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Effect of mood on long-term disability in younger stroke survivors: results from the Psychosocial Outcomes In StrokE (POISE) study

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Abstract

Background & Purpose: Anxiety and depression are common among stroke survivors and their effect on long-term outcome remains unknown in those under 65 years of age. We investigated the association between early anxiety/depression after stroke and 12-month disability, and whether this is modified by sex.

Methods: The Psychosocial Outcomes In StrokE (POISE) study was a prospective observational cohort study that recruited 441 younger (< 65 years) stroke survivors ≤28 days of acute stroke. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale, and disability using the World Health Organization Disability Assessment Scale version II (WHODAS-II). Associations between baseline anxiety/depression, and disability at 12-months was tested using analysis of covariance. Subgroup analysis was conducted using interaction term.

Results: 92 (25%) had anxiety and 53 (14%) depression at baseline. Multivariable models showed significant association between baseline anxiety and 12-month disability (WHODAS-II score 15.24 vs. 11.49, $p < 0.05$). Those with anxiety had more impairment in 'cognition' (WHODAS-II score 18.26 vs. 8.71, $p < 0.001$), 'getting along' (WHODAS-II score 11.87 vs. 7.42, $p < 0.05$) and 'participation' (WHODAS-II score 22.37 vs. 15.92, $p < 0.005$) WHODAS-II. No significant relationship was found between baseline depression and long-term disability. There was no differential effect of anxiety by sex found in this study.

Conclusions: Post-stroke anxiety has an adverse effect on disability at one year among young stroke survivors.

Keywords: anxiety, depression, function, disability, WHODAS-II, HADS, stroke, POISE.

Introduction

Stroke is a devastating disease and a leading cause of mortality and morbidity globally.[1] With advances in stroke care, reductions have been seen in stroke mortality.[2,3] Approximately one in three stroke survivors experience anxiety and depression at any time point, likely caused by a complex interplay of biological and psychosocial factors,[4,5] [4]which can adversely impact on recovery and quality of life.[4,6]

Previous research has shown potentially bidirectional associations between post-stroke depression and disability due to reduced participation in rehabilitation and decreased social and cognitive function. [4,7–9] However, literature on the effect of post-stroke anxiety on long-term disability is limited and findings are inconsistent.[10–15] Although those aged less than 65 years(hereafter referred to as 'younger') stroke survivors have a higher risk of post-stroke anxiety [6,10], and their functional impairment imposes longer socioeconomic challenges due to health-care costs and loss of productivity, studies of mood disorders and disability in younger stroke survivors are sparse. [10,16] It is also possible that the effect of anxiety or depression on disability may be modified by sex as female stroke survivors may have a higher risk of mood disorders and lower quality of life.[8,17]

We examined the prognostic effect of post-stroke anxiety and depression on disability in younger stroke survivors, and whether the effects are modified by sex.[18]

Materials and Methods

Study design and population

Psychosocial Outcomes In StrokE (POISE) was a prospective observational cohort study[18] to determine the psychosocial factors associated with recovery and return to work in younger

stroke survivors. Briefly, participants were recruited from 20 general public hospitals in New South Wales, from October 2008 to June 2010. Eligible participants were between 18 and 65 years of age, had an acute stroke within 28 days of recruitment, spoke sufficient English to respond to questions, and they or their proxies were able to give consent. Proxies were also able to complete the assessments on behalf of the participants-. POISE was registered with the Australian New Zealand Clinical Trials Registry ANZCTRN 12608000459325. A detailed description of the study methods can be found elsewhere.[18,19] This manuscript conforms to the STROBE Guidelines.

Data collection

Baseline (28 days post-stroke) sociodemographic, medical, and clinical characteristics of participants were recorded by hospital-based research nurses. Economic hardship was defined as either an instance of a household's inability to make a necessary household payment (financial stress) or the deployment of dissaving behaviour (borrowing or use of savings). Having psychiatric history was defined as receiving psychiatric medications or psychological counselling, at admission or ever. At 6 and 12-months after stroke we also collected information on current cognitive, social, work, household economic and rehabilitation status, anxiety and depressive symptoms and psychosocial disability.

Measurement tools

Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS).[20] The HADS is a 14-item self-report questionnaire with subscales for anxiety (HADS-A) and depression (HADS-D), validated for younger stroke survivors.[20,21] HADS subscale scores range from 0 to 21 with higher scores indicating more severe symptoms.

