Post-stroke Depression in the Very Elderly Rate and Predictive Factors

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Abstract

Background: Post-stroke depression (PSD) affects 25–32% stroke survivors. PSD is quality-of-life altering and negatively impacts stroke recovery and mortality. Stroke incidence increases exponentially with age, especially >65 years, but no studies have yet specifically evaluated PSD in older stroke survivors. Because the very elderly are more prone to developing depression, we hypothesized a relatively high PSD rate for them.

Methods: Consecutive stroke patients ≥75 years old, admitted to an acute stroke unit, were screened for depression with the Montgomery-Åsberg Depression Rating Scale or Aphasic Depression Rating Scale for aphasic patients, ≥15 days to 1-year post-stroke. Potential factors predictive of PSD were assessed.

Results: Among 441 consecutive stroke patients, only 78 (17%) patients were evaluated because of high mortality and exclusion criteria. Among them, 44.8% (35/78) developed PSD: 22/78 (28.2%) mild and 11/78 (14.1%) moderate. Multivariate analysis retained only ≥1 mRS-point gain as being independently associated with PSD (OR, 6.2 (95% CI, 1.3–29.2), *P*=0.020).

Conclusion: Our results confirmed the expected high PSD rate in patients ≥75 years, and suggest that PSD should be sought systematically or prophylactic antidepressants prescribed >15 days post-stroke for patients with ≥1 mRS-point gain.

Background

Strokes represent the second leading cause of death worldwide, with 6.5 million deaths annually.[1] Stroke incidence of increases with age, especially > 75 years. Post-stroke depression (PSD) is survivors' most common psychiatric complication, with first symptoms usually appearing shortly after the acute event.[2] Long-term, PSD (affecting 29% (25–32%)[2] is associated with lower and slower neurological recovery, and higher mortality.[3] No study has focused specifically on PSD in geriatric patients, those most at-risk for stroke. Moreover, the very elderly are more prone to developing depression.[4] Because many stroke victims are aged, we hypothesized more older survivors would have PSD, making it a major clinical issue.

This study was undertaken to evaluate PSD frequency in stroke survivors ≥ 75 years and to identify their PSD-associated factors.

Methods

This noninterventional, monocenter stroke-unit study was approved by our hospital Ethics Committee (April 2019, N° 456–2019). All consecutive ischemic or hemorrhagic stroke patients (01/09/18–01/09/19), ≥ 75 years old, managed during the acute phase in our unit were recruited. Other inclusion criteria were: evaluated > 15 days and ≤1-year post-stroke onset, no/mild aphasia: Language Screening Test (LAST)[5] score ≥ 10; no severe dementia: Mini Mental State Examination (MMSE) score ≥ 15; and patient/guardian provided informed oral consent. Exclusion criteria were: severe disability precluding

participation at the outpatient clinic; moderate/severe aphasia (LAST score < 10); severe dementia (MMSE score < 15); non-French speaker; refused participation or inability to provide informed consent.

Non-aphasic patients (LAST score = 15) were screened for depression using the Montgomery-Åsberg Depression Rating scale (MADRS), assessing the 9 Diagnostic and Statistical Manual of Mental Disorders depression-symptom criteria.[6] MADRS is used commonly in clinical practice, for all ages,[7] and can also evaluate depression-symptom intensity. It is rapid (~15 minutes), making it highly advantageous for elderly stroke patients. The 10 MADRS items, each graded 0–6, yield a maximal total score of 60, with none (0–6), mild (7–19), moderate (20–34) or severe (> 34) defining depression intensity.

The 9-item Aphasic Depression Rating Scale (ADRS; maximal score = 32) was used for mildly aphasic patients (LAST score = 10–14),[8] with ≥ 9 defining depression but no intensity-defining threshold. The same psychiatrist (E.S.) interviewed all patients.

Data Collected in the post-stroke depression (PSD) Study

Sociodemographic Characteristics

Socioeconomic level (according to the 10-level classification of the Institut National des Statistiques et des Etudes Economiques), living conditions (alone, within a family, assisted by caregiver or paid helper), residence (home, institution).

Geriatric Factors

Multi-comorbidities (≥ 3 chronic diseases), polypharmacy (≥ 5 drugs/d), denutrition (serum albumin < 30 g/l).

Clinical Neurovascular Factors

National Institute of Health Stroke Scale (NIHSS) score for neurological severity at admission or after a recanalization procedure; Language Screening Test score (LAST) score for aphasia detection and assessment[5]; Mini-Mental State Examination (MMSE) score to detect and evaluate cognitive impairment; modified Rankin Scale (mRS) score for functional independence, before and after stroke, with mRS score > 2 defining dependence. We also categorized patients according to their transition from independence (mRS≤2) to dependence (mRS > 2), or a ≥ 1 mRS-point gain post-stroke.

