Lacunar Strokes, Depression and Anxiety Symptoms One Year After Stroke.

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Abstract

Background: mood disorders are frequent after stroke, and are associated with poorer quality of life. Previous studies have reported conflicting results as to stroke subtype in the incidence of post-stroke mood disorders. We explored the relationship between ischemic stroke subtype and presence of such symptoms at one year after stroke.
Methods: anonymised data were accessed from the Virtual International Stroke Trials Archive (VISTA). Stroke subtypes were classified according to the Trial of Org 10172 (TOAST) classification. Depression and anxiety symptoms were assessed using Hospital Anxiety and Depression Scale (HADS). We investigated independent predictors of depression and anxiety symptoms using a logistic regression model.
Results: data were available for 2160 patients. Almost one fifth of patients developed both anxiety and depression at 1 year follow-up. After adjusting for confounders, the lacunar subtype was least associated with both anxiety (OR=0.65; 95% CI=0.51-0.85) and depression symptoms (OR=0.71; CI=0.55-0.93) versus other stroke subtypes.
Conclusions: lacunar strokes have a weaker association with presence of anxiety and depression symptoms compared with other subtypes.

Introduction

Stroke consequences frequently encompass mood disorders such as depression and anxiety, which may negatively affect quality of life. Depression affects around one third of patients at one month after stroke[1]. Anxiety occurs more frequently than depression, affecting up to 40% of stroke survivors[2]. Due to anatomical location and infarct size, different stroke pathological subtypes may be associated with various psychological sequela. A recent meta-analysis suggested that the risk of developing depression was unaffected by the underlying stroke subtype[3]. However, Appelros et al. reported lower rates of depression symptoms in patients with lacunar strokes after one year follow up[4], whereas results from the SMART-MR study showed that subcortical infarcts faced a higher risk of depressive symptoms[5]. We aimed to explore the relationship between stroke etiological subtype and presence of depression and anxiety symptoms at one year after ischaemic stroke by analyzing data from the Virtual International Stroke Trial Archive (VISTA).

Methods

We accessed anonymous, patient level, data from the VISTA resource. We classified the qualifying ischaemic stroke according to the method described in the Trial of Org 10172 (TOAST)[6].

We extracted baseline variables including demographic data, clinical symptoms and past medical history. Stroke severity was quantified using Oxford Handicap Scale (OHS). Outcome data included depression and anxiety symptoms, as measured using the Hospital Anxiety and Depression Scale (HADS). We defined the presence of anxiety and depression as a score of ≥8 on HADS-A or HADS-D, respectively.

Statistical analyses: We dichotomized stroke subtype into small arteries occlusion (lacunar) versus other stroke subtypes. Our primary outcomes of interest were dichotomized one year HADS-A and HADS-D using a score of ≥8 as our “screen positive” cut-off.

We developed a multivariate logistic regression model for both depression and anxiety symptoms adjusting for potentially significant factors ($p<0.1$) retained from univariate analysis and other clinically relevant factors. Variables with $p<0.05$ were considered independent predictors of outcomes. Statistical analysis was carried out by using SPSS for Windows (version 22.0; SPSS, Armonk NY, IBM Corp.).

Results

We identified 5721 patients with diagnosis of ischemic stroke at baseline and sufficient data to assign TOAST classification. Follow up data describing HADS scores were available for 2160 (38%) patients. Patients where no HADS data were available were younger and had higher baseline neurological impairment. More small arteries occlusive events had HADS data than other stroke types (52% vs 48%, $p<0.001$) (supp. Tab1).

Comparison of available baseline patient characteristics between lacunar and other stroke subtypes are showed in Table 1. Functional independence, history of depression, and impaired cognitive function showed no significant differences across the two groups.

At one year post-stroke, anxiety symptoms were present in 421 (19.5%) patients and depression symptoms in 416 (19.3%) patients. Unadjusted analysis suggested that lacunar stroke subtype had a poorer association with both anxiety (16.9% vs 22.3%, OR=0.71, 95% CI=0.58-0.88) and depression (17.6% vs 21.1%, OR=0.80, 95% CI=0.64-0.99) symptoms compared to other stroke types.

Anxiety and depression were strongly correlated (Spearman's $\rho=0.71$, $p<0.001$).

After adjusting for age, sex, disability grade at baseline, diabetes, history of depression, arm paralysis, leg paralysis, aphasia and neglect, our multivariate analyses suggested lacunar stroke subtype was independently associated with reduced risk of one-year anxiety (OR=0.78, 95% CI=0.62-0.98) and depression (OR=0.69, 95% CI=0.52-0.90) (Tab.2).

Discussion

We found that one year post-stroke depression and anxiety symptoms were strongly correlated with each other and affected almost one fifth of patients. Diagnosis of lacunar stroke subtype according to TOAST classification was associated with reduced risk of both anxiety and depression symptoms.

The associations between clinical and demographic features and development of mood symptoms are in keeping with available literature describing mood disorders in stroke. There was a sex-based effect with males less affected by both anxiety and depression symptoms; this is consistent with previous reports[1,7]. History of depression at baseline was strongly associated with both depression and anxiety symptoms, alluding to the complex relationship between the different mood disorders. These findings support previous published studies[8,9]. Our observed frequency of anxiety was lower than previously reported, which may relate to our population having milder strokes compared to other studies.

