ARTYKUŁ ORYGINALY / ORIGINAL PAPER
Otrzymano/Submitted: 07.06.2022 • Zaakceptowano/Accepted: 11.06.2022

© Akademia Medycyny

Depressive disorder in old age: an early report of a 6-month prospective study

Zaburzenia depresyjne wieku podeszłego – 6-miesięczne badania prospektywne

Leszek Bidzan[1], Shan Ali[2], Tomasz Piasecki[1], Monika Bidzan-Wiącek[3], Jakub Grabowski[1]

[1] Department of Developmental, Psychotic and Geriatric Psychiatry, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland

[2] Neurology Department, Mayo Clinic, Jacksonville, FL 32224, USA

[3] Division of Bioenergetics and Physiology of Exercise, Faculty of Health Sciences with the Institute of Maritime and Tropical Medicine, Medical University of Gdańsk, Gdańsk, Poland

Abstract

Introduction. During a 6-month observation, we assessed the course of depressive episode in a group of outpatients (aged 60 and above). We sought to determine the prognostic value of cognitive functioning and comorbidities. ***Method.*** 72 patients were diagnosed with a depressive episode. Clinical assessment was based on four validated scales. After 6 months, the diagnosis of depressive episode was re-verified. All patients were treated pharmacologically. Data underwent the chi-squared test. ***Results.*** The study was completed by 60 patients. Depressive disorder symptoms persisted in 31 patients (52%) after 6 months of treatment. Significant differences (related to a greater severity of depressive symptoms, worse cognitive functioning and comorbidity) were found between patients who did not respond to antidepressant drugs and those who achieved remission. ***Conclusions.*** Our study confirms a worse prognosis of depressive disorders in elderly patients. Moreover, cognitive dysfunctions and chronic somatic diseases negatively affected the prognosis in depressive patients. *Geriatria 2022;16:69-74. doi: 10.53139/G.20221611*

Keywords: cognitive functioning, depression, elderly depression, prognosis, comorbidity

Streszczenie

Wstęp. W badaniach oceniono przebieg epizodu depresyjnego w trakcie 6-miesięcznej obserwacji w grupie leczonych ambulatoryjnie osób w wieku 60 lat i powyżej. Oceniono znaczenie rokownicze szeregu czynników klinicznych, w tym zwłaszcza poziomu funkcjonowania poznawczego oraz współchorobowości. ***Metoda.*** Do badań włączono 72 osoby, u których w oparciu o kryteria DSM V rozpoznano epizod depresyjny, zarówno pierwszorazowy jak i w przebiegu zaburzeń depresyjnych nawracających. Oceny klinicznej dokonano w oparciu o skale: MADRS, MMSE, HAMA oraz CIRS. Osoby, które w badaniu skalą MMSE uzyskały poniżej 24 pkt lub w badaniu skalą HAMA powyżej 17 pkt zostały wykluczone z badania. Po 6 miesiącach dokonano ponownej weryfikacji rozpoznania epizodu depresyjnego. Wszyscy badani byli poddani leczeniu farmakologicznemu przeciwdepresyjnemu. ***Wyniki.*** Ocenę końcową przeprowadzono u 60 osób, które włączono do analizy statystycznej. W 6 miesiącu obserwacji depresję rozpoznano nadal u 31 badanych. Osoby, u których nie uzyskano efektu terapeutycznego różniły się w badaniu wyjściowym istotnie od pozostałych znajdujących się w chwili zakończenia badania w stanie remisji objawów. Różnice dotyczyły większego nasilenia objawów depresyjnych, gorszego funkcjonowania poznawczego oraz większego nasilenia współchorobowości. ***Wnioski.*** Przeprowadzone badania potwierdzają gorsze rokowanie w zaburzeniach depresyjnych wieku podeszłego. Jednocześnie wyraźnie wskazują na znaczenie towarzyszących depresjom dysfunkcjom poznawczym oraz przewlekłym schorzeniom somatycznym, które powinny być uwzględnianie w rokowaniu. *Geriatria 2022;16:69-74. doi: 10.53139/G.20221611*

