

# Poststroke Delirium Clinical Motor Subtypes: The PROspective Observational POLish Study (PROPOLIS)

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**Objective:** Although delirium is the most common neurobehavioral complication after stroke, its motor subtypes—hypoactive, hyperactive, mixed, and none—as well as their risk factors are not well characterized. Motor subtypes influence recognition and prognosis of delirium in hospitalized patients.

**Methods:** The aim of this prospective study was to assess the frequency of poststroke delirium subtypes and to describe their predictive models. Consecutive patients with stroke were screened for delirium with the Confusion Assessment Method for the Intensive Care Unit. Delirium was diagnosed according to DSM-5 criteria, and subtypes were classified with the Delirium Motor Subtype Scale-4. Baseline demographic characteristics, biochemistry, stroke-related data, medications, neurological deficits, and premorbid cognitive and functional impairments were assessed.

**Results:** Out of 750 patients (mean age, 71.75 years [SD = 13.13]), 203 (27.07%) had delirium: 85 (11.34%) were hypoactive, 77 (10.27%) were mixed hypoactive-hyperactive, 31 (4.13%) were hyperactive, and 10 (1.33%) had an unspecified type. Cognitive impairment at the time of hospital admission and spatial neglect, among other factors, were identified as the best predictors for all motor delirium subtypes.

**Conclusions:** Screening for poststroke delirium is important because the hypoactive subtype bears the worst prognosis and is misdiagnosed the most compared with other subtypes. All identified factors for the predictive models of delirium subtypes are routinely assessed during hospital admission. Their occurrence in patients with stroke should alert the treating physician to the high risk for a particular delirium subtype.

*J Neuropsychiatry Clin Neurosci* 2019; 31:104–111;  
doi: 10.1176/appi.neuropsych.18040073

Delirium is the most common neurobehavioral complication in acute hospital admissions of the elderly,<sup>1</sup> but it often goes unrecognized in clinical practice. It is characterized by disturbances in attention and awareness, changes in cognition that develop acutely, and a fluctuating course.<sup>2</sup> Because the presentation of delirium varies, clinical subtypes of delirium based on motor behavior and arousal disturbances have been distinguished: hyperactive, hypoactive, mixed, or neither type (nonmotor subtype).<sup>3</sup>

The hyperactive type is characterized by severe confusion and disorientation, motor agitation, restlessness, and wandering. The hypoactive type is characterized by motor retardation, withdrawal from interaction with the surrounding world, apathy, decreased speed of actions, and a decreased amount of speech. Mixed delirium includes both hyperactive and hypoactive symptoms. The nonmotor subtype is diagnosed if the patient only experiences cognitive symptoms of delirium.<sup>3</sup>

It is estimated that between one half and two thirds of delirium cases are undetected due to misdiagnosis, late detection, or in many cases a completely missed diagnosis.<sup>4</sup> Patients with the hypoactive profile with the absence of overt distress or disturbances are more likely to be

unrecognized compared with patients with the hyperactive subtype entailing overt behavioral disturbances that attract the attention of medical personnel.<sup>5</sup> Patients with the hyperactive or mixed type of delirium are usually misdiagnosed with functional psychosis, hypomania, anxiety disorders, or akathisia, while the hypoactive subtype is easily mistaken for depression or dementia.<sup>6</sup>

Stroke is a syndrome that often causes cognitive impairment and psychiatric disturbances. One of these is delirium, and its prevalence is estimated to be between 10% and 48%.<sup>7</sup> Although delirium after stroke is a very frequent complication, there is a paucity of studies assessing the subtypes of poststroke delirium and the risk factors for its development. Differentiating poststroke neurocognitive and behavioral complications from delirium is difficult and time-consuming. Patients with the hypoactive subtype of delirium may be easily missed because they are often perceived as cooperative and exhibit fewer behavioral problems than patients with the hyperactive type.<sup>5,8</sup> This is especially important because studies that performed detailed assessment of delirium subtypes showed that the hypoactive subtype is more common than the hyperactive subtype in a variety of clinical settings.<sup>9,10</sup>

