# Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Correlations Between Hematoma Volume at Baseline and Patient Characteristics (Rank Correlation Coefficient Kendall's τ)

| | **Hematoma volume at baseline (n = 61)** | ***P* Value** |
|---|---|---|
| Age (years) | 0.060 | .49 |
| Gender: female | -0.079 | .46 |
| $CHA_2DS_2VASc$ score[a] | 0.030 | .75 |
| HAS-BLED score[b] | 0.152 | .13 |
| Coexisting condition | | |
| Previous ischemic stroke/ TIA | -0.027 | .80 |
| Previous intracranial hemorrhage | 0 078 | .46 |
| Hypertension | 0.034 | .75 |
| Hyperlipidemia | -0.087 | .42 |
| Diabetes mellitus | 0.041 | .70 |
| Heart failure | 0.219 | .04 |
| Renal function at admission | | |
| GFR | 0.099 | .29 |
| Creatinine level (mg/dl) | -0.091 | .31 |
| Modified Rankin scale score[c] | | |
| Before stroke | 0.030 | .76 |
| At admission | 0.366 | <0.001 |
| NIHSS at admission[d] | 0.347 | <0.001 |
| Onset to baseline CT/MRI (hours) | | |
| Including cases with unknown onset | -0.010 | .91 |
| Exact onset (n=43) | 0.027 | .81 |
| Last intake NOAC (hours) (only cases with exact time window, n=41) | -0.076 | .49 |

Abbreviations: TIA, transient ischemic attack; GFR, glomerular filtration rate (electronic GFR as reported by the centers); NIHSS, National Institutes of Health Stroke Scale; NOAC, non vitamin-K antagonist oral anticoagulant.

[a] $CHA_2DS_2VASc$ score, range 0-9, from low to high risk of ischemic stroke in atrial fibrillation.

[b] HAS-BLED score, range 0-9, from low to high risk of hemorrhage under oral anticoagulation.

[c] Modified Rankin scale score, from 0 (no symptoms) to 6 (death).

[d] NIHSS, stroke related neurological deficits, from 0 (no symptoms) to 42.

**eTable 2.** Characteristics of Patients Receiving Prothrombin Complex Concentrate (PCC)

| | PCC administration (n = 35) | No PCC (n = 26) | *P* Value |
|---|---|---|---|
| Age, mean (SD), years | 76.4 (10.3) | 75.6 (13.2) | .77 |
| Women, No. (%) | 13 (37.1) | 12 (46.2) | .60 |
| Indication for oral anticoagulation, No. (%) | | | .18 |
| Atrial fibrillation | 35 (100.0) | 24 (92.3) | |
| Venous thromboembolism | 0 | 2 (7.7) | |
| Non vitamin-K antagonist oral anticoagulant, No. (%) | | | .56 |
| Apixaban | 4 (11.4) | 1 (3.8) | |
| Dabigatran | 4 (11.4) | 3 (11.5) | |
| Rivaroxaban | 27 (77.1) | 22 (84.6) | |
| Concomitant platelet inhibition, No. (%) | | | |
| Aspirin | 4 (11.4) | 0 | |
| Clopidogrel | 1 (2.9) | 0 | |
| Aspirin + Clopidogrel | 1 (2.9) | 0 | |
| $CHA_2DS_2VASc$ score, median (IQR)[a] | 5 (4–6) | 5 (3–6.25) | .78 |
| HAS-BLED score, median (IQR)[b] | 2 (2–3) | 2 (2–3) | .51 |
| Coexisting condition, No. (%) | | | |
| Previous ischemic stroke/ TIA | 11 (22.9) | 13 (50.0) | .19 |
| Previous intracranial hemorrhage | 3 (8.6) | 2 (7.7) | >.99 |
| Hypertension | 32 (91.4) | 21 (80.8) | .27 |
| Hyperlipidemia | 12 (34.3) | 8 (30.8) | .77 |
| Diabetes mellitus | 10 (28.6) | 9 (34.6) | .78 |
| Heart failure | 8 (22.9) | 5 (19.2) | .74 |
| Peripheral vascular disease | 3 (8.6) | 3 (11.5) | >.99 |
| Renal function at admission | | | >.99 |
| GFR ≥ 60 ml/min, No. (%) | 23 (71.9) | 17 (70.8) | |
| GFR < 60 ml/min, No. (%) | 9 (28.1) | 7 (29.2) | |
| Creatinin level, median (IQR), mg/dl | 1.01 (0.72–1.23) | 0.91 (0.70–1.19) | .63 |
| Modified Rankin scale score, median (IQR)[c] | | | |
| Before stroke[e] | 1 (0-3) | 2 (1-4) | .30 |
| At admission | 5 (4–5) | 4 (2.5–5) | .02 |
| NIHSS at admission, median (IQR)[d] | 13 (5–20) | 7.5 (2–17) | .05 |
| Death during acute stay, No. (%) | 6 (17.1) | 4 (15.4) | >.99 |
| Death until follow-up[e], No. (%) | 9 (26.5) | 8 (30.8) | .78 |
| Death within 5 days, No. (%) | 2 (5.7) | 4 (15.4) | .39 |
| Length of stay (days), median (IQR) | 11 (8-16) | 7.5 (3.5–13.5) | .06 |