Słowa kluczowe: funkcjonowanie poznawcze, depresja wieku podeszłego, rokowanie, współchorobowość

Introduction

Depressive disorders in old age have a diverse pathogenetic basis [1]. What distinguishes them from depression in younger patients is the frequent coexistence of somatic diseases and the deterioration of cognitive functions that accompany mood disorders [2,3]. In the elderly population, key symptoms of major depressive disorder (MDD) may be obscured by somatic complaints (regardless of their nature), anxiety or cognitive decline. This makes the diagnosis of depression more complicated. Cognitive decline is often accompanied by a depressed mood. Additionally, it is particularly difficult to assess the incidence and determine the severity of depressive disorders since cognitive deterioration is a process shared between dementia and MDD.

It has been established that the prognosis of depressive disorders in the elderly is worse than in the young [4]. MDD in old age is often characterized by a chronic course and a high risk of relapse [5-7]. So far, the severity of depressive disorders, later age of onset, cognitive impairment and comorbidity have been identified as factors of significant prognostic importance [8,9]. However, research results still vary considerably from study to study. The reason for this inconsistency may be due to the frequent use of a stipulated criteria rather than a formal diagnostic criterion consistent with a standardized disorder classification system [10,11].

In our study, we sought to test the current hypothesis with a prospective 6-month study based on validated and a standardized diagnostic criterion. We examined the clinical and sociodemographic factors that may influence the course of depressive disorders in people over 60 years of age in the outpatient setting.

Methods

The study was approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdansk [NKBBN/323/2017]. Due to ethical considerations, refusal to participate in the study was possible at any time and patients were not contacted outside of the mental health clinic.

Inclusion criteria

Patients who reported to the mental health clinic from January to May 2018, were considered for this study. Only those patients who underwent a full period of observation (6 months from baseline) were included in the analysis. Patients were qualified based on the following criteria: voluntary consent for participation in the study, age 60 or higher, diagnosis of MDD according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition criteria (DSM-V) [12], severity of depressive symptoms assessed according to the Montgomery-Åsberg Depression Rating Scale (MADRS) [13] 18 points and above and the possibility of using citalopram as a first-line treatment for the current depressive episode.

Exclusion criteria

We excluded subjects if: the current depressive disorder persisted for more than 6 months; previous pharmacological treatment was used due to depressive disorders in the last year; the Hamilton Anxiety Rating Scale (HAM-A) score [14] was above 17 points; the Mini Mental State Examination (MMSE) score [15] was below 24; dementia was diagnosed regardless of the etiology. The presence of one of the following diseases at initial examination or in medical history also excluded patients: bipolar disorder, schizophrenia, alcohol and other psychoactive substance dependency (nicotine and caffeine use was allowed), prolonged QTc interval on electrocardiogram (with QTcF>450ms on screening or any subsequent visit), epilepsy, Parkinson's disease and mental retardation. Patients experiencing consciousness impairment, musculoskeletal disorders or had significant sight and hearing problems were also not included in the study.

Clinical assessment

A full examination was carried out in all included subjects with the collection of basic sociodemographic data, physical examination, assessment of vital signs and laboratory tests (blood count, total cholesterol, triglycerides, HDL, LDL, glucose, ALAT, ASPAT). The mental state of patients included in the study was assessed with MADRS, HAM-A and MMSE, while results of the latter were recalculated in accordance with the algorithm of Mungas et al. (1996) [16]. In addition, the presence of coexisting somatic diseases was assessed using the Modified Cumulative Illness Rating Scale (CIRS) [17].

A clinical assessment of mental state and a physical examination were performed on monthly routine consultations. In patients whose clinical condition raised doubts as to the appropriateness of further diagnosis of MDD, MADRS was administered. Patients who did not meet the criteria for a depressive episode according

to DSM-V and had a score of MADRS lower than 15 points, were recognized as achieving significant clinical improvement while the remaining subjects were qualified as not presenting a therapeutic response. All tests were performed by a team of certified psychiatrists experienced in performing each of the methods used.

