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Long-term depression is a stroke risk factor

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Background and Aim: Only a few studies have evaluated depression prevalence in pre-stroke period in comparison to controls. We investigated this association based on a hospitalised stroke population.
Methods: One hundred and forty-eight stroke patients were evaluated. The presence of depression was compared with those of 100 healthy controls without stroke, from the same region. Depression was accepted as present or not present after history and clinical evaluation according to Diagnostic and Statistical Manual of Mental Disorders-IV. Socio-demographic variables, other stroke risk factors and the time of diagnosis of depression (how many year or month they got depression) were recorded.
Results: Gender and mean age of patients and controls were similar in comparison. Depression was diagnosed in 27 patients and 24 controls ($p > 0.05$). The time period passed after diagnosis of depression was longer in stroke patients in comparison to controls ($p < 0.001$).
Conclusions: The risk of stroke should be considered in elderly with long-term depression. This indicates that treatment of depression is another factor which should be considered in prevention of brain stroke.

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Keywords: depression; long-term depression; risk factor; stroke; stroke prevention

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Significant outcomes

- Long-term depression may be a risk for stroke development.
- Regular follow-up and treatment of depression in elderly people are important in prevention of stroke.

Limitations

- Inclusion criteria based on history and health/hospital registration records.
- The patients with subclinical or minor depression were not evaluated.

A bidirectional link exists between depression and many neurological illnesses (1). Post-stroke depression is well-known, but an association between a history of depression and future risk of cardiovascular or cerebrovascular events has not been studied widely using case–control protocols (2,3). Recently published prospective studies have shown an association between depression and the incidence of hypertension (4,5), cardiovascular mortality (6,7), stroke and stroke mortality (4,7,8). Additionally, some important follow-up studies including The Baltimore Epidemiologic Catchment Area Study showed that a history of depressive disorder was associated with an increased incidence of ischaemic stroke (9–11). In a community-based study conducted on Framingham Heart Study participants, depressive symptoms were found to be an independent risk factor for incident stroke/transient ischaemic attack (TIA) even after adjusting for traditional vascular risk factors and education (11).

Sympathoadrenal hyperactivity, ventricular instability and biological markers including platelet activation and inflammatory proteins have been proposed to explain the increased risk of cardiovascular disease in patients with depression (12–15). Platelet aggregation and mean platelet volumes are higher in patients with depression (16–18). Finally, depressive symptoms are associated with a higher prevalence of other modifiable lifestyle risk factors, such as smoking and lower levels of physical activity (19–22). Thus, we investigated the relationship between stroke and previous depression.

Materials and methods

We enrolled patients admitted to Düzce Medical Faculty Hospital with depression that was clinically diagnosed using a psychiatric structured interview (Turkish version of SCI-I) and criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) within 1 year before stroke occurrence in patients; we enrolled non-stroke controls with risk factors from the hospital ward in the same region. The criteria for the diagnosis of a depressive episode included depressed mood lasting at least 2 weeks, loss of interest or diminished sense of pleasure, plus four of seven other features sufficient to cause clinically important psychological or physical distress or functional impairment (23,24). Additionally, depression was accepted as present and considered a potential factor related to the stroke if there was a history of depression diagnosed by a psychiatric structured interview or by a psychiatrist using the DSM-IV criteria or if there was a history of diagnosed depression and antidepressant use had been prescribed by a psychiatrist during the past 10 years. Unconsciousness and aphasia were exclusion criteria for this study. Whether the patients had a stroke or used any antidepressants was recorded. Complications of mood disorders, alcoholism and substance abuse, socio-demographic variables, other risk factors and the duration of depression (in years or months) were also recorded.

Diagnostic imaging

The criteria used for the diagnosis of stroke included clinical evidence of stroke and computed tomography (CT) of brain and/or cranial magnetic resonance imaging (MRI) evidence of cerebral infarction without demonstrable source of embolism. The patients were evaluated with cranial CT ($n = 148$) and MRI ($n = 56$) to define stroke and were grouped as ischaemic, haemorrhagic and lacunar infarctions (Table 1).

Risk factor records

The data were collected using face-to-face interview technique. Semi-structured questionnaires consisting of multiple questions related to age, gender and risk factors were completed. The participants responded to a preformed list of questions related to risk factors. The risk factor records were based on their self-report, clinical and laboratory analysis. Hypertension was considered to be present if, at the time of diagnosis, the subject had a systolic blood pressure greater than 160 mm Hg or a diastolic pressure greater than 95 mm Hg, if he or she have had a systolic blood pressure greater than 140 mm Hg or a diastolic pressure greater than 90 mm Hg during follow-up in clinics and if treatment for high blood pressure had been administered previously. Hypercholesterolaemia was considered present if subjects had serum total cholesterol greater than 200 mg/dl. Hyperglycaemia was considered present if subjects had a serum glucose level greater than 115 mg/dl or if treatment for diabetes had been previously implemented. A subject was accepted as a smoker if he or she reported smoking one package of cigarettes daily for 5 years. Modifiable risk factors were noted. Past histories related to cardiac disease and strokes were evaluated based on follow-up files, healthcare records and self-reports.