**TABLE 1. Risk Factors Predicting Hyperactive Poststroke Delirium**

| Risk Factors  | Total<br>N | Hyperactive Delirium |       |       |       | No Delirium |       |       |       | Odds<br>Ratio | 95% CI     | p <sup>a</sup>   |
|---|------------|----------------------|-------|-------|-------|-------------|-------|-------|-------|---------------|------------|------------------|
|   |            | N                    | %     | Mean  | SD    | N           | %     | Mean  | SD    |               |            |                  |
| Age (years)   | 578        |                      |       | 77.19 | 11.87 |             |       | 69.81 | 13.42 | 1.05          | 1.02–1.09  | <b>0.003</b>     |
| Gender (male)   | 578        | 15/31                | 48.39 |       |       | 268/547     | 48.99 |       |       | 0.98          | 0.46–2.08  | 0.950            |
| National Institutes of<br>Health Stroke Scale                                   | 578        |                      |       | 9.61  | 5.99  |             |       | 6.87  | 6.83  | 1.05          | 1.00–1.10  | <b>0.032</b>     |
| Predementia   |            |                      |       |       |       |             |       |       |       |               |            |                  |
| Informant Questionnaire<br>on Cognitive<br>Decline in the<br>Elderly >88 points | 465        | 7/26                 | 26.92 |       |       | 49/439      | 11.16 |       |       | 2.93          | 1.17–7.35  | <b>0.022</b>     |
| Montreal Cognitive<br>Assessment score  | 436        |                      |       | 12.37 | 7.91  |             |       | 21.02 | 5.49  | 0.83          | 0.77–0.89  | <b>&lt;0.001</b> |
| Diabetes mellitus   | 577        | 14/31                | 45.16 |       |       | 132/546     | 24.18 |       |       | 2.58          | 1.24–5.39  | <b>0.011</b>     |
| Atrial fibrillation   | 577        | 14/31                | 45.16 |       |       | 104/546     | 19.05 |       |       | 3.5           | 1.67–7.34  | <b>&lt;0.001</b> |
| Percutaneous coronary<br>intervention or coronary<br>artery bypass grafting     | 577        | 7/31                 | 22.58 |       |       | 46/546      | 8.42  |       |       | 3.17          | 1.30–7.77  | <b>0.011</b>     |
| Modified Cumulative<br>Illness Rating Scale                                     |            |                      |       |       |       |             |       |       |       |               |            |                  |
| Total score   | 577        |                      |       | 11.19 | 4.81  |             |       | 8.80  | 4.89  | 1.09          | 1.02–1.17  | <b>0.009</b>     |
| Severity index  | 577        |                      |       | 0.82  | 0.35  |             |       | 0.64  | 0.36  | 3.39          | 1.35–8.52  | <b>0.009</b>     |
| Comorbidity index   | 577        |                      |       | 4.42  | 1.69  |             |       | 3.24  | 1.94  | 1.33          | 1.12–1.58  | <b>0.001</b>     |
| Medications   |            |                      |       |       |       |             |       |       |       |               |            |                  |
| Heparin   | 514        | 3/26                 | 11.54 |       |       | 15/488      | 3.07  |       |       | 4.11          | 1.11–15.27 | <b>0.034</b>     |
| Pneumonia at hospital<br>admission  | 578        | 5/31                 | 16.13 |       |       | 31/547      | 5.67  |       |       | 3.20          | 1.48–8.93  | <b>0.026</b>     |
| Pneumonia during<br>hospitalization   | 578        | 5/31                 | 16.13 |       |       | 21/547      | 3.84  |       |       | 4.82          | 1.68–13.82 | <b>0.003</b>     |
| Urinary tract infection at<br>hospital admission                                | 561        | 13/29                | 44.83 |       |       | 122/532     | 22.93 |       |       | 2.73          | 1.28–5.84  | <b>0.010</b>     |
| Spatial neglect   | 578        | 6/31                 | 19.35 |       |       | 32/547      | 5.85  |       |       | 3.86          | 1.48–10.11 | <b>0.006</b>     |
| Vision disorders  | 578        | 19/31                | 61.29 |       |       | 153/547     | 27.97 |       |       | 4.08          | 1.93–8.61  | <b>&lt;0.001</b> |
| Laboratory data   |            |                      |       |       |       |             |       |       |       |               |            |                  |
| WBC count (day 1)   | 563        |                      |       | 10.03 | 3.49  |             |       | 8.39  | 2.91  | 1.16          | 1.05–1.28  | <b>0.004</b>     |
| Urine leukocyte (day 1)   | 555        | 17/29                | 58.62 |       |       | 180/526     | 34.22 |       |       | 2.72          | 1.27–5.84  | <b>0.010</b>     |
| Nitrate in urine (day 1)  | 556        | 6/29                 | 20.69 |       |       | 42/527      | 7.97  |       |       | 3.01          | 1.16–7.82  | <b>0.023</b>     |
| Urine bacteremia (day 1)  | 544        | 26/29                | 89.66 |       |       | 255/515     | 49.51 |       |       | 8.84          | 2.63–29.64 | <b>&lt;0.001</b> |
| Anxiety   | 461        | 12/26                | 46.15 |       |       | 104/435     | 23.91 |       |       | 2.73          | 1.22–6.10  | <b>0.014</b>     |
| Motoric disorders   | 461        | 5/26                 | 19.23 |       |       | 31/435      | 7.13  |       |       | 3.10          | 1.09–8.82  | <b>0.033</b>     |

<sup>a</sup> Statistical significance is indicated in bold.

Delirium subtypes impact prognosis and are considered to be relevant to detection, etiology, and phenomenology.<sup>6,11,12</sup> While some data show that the hypoactive subtype has a worse prognosis in both short-<sup>13</sup> and long-term perspectives,<sup>14</sup> not all studies confirmed these observations.<sup>12,15</sup> So far, the frequency of poststroke delirium subtypes and their precipitating factors have not been investigated in a large cohort of stroke patients.

The advanced knowledge of who is at risk for developing this common poststroke complication can improve recognition, change treatment, and improve the prognosis of delirium.

Therefore, the aim of the PROspective Observational POLish Study on poststroke delirium (PROPOLIS) was to assess the frequency of delirium motor subtypes in the Polish stroke population within 7 days of a hospital stay. Another aim was to build predictive models for delirium

subtypes in order to better identify patients at risk for developing these serious complications.

