences would have different effects in acute ischemic stroke in the anterior and posterior circulation, and it seems unlikely that differences of coagulation and the fibrinolytic system exist between patients with anterior and posterior circulation stroke. In the absence of a pathophysiological explanation of the contrary, we believe our study suggests a lack of a difference in treatment response between men and women with BAO.

BASICS was an observational registry and has the inherent limitations of a nonrandomized study. Therefore, our results are prone to known and unknown biases that limit the strength of the evidence and preclude definite conclusions on gender differences in patients with BAO. However, we did adjust for age, National Institutes of Health Stroke Scale (NIHSS) score at time of treatment, and location of occlusion; adjustment for age, NIHSS score at time of treatment, location of occlusion, and deficit at time of treatment.

In conclusion, in this observational study, men and women with acute BAO did not show any significant differences in clinical outcome and vessel recanalization regardless of treatment modalities.

### Appendix

Participating centers (with number of patients and names of investigators) were as follows. Australia (6): University of Melbourne (A.M. Weber, G.A. Donnan); Belgium (21): University Hospital,
Leuven (11; V. Thijs), University Hospital St. Luc, Brussels (10; A. Peeters); Brazil (18): University of Rio de Janeiro (11; G. de Freitas), University of Sao Paulo, Hospital das Clinicas (5; A.B. Conforto), Federal University of Sao Paulo (2; M. Miranda-Alves, A. Massaro); Finland (14): University of Helsinki (14; P. Iijas, T. Bogoslovsky, P.J. Lindsberg); Germany (224): German Stroke Database (77; C. Weimar, J. Benennam, K. Kraywinkel), University Hospital Freiburg (20; C. Havercamp), Leipzig University (15; D. Michalski), University Hospital Essen (10; C. Weimar), Medical University Hannover (8; K. Weissenborn), 6; University Hospital Magdeburg (M. Goertler); 4; University Hospital Rostock (A. Kloth), Klinikum Neuruppin (3; A. Bitsch), Burger Hospital, Stuttgart (3; T. Mieck), Heinrich Braun Krankenhaus, Zwickau (2; J. Machetanz), Sofien and Hufeland Hospital, Weimar (2; P. Möller), University Hospital, Ulm (2; R. Huber), Hospital Heidenheim (2; S. Kaendler), St. Elisabeth Hospital, Ravensburg (47; C. Rueckert), TEMPS Netwokk Baatar (38; H. Audebert, R. Möller, B. Vatanakhan), University of Munich (26; T. Pfefferkorn, T.E. Mayer), Universitätshocklinik Mannheim (19; K. Szabo), Dresden University (13; C. Disque), Klinikum (2; O. Busse), University of Heidelberg (2; C. Berger, W. Hacke); Israel (19): Sheba Medical Center (19; Y. Schwammenthal, D. Orion, D. Tanne); Italy (6): University of Turin (5; M. Bergui), University of Bologna (1; E. Pazzuti); Netherlands (82): St. Antonius Hospital, Nieuwegein (40; W.J. Schonewille), University Medical Center Utrecht (22; W.J. Schonewille, A. Algra, L.J. Kappelle), University Medical Center Groningen (6; G.J. Luijkx, P. Vroomen), Academic Medical Center, Amsterdam (5; M.D. Vergouwen, Y. Roos, J. Stam), Gelte Hospital (4; P. Bienfait), University Medical Center Nijmegen (3; F.E. de Leeuw), St. Elisabeth Hospital, Tilburg (1; P.de Kort), Erasmus Medical Center, Rotterdam (1; D. Dippel); Scotland (23): Southern General Hospital, Glasgow (23; T. Baird, K. Muir); Spain (25): Hospital Val ‘d Hebron, Barcelona (13; J. Pagola, M. Ribó, C. Molina), Hospital Virgen del Rocío, Sevilla (12; A. Gonzales, A. Gil-Peralta); Sweden (3): Lund University (3; B. Norrving); Switzerland (127): Inselspital, Bern (52; M. Arnold, U. Fischer, J. Gralla, H. Mattle, G. Schroth), Centre Hospitalier Universitaire Vaudois, Lausanne (39; P. Michel), University Hospital, Zurich (8; J. Gandjour, N. Michael, R. Baumgartner), Kantonsspital, St. Gallen (2; B. Tetenbaum), Kantonsspital, Aarau (2; H. Hungerbuehler); United States (51): Stanford Stroke Center, Palo Alto, Calif (29; C.A. Wijman, A. Finley Caulfield, M. Lansberg, N. Schwartz, C. Venkatabramanian), University of Texas, Houston (22; Z. Garami, S. Bogaard, F. Yatsu, J. Grotta).

**Authors’ Contribution**

M.A. and U.F. had the idea for this study, wrote the first draft of the manuscript and the final report, and contributed equally to this study. W.J.S. had the idea for the BASICS registry, developed the Internet database, encouraged international colleagues to contribute data to the study, analyzed and interpreted data, and contributed to subsequent versions of the manuscript. A.A. and A.C. performed the statistical analysis and contributed to subsequent versions of the manuscript. J.G., O.F., D.T., L.J.K., and H.P.M. assisted in the recruitment of patients and contributed to the design of the study and to subsequent versions of the manuscript.

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**Disclosures**

None.

**References**


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