In the Stroke Prevention in Small Subcortical Strokes Study (SPS-3), which enrolled patients with lacunar strokes and mild deficits, 17% of patients suffer from depression one year after stroke, roughly the same percentage that we found in our study[10]. Our population is similar to those recruited to SPS-3, and our findings support the position that lacunar strokes are a relatively benign stroke subtype[11,12], with lesser mood disorders in the lacunar group. However, with almost one out of five patients at one year suffering from mood symptoms, lacunar strokes are still associated with a substantial burden of anxiety and depression.

Our study has limitations. The main shortcoming was missing mood data for 62% of the whole cohort at follow up. Patients lost were more likely to have had a greater prevalence of non-lacunar stroke subtypes, leading to a relative over-representation of lacunar strokes in the study population. It seems plausible that patients lost at follow up may have had a greater prevalence of mood disorders. Our results are therefore likely to underestimate the true burden of symptoms of mood disorders. Another limitation is that our assessment of symptoms was based on a metric "screening" scale, and not on a comprehensive clinical evaluation. We are aware that a short scale is not a substitute for expert clinical assessment; however, we consider our cut-off to offer a conservative estimate, which is appropriate to our study population with relatively mild strokes.

In conclusion, we observed that in patients with mild ischemic strokes, lacunar subtype has a weaker association with the development of anxiety or depression, within a year of stroke.

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Tab. 1. Characteristics of the study population

	All **N=2160**	**Lacunar** **N=1127**	**Other subtypes** **N=1033**	**p**
Age (mean±SD)	64.2±11.9	64.1±11.8	64.3±11.8	0.912
Sex, male (%)	67	64	69	0.009
OHS, (median, IQR)	1 (1-2)	1 (1-2)	1 (1-2)	0.594
MMSE, one year (median, IQR)	29 (27-30)	28 (26-29)	29 (27-30)	0.302
Hypertension (%)	71	71	71	0.819
Diabetes (%)	25	26	25	0.794
History of depression (%)	8	7	9	0.138
Atrial Fibrillation (%)	10	8	12	0.002
Smoke (%)	24	25	23	0.388
Ischemic heart disease (%)	18	16	20	0.030
Hypercholesterolemia (%)	45	45	45	0.759
Aphasia/dysarthria (%)	27	22	32	<0.001
Neglect (%)	9	5	13	<0.001
Arm Paralysis (%)	74	88	60	<0.001
Leg Paralysis (%)	67	81	54	<0.001

SD=Standard Deviation; IQR=Interquartile Range; OHS=Oxford Handicap Scale; MMSE=Mini Mental State Examination; OCSP=Oxford Community Stroke Project.

Tab.2. Predictors of depression and anxiety symptoms after one year

Factor	Depression OR (95% CI)	Anxiety OR (95% CI)
Age	0.99 (0.98.1.01)	0.99 (0.98-1.00)
Sex, male	0.68 (0.53-0.88)	0.46 (0.35-0.59)
History of diabetes	1.16 (0.89-1.53)	0.85 (0.63-1.14)
History of depression	2.24 (1.53-3.29)	4.72 (3.27-6.76)
OHS baseline	1.36 (1.18-1.57)	1.07 (0.92-1.24)
Lacunar by TOAST	0.71 (0.55-0.93)	0.65 (0.51-0.85)
Arm paralysis*	1.64 (1.12-2.39)	-
Leg paralysis*	0.93 (0.66-1.31)	-
Aphasia/dysarthria	1.27 (0.97-1.67)	1.61 (1.22-2.12)
Neglect	1.63 (1.06-2.49)	1.69 (1.11-2.57)

OHS=Oxford handicap Scale; TOAST=Trial of Org 10172 in Acute Stroke Treatment.

*Not significant at the univariate analysis for anxiety.

Supp. Tab 1. Comparison between patients included and excluded at follow-up at one year.

	All **N=5721**	**Included** **N=2160**	**Excluded** **N=3561**
Age (mean±SD)	64.2±11.9	64.2±11.4	61.6±12.9
Sex, male (%)	67	67	63
OHS, median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)
MMSE, one year (median, IQR)	29 (27-30)	29 (27-30)	28 (25-29)
Lacunar by TOAST (%)	49	52	48
Hypertension (%)	71	71	72
Diabetes (%)	25	25	28
Atrial Fibrillation (%)	10	9	10
Hypercholesterolemia (%)	45	45	39
History of Depression (%)	8	7	8
Ischemic heart disease (%)	18	18	18
Smoke (%)	24	24	24
Aphasia/dysarthria (%)	27	23	29
Neglect (%)	9	9	9
Arm Paralysis (%)	74	69	77
Leg Paralysis (%)	67	61	70

SD=Standard Deviation; OHS=Oxford handicap Scale; MMSE=Mini Mental State Examination; OCSP=Oxford Community Stroke Project; IQR=Interquartile Range; TOAST= Trial of Org 10172 in Acute Stroke Treatment.