Participants were classified as having 'anxiety' or 'depression' with subscale scores of 8 or more.[22] We assessed disability using the 36-item World Health Organisation Disability Assessment Schedule II (WHODAS-II), which has been validated in stroke populations. [23] The WHODAS-II has six domains: cognition (understanding or communicating), mobility (getting around), self-care (measuring individual's capacity to carry out needs), getting along (interpersonal interactions), life activities (household tasks), and participation (participating in society). Items focus upon difficulties in everyday life encountered within the last 30 days, response categories based on 5-step Likert-scales ('no difficulties' to 'extreme difficulties/not possible at all'). Each domain was scored separately, excluding the four questions relevant to household and paid/school work ability in the domain of life activities. A total WHODAS-II score was calculated and converted to a score ranging from 0 to 100, with higher scores indicating greater disability. 'At risk drinking' was assessed using the Alcohol Disorders Identification Test (AUDIT-C) scored on a scale of 0-12 with scores of ≥ 5 for males and ≥ 4 for females indicating hazardous drinking.[24] Cognitive status was measured using the Telephone Interview for Cognitive Status (TICS), which assigns scores from 0 to 39, with higher scores indicating better cognitive function.[25] We measured social function using the Frenchay Activities Index (FAI), a 15-item questionnaire covering domestic, leisure, social and work activities used a four-point scale from 'never' to 'frequent' with total scores ranging from 0 (no activities) to 45 (full activities).[26]

Statistical analysis

Baseline characteristics were summarized as mean (standard deviation) or median (interquartile range) for continuous and as number (%) for categorical or ordinal variables. Between-group comparisons were made using the t-test for continuous and Chi-square test for discrete variables. The correlation between anxiety or depression and disability was

calculated using Pearson's correlation tests at baseline, 6 and 12-months, adjusted for baseline age, sex, and stroke severity as indicated by Glasgow Coma Scale (GCS) score[27]. We analysed the association between post-stroke anxiety and depression and disability at 12-months using the Analysis of Covariance (ANCOVA), adjusted for confounders including sociodemographic (age, sex), medical (GCS score, TICS score, psychiatric history), clinical (FAI score, WHODAS-II score, baseline HADS score) characteristics at baseline. These covariates were selected based on knowledge of prior literature and statistical significance in crude models. We investigated the potential combined effect of depression and anxiety on disability by inserting an interaction term for anxiety and depression in our model.

As we found a significant effect of anxiety on disability, we further tested the modification of this effect by sex -using interaction terms. A 2-sided *P* value <0.05 was considered indicative of statistical significance. All analyses were performed using SAS version 9.4 (SAS institute, Cary, NC).

Results

Baseline Characteristics

Of the 441 younger stroke survivors in POISE, 372 with complete information on anxiety and depression were included in these analyses. There were 92 (25%) with anxiety at baseline, 53 (14%) participants with depression at baseline, and 35 participants with both anxiety and depression.~~.~~ Compared to those without anxiety, those with anxiety were less likely to be living alone (9% vs 20%), have helpful neighbours (64% vs 79%), to be able to make their own decisions (65% vs 89%), and be highly active (57% vs 61%); they were more likely to have at least one activity-restricting illness (37% vs 18%), have a psychiatric history (54% vs 30%), experience economic hardship (47% vs 32%), and be disabled (mean WHODAS score

34.6 vs 19.5) (~~(Table 1)~~. ~~These p~~Participants with depression were more likely to speak a non-English language at home (32% vs 18%), have a psychiatric history (49% vs 34%), and to be disabled (mean WHODAS score 47.6 vs 19.6); and less likely to have helpful neighbours (57% vs 78%), be able to make their own decisions (54% vs 88%), and be highly active (57% vs 61%). The groups did not differ significantly in other ways. (Table 1)

Anxiety, depression and disability

Significant positive correlations exist between anxiety and depression and disability at all time points (baseline, 6 and 12-months) and across all domains of the WHODAS-II and with the total score (all $p < 0.01$, Supplementary Table 1). The correlation was lower for anxiety and depression and the WHODAS-II domains of 'self-care' and 'life-activities' at all time-points.