## METHODS

The 750 consecutive patients with stroke (ischemic or hemorrhagic) or transient ischemic attack admitted to the Stroke Unit at the University Hospital in Krakow who met inclusion criteria for this study were investigated for the presence and risk factors of delirium. Stroke was defined according to the criteria of the U.S National Institute of Neurological Disorders and Stroke.<sup>16</sup> All patients were treated according to the standard protocols of international guidelines.<sup>17</sup>

Inclusion and exclusion criteria for this study are described in detail elsewhere.<sup>18</sup> Briefly, exclusion criteria were <18 years of age, hospital admission more than 48 hours from the first stroke symptoms, subarachnoid hemorrhage, cerebral

**TABLE 2. Predictive Model for Poststroke Hyperactive Delirium**

| Variable                            | Total   |       |       |      | Delirium |       |       |      | No Delirium |       |       |      | Odds Ratio | 95% CI     | p <sup>a</sup> |
|-------------------------------------|---------|-------|-------|------|----------|-------|-------|------|-------------|-------|-------|------|------------|------------|----------------|
|                                     | N       | %     | Mean  | SD   | N        | %     | Mean  | SD   | N           | %     | Mean  | SD   |            |            |                |
| Montreal Cognitive Assessment score |         |       | 20.64 | 5.88 |          |       | 12.37 | 7.91 |             |       | 21.02 | 5.49 | 0.83       | 0.76–0.91  | <0.001         |
| Diabetes mellitus                   | 146/577 | 25.30 |       |      | 14/31    | 45.16 |       |      | 132/546     | 24.18 |       |      | 5.91       | 1.79–19.50 | 0.004          |
| Neglect                             | 38/578  | 6.57  |       |      | 6/31     | 19.35 |       |      | 32/547      | 5.85  |       |      | 4.59       | 1.19–17.75 | 0.027          |
| Urine bacteremia (day 1)            | 281/544 | 51.65 |       |      | 26/29    | 89.66 |       |      | 255/515     | 49.51 |       |      | 5.19       | 1.08–25.03 | 0.040          |

<sup>a</sup> All values meet statistical significance.

venous thrombosis, cerebral vasculitis, trauma, coma, brain tumor, delirium due to alcohol withdrawal, and diseases with a life expectancy <1 year.

Patients were screened for delirium every day, starting from hospital admission until the 7th day of hospital stay. Screening was performed at the same time (3–6 p.m.) of every day by a neurologist. An abbreviated version of the Confusion Assessment Method (bCAM) was used for the delirium screening; the Confusion Assessment Method—Intensive Care Units (CAM-ICU) was used for those with speech output problems.<sup>19,20</sup> Delirium Motor Subtype Scale 4 was completed for assessment of motor subtype presentation, where delirium was categorized as hyperactive, hypoactive, mixed, or nonmotor subtype.<sup>21</sup>

To screen for possible delirious symptoms during all 24 hours, a short questionnaire regarding patient's behavior and cognitive fluctuations was completed by ward nurses for each patient.

Diagnosis of delirium was concluded by clinical observation and structural assessment. Delirium was diagnosed according to the DSM-5 criteria.<sup>22</sup>

To screen for prestroke dementia, a Polish version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) was used.<sup>23</sup> Cognitive and behavioral and emotional functioning were also screened by the psychologist during the hospital stay. The Montreal Cognitive Assessment (MoCA),<sup>24</sup> Frontal Assessment Battery,<sup>25</sup> and Cognitive Test for Delirium<sup>2</sup> were used between days 1 and 2 and on the 7th day after hospital admission. On admission, information was obtained from the spouse or caregiver regarding prestroke behavioral functioning on the Neuropsychiatric Inventory.<sup>26</sup>

Data were collected regarding sociodemographic factors, comorbidity (hypertension, diabetes mellitus, atrial fibrillation, myocardial infarct, percutaneous coronary intervention, coronary artery bypass grafting, respiratory system disorders, gastrointestinal complications, liver and renal dysfunctions, genitourinary problems, past neurological history, musculoskeletal dysfunctions, and endocrine problems), and smoking (current, ex-smoker, never smoked). The Cumulative Illness Rating Scale, a valid and reliable method of measuring prestroke comorbidity, was used as the general indicator of health status.<sup>27</sup>

Medications taken were evaluated and grouped according to their pharmacological family. Auditory and visual impairment, stroke-related factors, laboratory test results, pneumonia, and urinary tract infection during hospitalization were recorded.

At the time of hospital admission, all patients had neuroimaging (CT/MRI). Ischemic stroke etiology was classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria.<sup>28</sup> The severity of the clinical deficit was graded using the National Institutes of Health Stroke Scale (NIHSS)<sup>29</sup> at the time of hospital admission. Motor functions prior to admission were assessed using the modified Rankin Scale.

This study was approved by the medical ethical committee at the Jagiellonian University. Informed consent was given by the patient after the procedures were fully explained. If the patient was unable to fully understand the procedures, the caregiver was asked for informed assent; then, when the patient's condition improved, he or she was asked to provide informed consent.

## Statistics

All of the statistical analyses were performed using STATISTICA for Windows version 12 (StatSoft, Tulsa, Okla.). First, associations between types of delirium and predisposing factors were found. Odds ratios with p values were obtained using univariate logistic regression to identify variables significantly associated with delirium, which were subsequently entered into the multivariable logistic regression analysis. The final predictive model for each delirium type was fitted using forward stepwise selection method. The goodness of fit was determined by the chi-square test. The value of alpha=0.05 was considered as a threshold for statistical significance.