Neuroradiological Factors

Pathological stroke type (infarct/intracerebral hemorrhage); stroke volume (minor/moderate/major on a visual scale); stroke location (right or left hemisphere/posterior fossa); Fazekas (leukoaraiosis) scale on neuroimaging (grade 1–3);

psychiatric and addictology factors: history of depression and antidepressant treatment during the 6 months preceding stroke; antidepressant treatment post-stroke; any-type addiction pre-stroke; “Cut-down, Annoyed, Guilty, Eye-opener” (CAGE) test, a self-reporting questionnaire to detect chronic alcoholism.

Therapeutic Factors

Recanalization procedure(s) (intravenous thrombolysis, mechanical thrombectomy) done or not.

Statistical Analysis

Comparisons used Student’s *t*-test for quantitative variables and Pearson’s χ^2 test for qualitative variables, with a bilateral 5% alpha risk and 10% beta risk. Univariate analyses used a logistic-regression model to identify associations between the different explanatory variables (qualitative and quantitative) and the dependent variable PSD. Only explanatory parameters achieving $P < 0.25$ in univariate analyses were included in the multivariate logistic analysis, whose significance threshold was set at $P < 0.05$. To avoid incorporating factors likely to bias multivariate analysis findings because of multi-colinearity, parameters selected by the univariate analyses were tested for colinearity before being entered into the model.

Results

Among the 451 eligible patients, only 78 (17.3%) were included; 266 of the 373 excluded had died (n = 95), were severely demented (n = 87), moderately/severely aphasic (n = 84) or severely disabled and unable to participate (n = 62); 25 patients could not be contacted despite multiple attempts; and 20 refused participation.

The 78 participants’ mean age of 82.5 ± 4.6 years (male/female ratio = 0.90) was younger than those excluded (84.4 ± 6.2 years; $P = 0.03$; comparable sex ratio = 0.88). Multi-comorbidities (60.3%), polypharmacy (68%) and denutrition (42/70 = 60%) characterized them.

Participants were evaluated during their hospitalization for acute stroke (6/78), in an outpatient clinic (52/78) or a rehabilitation center (20/78). Ischemic (71/78) or hemorrhagic (7/78) strokes affected the right (36/78) or left hemisphere (34/78), or posterior fossa (8/78). Stroke volume of was minor (51/78), moderate (24/78) or major (3/78). Fazekas (leukoaraiosis) score was 0/1 (46/78) or 2/3 (32/78). Twenty-one (26,9%) underwent recanalization procedure(s).

Among the 69/78 patients functionally independent (modified Rankin scale score (mRS)≤2) pre-stroke, 23 became dependent (mRS > 2) post-stroke; 46 remained independent; 40 gained ≥ 1 mRS points, including 18 retaining in the same functional category post-stroke. Other characteristics are detailed in the Table 1 and in *additional Table S1.*

Table 1
Characteristics of the 78 Post-Stroke Patients

	Mean ± SD	Range	Median
Age (y)	82.5 ± 4.6	75–94	82.0
NIHSS	2.25 ± 2.9	0–13	1.0
Time to evaluation post-stroke onset (d)	126 ± 86	15–321	105.0
Mini-Mental State Examination	25.6 ± 3.3	16–30	26.0
LAST	14.7 ± 0.9	10–15	15
MADRS (n = 72)	8.8 ± 8.7	0–30	5
Aphasic Depression Rating Scale (n = 7)	9.5 ± 5.9	1–18	10
CAGE	0.24 ± 0.5	0–2	0
Pre- to post-stroke mRS change	1.03 ± 1.3	0–4.0	1.0

NIHSS: National Institute of Health Stroke Scale; LAST: Language Screening Test; MADRS: Montgomery–Åsberg Depression-Rating Scale; CAGE: Cut-down, Annoyed, Guilty, Eye-opener; mRS: modified Rankin Scale.

Based on MADRS (n = 72/78) and ADRS (n = 6/78) evaluations, the PSD rate was 44.8% (n = 35/78). MADRS detected 32 PSDs and ADRS 3. PSD severity, assessed for 32/35, was mild (21) or moderate (11). Mean stroke-to-evaluation interval was 126 ± 86 days, with 34 (44%) assessed before 3 months, 44 (56%) thereafter, yielding respective PSD rates of 41% and 48% ($P = 0.37$). Ten patients took selective serotonin-reuptake inhibitors (SSRIs) for “depression” in the 6 months preceding stroke.

Table 2 reports PSD-associated factors identified by univariate analyses. Because all factors concerning functional dependence post-stroke demonstrated colinearity, only “≥1 mRS-point gain” (univariate analysis PSD association $P = 0.0001$) was included in the multivariate analysis. That factor encompasses mRS change and independence-to-dependence transition, while providing more subtle notions (eg the loss of only minor functional independence) and maintaining the same independence/dependence category; it was also the only one retained by multivariate analysis as being independently and significantly PSD-associated. The close outcome–PSD relationship is clearly illustrated by patients’ depression diagnoses: 17/23 (73.4%) who became dependent post-stroke, and 25/40 (62.5%) with ≥ 1 mRS-point gain.