The study was based on the observation of patients treated in a mental health outpatient clinic and did not alter our routine psychiatric practice. The only differences were the implementation of clinical scales, mentioned before.

Pharmacological treatment

In the analyzed group, all subjects received citalopram (in various generic forms available on the market) as the first drug. The dosing protocol was based on an initial administration of 20 mg and was increased to 40 mg after 14 days, with some regimen deviations dependent on the patient's weight or adverse effects. In the absence of improvement over a period of 6 to 10 weeks, the drug was changed to another selective serotonin reuptake inhibitor. If this was still not effective it was changed to substances of different neurophysiological activity.

Statistical analysis

Results were collected on Microsoft Excel 2010 (Microsoft, Redmond, Washington, USA). Statistical analysis was performed on Statistica 12.0 (StatSoft Inc., Dell Software). A P value ≤0.05 was considered significant. The hypothesis was tested for two means with the chi-squared test. A test for two independent means was used and two-sided confidence interval was applied. The equal variance hypothesis was verified by a test for two variances.

Results

72 people were included in the study, of which 60 completed the six-month observation period. The most common reason for withdrawal was the loss of contact with patients since they did not attend the designated control examination in the clinic (N = 9). The mean age was 72.05, the mean year of onset of MDD was 67.80 and the mean duration since the last depressive episode was 4.75 years. Duration of current episode

Table I. Comparison of subjects with remission and no remission of symptoms during the 6-month follow-up

	No remission (mean) N = 31	Remission (mean) N = 29	t	df	p	No remission SD	Remission SD	F-ratio	p (variances)
Age*	74.19	69.76	3.30	58.00	0.00	6.62	3.04	4.73	0.00
Number of episodes	1.87	2.17	-1.07	58.00	0.29	1.15	1.04	1.22	0.60
Years since first MDD episode	5.65	2.76	1.86	58.00	0.07	7.78	3.20	5.90	0.00
Age of MDD onset	68.48	67.07	0.64	58.00	0.52	8.71	8.27	1.11	0.79
Months of current episode at baseline	2.52	2.07	1.24	58.00	0.22	1.46	1.33	1.19	0.64
Months to achieve improvement		1.90		27.00			0.94	0.00	1.00
MADRS-0*	25.84	21.83	2.75	58.00	0.01	7.13	3.42	4.34	0.00
MADRS-6*	25.45	10.55	7.68	58.00	0.00	9.29	4.95	3.52	0.00
MMSE-0*	25.39	26.24	-3.13	58.00	0.00	1.12	0.99	1.28	0.52
HAMA-0*	15.26	12.52	2.23	58.00	0.03	3.76	5.62	2.24	0.03
CIRS-0*	19.48	18.21	1.92	58.00	0.06	2.90	2.18	1.77	0.13

Abbreviations: MDD – Major Depressive Disorder; MADRS-0 – Montgomery-Åsberg Depression Rating Scale score at baseline; MADRS-6 – MADRS score at the end of follow-up (after 6 months); MMSE – Mini-Mental State Examination; HAM-A – Hamilton Anxiety Rating Scale; CIRS – Modified Cumulative Illness Rating Scale

*- results statistically significant (p≤0.05);

** - during the baseline assessment following items of the MADRS varied significantly (p≤0.05) between the two groups: reduced appetite, concentration difficulties, lassitude;

*** - during the baseline assessment CIRS results varied (p≤0.05) in relation to cardiac diseases

Table II. Comparison of patients with remission and without remission of symptoms during the 6-month follow-up. These patients all experienced their first MDD episode

	No remission (mean) N = 16	Remission (mean) N = 9	t	df	p	No remission SD	Remission SD	F-ratio	p (variances)
Age	72.44	70.00	1.21	23.00	0.24	5.54	3.16	3.07	0.11
Months of current episode at baseline	2.13	2.00	0.22	23.00	0.83	1.59	0.87	3.36	0.09
Months to achieve improvement		2.11		7.00			1.36	0.00	1.00
MADRS-0*	23.31	21.11	1.13	23.00	0.27	5.55	2.20	6.33	0.01
MADRS-6*	25.81	9.78	5.09	23.00	0.00	8.65	4.92	3.09	0.11
MMSE-0*	25.56	26.56	-3.04	23.00	0.01	0.89	0.53	2.87	0.14
HAMA-0*	14.06	12.11	0.94	23.00	0.36	3.43	7.04	4.21	0.02
CIRS-0*	19.25	18.44	0.71	23.00	0.48	3.11	1.74	3.19	0.10