## RESULTS

The 750 patients with a mean age of 71.75 years (SD=13.13) were included in the study (women, N=398, mean age=74.72 years [SD=13.20]; men, N=352, mean age=68.40 years [SD=12.23]). Six hundred fifty patients had ischemic stroke, 52 had hemorrhagic stroke, and 48 had a transient ischemic attack. The National Institutes of Health Stroke

**TABLE 3. Risk Factors Predicting Hypoactive Poststroke Delirium**

| Risk Factors                | Total<br>N | Hyperactive Delirium |       |       |       | No Delirium |       |       |       | Odds<br>Ratio | 95 % CI    | p <sup>a</sup> |
|-----------------------------|------------|----------------------|-------|-------|-------|-------------|-------|-------|-------|---------------|------------|----------------|
|                             |            | N                    | %     | Mean  | SD    | N           | %     | Mean  | SD    |               |            |                |
| Gender (male)               | 632        | 23/85                | 27.06 |       |       | 268/547     | 48.99 |       |       | 0.39          | 0.23–0.64  | <0.001         |
| Age (years)                 | 632        |                      |       | 77.13 | 10.34 |             |       | 69.81 | 13.42 | 1.05          | 1.03–1.07  | <0.001         |
| Premodified Rankin scale    | 631        |                      |       | 1.44  | 1.72  |             |       | 0.52  | 1.55  | 1.52          | 1.32–1.75  | <0.001         |
| NIHSS                       | 632        |                      |       | 14.13 | 6.79  |             |       | 6.87  | 6.83  | 1.13          | 1.10–1.17  | <0.001         |
| Localization of stroke      |            |                      |       |       |       |             |       |       |       |               |            |                |
| Left versus right           | 550        | 33/79                | 41.77 |       |       | 273/471     | 57.96 |       |       | 0.52          | 0.32–0.84  | 0.008          |
| hemispheric stroke          |            |                      |       |       |       |             |       |       |       |               |            |                |
| Hemorrhagic versus          | 591        | 10/83                | 12.05 |       |       | 28/508      | 5.51  |       |       | 2.35          | 1.09–5.04  | 0.029          |
| ischemic stroke             |            |                      |       |       |       |             |       |       |       |               |            |                |
| Education (years)           | 557        |                      |       | 10.25 | 3.02  |             |       | 11.66 | 3.67  | 0.87          | 0.80–0.95  | 0.002          |
| Predementia                 |            |                      |       |       |       |             |       |       |       |               |            |                |
| Informant Questionnaire     | 512        | 20/73                | 27.40 |       |       | 49/439      | 11.16 |       |       | 3.00          | 1.66–5.45  | <0.001         |
| on Cognitive                |            |                      |       |       |       |             |       |       |       |               |            |                |
| Decline in the              |            |                      |       |       |       |             |       |       |       |               |            |                |
| Elderly >88 points          |            |                      |       |       |       |             |       |       |       |               |            |                |
| Montreal Cognitive          | 453        |                      |       | 11.28 | 5.79  |             |       | 21.02 | 5.49  | 0.79          | 0.75–0.84  | <0.001         |
| Assessment score            |            |                      |       |       |       |             |       |       |       |               |            |                |
| Atrial fibrillation         | 630        | 33/84                | 39.29 |       |       | 104/546     | 19.05 |       |       | 2.75          | 1.69–4.48  | <0.001         |
| Smoker ever                 | 610        | 24/79                | 30.38 |       |       | 252/531     | 47.46 |       |       | 0.48          | 0.29–0.80  | 0.005          |
| Modified Cumulative Illness |            |                      |       |       |       |             |       |       |       |               |            |                |
| Rating Scale                |            |                      |       |       |       |             |       |       |       |               |            |                |
| Total score                 | 629        |                      |       | 10.88 | 4.74  |             |       | 8.80  | 4.89  | 1.09          | 1.04–1.3   | <0.001         |
| Severity index              | 629        |                      |       | 0.79  | 0.36  |             |       | 0.64  | 0.36  | 2.86          | 1.55–5.26  | 0.001          |
| Comorbidity index           | 629        |                      |       | 4.11  | 1.79  |             |       | 3.24  | 1.94  | 1.25          | 1.11–1.40  | <0.001         |
| Medications                 |            |                      |       |       |       |             |       |       |       |               |            |                |
| Anticoagulants              | 561        | 12/73                | 16.44 |       |       | 34/488      | 6.97  |       |       | 2.63          | 1.29–5.35  | 0.008          |
| Insulin                     | 560        | 12/72                | 16.67 |       |       | 33/488      | 6.76  |       |       | 2.76          | 1.35–5.64  | 0.006          |
| Beta blockers               | 558        | 36/70                | 51.43 |       |       | 177/488     | 36.27 |       |       | 1.86          | 1.12–3.08  | 0.016          |
| Pneumonia at admission      | 632        | 15/85                | 17.65 |       |       | 31/547      | 5.67  |       |       | 3.57          | 1.83–6.95  | <0.001         |
| Pneumonia during            | 632        | 12/85                | 14.12 |       |       | 21/547      | 3.84  |       |       | 4.12          | 1.94–8.73  | <0.001         |
| hospitalization             |            |                      |       |       |       |             |       |       |       |               |            |                |
| Urinary tract infection at  | 613        | 41/81                | 50.62 |       |       | 122/532     | 22.93 |       |       | 3.44          | 2.13–5.73  | <0.001         |
| admission                   |            |                      |       |       |       |             |       |       |       |               |            |                |
| Aphasia                     | 632        | 39/85                | 45.88 |       |       | 166/547     | 30.35 |       |       | 1.95          | 1.22–4.00  | 0.005          |
| Spatial neglect             | 632        | 29/85                | 34.12 |       |       | 32/547      | 5.85  |       |       | 8.33          | 4.69–14.80 | <0.001         |
| Vision disorders            | 632        | 67/85                | 78.82 |       |       | 153/547     | 27.97 |       |       | 9.59          | 5.51–16.60 | <0.001         |
| Laboratory data             |            |                      |       |       |       |             |       |       |       |               |            |                |
| White blood count on        | 457        |                      |       | 9.48  | 3.57  |             |       | 8.30  | 3.27  | 1.09          | 1.02–1.17  | 0.016          |
| admission                   |            |                      |       |       |       |             |       |       |       |               |            |                |
| Glucose level on            | 558        |                      |       | 8.25  | 4.23  |             |       | 7.30  | 2.75  | 1.09          | 1.02–1.16  | 0.016          |
| admission                   |            |                      |       |       |       |             |       |       |       |               |            |                |
| White blood count           | 616        |                      |       | 11.71 | 4.53  |             |       | 8.39  | 2.91  | 1.28          | 1.19–1.36  | <0.001         |
| during hospitalization      |            |                      |       |       |       |             |       |       |       |               |            |                |
| Urine-leukocyte count       | 607        | 48/81                | 59.26 |       |       | 180/526     | 34.22 |       |       | 2.80          | 1.73–4.52  | <0.001         |
| (first day)                 |            |                      |       |       |       |             |       |       |       |               |            |                |
| Urine-nitrate count (first  | 608        | 12/81                | 14.81 |       |       | 42/527      | 7.97  |       |       | 2.01          | 1.01–4.01  | 0.048          |
| day)                        |            |                      |       |       |       |             |       |       |       |               |            |                |
| Urine-bacteremia (first     | 594        | 61/79                | 77.22 |       |       | 255/515     | 49.51 |       |       | 3.46          | 1.98–6.02  | <0.001         |
| day)                        |            |                      |       |       |       |             |       |       |       |               |            |                |
| Temperature <sup>b</sup>    | 632        |                      |       | 37.39 | 0.66  |             |       | 37.06 | 0.68  | 1.88          | 1.38–2.57  | <0.001         |
| Depression                  | 508        | 22/73                | 30.14 |       |       | 82/435      | 18.85 |       |       | 1.86          | 1.06–3.24  | 0.029          |
| Sleep disorders             | 508        | 31/73                | 42.47 |       |       | 132/435     | 30.34 |       |       | 1.69          | 1.02–2.82  | 0.042          |

