

## **The prevalence of cardiac complications and their impact on outcomes in patients with non-traumatic subarachnoid hemorrhage.**

Maarit Lång, MD, Kuopio University Hospital, Department of Intensive Care Medicine, Finland

Stephan M Jakob, MD, PhD, Professor, Department of Intensive Care Medicine, Bern University Hospital, University of Bern, Bern, Switzerland

Riikka Takala MD, PhD, Associate Professor, Perioperative Services, Intensive Care Medicine and Pain Management, Turku University Hospital, Anaesthesiology, Intensive Care, Emergency Care and Pain Medicine, University of Turku, Finland

Magnus N Lyngbakken, MD, PhD, Associate Professor, Department of Cardiology, Division of Medicine, Akershus University Hospital, Lørenskog, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Anu Turpeinen, MD, PhD, Associate Professor, Kuopio University Hospital, Department of Cardiology, Finland

Torbjørn Omland, MD, PhD, Professor, Department of Cardiology, Division of Medicine, Akershus University Hospital, Lørenskog, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Tobias M Merz, MD \*, Department of Intensive Care Medicine, Bern University Hospital, University of Bern, Bern, Switzerland, \*Current affiliation: Cardiothoracic and Vascular Intensive Care Unit, Auckland City Hospital, Auckland, New Zealand

Jan Wiegand, MD <sup>+</sup>, Department of Intensive Care Medicine, Bern University Hospital, University of Bern, Bern, Switzerland, <sup>+</sup>Current affiliation: Intensive Care Unit, Lindenhofspital, Bern, Switzerland.

Juha Grönlund, MD PhD, Perioperative Services, Intensive Care Medicine and Pain Management, Turku University Hospital, Anaesthesiology, Intensive Care, Emergency Care and Pain Medicine, University of Turku, Finland

Melissa Rahi, MD, PhD, Neurocenter, Department of Neurosurgery, Turku University Hospital, Finland

Mika Valtonen, MD PhD, Associate Professor, Perioperative Services, Intensive Care Medicine and Pain Management, Turku University Hospital, Anaesthesiology, Intensive Care, Emergency Care and Pain Medicine, University of Turku, Finland

Timo Koivisto, MD, PhD, Associate Professor, Kuopio University Hospital, Department of Neurosurgery, Finland

Helge Røsjø, MD, PhD, Professor, Division for Research and Innovation, Akershus University Hospital, Lørenskog, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Stepani Bendel, MD, PhD, Associate Professor 1. Kuopio University Hospital, Department of Intensive

Correspondence:

Maarit Lång, MD

Kuopio University Hospital

PO BOX 100, 70029 KYS, Finland

E-mail: [maarit.lang@kuh.fi](mailto:maarit.lang@kuh.fi)

Key Words: subarachnoid haemorrhage, cardiac failure, cardiac dysfunction, Tnt, myocardial injury, outcome