*- results statistically significant (p≤0.05);
** - compared groups differed in body mass (lower weight was noted in subjects with unfavorable course)

Table III. Comparison of patients with and without remission of symptoms during the 6-month follow-up. These patients all had recurrent MDD

	No remission (mean) N = 16	Remission (mean) N = 9	t	df	p	No remission SD	Remission SD	F-ratio	p (variances)
Age*	76.07	69.65	3.54	33.00	0.00	7.32	3.07	5.71	0.00
Number of episodes	2.80	2.70	0.33	33.00	0.75	1.01	0.80	1.60	0.34
Years since first MDD episode	11.67	4.00	4.18	33.00	0.00	7.37	3.15	5.50	0.00
Age of MDD onset	64.20	66.40	-0.73	33.00	0.47	9.11	8.66	1.11	0.82
Months of current episode at baseline	2.93	2.10	1.74	33.00	0.09	1.22	1.52	1.54	0.41
Months to achieve improvement		1.80		18.00			0.70	0.00	1.00
MADRS-0*	28.53	22.15	3.19	33.00	0.00	7.80	3.86	4.09	0.01
MADRS-6*	25.07	10.90	5.40	33.00	0.00	10.22	5.05	4.10	0.01
MMSE-0*	25.20	26.10	-2.18	33.00	0.04	1.32	1.12	1.39	0.50
HAMA-0*	16.53	12.70	2.46	33.00	0.02	3.78	5.06	1.79	0.27
CIRS-0*	19.73	18.10	1.88	33.00	0.07	2.74	2.38	1.32	0.56

*- results statistically significant (p≤0.05);
** - during the baseline assessment following items of the MADRS varied significantly (p≤0.05) between the two groups: apparent sadness, reported sadness, concentration difficulties, lassitude, inability to feel;
*** - during the baseline assessment CIRS results varied (p≤0.05) in relation to cardiac and respiratory diseases

before enrollment was 2.3 months. Mean scale values were 23.90 for MADRS, 25.80 for MMSE and 18.87 for CIRS. Remission of symptoms (MADRS at 14 points or less and failure to meet DSM-V diagnostic criteria) during the study was achieved in 29 patients, while in 31 patients in the sixth month of follow-up depressive disorder was still present. The basis for further data analysis was a division into two groups in terms of therapeutic response during the 6-month follow-up period: remission and no remission (table I).

A distinction was made between people with the first episode of depression (table II) and a recurrent disorder of depression (table III). These groups were also compared against each other. However, the only difference found was the greater severity of apparent sadness item of MADRS at baseline in subjects with recurrent depressive disorder.

Discussion

We found that elderly patients with depressive disorder had a worse prognosis. This finding is consistent with previous studies concerning depressive disorders of old age [4,10]. In our study, symptom remission was achieved in 48% of elderly patients; this number takes into account the need for a treatment change due to an unsatisfactory therapeutic response. In younger patients, the average effectiveness of treatment with first-line antidepressant is about 50% and if there is a need for a treatment change, with the use of second-generation drugs, 66% of remissions may be expected [18, 19]. A better prognosis was expected in younger patients, which was confirmed in our study (table I). The causes of a lower therapeutic efficacy in the elderly is complex with several factors responsible, both biological and social. Some studies consider the later age of disease as an additional factor worsening the outcome [8]. Our study showed that the group with recurrent MDD had a worse prognosis than the patient group with the first episode of depression. Lack of confirmed statistical significance in the latter group may be related to the relatively small number of patients included in the study. The relationship between the age and the prognosis is a complex problem, conditioned by several factors, such as somatic burden, but also, what has been demonstrated in the group of people with recurrent disorder, by the time that elapsed since first episode of MDD (table III).