Association between baseline anxiety and depression, and disability at 12-months

Multivariable models showed a significant association between anxiety and 12-month disability (WHODAS-II score 15.24 vs. 11.49, $p < 0.05$). Those with anxiety had more impairment in individual domains of 'cognition' (WHODAS-II score 18.26 vs. 8.71, $p < 0.001$), 'getting along' (WHODAS-II score 11.87 vs. 7.42, $p < 0.05$) and 'participation' (WHODAS-II score 22.37 vs. 15.92, $p < 0.005$). No significant differences were found for the domains of mobility, self-care, or life activities (Table 2-, Figure 1). We found no significant interaction between anxiety and depression on domains of WHODAS-II score and total WHODAS-II score at 12 months (all P≥0.09). Subgroup analysis by sex showed no significant association between anxiety and 12-month disability. (Table 3) No significant association was found between baseline depression and disability at 12-months.

Discussion

In this prospective study young stroke survivors we found that anxiety and depression were correlated with disability during the first year after stroke. Baseline anxiety was associated with disability at 12-months post-stroke with no difference between sexes. We did not observe any relationship between early depression and 12-month disability. Baseline anxiety was significantly associated with poorer ability to communicate and interact with others and less willingness to participate in social activities one year after stroke.

Our results suggest that early post-stroke anxiety may reduce peoples' ability and willingness to engage socially in the first year after stroke. This is consistent with a cross-sectional study in young stroke survivors,[10] and similar studies in the general stroke population.[11,13] Phobic disorders may be the predominant anxiety subtype and correlated with more avoidant behaviours and restriction of social participation.[6] Other explanations for the association include under-recognition or treatment of post-stroke anxiety (possibly due to the lack of guidance for effective treatment) and decreased motivation to participate in rehabilitation.[6,28,29] In this study, early anxiety is also influenced by the socioeconomic circumstances and comorbidities of the participants. Recognition of these factors may facilitate the identification of those at risk for post-stroke anxiety. It will be important to determine whether improved recognition and management of post-stroke anxiety leads to less disability.

We did not find a relationship between depression and disability. This differs from findings in the general and younger stroke populations. Post-stroke depression has been associated with increased disability and reduced quality of life.[8,9,30] Although it is postulated that

depression may be linked to long-term disability through reduced participation in rehabilitation and low activity level,[8,29] it is possible that this relationship may be complicated by other elements including presence of a spouse, income status and family/social support that have also been shown to influence post-stroke depression.[31] This study is one of few which collected detailed information on socioeconomic factors. Therefore, the discrepant findings may be associated with our ability to control for these confounding factors. Compared to prior observational studies, our study participants had a much lower frequency of depression at baseline (14% vs 31%). The~~We also had a~~ small number of participants with baseline depression~~-~~ could have reduced our power to detect a significant association.[8,32]

The strengths of this study include the prospective design, relatively large sample of well characterized younger stroke survivors from urban and rural centers with low loss to follow-up. Although the HADS is well validated in stroke survivors,[21,22] we acknowledge that the gold standard method of depression diagnosis is via a clinical interview by a trained, culturally-competent interviewer. The generalizability of the present findings to the current Australian stroke population may be limited by the study participant selection criteria such as the exclusion of participants or proxies who did not speak English and people over 65 years of age. Although our analysis is based on data which was collected over ten years ago~~-~~, our findings may still contribute to the establishment of focused screening for mood disturbances in stroke survivors as no formal protocol has been established in the interim for the screening of anxiety or depression in stroke survivors.[33]

In conclusion, early post-stroke anxiety affects one in four younger stroke survivors and may lead to reduced cognition and social engagement, and increased disability. Future research

could investigate whether early detection, diagnosis and management of post-stroke anxiety decreases disability one year post stroke.

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Concept or design of the work (CL, AVL, DZ, MH); data analysis (QL); interpretation of data (CL, AVL, DZ, MH), initial draft (CL, AVL, DZ), revised it critically for important intellectual content (DZ, MH).

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The authors declare no conflict of interest.

Data availability statement

The POISE dataset used for this project is held at The George Institute for Global Health.

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Table 1. Baseline characteristics of stroke survivors by anxiety and depression status

Values in the table are presented as mean±standard deviation or number (percentage)

AUDIT-C indicates Alcohol Disorders Identification Test; HADS-A, Hospital Anxiety and Depression Scale – Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale – Depression Subscale; TICS, Telephone Interview for Cognitive Status; WHODAS, World Health Organization Disability Assessment Schedule.