| SUPPLEMENT TABLE 1. Baseline characteristics according to WFNS grading score for SAH |                     |                     |                     |                     |                     |             |
|--------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-------------|
|                                                                                      | WFNS 1              | WFNS 2              | WFNS 3              | WFNS 4              | WFNS 5              |             |
| N                                                                                    | 55                  | 53                  | 26                  | 42                  | 16                  | p for trend |
| Clinical characteristics                                                             |                     |                     |                     |                     |                     |             |
| Male sex, n (%)                                                                      | 29 (52.7%)          | 20 (37.7%)          | 10 (38.5%)          | 19 (45.2%)          | 7 (43.8%)           | 0.58        |
| Age, years                                                                           | 54.0 (42.0-63.0)    | 52.0 (47.0-59.0)    | 59.0 (48.0-65.0)    | 57.5 (50.0-65.0)    | 55.0 (45.5-63.0)    | 0.24        |
| Current smoking, n (%)                                                               | 20 (38.5%)          | 24 (47.1%)          | 12 (52.2%)          | 18 (47.4%)          | 4 (26.7%)           | 0.49        |
| Body mass index, kg/m <sup>2</sup>                                                   | 26.3 (23.8-28.7)    | 25.7 (23.1-28.7)    | 26.4 (22.9-29.9)    | 27.7 (24.5-29.4)    | 24.7 (23.7-27.7)    | 0.38        |
| Systolic blood pressure, mmHg                                                        | 138.5 (123.0-149.0) | 136.5 (128.0-150.0) | 138.0 (122.0-151.0) | 128.5 (118.0-146.0) | 134.0 (123.0-145.0) | 0.31        |
| Diastolic blood pressure, mmHg                                                       | 62.5 (54.0-71.0)    | 59.0 (52.0-66.0)    | 57.0 (48.0-65.0)    | 60.0 (51.0-65.0)    | 58.0 (54.5-70.5)    | 0.41        |
| Medical history                                                                      |                     |                     |                     |                     |                     |             |
| Hypertension, n (%)                                                                  | 15 (27.3%)          | 12 (22.6%)          | 9 (34.6%)           | 18 (42.9%)          | 2 (12.5%)           | 0.12        |
| Coronary artery disease, n (%)                                                       | 0 (0.0%)            | 2 (3.8%)            | 3 (11.5%)           | 4 (9.5%)            | 1 (6.3%)            | 0.06        |
| Hypercholesterolemia, n (%)                                                          | 4 (7.3%)            | 2 (3.8%)            | 1 (3.8%)            | 3 (7.1%)            | 1 (6.3%)            | 0.93        |
| Atrial fibrillation, n (%)                                                           | 0 (0.0%)            | 0 (0.0%)            | 1 (3.8%)            | 1 (2.4%)            | 0 (0.0%)            | 0.28        |
| Ischemic stroke, n (%)                                                               | 3 (5.5%)            | 2 (3.8%)            | 0 (0.0%)            | 1 (2.4%)            | 0 (0.0%)            | 0.88        |
| Diabetes mellitus, n (%)                                                             | 3 (5.5%)            | 4 (7.5%)            | 2 (7.7%)            | 3 (7.1%)            | 0 (0.0%)            | 0.92        |
| Chronic renal disease, n (%)                                                         | 1 (1.8%)            | 0 (0.0%)            | 0 (0.0%)            | 0 (0.0%)            | 1 (6.3%)            | 0.22        |
| Electrocardiography                                                                  |                     |                     |                     |                     |                     |             |
| Corrected QT time, ms                                                                | 428.0 (419.5-457.5) | 445.0 (416.0-475.0) | 447.0 (432.0-464.0) | 446.0 (428.0-495.0) | 467.5 (445.0-534.5) | 0.014       |