Table 1. Descriptive characteristics and comparison of study groups

Variable	Patients ($n = 148$)	Controls ($n = 100$)	p-value
Presence of other stroke risk factors (# of people)			
Hypertension	124	55	0.000
Diabetes mellitus	30	44	0.000
Hyperlipidaemia	19	17	0.363
Smoking	22	6	0.030
Atrial fibrillation	14	0	0.000
Coronary artery disease	27	2	0.000
Mitral valve problem	2	8	0.009
Previous stroke	41	0	0.000
Lesion shown in CT or MRI			
Cortical infarction	24		
Subcortical infarction	58		
Brain stem infarction	6		
Cerebellar infarction	1		
Intracerebral haemorhage	30		
Cerebellar and brain stem haemorhage	2		
Lacunes	27		

Statistical analysis

The prevalence of depression in stroke patients was evaluated and it was compared to the depression prevalence by using the same criteria in age and sex-matched healthy people in the same population living in Düzce. Intergroup differences and correlations were tested using frequency tests, Student's t-tests and correlation analysis. Data were expressed as mean $\pm$ SD. All analyses were made using the SPSS 10.0 version statistical software package and probability value of less than 0.05 was accepted as to be statistically significant.

Results

In our study population, the gender of patients (70 females, 78 males) and controls (54 females, 46 males) were similar in comparison. The mean age of patients (67.49 $\pm$ 11.41 years) and controls (64.76 $\pm$

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Table 2. Comparison of study groups with depression

Variable	Patients with depression ($n = 27$)	Controls with depression ($n = 24$)	p-value
Ages (years)	66.26 ± 10.79	65.79 ± 8.46	0.865
Gender			
Male	12	10	0.842
Female	15	14	
Duration of depression symptoms (years)	6.70 ± 3.62	1.42 ± 0.51	0.000
How many people had treatment for depression?	21	5	0.000
Duration of treatment for depression (years)	2.94 ± 2.31	1.25 ± 0.44	0.001
Presence of other stroke risk factors (# of people)			
Hypertension	24	6	0.000
Diabetes mellitus	7	10	0.234
Hyperlipidaemia	1	2	0.483
Smoking	4	2	0.473
Atrial fibrillation	2	0	0.000
Coronary artery disease	4	2	0.473
Mitral valve problem	0	3	0.058
Previous stroke	10	0	0.000

9.73 years) were similar too ($p = 0.52$). The descriptive characteristics, risk factors and diagnostic findings of study groups were revealed in Table 1.

Depression was diagnosed in 27 patients and 24 controls ($p = 0.37$). When we evaluated only the patients and controls with depression, the duration of depression was longer in stroke patients in comparison to controls ($p < 0.001$). Nearly all controls talked about depression symptoms which continued less than 2 years (Table 2). In comparison, 89% of the patients delineated depression symptoms which continued more than 2 years. Twenty-one of 27 patients had treatment for depression while 5 of 24 controls had treatment ($p < 0.001$). Nine patients and seven controls were hospitalised in history ($p > 0.05$). In addition, the time duration of reported treatments was longer in the patients as seen in Table 2.

There was no correlation between the presence of depression and modifiable stroke risk factors (hypertension, diabetes, hyperlipidaemia, coronary artery disease, mitral valve prolapsus, smoking), age, gender and the lesions (seven cortical, eight subcortical, two lacunars and two brain stem ischaemic infarctions and eight haemorrhagic infarctions) in the patient group.

Discussion

Although significant psychological distress causing hypertension and reduced vascular function, autonomic nervous system dysfunction and increased platelet activity and aggregation are reported as predictors of fatal ischaemic stroke, whether an association exists between depressive symptoms and stroke remains uncertain (8,25–28). In this study, we tried to identify the clinical implications of an association between depression and stroke in older individuals. Findings from our case–control study suggest that depressive disorder is not associated with an elevated stroke risk, but that the risk of stroke should be considered in elderly people with long-term depression. Similar to our findings, some studies have concluded that depressive symptoms are not associated with an increased risk of stroke in general (25,26) or with non-fatal ischaemic stroke or TIA (27). We also found that the presence of depression was independent of modifiable stroke risk factors and was not associated with age, gender and ischaemic lesions in the patient group. Twenty-four of 100 controls were reported as fulfilling the criteria of depression, which seems like a very high prevalence compared to a normal background population. But there are lots of studies conducted in neurology clinics or hospitals in which they reported high prevalence of depression (10–60%) related to chronic aspect of underlying disease or risk factors (29–31). This was an important finding and supported the conclusion that depression was commonly seen in stroke. In our study group, this high prevalence may be related to hypertension or other risk factors which are chronic disorders and resulted in atherosclerosis like hypertension, diabetes or hyperlipidaemia, seen in control as shown in Table 1.