<sup>a</sup> All values meet statistical significance.<sup>b</sup> The highest body temperature for each patient between day 1 and day 3 of the hospital stay (mean for all group).

Scale score for the entire cohort was 8.52 [SD=7.31] (ischemic stroke, 8.85 [SD=7.23], hemorrhagic stroke, 11.15 [SD=7.35], and transient ischemic attack, 1.17 [SD=2.19]).

Out of 203 patients with delirium (women, N=119 [29.90%]; men, N=84 [23.86%]), hyperactive type was identified in

31 (15.27%), hypoactive in 85 (41.87%), mixed type in 77 (39.93%), and unspecified in 10 (4.93%). The group of patients with delirium was characterized elsewhere.<sup>30</sup> The demographic and clinical characteristics of patients with delirium subtypes are presented in Tables 1–3.

**TABLE 4. Predictive Model for Poststroke Hypoactive Delirium**

| Risk Factors                        | Total   |       |       |      | Hypoactive Delirium |       |       |      | No Delirium |       |       |      | Odds Ratio | 95% CI     | p <sup>a</sup> |
|-------------------------------------|---------|-------|-------|------|---------------------|-------|-------|------|-------------|-------|-------|------|------------|------------|----------------|
|                                     | N       | %     | Mean  | SD   | N                   | %     | Mean  | SD   | N           | %     | Mean  | SD   |            |            |                |
| Montreal Cognitive Assessment score |         |       | 20.25 | 6.11 |                     |       | 11.28 | 5.79 |             |       | 21.02 | 5.49 | 0.78       | 0.71–0.85  | <0.001         |
| Vision disorders                    | 220/632 | 34.81 |       |      | 67/85               | 78.82 |       |      | 153/547     | 27.97 |       |      | 6.49       | 2.02–20.85 | 0.002          |
| WBC count during hospitalization    |         |       | 8.84  | 3.37 |                     |       | 11.71 | 4.53 |             |       | 8.39  | 2.91 | 1.22       | 1.07–1.39  | 0.003          |
| Anticoagulants                      | 46/561  | 8.20  |       |      | 12/73               | 16.44 |       |      | 34/488      | 6.97  |       |      | 7.28       | 1.61–32.98 | 0.010          |
| Neglect                             | 61/632  | 9.65  |       |      | 29/85               | 34.12 |       |      | 32/547      | 5.85  |       |      | 4.09       | 1.14–14.65 | 0.031          |

<sup>a</sup> All values meet statistical significance.

A number of predisposing factors for hyperactive delirium were identified in univariate analysis (Table 1.).

Multivariable logistic regression analysis based on the results of univariate logistic regression was performed. For the hyperactive delirium constellation of MoCA score, urine bacteremia, diabetes mellitus, and spatial neglect allowed us to achieve the best predictive model (Table 2).

Univariate analysis identified predisposing factors for hypoactive delirium (Table 3).