|                                           |                     |                    |                    |                   |                    |        |
|-------------------------------------------|---------------------|--------------------|--------------------|-------------------|--------------------|--------|
| Any rhythm disturbance, n (%)             | 11 (20.0%)          | 7 (13.2%)          | 3 (11.5%)          | 6 (14.3%)         | 0 (0.0%)           | 0.38   |
| Signs of ischemia, n (%)                  | 2 (4.5%)            | 3 (6.8%)           | 4 (17.4%)          | 5 (14.7%)         | 2 (16.7%)          | 0.24   |
| Any rhythm disturbance or ischemia, n (%) | 12 (21.8%)          | 9 (17.0%)          | 7 (26.9%)          | 10 (23.8%)        | 2 (12.5%)          | 0.75   |
| First degree AV block, n (%)              | 8 (15.7%)           | 8 (15.4%)          | 3 (11.5%)          | 13 (31.7%)        | 0 (0.0%)           | 0.05   |
| Echocardiography                          |                     |                    |                    |                   |                    |        |
| LV ejection fraction, %                   | 64.0 (58.0-70.0)    | 61.5 (55.0-70.0)   | 60.0 (57.0-67.0)   | 68.0 (60.0-72.0)  | 60.5 (54.0-73.0)   | 0.42   |
| E/A ratio                                 | 1.3 (1.0-1.7)       | 1.3 (1.1-1.7)      | 1.2 (1.0-1.6)      | 1.1 (0.9-1.5)     | 1.2 (1.0-1.5)      | 0.29   |
| e'                                        | 10.9 (9.0-13.6)     | 11.0 (9.0-12.0)    | 11.0 (9.0-13.0)    | 10.0 (7.0-12.0)   | 9.0 (7.9-10.3)     | 0.21   |
| E/e'                                      | 7.6 (6.0-8.8)       | 7.8 (6.6-9.0)      | 7.9 (7.0-8.2)      | 7.6 (6.3-9.1)     | 8.2 (6.2-8.5)      | 0.87   |
| TAPSE, mm                                 | 27.0 (25.0-30.0)    | 26.0 (23.0-29.0)   | 24.0 (21.0-27.0)   | 26.0 (20.1-29.5)  | 24.0 (21.0-26.0)   | 0.11   |
| Regional wall motion disturbance, n (%)   | 0 (0.0%)            | 2 (3.8%)           | 1 (3.8%)           | 3 (7.1%)          | 2 (12.5%)          | 0.10   |
| Radiography                               |                     |                    |                    |                   |                    |        |
| Pneumonia, n (%)                          | 1 (7.7%)            | 2 (8.3%)           | 1 (8.3%)           | 2 (8.7%)          | 2 (12,5%)          | 0.44   |
| Congestion, n (%)                         | 0 (0.0%)            | 0 (0.0%)           | 1 (8.3%)           | 0 (0.0%)          | 0 (0.0%)           |        |
| Clinical chemistry                        |                     |                    |                    |                   |                    |        |
| eGFR, ml/min/1.73m <sup>2</sup>           | 108.9 (102.7-116.3) | 109.3 (98.3-117.6) | 104.9 (95.5-110.6) | 99.3 (92.4-112.6) | 103.2 (86.1-111.0) | 0.13   |
| Epinephrine, nmol/L                       | 0.5 (0.3-0.7)       | 0.5 (0.3-0.8)      | 0.3 (0.1-0.6)      | 0.2 (0.1-0.4)     | 0.5 (0.3-0.7)      | 0.003  |
| Norepinephrine, nmol/L                    | 2.6 (1.7-3.8)       | 3.5 (2.3-7.4)      | 5.9 (3.2-9.2)      | 17.7 (3.8-45.3)   | 10.2 (2.6-33.8)    | <0.001 |
| Lactate, mmol/L                           | 1.2 (0.9-1.4)       | 1.2 (0.9-1.6)      | 1.4 (1.1-2.4)      | 1.8 (1.3-2.2)     | 1.8 (1.3-3.1)      | <0.001 |
| CRP, mg/L                                 | 4.0 (1.5-11.0)      | 7.0 (3.0-13.0)     | 20.0 (7.5-32.0)    | 15.0 (7.0-37.0)   | 28.0 (9.0-69.0)    | <0.001 |



| SUPPLEMENT TABLE 2. Predictive factors of decreased LVEF at 90 days |              |               |       |
|---------------------------------------------------------------------|--------------|---------------|-------|
| N=126                                                               | EF≤50%       | D90 EF>50%    | p     |
|                                                                     | n=22 (17.5%) | n=104 (82.5%) |       |
| Age, years                                                          | 53.1±10.0    | 54.4±13.2     | 0.64  |
| Gender, n (%)                                                       |              |               |       |
| Male                                                                | 9 (40.9%)    | 44 (42.3%)    | 0.90  |
| Female                                                              | 13 (59.1%)   | 60 (57.7%)    |       |
| BMI                                                                 | 26.3±4.7     | 26.7±4.6      | 0.72  |
| Aneurysm location, n (%)                                            | n=19         | n=103         |       |
| ICA                                                                 | 4 (21.1%)    | 21 (20.4%)    | 0.82  |
| MCA                                                                 | 5 (26.3%)    | 25 (24.3%)    |       |
| ACoA                                                                | 6 (31.5%)    | 34 (33.0%)    |       |
| ACA                                                                 | 0            | 7 (6.8%)      |       |
| VBA                                                                 | 4 (21.1%)    | 16 (15.5%)    |       |
| No aneurysm, n (%)                                                  | 3 (13.6%)    | 0             | <0.05 |
| Hunt Hess, n (%)                                                    | n=20         | n=92          |       |
| 1-2 (headache)                                                      | 9 (45.0%)    | 54 (58.7%)    | 0.37  |
| 3 (drowsy)                                                          | 4 (20.0%)    | 19 (20.7%)    |       |