* HADS-A and HADS-D scores range from 0 to 21, with higher scores indicating more severe symptoms.

† Economic hardship was defined as either an instance of a household's inability to make a necessary household payment (financial stress) or the deployment of dissaving behaviour (borrowing or use of savings).

‡ At risk drinking was assessed using the AUDIT-C questionnaire scored on a scale of 0-12. The cut-off for identifying hazardous drinking was ≥ 5 for males and ≥ 4 for females.

§ Psychiatric history was defined as psychiatric medications or psychological counselling, at admission or ever

‖ Cognitive status was measured by the TICS, which assigns scores ranging from 0 to 39, with higher scores indicating better cognitive function.

WHODAS II score ranges from 0-100, with higher scores indicating greater disability

** There are 9% participants with missing data

	No anxiety (HADS-A score 0-7)* N=280	Anxiety (HADS-A score 8-21)* N=92	*p*-value	No depression (HADS-D score 0-7)* N=319	Depression (HADS-D score 8-21)* N=53	*p*-value	***Total***
Demographics							
Age, years	52.5±10.4	50.9±9.7	0.22	52.1±10.4	51.7±9.2	0.78	52.1±10.2
Female sex	85 (30)	34 (37)	0.24	96 (30)	23 (43)	0.05	119 (32)
Born in Australia	209 (75)	60 (65)	0.08	231 (72)	38 (72)	0.91	269 (72)
Speaks another language at home	50 (18)	24 (26)	0.09	57 (18)	17 (32)	0.02	74 (20)
Highest educational qualification			0.66			0.70	
Nil/School Certificate	100 (36)	33 (36)		117 (37)	16 (31)		133 (36)
High School or equivalent	77 (28)	21 (23)		83 (26)	15 (29)		98 (26)

Diploma/Degree	102 (37)	37 (41)		118 (37)	21 (40)		139 (38)
Psychosocial and socioeconomic factors							
Partnered	172 (61)	65 (71)	0.09	201 (63)	36 (68)	0.32	237 (64)
Living alone	56 (20)	8 (9)	0.01	58 (18)	6 (11)	0.22	64 (17)
Household Economics							
Experiencing economic hardship[†]	90 (32)	43 (47)	0.01	109 (34)	24 (45)	0.12	133 (36)
Social contacts							
Able to borrow money	232 (84)	68 (79)	0.35	266 (84)	34 (72)	0.05	300 (82)
Have helpful neighbours	220 (79)	59 (64)	0.005	249 (78)	30 (57)	< 0.001	279 (75)
Able to make decisions	247 (89)	60 (65)	< 0.001	279 (88)	28 (54)	< 0.001	307 (83)
Needs to be alert in neighbourhood	90 (32)	28 (31)	0.78	96 (30)	22 (42)	0.08	118 (32)
Medical History							

Current smoker	113 (41)	45 (49)	0.16	132 (42)	26 (49)	0.30	158 (43)
At-risk drinking‡	43 (15)	18 (20)	0.35	53 (17)	8 (15)	0.77	61 (16)
Any comorbidities	131 (47)	50 (54)	0.22	158 (50)	23 (43)	0.40	181 (49)
Activity restricting illness	49 (18)	34 (37)	<0.001	66 (21)	17 (32)	0.07	83 (22)
Psychiatric history§	85 (30)	50 (54)	< 0.001	109 (34)	26 (49)	0.04	135 (36)
Glasgow Coma Scale score			0.43			0.10	
Severe (3-8)	1 (< 1)	0 (0)		1 (< 1)	0 (0)		1 (0)
Moderate (9-12)	2 (1)	2 (2)		2 (1)	2 (4)		4 (1)
Mild (13-15)	268 (99)	87 (98)		307 (99)	48 (96)		355 (99)
Good cognitive function (TICS≥ 21)‖	232 (83)	75 (82)	0.77	268 (84)	39 (74)	0.06	307 (83)
Frenchay Activities Index			0.02			< 0.001	
Low activity (0-15)	5 (2)	7 (8)		4 (1)	8 (15)		12 (3)
Moderate activity (16-30)	104 (37)	33 (36)		122 (38)	15 (28)		137 (37)

High activity (31-45)	171 (61)	52 (57)		193 (61)	30 (57)		223 (60)
WHODAS II score[#,**]	19.5±17.3	34.6±20.5	< 0.001	19.6±16.3	47.6±19.6	< 0.001	23.4±(19.3)

Table 2. Association between baseline anxiety and depression and disability at 12 months

HADS-A indicates Hospital Anxiety and Depression Scale – Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale – Depression Subscale; WHODAS, World Health Organization Disability Assessment Schedule.