Multivariable logistic regression analysis based on the results of univariate logistic regression was performed. In the predictive model for the hypoactive type of delirium MoCA score, the presence of vision disorders, WBC count during hospitalization, anticoagulant therapy, and spatial neglect syndrome were identified as the best predictors of this type of delirium (Table 4).

Predisposing factors for mixed type of delirium were identified by univariate analysis (Table 5.).

Multivariable logistic regression analysis based on the results of univariate logistic regression was performed. For mixed type of delirium MoCA score, spatial neglect, atrial fibrillation, and comorbidity index allowed us to achieve the best predictive model (Table 6).

## DISCUSSION

This study demonstrated the highest prevalence of hypoactive delirium subtype among stroke patients, followed by a mixed type that was almost as common as the hypoactive type, whereas the easily detectable hyperactive variant was nearly three times less common.

This is in line with two previous studies assessing poststroke delirium subtypes, Ojagberni et al.<sup>31</sup> and Kozak et al.,<sup>32</sup> where the hypoactive form of poststroke delirium was also the prevalent type. However, its prevalence was much higher than in our study (65.6% and 72.7%, respectively, versus 41.8%). Both previous studies were small, the delirium prevalence was discrepant (33% versus 18%, respectively), and risk factors for delirium subtypes were not analyzed. The prevalence of delirium in our study (27.07%) was in the midrange of both studies and the number of included patients was much higher, which makes our results

more reliable. It is also noteworthy to mention that our study identified mixed-type delirium in 39.9% of all delirium cases, suggesting that changes in the psychomotor activity of patients with stroke are frequent and signs of mental or motor hyper- and hypoactivity often coexist.

Delirium is a multifactorial acute condition that usually involves a predisposing factor and one or more acute superimposed conditions that directly precipitate delirium.<sup>33</sup> Different theories have been proposed in an attempt to explain the processes leading to the development of poststroke delirium. Most of these theories are complementary rather than competing. Current theories explain delirium development by the interaction of hypoxia, inflammatory processes, disturbance of neurotransmitters, neuroendocrine dysregulation, and the presence of internal or external risk factors,<sup>34</sup> all of which can affect the integrity of functional brain networks in patients with delirium.

This study aimed to identify the risk factors for different delirium subtypes and to build a predictive model for each poststroke delirium subtype. We found that the MoCA score on the first day of the hospital stay as well as spatial neglect were found to be the predicting factors in all delirium subtypes.

Cognitive decline is a well-known risk factor for delirium.<sup>7</sup> In our cohort, prestroke cognitive decline and MoCA scores were identified as risk factors for all subtypes of delirium, but the MoCA score on the first day of hospitalization had a better predictive value in the final predictive models. The MoCA is an objective, direct tool for estimating general cognitive functioning, whereas IQCODE relies on the caregiver's subjective assessment. Although patients with prestroke dementia score worse on MoCA, stroke can lower cognitive reserve in some patients classified as free of prestroke dementia on admission by the application of IQCODE.

We decided to use MoCA for cognitive screening in the poststroke cohort because vascular cognitive impairment is different than that seen in neurodegenerative conditions. A more commonly used cognitive screening tool, the Mini-Mental State Examination, was designed to detect Alzheimer's disease, which is primarily a disorder of memory. People with vascular impairment have more executive

