Associations between cognitive impairment, vulnerability and mortality post-stroke: Findings from a five-year follow-up of the ASPIRE-S cohort

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Introduction

Patients with ischaemic stroke (IS) have a 2-3-fold increased risk of death compared to non-stroke patients.¹ Numerous cardiovascular risk factors have been associated with increased risks of mortality post-stroke.² Cognitive impairment (CI), which may be experienced by over half of patients six months post-stroke, is similarly associated with increased mortality risks.³ Vulnerability has been found to predict both morbidity and mortality in general older adult populations. No study to date has examined vulnerability and its association with mortality in a dedicated stroke population.

Aim

The aim of this study was to study aims to review predictors of mortality in patients five years post-stroke, focusing on cognitive impairment and vulnerability in addition to cardiovascular risk factors.

Methods

Study Population and Recruitment

This analysis is based on data from a five-year follow-up of the ASPIRE-S (Action on Secondary Prevention Interventions and Rehabilitation in stroke) cohort.⁴ Full details of the methodology on recruitment and selection have been published previously.^{5,6}

Cardiovascular Risk Factors

At 6-months post stroke, eligible patients were followed up. A comprehensive assessment was completed, modelled on the EUROASPIRE protocol for evaluation of the adequacy of secondary prevention in post-discharge cardiac patients.⁷ Clinical measurements including blood pressure measurements, lipid profiles, weight, waist circumference, height, pulse, carbon monoxide levels in smokers were recorded and recent international normalised ratio (INR) readings were reviewed in those on warfarin therapy. Demographic data, background medical history and stroke classification and severity were also recorded.

Cognitive Function

Cognitive function was assessed at six months post-stroke using the Montreal Cognitive Assessment (MoCA). We applied the recommended cut-off score of <26 to identify participants with cognitive impairment.

Vulnerability

Vulnerability was assessed using the Vulnerable Elders Scale (VES). The VES is a standardised, validated, 13-point self-completion screening tool that identifies vulnerable individuals at risk for health deterioration and death.⁸ The VES assesses limitations in functional abilities, difficulties with activities of daily living, and self-rated health. Scores range from 0 to 10, with a score ≥3 used to identify vulnerable individuals.

Statistical analysis

Univariate associations with mortality were examined with log rank tests for categorical variables, and univariate Cox regression for continuous variables. Predictors of mortality were examined using multivariate Cox proportional hazards models. Adjusted hazard ratios (HR) and 95% confidence intervals (CI) for each model are presented. An alpha level of $p<0.05$ was assumed to denote statistical significance. Data were analysed using Stata® version 13.

Results

Out of 256 patients last followed up at six months, 63 (24.6%) had died during the follow-up period. In univariate analyses, older age, history of atrial fibrillation, history of stroke/transient ischaemic attack (TIA), vulnerability and cognitive impairment were associated with all-cause mortality within five years.

A number of cox proportional hazards models examined predictors of mortality (Table 2). Both cognitive impairment [HR (95% CI): 2.19 (1.42, 3.39)] and vulnerability [HR (95% CI): 5.23 (2.92, 9.36)] were significantly associated with mortality at five years. While atrial fibrillation [HR (95% CI): 2.27 (1.71, 3.03)] also increased the risk of mortality, a history of stroke/TIA was not associated with mortality in multivariate analyses.

Table 1. Univariate analysis of demographics, stroke event and cardiovascular risk factor profiles, cognitive status and vulnerability by survival status at 5 years.

		Survived five years post-stroke n (%)	Deceased within five years n (%)
Demographics	Age (Mean, SD)	66.2 (12.7)	77.7 (9.7)***
	Male	112 (58.0)	36 (57.1)
	Married (vs. not married)	122 (63.2)	38 (60.3)
	Living alone (vs. living with others)	50 (25.9)	16 (25.4)
	Private insurance (vs. public)	59 (30.6)	18 (28.5)
Bamford classification	TACS (Total anterior circulation stroke)	11 (5.7)	4 (6.5)
	PACS (Partial anterior circulation stroke)	74 (38.3)	29 (46.0)
	POCS (Posterior circulation stroke)	59 (30.6)	11 (17.5)
	LACS (Lacunar stroke)	45 (23.3)	17 (27.0)
	Unclassifiable	4 (2.1)	2 (3.2)
TOAST classification	Cardioembolism	69 (35.8)	31 (49.2)*
	Other	124 (64.2)	32 (50.8)
Uncontrolled vascular risk factors at six months	Hypertension (n=254)	138 (72.3)	42 (66.7)
	TC/HDL-C (n=221)	38 (21.8)	18 (38.3)*
	Impaired fasting glucose (n=231)	25 (14.0)	12 (23.1)
	Overweight/obese (n=250)	112 (59.0)	28 (46.7)
	Smoker	54 (28.0)	17 (27.0)
	History of alcohol abuse	28 (14.5)	9 (14.3)
	History of stroke/TIA	42 (21.8)	22 (34.9)*
	History of heart disease	53 (27.5)	22 (34.9)
	History of carotid stenosis	31 (16.1)	10 (15.9)
	History of AF	62 (32.1)	36 (57.5)***
Total number of cardiovascular risk factors (M, SD)		3 (1.3)	3.4 (1.6)*
Stroke severity (n=253)	Moderate or severe	38 (19.7)	17 (28.3)
Cognitive impairment (n=226)	MoCA <26	90 (50.6)	38 (79.2)***
Vulnerability (n=218)	VES ≥3	65 (37.8)	37 (80.4)***

Note: * $p<.05$, ** $p<.01$, *** $p<.001$

Table 2. Adjusted Hazard Ratios (95% CI) from Cox proportional hazards models for all-cause mortality based on cognitive impairment, vulnerability, atrial fibrillation, history of stroke/TIA, and TC/HDL-C

Model	Adjusted HR (95% CI)*	p
1 Cognitive impairment [§] (n=225)	2.19 (1.42, 3.39)	<.001
2 Vulnerability [§] (n=216)	5.23 (2.92, 9.36)	<.001
3 Atrial fibrillation [†] (n=256)	2.27 (1.71, 3.07)	<.001
4 History of stroke/TIA [§] (n=253)	1.26 (0.80, 1.99)	.315
5 TC/HDL-C [§] (n=219)	1.90 (1.10, 3.27)	.021

[§] adjusted for age, sex, and stroke severity
[†]adjusted for age, sex, and anticoagulant medications

A final model included both cognitive impairment [HR (95% CI): 2.16 (1.46, 3.18)] and vulnerability [HR (95% CI): 4.87 (2.69, 8.81)], with both predictors independently associated with an increased mortality risk (Table 3).

Table 3. Adjusted Hazard Ratios (95% CI) from Cox proportional hazards models for all-cause mortality based on cognitive impairment, vulnerability

Cognitive impairment and vulnerability [§]	Adjusted HR (95% CI)*	p
Cognitive impairment	2.16 (1.46, 3.18)	<.001
Vulnerability	4.87 (2.69, 8.81)	<.001

[§] adjusted for age, sex, and stroke severity. N=204.

Conclusion

Cognitive impairment and vulnerability are associated with significantly increased risk of five-year mortality post-ischaemic stroke. Identification and management of these risk factors should be emphasised in post-stroke care.

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