In contrast, Jonas and Mussolino (4) reported a significant association between a high level of depressive symptoms and the incidence of subsequent stroke. Nilsson and Kessing (32) reported that patients with depression severe enough to require hospitalisation were at increased risk for developing cerebrovascular disease. In this study, we asked the previous hospitalisations due to depression. There was not any statistical difference between the patients and controls with depression severe enough to be hospitalised in our study. Supporting these studies, Surtees et al. (33) reported that depression was associated with an 11% increase in the risk of stroke after adjusting for risk factors and socio-demographic variables (hazard ratio, 1.11; 95% confidence interval, 1.00–1.22). In our study, we did not measure levels of depression, but it was an important finding that the duration of depression differed and was higher in the patients in comparison. Our findings provide another additional evidence that there might be some pathogenic mechanisms explaining the association between depression and stroke (12–22).

Some studies have concluded that the risk of developing stroke/TIA increases in participants <65 years of age with symptoms of depression (7,25,26).

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In contrast, when Jonas and Mussolino (4) examined the risk of stroke in depressed individuals stratified by age (25–59 years and 60–74 years), a positive association was found in both age groups. Stroke risk was associated with high level of depression in both age groups (4). All studies reported above supported that depression was an important risk factor for stroke in all age groups (4,7,25,26). Similarly, we found a high incidence of depression in older aged study population of us and age was not correlated with depression in our study.

The most important limitation of our study was a possible bias because of inclusion criteria based on history and records and the absence of follow-up. It is possible that we missed the data of patients with subclinical or minor depression. Another possible source of bias was a misclassification due to inaccurate diagnosis codes on medical records and health certificates. In addition, more patients had been treated for depression. Despite these limitations and confusions, our results provide additional evidence that there is no association between the presence of depression and stroke. However, a relationship between long-term depression and stroke indicates that effective treatment for depression may be important in the primary prevention of stroke. Because depressive symptoms are associated with a higher prevalence of other modifiable lifestyle risk factors, social support, psychological status, treatment modalities and medical follow-up, personal characteristics should be analysed more thoroughly in future studies on stroke.