|                               |           |            |      |
|-------------------------------|-----------|------------|------|
| 4-5 (stupor/coma)             | 7 (35.0%) | 19 (20.7%) |      |
| Fisher scale, n (%)           | n=21      | n=102      |      |
| 1 (No blood, thin)            | 5 (23.8%) | 18 (17.6%) | 0.80 |
| 2 (Clots)                     | 8 (38.1%) | 41 (40.2%) |      |
| 3 (Diffuse ICH, IVH)          | 8 (38.1%) | 43 (42.2%) |      |
| SDH, n (%)                    | 1 (4.5%)  | 4 (3.8%)   | 0.88 |
| ICH, n (%)                    | 3 (13.6%) | 21 (20.2%) | 0.56 |
| Hydrocephalus, n (%)          | 9 (40.9%) | 50 (48.1%) | 0.54 |
| IVH, n (%)                    | 5 (22.7%) | 28 (26.9%) | 0.68 |
| Cardiovascular disease, n (%) | 6 (27.3%) | 28 (26.9%) | 0.97 |
| Neurologic disease, n (%)     | 4 (18.2%) | 10 (9.8%)  | 0.26 |
| Pulmonary disease, n (%)      | 2 (9.1%)  | 11 (10.6%) | 0.84 |
| Diabetes, n (%)               | 2 (9.1%)  | 3 (2.9%)   | 0.18 |
| Chronic renal disease, n (%)  | 1 (4.5%)  | 1 (1.0%)   | 0.22 |
| Smoker, n(%)                  | 9 (40.9%) | 49 (47.1%) | 0.92 |
| Ex-smoker                     | 2 (9.1%)  | 10 (9.6%)  |      |

|                                                             |                     |                     |       |
|-------------------------------------------------------------|---------------------|---------------------|-------|
| No smoking                                                  | 10 (45.5%)          | 39 (37.5%)          |       |
| Drug abuse (alcohol, drugs), n (%)                          | 3 (13.6%)           | 7 (6.7%)            | 0.53  |
| ECG rhythm disturbances<br>at day 1, n (%)                  | 5 (22.7%)           | 16 (15.4%)          | 0.40  |
| ECG ischemia at day 1, n (%)                                | 4 (18.2%)           | 7 (6.7%)            | 0..08 |
| Tnt ng/L at day 1                                           | 9 [5-17]            | 7 [5-14]            | 0.60  |
| ProBNB ng/L at day 1                                        | 375.0 [156.5-985.0] | 406.0 [241.0-727.0] | 0.75  |
| Endogenous P-norepinephrine<br>concentration nmol/L at day1 | 1.44 [1.1-3.39]     | 2.66 [1.88-3.56]    | 0.23  |
| GCS at arrival, n (%)                                       | n=22                | n=101               |       |
| Good (9-15)                                                 | 18 (81.8%)          | 86 (85.1%)          | 0.70  |
| Bad (3-8)                                                   | 4 (18.2%)           | 15 (14.9%)          |       |
| Worst GCS during the first 24 hours, n (%)                  | n=22                | n=102               |       |
| Good (9-15)                                                 | 12 (57.1%)          | 83 (81.4%)          | 0.02  |
| Bad (3-8)                                                   | 10 (42.9%)          | 19 (18.6%)          |       |
| WFNS, n (%)                                                 |                     |                     |       |
| 1                                                           | 4 (18.2%)           | 31 (30.1%)          | 0.50  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |           |            |      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------|------|
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 8 (36.4%) | 35 (33.7%) |      |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 2 (9.1%)  | 16 (15.4%) |      |
| 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 6 (27.3%) | 15 (14.4%) |      |
| 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 2 (9.1%)  | 7 (6.7%)   |      |
| GOSE dependent, n (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 4 (19.0%) | 24 (25.3%) | 0.55 |
| mRS dependent, n (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 3 (15.0%) | 15 (16.9%) | 0.84 |
| SD=standard deviation and IQR= interquartile range. ICA: internal cerotic artery, MCA: middle cerebral artery, ACoA: anterior communicating artery, ACA: anterior cerebral artery, VBA: vertebrobasilar artery. SDH: subdural hematoma, ICH: intracerebral hematoma, IVH: intraventricular hematoma; ECG: electrocardiogram, Tnt; troponin_t, ProBNB: B-type N-terminal peptide, ECHO: cardiac ultrasound, GCS: Glasgow coma scale; WFNS; World Federation of Neurosurgical Societies |           |            |      |