We found that the initial clinical condition and the cognitive functions assessment had the most promising prognostic value. Additionally, the prognosis was worse with higher initial severity of somatic diseases (i.e. cardiac and respiratory disorders) and matches the findings of a previous study [8]. However, we cannot confidently confirm the prognostic values of somatic diseases as the sample size was relatively small.

Comorbidity, as a risk factor, is not frequently considered in research. Relatively few studies on MDD with a robust methodology have indicated their unfavorable prognostic significance [2,3,20]. In our study, the assessment of somatic burden was based on the CIRS scale; this allows for estimating the severity of each disease. Significant differences were found in relation to cardiac and respiratory disorders, which were of greater severity in people with a worse MDD outcome, especially in the group of subjects with recurrent depressive disorder. Previous research has established that the relationship between cardiovascular and mental disorders (particularly mood disorders) is strong [21].

Assessment of depressive disorder severity was based on MADRS, which we consider a suitable measurement tool in this age category for several reasons. MADRS is more focused on depressive disorders unlike the Hamilton scale which includes a whole range of symptoms that may be the result of anxiety expression or depressive disorders. Differentiation of depressive and anxiety disorders is difficult, especially in the elderly population, where both often manifest themselves through various somatic symptoms. Notably, the issue of anxiety in mood disorders has often been overlooked in previous studies on elderly people [3]. In our study, patients with high levels of anxiety (as measured by HAM-A over 17 points) were excluded during the screening process, but the anxiety level was monitored in enrolled patients. Our analysis showed a greater severity of anxiety in people with a worse prognosis during the six-month observation period.

MMSE scale results were slightly lower at baseline in patients characterized by a worse outcome. Cognitive decline is a widely accepted negative prognostic factor in mood disorders in the elderly [2,3]. It is worth noting that the correlation between MMSE score and the course of the disease was visible, although, people with clinically significant cognitive impairment were not included in the study. We reiterate that the MMSE was designed only for screening cognition and therefore should not be used to make decisive conclusions.

Symptom remission was achieved by most patients during the first 3 months in those with a good therapeutic response. This result matches previous observations. In patients with recurrent MDD, one could expect a more rapid improvement than with the patients with the first episode of a depressive disorder [22,23].

Our prospective study was based on the observation of a group of patients undergoing routine outpatient care, which is related to a number of methodological limitations. Furthermore, the treatment was subject to standardization only in the first stage of therapy. In the absence of its effectiveness, further therapy was dependent on the patient's current clinical condition, which made it impossible to subject this group of variables to statistical analysis.

Conclusions

Our study confirms a worse prognosis of depressive disorders in the elderly. Moreover, it identifies cognitive dysfunctions and somatic comorbidities as significant factors that should be taken into consideration during treatment as they may negatively affect the prognosis.

Conflict of interest
Brak/Non

Correspondence address
Leszek Bidzan
Department of Developmental, Psychotic and Geriatric Psychiatry, Faculty of Medicine, Medical University of Gdańsk
Srebrniki 1 Str.; 80-282 Gdańsk
☎ (+48 58) 344 60 85
leszekbidzan@gumed.edu.pl