References

1. Evans DL, Charney DS, Lewis L et al. Mood disorders in the medically ill: scientific review and recommendations. Biol Psychiatry 2005;**58**:175–189.
2. Carod Artal FJ. Post-stroke depression (I). Epidemiology, diagnostic criteria and risk factors. Rev Neurol 2006;**42**:169–175.
3. Krishnan KR. Depression as a contributing factor in cerebrovascular disease. Am Heart J 2000;**140**:70–76.
4. Jonas BS, Mussolino ME. Symptoms of depression as a prospective riskfactor for stroke. Psychosom Med 2000;**62**:463–471.
5. Davidson K, Jonas BS, Dixon KE, Markovitz JH. Do depression symptoms predict early hypertension incidence in young adults in the CARDIA study? Arch Intern Med 2000;**160**:1495–1500.
6. Penninx BWJH, Beekman ATF, Honig A et al. Depression and cardiac mortality: results from a community-based longitudinal study. Arch Gen Psychiatry 2001;**58**:221–227.
7. Gump BB, Matthews KA, Eberly LE, Chang YF; for the MRFIT Research Group. Depressive symptoms and mortality in men: results from the Multiple Risk Factor Intervention Trial. Stroke 2005;**36**:98–102.
8. Carod-Artal FJ, Egido JA. Quality of life after stroke: the importance of a good recovery. Cerebrovasc Dis 2009;**27**:204–214.
9. Larson SL, Owens PL, Ford D, Eaton W. Depressive disorder, dysthymia, and risk of stroke: thirteen-year follow-up from the Baltimore Epidemiologic Catchment Area study. Stroke 2001;**32**:1979–1983.
10. Ohira T, Iso H Satoh S et al. Prospective study of depressive symptoms and risk of stroke among Japanese. Stroke 2001;**32**:903–908.
11. Salaycik KJ, Kelly-Hayes M, Beiser A et al. Depressive symptoms and risk of stroke: the Framingham Study. Stroke 2007;**38**:16–21.
12. Musselman DL, Evans DL, Nemeroff CB. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. Arch Gen Psychiatry 1998;**55**:580–592.
13. Jiang W, Krishnan RRK, O'Connor CM. Depression and heart disease: evidence of a link, and its therapeutic implications. CNS Drugs 2002;**16**:111–127.
14. Ladwig KH, Marten-Mittag B, Lowel H, Doring A, Koenig W. C-reactive protein, depressed mood, and the prediction of coronary heart disease in initially healthy men: results from the MONICA-KORA Augsburg Cohort Study 1984–1998. Eur Heart J 2005;**26**:2537–2542.
15. Empana JP, Sykes DH, Luc G et al. Contributions of depressive mood and circulating inflammatory markers to coronary heart disease in healthy European men: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). Circulation 2005;**111**:2299–2305.
16. Williams L. Depression and stroke: cause or consequence? Semin Neurol 2005;**25**:396–409.
17. Serebruany VL, Glassman AH, Malinin AI et al. Platelet/endothelial biomarkers in depressed patients treated with the selective serotonin reuptake inhibitor sertraline after acute coronary events: the Sertraline AntiDepressant Heart Attack Randomized Trial (SADHART) Platelet substudy. Circulation 2003;**108**:939–944.
18. Ataoglu A, Canan F. Mean platelet volume in patients with major depression: effect of escitalopram treatment. J Clin Psychopharmacol 2009;**29**:368–371.
19. Wannamethee SG, Shaper AG. Physical activity in the prevention of cardiovascular disease: an epidemiological perspective. Sports Med 2001;**31**:101–114.
20. Fox KR. The influence of physical activity on mental well-being Public Health Nutr 1999;**2**:411–418.
21. Weyerer S. Physical inactivity and depression in the community. Evidence from the Upper Bavarian Field Study. Int J Sports Med 1992;**13**:492–496.
22. Camacho TC, Roberts RE, Lazarus NB, Kaplan GA, Cohen RD. Physical activity and depression: evidence from the Alameda County Study. Am J Epidemiol 1991;**134**: 220–231.
23. Özkürkçügil A, Aydemir Ö, Yildiz M, Danaci E, Koroglu E. Adaptation and reliability study of structured clinical interview for DSM-IV Axis I disorders (Turkish). Turk J Drugs Ther 1999;**12**:233–236.
24. Diagnostic and statistical manual for mental disorders: DSM-IV, 4th edn. Washington, DC: American Psychiatric Association, 1994.
25. Colantonio A, Kasi SV, Ostfeld AM. Depressive symptoms and other psychosocial factors as predictors of stroke in the elderly. Am J Epidemiol 1992;**136**:884–894.
26. Wassertheil-Smoller S, Applegate WB, Berge K et al. Change in depression as a precursor of cardiovascular events: SHEP Cooperative Research Group (Systolic Hypertension in the elderly). Arch Intern Med 1996;**156**:553–561.

https://doi.org/10.1111/j.1601-5215.2011.00573.x Published online by Cambridge University Press

27. May M, McCarron P, Stansfeld S et al. Does psychological distress predict the risk of ischemic stroke and transient ischemic attack? The Caerphilly Study. Stroke 2002;**33**:7–12.
28. Everson SA, Roberts RE, Goldberg DE, Kaplan GA. Depressive symptoms and increased risk of stroke mortality over a 29-year period. Arch Intern Med 1998;**158**: 1133–1138.
29. Wu HQ, Zhang Y, Li YS, Zhu Y, Shen F. Clinical characteristics of patients with depressive disorders at Department of Neurology in general hospitals. Zhonghua Yi Xue Za Zhi 2010;**90**:1760–1763.
30. Carson AJ, Ringbauer B, MacKenzie L, Warlow C, Sharpe M. Neurological disease, emotional disorder, and disability: they are related: a study of 300 consecutive new referrals to a neurology outpatient department. J Neurol Neurosurg Psychiatry 2000;**68**:202–206.
31. Hamilton J, Campos R, Creed F. Anxiety, depression and management of medically unexplained symptoms in medical clinics. J R Coll Physicians Lond 1996;**30**:18–20.
32. Nilsson FM, Kessing LV. Increased risk of developing stroke for patients with major affective disorder: a registry study. Eur Arch Psychiatry Clin Neurosci 2004;**254**:387–391.
33. Surtees PG, Wainwright WJ, Luben RN, Wareham NJ, Bingham SA, Khaw T. Psychological distress, major depressive disorder, and risk of stroke. Neurology 2008;**4**: 788–794.

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