Abbreviations: TIA, transient ischemic attack; GFR, glomerular filtration rate (electronic GFR as reported by the centers); NIHSS, National Institutes of Health Stroke Scale.

[a] $CHA_2DS_2VASc$ score, range 0-9, from low to high risk of ischemic stroke in atrial fibrillation.

[b] HAS-BLED score, range 0-9, from low to high risk of hemorrhage under oral anticoagulation.

[c] Modified Rankin scale score, from 0 (no symptoms) to 6 (death).

[d] NIHSS, stroke related neurological deficits, from 0 (no symptoms) to 42.

[e] Before intracerebral hemorrhage functional status missing in two patients. Outcome at day 90 missing in one patient.

**eTable 3.** Hematoma Characteristics of Patients Receiving Prothrombin Complex Concentrate (PCC)

| | PCC administration (n = 35) | No PCC (n = 26) | *P* Value |
|---|---|---|---|
| Onset to baseline CT/MRI, median (IQR), hours | | | |
| Including cases with unknown onset[a] | 4.0 (1.4–10.9) | 6.1 (2.5–12.9) | .23 |
| Exact onset (n = 43) | 2.3 (1.4–5.9) | 3.3 (2.3–17.9) | .20 |
| Last intake NOAC, median (IQR), hours (only cases with exact time window, n = 29) | 8.2 (3.9–23.7) | 17.1 (12.1–22.7) | .07 |
| **Hematoma characteristics at baseline** | | | |
| Hematoma volume, ml | | | |
| Median (IQR) | 11.6 (5.6–29.7) | 8.1 (2.6–38.5) | .51 |
| Mean (SD) | 21.9 (25.7) | 26.0 (38.1) | |
| Intraventricular extension, No. (%) | 19 (54.3) | 8 (30.8) | .08 |
| Modified Graeb score, median (IQR)[b] | 9 (3 - 15 | 9 (5–14) | .89 |
| Location of hemorrhage, No. (%) | | | |
| Supratentorial | 30 (85.7) | 17 (65.4) | .07 |
| Infratentorial | 5 (14.3) | 9 (34.6) | |
| Deep | 18 (51.4) | 5 (19.2) | .07 |
| Lobar | 12 (34.3) | 13 (50.0) | |
| Cerebellar | 4 (11.4) | 6 (23.1) | |
| Brainstem | 1 (2.9) | 2 (7.7) | |
| **Hematoma characteristics at follow-up-imaging** | | | |
| | n = 28 | n =17 | |
| Time since baseline CT/MRI, median (IQR), hours | 19.2 (12.9–26.5) | 23.8 (12.5–33.6) | .36 |
| Hematoma volume, ml | | | |
| Median (IQR) | 14.8 (8.1–28.2) | 7.5 (2.6 -14.0) | .04 |
| Mean (SD) | 23.0 (24.8) | 14.3 (22.5) | |
| *Absolute and relative differences* | | | |
| Median (IQR) | 0.86 (-2.32–5.82) | 0.14 (-0.88–1.87) | |
| % volume change, median (IQR) | 15.6 (-13.3–109.3) | 8.1 (-5.1–61.2) | |
| Volume increase ≥ 33%, No. (%) | 11 (39.3) | 4 (23.5) | .34 |
| Volume increase ≥ 6 ml, No. (%) | 6 (21.4) | 1 (5.9) | .23 |
| Substantial hematoma expansion, No. (%)[c] | 12 (42.9) | 5 (29.4) | .53 |
| Intraventricular extension | | | |
| New intraventricular hemorrhage, No. (%) | 2 (7.1) | 1 (5.9) | >.99 |
| Modified Graeb score (change from baseline) (n=20) | | | |
| Absolute change of score, median (IQR) | 0 (-0.75–2.75) | -0.5 (-3.25–0) | .12 |
| Increase ≥ 2 pts, No. (%) | 5 (17.9) | 0 | .53 |

Abbreviations: CT, computer tomography; MRI, magnetic resonance imaging; NOAC, non vitamin-K antagonist oral anticoagulant; PCC, prothrombin complex concentrate.