Table 2
Post-Stroke Depression-Associated Factors

Univariate analyses	**OR**	**95% CI**	***P* Value**
Sex	1.7	0.68–4.20	0.26
Age, y	1.0	0.91–1.11	0.92
Residence (home, institution, hospital)	4.30	0.43–43.35	0.26
Antidepressant treatment			
Pre-stroke	0.10	0.01–0.906	0.04
Post-stroke	0.10	0.01–0.906	0.08
LAST score (10–15)	3.59	0.84–15.44	0.086
Stroke volume (minor, moderate, major)	0.29	0.84–4.23	0.07
Fazekas score (0–3)	1.29	0.82–2.04	0.28
NIHSS score (0–41)	1.14	0.97–1.34	0.12
Dependence (mRS > 2)			
Pre-stroke	0.35	0.07–1.82	0.214
Post-stroke*	2.92	1.12–7.66	0.029
Pre- to post-stroke mRS change*	2.19	1.38–3.47	0.001
Independence (mRS≤2)-to-functional dependence transition*	7.6	2.38–24.29	0.001
mRS-point gain			
≥1*	6.21	2.23–17.30	0.0001
≥2*	5.91	1.84–18.95	0.003
Multivariate analysis			
≥ 1 mRS-point gain	6.20	1.3–29.2	0.020

*Univariate-selected factors tested for colinearity before multivariate analysis. LAST: Language Screening Test; NIHSS: National Institute of Health Stroke Scale; mRS: modified Rankin Scale.

Discussion

Our very elderly stroke population's overall PSD rate, assessed a mean of ~4 months post-stroke, reached 44.8%, with no significant difference for those evaluated before or 3 months post-event. Our PSD patients' MADRS-assessed depression intensity was moderate/severe for 39%. Stroke-attributable ≥ 1 mRS-point gain was the only independent PSD predictor.

Study-population neurological parameters (relatively small parenchymal lesion volume, mean admission NIHSS = 2.25, mean mRS = 1.8 post-stroke) highlighted relatively low overall stroke severity, keeping in mind that patients with communication impairment or severe disability were excluded, which represents an important limitation.

However, our results reflect real-world stroke in the very elderly, as < 20% can be assessed for PSD after the acute phase. Nonetheless, considering post-stroke functional disability as the main PSD predictor, we think our results probably underestimate the real PSD rate. Indeed, PSD was common after minor strokes, but its cumulative rate was lower than for all-type–stroke survivors.[9]

Despite diverse screening methods used to detect PSD, a meta-analysis showed a relatively constant ~30% PSD rate, regardless of the time-to-assessment until 10 years.[2] Those patients' mean age was 65–71 years, ~15 younger than our specifically geriatric PSD population. The relatively high PSD rate in very old stroke survivors might be explained by the elderly's overall high vulnerability to depression, and their relatively low capacity for mental readjustment to their new acute stroke-generated state.[4] Also, their relatively short life expectancy and low probability of returning to their pre-stroke state can contribute to frequent loss of morale. Depression prevalences for the elderly in the general population are 4.4% (75–84 years) and 5% (≥ 85 years) ;[10] its risk is multiplied by ~10 for aged stroke victims.

PSD impact on our patients' quality of life (QOL) is difficult to evaluate and represents another limitation. However, even a mild mood disorder has been shown to negatively affect stroke survivors' long-term QOL,[2,9] meaning clinical detection of even a mild morale dip could improve their QOL.

What do our results bring to clinical practice? The recent large, randomized FOCUS, AFFINITY and EFFECTS trials did not confirm the initially positive effect of fluoxetine, an SSRI, on stroke recovery.[11–13] Although their results clearly demonstrated fluoxetine efficacy against PSD, it was unfortunately offset by the doubled bone-fracture risk. [11–13] Therefore, post-stroke patients at-risk of PSD must be identified instead of systematically prescribed preventive antidepressants. Our observations suggest that a ≥ 1 mRS-point gain after the stroke's acute phase, regardless of the final functional grade, can identify very elderly patients at high risk of developing PSD, for whom depression screening or even preventive antidepressant therapy could be justified.

Declarations

Ethics approval and consent to participate **:**

The name of the Ethics Committee is : “Unité de Recherche Clinique”, Centre Hospitalier Sud-Francilien (40 avenue Serge Dassault, 91106 Corbeil-Essonnes, France); the agreement of the study methods was registered under the number 456-2019 (April 2019).

The consent to participate was only oral, because very elderly stroke patients were frequently unable to write or even sign. The ethics committee was informed and approved this procedure. All participants or their guardians provided informed oral consent; the 20 patients (or guardians) who refused to give oral consent were excluded.

Authors' contributions :

All authors contributed to the development of the methodology and the writing of the article

All authors have read and approved the manuscript for publication

Availability of data and material :

All data generated or analysed during this study are included in this published article and its supplementary information files (additional table 1).

Competing interests **:** no

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