References

1. Wittchen HU. The burden of mood disorders. Science (80-). 2012;338(6103):15. doi:10.1126/science.1230817.
2. Lenze EJ, Mulsant BH, Shear MK, Alexopoulos GS, Frank E, Reynolds CF. Comorbidity of depression and anxiety disorders in later life. Depress Anxiety. 2001;14(2):86-93. doi:10.1002/da.1050.
3. Steffens DC. A multiplicity of approaches to characterize geriatric depression and its outcomes. Curr Opin Psychiatry. 2009;22(6):522-526. doi:10.1097/YCO.0b013e32832fcd93.
4. Spijker J, De Graaf R, Bijl R V., Beekman ATF, Ormel J, Nolen WA. Duration of major depressive episodes in the general population: Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). Br J Psychiatry. 2002;181(SEPT.):208-213. doi:10.1192/bjp.181.3.208.
5. Beekman ATF, Geerlings SW, Deeg DJH, et al. The natural history of late-life depression: A 6-year prospective study in the community. Arch Gen Psychiatry. 2002;59(7):605-611. doi:10.1001/archpsyc.59.7.605.
6. Mueller TI, Kohn R, Leventhal N, et al. The Course of Depression in Elderly Patients. Am J Geriatr Psychiatry. 2004;12(1):22-29. doi:10.1097/00019442-200401000-00003.
7. Magnil M, Janmarker L, Gunnarsson R, Björkelund C. Course, risk factors, and prognostic factors in elderly primary care patients with mild depression: A two-year observational study. Scand J Prim Health Care. 2013;31(1):20-25. doi:10.3109/02813432.2012.757074.
8. Alexopoulos GS, Meyers BS, Young RC, et al. Recovery in geriatric depression. Arch Gen Psychiatry. 1996;53(4):305-312. doi:10.1001/archpsyc.1996.01830040039008.
9. Alexopoulos GS, Kiosses DN, Heo M, Murphy CF, Shanmugham B, Gunning-Dixon F. Executive dysfunction and the course of geriatric depression. Biol Psychiatry. 2005;58(3):204-210. doi:10.1016/j.biopsych.2005.04.024.
10. Comijs HC, Nieuwesteeg J, Kok R, et al. The two-year course of late-life depression; results from the Netherlands study of depression in older persons. BMC Psychiatry. 2015;15(1):20. doi:10.1186/s12888-015-0401-5.
11. Bhalla RK, Butters MA, Becker JT, et al. Patterns of mild cognitive impairment after treatment of depression in the elderly. Am J Geriatr Psychiatry. 2009;17(4):308-316. doi:10.1097/JGP.0b013e318190b8d8.
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association; 2013. doi:10.1176/appi.books.9780890425596.
13. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry. 1979;134(4):382-389. doi:10.1192/bjp.134.4.382.
14. HAMILTON M. The Assessment of Anxiety States by Rating. Br J Med Psychol. 1959;32(1):50-55. doi:10.1111/j.2044-8341.1959.tb00467.x.
15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189-198. doi:10.1016/0022-3956(75)90026-6.
16. Mungas D, Marshall SC, Weldon M, Haan M, Reed BR. Age and education correction of Mini-Mental State Examination for English and Spanish-speaking elderly. Neurology. 1996;46(3):700-706. doi:10.1212/wnl.46.3.700.
17. Salvi F, Miller MD, Grilli A, et al. A manual of guidelines to score the modified Cumulative Illness Rating Scale and its validation in acute hospitalized elderly patients. J Am Geriatr Soc. 2008;56(10):1926-1931. doi:10.1111/j.1532-5415.2008.01935.x.
18. Thase ME, Entsuah AR, Rudolph RL. Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. Br J Psychiatry. 2001;178(MARCH.):234-241. doi:10.1192/bjp.178.3.234.
19. Quitkin FM, McGrath PJ, Stewart JW, et al. Remission rates with 3 consecutive antidepressant trials: effectiveness for depressed outpatients. J Clin Psychiatry. 2005;66(6):670-676. doi:10.4088/jcp.v66n0601.
20. Tilvis RS, Pitkälä K, Nevantaus H. Prognosis of depression in old age. Arch Gerontol Geriatr. 1998;26(SUPPL.1):491-498. doi:10.1016/S0167-4943(98)80072-1.
21. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and diagnosis. Cardiovasc Psychiatry Neurol. 2013;2013:695925. doi:10.1155/2013/695925.
22. Vermeiden M, Kamperman AM, Vulink ME, Van Den Broek WW, Birkenhäger TK. Early improvement as a predictor of eventual antidepressant treatment response in severely depressed inpatients. Psychopharmacology (Berl). 2015;232(8):1347-1356. doi:10.1007/s00213-014-3765-1.
23. Mulsant BH, Blumberger DM, Ismail Z, Rabheru K, Rapoport MJ. A systematic approach to pharmacotherapy for geriatric major depression. Clin Geriatr Med. 2014;30(3):517-534. doi:10.1016/j.cger.2014.05.002.