| <b>SUPPLEMENT TABLE 3. Association of WFNS score and cTnT with poor neurological outcome</b>                                                                                                                                                                                                                                                                  |               |                     |                     |                      |             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|---------------------|---------------------|----------------------|-------------|
| Odds ratio (95% CI)                                                                                                                                                                                                                                                                                                                                           |               |                     |                     |                      |             |
|                                                                                                                                                                                                                                                                                                                                                               | WFNS - cTnT - | WFNS - cTnT +       | WFNS + cTnT -       | WFNS + cTnT +        | P for trend |
| Model 1                                                                                                                                                                                                                                                                                                                                                       | 1.00          | 1.75 (0.71 to 4.31) | 1.73 (0.63 to 4.77) | 6.33 (2.71 to 14.80) | <0.001      |
| Model 2                                                                                                                                                                                                                                                                                                                                                       | 1.00          | 1.16 (0.44 to 3.06) | 1.66 (0.59 to 4.70) | 5.08 (2.10 to 12.29) | <0.001      |
| Model 3                                                                                                                                                                                                                                                                                                                                                       | 1.00          | 0.86 (0.25 to 2.94) | 2.00 (0.58 to 6.95) | 4.45 (1.45 to 13.36) | 0.006       |
| WFNS -, < 3. WFNS +, ≥ 3. cTnT -, < 8 ng/L. cTnT +, ≥ 8 ng/L. Model 1, unadjusted. Model 2, adjusted for age and sex. Model 3, adjusted for model 2, systolic blood pressure, BMI, coronary artery disease, diabetes mellitus, current smoking, eGFR, and concentrations of norepinephrine. BMI, body mass index. eGFR, estimated glomerular filtration rate. |               |                     |                     |                      |             |

| <b>SUPPLEMENT TABLE 4. Association of WFNS score and NT-proBNP with poor neurological outcome</b>                                                                                                                                                                                                                             |                    |                     |                     |                     |             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|---------------------|---------------------|-------------|
| Odds ratio (95% CI)                                                                                                                                                                                                                                                                                                           |                    |                     |                     |                     |             |
|                                                                                                                                                                                                                                                                                                                               | WFNS - NT-proBNP - | WFNS - NT-proBNP +  | WFNS + NT-proBNP -  | WFNS + NT-proBNP +  | P for trend |
| Model 1                                                                                                                                                                                                                                                                                                                       | 1.00               | 1.26 (0.52 to 3.03) | 3.85 (1.48 to 9.98) | 3.19 (1.30 to 7.84) | 0.002       |
| Model 2                                                                                                                                                                                                                                                                                                                       | 1.00               | 0.86 (0.33 to 2.22) | 3.06 (1.13 to 8.27) | 2.66 (1.02 to 6.92) | 0.007       |
| Model 3                                                                                                                                                                                                                                                                                                                       | 1.00               | 0.59 (0.18 to 1.87) | 3.97 (1.20 to 13.2) | 1.49 (0.43 to 5.17) | 0.10        |
| WFNS -, < 3. WFNS +, ≥ 3. NT-proBNP -, NT-proBNP < 380 ng/L. NT-proBNP +, NT-proBNP ≥ 380 ng/L. Model 1, unadjusted. Model 2, adjusted for age and sex. Model 3, adjusted for model 2, systolic blood pressure, BMI, coronary artery disease, diabetes mellitus, current smoking, eGFR, and concentrations of norepinephrine. |                    |                     |                     |                     |             |