**TABLE 5. Risk Factors Predicting Mixed Poststroke Delirium**

| Risk Factors  | Total<br>N | Mixed Delirium |       |       |       | No Delirium |       |       |       | Odds<br>Ratio | 95% CI     | p <sup>a</sup>   |
|---|------------|----------------|-------|-------|-------|-------------|-------|-------|-------|---------------|------------|------------------|
|   |            | N              | %     | Mean  | SD    | N           | %     | Mean  | SD    |               |            |                  |
| Age (years)   | 624        |                |       | 77.96 | 10.16 |             |       | 69.81 | 13.42 | 1.06          | 1.04–1.08  | <b>&lt;0.001</b> |
| Gender (male)   | 624        | 41/77          | 53.25 |       |       | 268/547     | 48.99 |       |       | 1.19          | 0.73–1.92  | 0.486            |
| National Institutes of<br>Health Stroke Scale                                   | 624        |                |       | 13.69 | 6.36  |             |       | 6.87  | 6.83  | 1.13          | 1.09–1.16  | <b>&lt;0.001</b> |
| Premodified Rankin scale  | 624        |                |       | 1.49  | 1.77  |             |       | 0.52  | 1.16  | 1.54          | 1.33–1.78  | <b>&lt;0.001</b> |
| Stroke localization   |            |                |       |       |       |             |       |       |       |               |            |                  |
| Cerebellum stroke<br>versus hemispheric/<br>brainstem                           | 622        | 1/76           | 1.32  |       |       | 65/546      | 11.9  |       |       | 0.10          | 0.01–0.72  | <b>0.023</b>     |
| Hemorrhagic versus<br>ischemic stroke   | 583        | 11/75          | 14.67 |       |       | 28/508      | 5.51  |       |       | 2.95          | 1.40–6.21  | <b>0.005</b>     |
| Education (years)   | 556        |                |       | 10.56 | 3.20  |             |       | 11.66 | 3.37  | 0.90          | 0.83–0.98  | <b>0.015</b>     |
| Predementia   |            |                |       |       |       |             |       |       |       |               |            |                  |
| Informant Questionnaire<br>on Cognitive<br>Decline in the<br>Elderly >88 points | 502        | 24/63          | 38.10 |       |       | 49/439      | 11.16 |       |       | 4.90          | 2.27–8.84  | <b>&lt;0.001</b> |
| Montreal Cognitive<br>Assessment Score  | 446        |                |       | 10.52 | 6.33  |             |       | 21.02 | 5.49  | 0.79          | 0.73–0.84  | <b>&lt;0.001</b> |
| Hypertension  | 623        | 46/77          | 59.74 |       |       | 388/546     | 71.06 |       |       | 0.60          | 0.37–0.99  | <b>0.045</b>     |
| Atrial fibrillation   | 623        | 27/77          | 35.06 |       |       | 104/546     | 19.05 |       |       | 2.30          | 1.37–3.84  | <b>0.002</b>     |
| Modified Cumulative Illness<br>Rating Scale                                     |            |                |       |       |       |             |       |       |       |               |            |                  |
| Total score   | 623        |                |       | 11.03 | 4.56  |             |       | 8.80  | 4.89  | 1.09          | 1.04–1.44  | <b>&lt;0.001</b> |
| Severity index  | 623        |                |       | 0.78  | 0.35  |             |       | 0.64  | 0.36  | 2.59          | 1.37–4.88  | <b>0.003</b>     |
| Comorbidity index   | 623        |                |       | 4.30  | 1.81  |             |       | 3.24  | 1.94  | 1.31          | 1.16–1.47  | <b>&lt;0.001</b> |
| Medications   |            |                |       |       |       |             |       |       |       |               |            |                  |
| Diuretics   | 552        | 22/64          | 34.38 |       |       | 103/488     | 21.11 |       |       | 1.96          | 1.12–3.43  | <b>0.019</b>     |
| Anticholinergic drugs   | 553        |                |       | 0.48  | 1.06  |             |       | 0.25  | 0.69  | 1.36          | 1.04–1.78  | <b>0.023</b>     |
| Pneumonia at admission  | 624        | 19/77          | 24.68 |       |       | 31/547      | 5.67  |       |       | 5.45          | 2.89–10.2) | <b>&lt;0.001</b> |
| Urinary tract infection at<br>admission   | 604        | 30/72          | 41.67 |       |       | 122/532     | 22.93 |       |       | 2.40          | 1.44–4.00  | <b>0.001</b>     |
| Aphasia   | 624        | 35/77          | 45.45 |       |       | 166/547     | 30.35 |       |       | 1.91          | 1.78–3.11  | <b>0.001</b>     |
| Neglect   | 624        | 24/77          | 31.17 |       |       | 32/547      | 5.85  |       |       | 7.29          | 3.99–13.3  | <b>&lt;0.001</b> |
| Vision disorders  | 624        | 53/77          | 68.83 |       |       | 153/547     | 27.97 |       |       | 5.69          | 3.39–9.55  | <b>&lt;0.001</b> |
| Laboratory data   |            |                |       |       |       |             |       |       |       |               |            |                  |
| WBC count on<br>admission   | 454        |                |       | 9.32  | 3.34  |             |       | 8.30  | 3.27  | 1.08          | 1.00–1.16  | <b>0.037</b>     |
| WBC count (day 1)   | 608        |                |       | 9.72  | 3.67  |             |       | 8.39  | 2.91  | 1.13          | 1.06–1.22  | <b>0.001</b>     |
| Potassium (day 1)   | 621        |                |       | 4.19  | 0.61  |             |       | 4.34  | 0.43  | 0.46          | 0.26–0.80  | <b>0.007</b>     |
| Urine leukocyte count<br>(day 1)  | 597        | 35/71          | 49.30 |       |       | 180/526     | 34.22 |       |       | 1.87          | 1.13–3.08  | <b>0.014</b>     |
| Urine nitrate count (day<br>1)  | 598        | 12/71          | 16.90 |       |       | 42/527      | 7.97  |       |       | 2.35          | 1.17–4.72  | <b>0.017</b>     |
| Urine bacteremia (day 1)  | 585        | 50/70          | 71.43 |       |       | 255/515     | 49.51 |       |       | 2.55          | 1.47–4.41  | <b>0.001</b>     |
| Temperature <sup>b</sup>  | 624        |                |       | 37.43 | 0.70  |             |       | 37.06 | 0.68  | 1.99          | 1.45–2.74  | <b>&lt;0.001</b> |
| Delusion  | 498        | 9/63           | 14.29 |       |       | 27/435      | 6.21  |       |       | 2.52          | 1.22–5.65  | <b>0.025</b>     |
| Apathy  | 498        | 23/63          | 36.51 |       |       | 60/435      | 13.79 |       |       | 3.59          | 2.01–6.43  | <b>&lt;0.001</b> |
| Disinhibition   | 498        | 10/63          | 15.87 |       |       | 19/435      | 4.37  |       |       | 4.13          | 1.82–9.37  | <b>0.001</b>     |
| Anxiety   | 498        | 24/63          | 38.10 |       |       | 104/435     | 23.91 |       |       | 1.96          | 1.12–3.41  | <b>0.018</b>     |
| Sleep   | 498        | 27/63          | 42.86 |       |       | 132/435     | 30.34 |       |       | 1.72          | 1.00–2.96  | <b>0.049</b>     |

<sup>a</sup> Statistical significance is indicated in bold.<sup>b</sup> The highest body temperature for each patient between day 1 and day 3 of the hospital stay (mean for all group).

dysfunction; therefore, this tool might be less sensitive in the poststroke population. Our study showed that MoCA better identifies patients at risk for delirium among poststroke survivors than prestroke IQCODE assessment does.