[a] In case of unknown exact onset, last seen well was taken as onset.

[b] Modified Graeb score, from 0 (no intraventricular blood) to 32 (all compartments are filled with blood and expanded)

[c] Substantial hematoma expansion defined as volume increase ≥ 33% and/or 6 ml

**eTable 4.** Hematoma Characteristics and Mortality of Rivaroxaban Patients Only

| | Rivaroxaban patients (n = 49) | Expansion analysis group (n = 37) | No FU image (n = 12) | *P* Value |
|---|---|---|---|---|
| **Hematoma characteristics at baseline** | | | | |
| Hematoma volume, ml | | | | |
| Median (IQR) | 9.4 (3.6–21.4) | 8.9 (4.0–17.9) | 11.9 (2.9–38.7) | .59 |
| Mean (SD) | 18.4 (25.0) | 15.1 (16.9) | 28.7 (40.5) | |
| Intraventricular extension, No. (%) | 22 (44.9) | 18 (48.6) | 4 (33.3) | .51 |
| Modified Graeb score, median (IQR)[a] | 8.5 (4 – 14) | 7.5 (4 – 14) | 9 (5 -13) | .93 |
| PCC administration, No. (%) | 27 (55.1) | 22 (59.5) | 5 (41.7) | .33 |
| **Hematoma characteristics at follow-up-imaging** | | | | |
| Time since baseline CT/MRI, median (IQR), hours | | 20.3 (13.7–28.5) | | |
| Hematoma volume, ml | | | | |
| Median (IQR) | | 9.6 (5.2–19.6) | . | |
| Mean (SD) | | 18.7 (22.1) | | |
| *Absolute and relative differences* | | | | |
| Median (IQR) | | 0.5 (-1.6–4.7) | | |
| Mean (SD) | | 3.6 (11.7) | | |
| Range | | -7.8 – 54.1 | | |
| % volume change, median (IQR) | | 10.6 (-6.7–89.8) | | |
| Volume increase ≥ 33% | | 13 (35.1) | | |
| Volume increase ≥ 6 ml | | 5 (13.5) | | |
| Substantial hematoma expansion, No. (%)[b] | | 14 (37.8) | | |
| Intraventricular extension | | | | |
| New intraventricular hemorrhage, No. (%) | | 3 (6.1) | | |
| Modified Graeb score (change from baseline) (n=20) | | | | |
| Absolute change of score, median (IQR) | | 0 (-1–1) | | |
| Increase ≥ 2 pts, No. (%) | | 4 (8.2) | | |
| **Mortality** | | | | |
| Death during acute stay | 8 (16.3) | 4 (10.8) | 4 (33.3) | .09 |
| Death until follow-up[†] | 13 (27.1) | 9 (25.0) | 4 (33.3) | .71 |
| Death within 5 days | 5 (10.2) | 2 (5.4) | 3 (25.0) | .09 |

Abbreviations: CT, computer tomography; MRI, magnetic resonance imaging; PCC, prothrombin complex concentrate.

[a] Modified Graeb score, from 0 (no intraventricular blood) to 32 (all compartments are filled with blood and expanded)

[b] Substantial hematoma expansion defined as volume increase ≥ 33% and/or 6 ml

**eTable 5.** Factors Associated With an Unfavorable Outcome (mRS 3-6) at 3-Month Follow-up of Rivaroxaban Patients Only (Univariate Analysis)

| | OR (95% CI) | *P* value |
|---|---|---|
| Age ≥ 76 years | 3.70 (1.01–13.65) | .05 |
| Gender: female | 2.03 (0.56–7.31) | .28 |
| Coexisting condition | | |
| Previous ischemic stroke/ TIA | 2.27 (0.53–9.70) | .27 |
| Previous intracranial hemorrhage | 5.41 (0.55-728.0) | .17 |
| Hypertension | 1.72 (0.26–11.62) | .58 |
| Hyperlipidemia | 0.42 (0.12–1.50) | .42 |
| Diabetes mellitus | 0.75 (0.20–2.80) | .67 |
| Heart failure | 1.56 (0.28–8.62) | .61 |
| Peripheral vascular disease | 1.73 (0.18-17.05) | .64 |
| Renal function: GFR < 60 ml | 0.48 (0.13–1.84) | .29 |
| $CHA_2DS_2VASc$ score[a] | 1.34 (0.88–2.05) | .17 |
| HAS-BLED score[b] | 3.23 (1.15–9.31) | .03 |
| Modified Rankin scale score before stroke[c] | 1.69 (1.03–2.76) | .04 |
| Modified Rankin scale score at admission[c] | 3.44 (1.68–7.04) | .001 |
| NIHSS at admission[d] | 1.28 (1.08–1.51) | .005 |
| Baseline hematoma volume[e] | 3.24 (1.15–9.13) | .03 |
| Location: Supratentorial | 0.46 (0.09–2.48) | .37 |
| Location: Deep | 1.42 (0.39–5.14) | .59 |
| Substantial hematoma expansion | 0.74 (0.16–3.39) | .69 |
| PCC administration | 0.84 (0.24–2.96) | .79 |
| Intraventricular extension (baseline) | 8.57 (1.65–44.43) | .01 |