* HADS-A and HADS-D scores range from 0 to 21, with higher scores indicating more severe symptoms.

† Model was adjusted for baseline factors including Glasgow Coma Scale score, Telephone Interview for Cognitive Status score, Frenchay Activity Index score, total WHODAS II score, psychiatric history, speaking another language at home, activity restricting illness, experiencing economic hardship, helpful neighbours, and being able to make good decisions.

‡ Disability was measured using WHODAS II.

	No anxiety (HADS-A score 0-7)*	**Anxiety (HADS-A score 8-21)***	***p*-value†**	**No depression (HADS-D score 0-7)***	**Depression (HADS-D score 8-21)***	***p*-value†**
WHODAS II Domains	**Mean (95% CI)**	**Mean (95% CI)**		**Mean (95% CI)**	**Mean (95% CI)**	

Cognition	8.7 (5.5-11.9)	18.3 (14.5-22.0)	< 0.001	11.8 (8.7-14.9)	13.8 (8.3-19.4)	0.49
Mobility	13.93 (9.8-18.1)	14.4 (9.5-19.3)	0.85	15.2 (11.3-19.0)	8.8 (1.9-15.7)	0.08
Self-care	4.6 (1.5-7.7)	2.4 (0.0-6.1)	0.26	4.5 (1.6-7.5)	0.2 (0.0-5.5)	0.12
Getting along	7.42 (3.9-10.9)	11.9 (7.7-16.0)	0.04	8.6 (5.3-11.9)	11.1 (5.1-17.0)	0.43
Life activities	16.7 (11.3-22.2)	14.1 (7.7-20.6)	0.44	16.7 (11.6-21.8)	11.0 (1.8-20.2)	0.23
Participation	15.9 (12.5-19.3)	22.4 (18.4-26.4)	0.002	18.5 (15.3-21.7)	17.1 (11.3-22.9)	0.65
WHODAS II score‡	11.5 (8.9-14.1)	15.2 (12.2-18.3)	0.02	13.1 (10.6-15.5)	11.8 (7.3-16.2)	0.60

Table 3. Association between baseline anxiety and 12-month disability by sex

HADS-A indicates Hospital Anxiety and Depression Scale – Anxiety Subscale; WHODAS, World Health Organization Disability Assessment Schedule.

		No anxiety (HADS-A score 0-7)[a]	Anxiety (HADS-A score 8-21)[a]	*p-interaction*
		Mean (95% CI)	Mean (95% CI)	
Cognition	Female	8.4 (3.5-13.4)	21.2 (15.2-27.2)	0.27
	Male	9.2 (5.2-13.2)	16.6 (11.9-21.4)	
Mobility	Female	20.6 (13.3-28.0)	20.9 (12.0-29.8)	0.65
	Male	9.4 (4.7-14.2)	11.1 (5.5-16.8)	
Self-care	Female	7.7 (2.5-12.9)	0.0 (0.0-5.8)	0.08
	Male	3.8 (0.009- 7.6)	3.7 (0.0-8.2)	
Getting along	Female	6.0 (1.1-10.8)	11.9 (6.1-17.8)	0.74
	Male	8.3 (3.6-12.9)	12.5 (6.9-18.0)	
Life-activities	Female	25.6 (15.0-36.2)	20.9 (8.0-33.8)	0.89

	Male	11.6 (5.6-17.6)	9.9 (2.7-17.1)	
Participation	Female	19.5 (14.2-24.8)	27.7 (21.3-34.0)	0.76
	Male	13.6 (9.2-18.0)	20.2 (15.0-25.4)	
WHODAS II score	Female	14.2 (10.0-18.4)	19.3 (14.2-24.4)	0.58
	Male	9.9 (6.7-13.1)	13.5 (9.6-17.3)	

Figure legend

Figure 1. Comparison of WHODAS II adjusted mean scores at 12 months by baseline anxiety symptoms

*Indicates the significant difference in mean WHODAS II score between groups.