Different studies on poststroke delirium suggest that any visual disturbances may increase the risk of delirium: poor vision prestroke,<sup>35</sup> hemianopsia,<sup>36</sup> and neglect.<sup>37</sup> Differentiating between different types of visual impairment (for example, between spatial neglect and hemianopsia) may be



**TABLE 6. Predictive Model for Poststroke Mixed Delirium**

| Risk Factors                        | Total   |       |       |      | Mixed Delirium |       |       |      | No Delirium |       |       |      | Odds Ratio | 95 % CI    | p <sup>a</sup> |
|-------------------------------------|---------|-------|-------|------|----------------|-------|-------|------|-------------|-------|-------|------|------------|------------|----------------|
|                                     | N       | %     | Mean  | SD   | N              | %     | Mean  | SD   | N           | %     | Mean  | SD   |            |            |                |
| Montreal Cognitive Assessment score |         |       | 20.34 | 6.12 |                |       | 10.52 | 6.33 |             |       | 21.02 | 5.49 | 0.78       | 0.71–0.85  | <0.001         |
| Spatial Neglect                     | 56/624  | 8.97  |       |      | 24/77          | 31.17 |       |      | 32/547      | 5.85  |       |      | 12.18      | 3.82–38.86 | <0.001         |
| Atrial fibrillation                 | 131/623 | 21.03 |       |      | 27/77          | 35.06 |       |      | 104/546     | 19.05 |       |      | 3.54       | 1.27–9.86  | 0.016          |
| Comorbidity index                   |         |       | 3.37  | 1.95 |                |       | 4.30  | 1.81 |             |       | 3.23  | 1.93 | 1.32       | 1.00–1.75  | 0.048          |

<sup>a</sup> All values meet statistical significance.

challenging, especially among patients in confused states or with cognitive impairment. Therefore, it seems important to remember that any visual deficit increases the likelihood of occurrence for all the delirium subtypes in poststroke patients.

Additionally, we identified urine bacteremia and WBC count during hospitalization as a risk for the hyper- and hypoactive types of delirium, respectively, in the final predictive model. Infections were identified as an important cause of delirium in the elderly patient population<sup>38</sup> and a risk factor for poststroke delirium.<sup>39</sup> Additionally, comorbid disorders increase the risk of poststroke delirium.<sup>40</sup> In our predictive models, the best predictive values for the hyperactive and mixed subtypes of delirium had diabetes and atrial fibrillation with the comorbidity index, respectively.

Our study showed that some risk factors for each delirium subtype predict the development of delirium better than others. All identified risk factors in the final predictive models for delirium subtypes are easily assessed or obtained in routine clinical practice.

The present study is the first one to identify risk factors for different subtypes of poststroke delirium. Recognizing different subtypes of delirium is crucial for reducing the potential for underestimation of such variations with the associated inaccuracy in subtype attribution. We used DSM-5 diagnostic criteria for delirium. The DSM-5 criteria changed the way delirium is regarded: the term is now more restrictively defined in terms of cognitive features. Therefore, every patient with stroke had a repeated screening of cognitive functioning every day. From the first day of hospital admission, careful attention was given to discriminate cognitive dysfunction due to dementia and delirium.

The strength of our study is our large number of consecutive patients with stroke and a very careful assessment of the range of potential risk factors, including cognitive and neuropsychiatric factors. Diagnosis of delirium is often difficult; many cases may be missed, especially in stroke patients, due to prevalent language disorders, neglect, mood disturbances, and cognitive impairment that can be confused with delirium, thus making proper assessment impossible. Only a systematic assessment and longitudinal observation by medical personnel can give reliable answers to questions regarding disturbances of patients' awareness. In our study, structural

assessment was conducted every day, and the final diagnosis was based on a daily observational chart provided by the medical personnel for every patient.

For delirium screening, we used bCAM for verbal patients and CAM-ICU for patients who could not speak but who were able to communicate nonverbally. Both methods have high sensitivity and specificity and are easy to administer. The same assessor administered the scale from day 1 to day 7, thus making bias of interobserver variation minimal.<sup>14,15</sup>

Age is a risk factor for poststroke delirium; therefore, the prevalence of delirium may be affected by age inclusion criteria and the number of young patients included in the study. This study included patients of a wide age range, but the mean age of the cohort was high and similar to other studies. Therefore, we do not think that age inclusion criteria could have caused a bias.

The incidence of poststroke delirium in our sample might be underestimated due to the restricted 7-day observation period. This is the average duration of a hospital stay in Krakow's stroke unit. Therefore, those with delayed onset delirium might have been missed.

In conclusion, the PROPOLIS showed that the hyperactive form of poststroke delirium is the rarest type. The best factors predicting different subtypes of delirium are easily assessed in everyday practice, and their co-occurrence in patients with stroke should alert a treating physician to a high risk for their prevalence and severe poststroke complications. The identification of risk factors with the best predictive value will help identify patients at risk of developing a particular delirium subtype during their hospital stay. Our results may also encourage new prevention studies for this frequent and serious poststroke complication.

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Supported by the Leading National Research Centre.

The authors thank Malgorzata Mazurek for assistance with this article.

The authors report no financial relationships with commercial interests.

Received April 5, 2018; revision received June 3, 2018; accepted June 12, 2018; published online Nov. 8, 2018.

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