Abbreviations: TIA, transient ischemic attack; GFR, glomerular filtration rate (electronic GFR as reported by the centers); NIHSS, National Institutes of Health Stroke Scale.

[a] $CHA_2DS_2VASc$ score, range 0-9, from low to high risk of ischemic stroke in atrial fibrillation; *per increment.*

[b] HAS-BLED score, range 0-9, from low to high risk of hemorrhage under oral anticoagulation; *per increment.*

[c] Modified Rankin scale score, from 0 (no symptoms) to 6 (death); *per increment.*

[d] NIHSS, stroke related neurological deficits, from 0 (no symptoms) to 42; *per increment.*

[e] *Per log-transformed increment (ml)*

**eTable 6.** Summary of Past Studies on Intracerebral Hemorrhage Cited Within the Main Text

| | Non-OAC | | | | Mixed | | | | | OAC |
|---|---|---|---|---|---|---|---|---|---|---|
| Reference[a] | [52] | [51] | [3] | [44] | [6] | [45] | [50] | [46] | [4] | [7] |
| Year | 1996 | 1997 | 2006 | 2008 | 2004 | 2008 | 2008 | 2011 | 2013 | 2015 |
| Study Type | Retrospective analysis | Prospective observational | Pooled meta-analysis | RCT | Prospective cohort study | Retrospective cohort study | RCT substudy | Retrospective observational | Registry | Retrospective cohort study |
| N | 204 | 103 | 218 | 268 (placebo-arm) | 183 (70 expansion analysis) | 258 | 303 (285 expansion analysis) | 982 | 206 (152 expansion analysis) | 853 |
| Age, mean, years | 64 | 63 | 66 | 65 | 76 | 69 | NR (OAC: 75) | 69 | 74[b] | 74 |
| Women, % | 37.7% | 36.0% | 41.7% | 37.0% | NR | 54.3% | 33.9% | 46.2% | 47.6% | 37.9% |
| Oral Anticoagulation, No. (%)[c] | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 42 (23.0) | 51 (19.8) | 21 (6.9) | 182 (18.5) | 51 (24.8) | 853 (100) |
| Hematoma volume | | | | | | | | | | |
| Median (IQR) | NR | NR | NR | NR | NR | NR | Non-OAC: 14.4 (7.9-30.9) OAC: 30.6 (7.4-70.1) | NR | Non-OAC 14.3 (4.9-35.7) OAC: 20.0 (8.3-48.8) | 19.3 (6.9-52.8) |
| Mean (SD) | 20.1 (18.0) | 26 (29) | 25.3 (NR) | 22 (24) | NR | [d] | NR | Non-OAC: 29.6 (37.0) OAC: 47.8 (58.0) | Non-OAC: 26.4 (31.7) OAC: 31.5 (30.2) | NR |
| Hematoma Expansion | | | | | | | | | | |
| Predefined time frame analysed | 0–120 h | 0–20h | 24 h | 21–48 h | 0–7 d | - | 0–72 h | NR | 24–48 h | NR |
| Definition of significant expansion | > 12.5 ml or > 40% | ≥ 33% | > 33% | - | ≥ 33% | NR | ≥ 33% | NR | ≥ 6 ml or ≥ 33% | ≥ 33% |
| Proportion of patients with significant expansion | 19.6% | 38.0% | 31.6% | NR[e] | Non-OAC 23% OAC: 54% | NR | Non-OAC: 26% OAC: 56% | NR | non-OAC: 11.7% OAC: 12.5% | 36% |

Abbreviations: NR, not reported; RCT, randomized clinical trial; OAC, oral anticoagulation.
[a] References within the main document
[b] median
[c] Oral anticoagulation = treatment with vitamin K antagonists
[d] Non-OAC (International Normalized Ratio (INR) < 1.2) 13.4 ml, OAC INR 2.1-3.0 14.0 ml, OAC INR > 3.0 33.2 ml.
[e] Estimated mean volume increase 26%

**eAppendix.** Principal Investigators and Participating Hospitals Who Enrolled at Least 1 ICH Patient

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