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Pre-stroke living situation and depression contribute to initial stroke severity and stroke recovery

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Abstract

Substantial evidence from both experimental and clinical studies has demonstrated that social isolation can increase stroke incidence and impair recovery. Social isolation leads to higher rates of recurrent stroke but is often not reported as a risk factor. We examined prospectively collected stroke center database variables, which included pre-stroke living situation, to determine if social isolation could be determined from existing data using living arrangement as a proxy. Patients were categorized into 4 groups hypothesized to represent increasing levels of social isolation: Living with Spouse, Living with Family, Living alone with visiting services and Living Alone. Initial stroke severity and recovery were measured using the National Institutes of Health Stroke Scale and Barthel Index, respectively. A multivariate model was used to determine the relationship between pre-stroke living situation, stroke severity and functional outcome. Patients living alone had less severe strokes on admission and better recovery at 3 months compared to the other cohorts. Patients living alone or those that lived with a spouse had less severe strokes on presentation and better recovery at both 3 and 12 months after stroke compared to the other cohorts. However, upon detailed examination, it was found that these patients also had significantly higher pre-stroke function. Pre-existing depression was significantly higher in women and depressed patients had poorer outcomes 3 months after stroke. Information regarding isolation is notably absent from most large stroke databases. A more comprehensive evaluation of social interaction should be obtained to more accurately measure social isolation.

Keywords

Ischemic Stroke; social isolation; loneliness; depression; gender differences

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Introduction

Stroke is the 4th leading cause of death in the United States and the leading cause of long term disability. Over 7 million Americans have had a stroke [1]. The American Heart Association predicts that by 2030, the direct cost of caring for stroke patients will triple from \$61.55 billion to \$183.13 billion, due in large part to increasing life expectancy, declining stroke-related mortality and aging U.S. population[2, 3]. Even more troubling, data from the U.S. Census show an increase in the number of people living alone from 17.1% of households in 1970 to 27.4% in 2012 (<http://www.census.gov/prod/2013pubs/p20-570.pdf>). With the aging population and the increased rates of individuals living alone, it is imperative to determine if living situation is a risk factor for stroke severity and poor recovery in order to identify at risk populations for both prevention and rehabilitation.

Social support refers to the resources, both material and psychological, a community or network supplies in order for an individual to cope with stressors[4]. Over twenty years ago, after the review of five large prospective studies, a causal association between social relationships and mortality was proposed after finding that social relationships predicted all-cause mortality[5]. Social isolation predicts mortality in a variety of diseases including cardiovascular disease[6], renal disease[7] and cancer[8] yet is still not commonly recognized or reported as a risk factor for disease.

Psychosocial distress has been related to an increased risk in both fatal and non-fatal stroke in the elderly[9]. Additionally, a recent case control trial spanning 22 different countries demonstrated psychological stress to be just as significant of a risk factor as a history of diabetes mellitus, hypertension and smoking[10]. In studies that have investigated social risk factors, strong social support and social networks are associated with lower mortality[11, 12] and improve recovery following stroke[13]. In contrast, socially isolated individuals have poorer functional and cognitive recovery after stroke [14].

The mechanism by which these social factors enhance morbidity and mortality from stroke compared to other more traditional risk factors remains unknown. It has been suggested that poor social support from social isolation can itself act as a stressor[15, 16]. Stress is known to modulate the hypothalamic-pituitary-adrenal axis, leading to increased levels of cortisol[17] which can affect stroke recovery [18]. In studies in rodents subjected to an experimental stroke, isolated animals demonstrate significant neuro-hormonal and inflammatory differences compared to those living with other animals before their stroke[19–21]. Ischemic damage was less severe and behavioral recovery was improved in pair-housed animals[22], which is associated with an increase in brain derived neurotrophic factor (BDNF) [23], neurogenesis and improved recovery[24]. Environmental enrichment has also been shown to increase neurogenesis in animal models, and social interaction likely contributes to this [25, 26]. However, before studies of mechanism can be considered in clinical populations, how isolation could be quantified with existing dataset must be determined.

Social isolation has been measured in a number of different ways using surveys that contain many questions that may not only be time consuming, but difficult for elderly and stroke populations to answer, especially in an emergency setting[27, 28]. Therefore, this study attempted to develop a simple method to measure social isolation that could be used in large stroke center data sets by exploring whether living situation, an easily obtainable demographic, was a sufficient measure to capture the construct of “social isolation”. This information could then be used to identify patients at risk for prolonged and difficult recovery or high risk for recurrent stroke or readmissions. Using information collected from a prospectively collected stroke database, we assessed whether patients who lived alone prior to their stroke had more severe strokes and/or poorer recovery. The main objective was to assess if pre-stroke living situation could serve as an appropriate proxy for social isolation, a known risk factor for stroke morbidity and mortality and as a tool to predict initial severity and outcomes.

Methods

Patient selection

A retrospective review was performed on data from a prospectively collected database at the Hartford Hospital Stroke Center Database in Hartford, Connecticut. Adult patients (18 years old) admitted to the Hartford Hospital Stroke Center with acute ischemic stroke from 2005–2011 with data obtainable on their pre-stroke living situation were examined in the study. Patients were excluded if they were homeless or living in an extended care facility as these living situations are more complex and may have significant confounding variables that could not be controlled for. Patients were also excluded if they had their stroke during an inpatient stay or the time of stroke onset was not obtainable or greater than 48 hours prior to admission as the opportunity for early intervention (i.e., thrombolytic use) is a factor in stroke recovery. (See Figure 1)Data were stored in an ACCESS based database, extracted to EXCEL and then imported into SPSSv14 for analysis. The data base and retrospective studies derived from the data have been approved by the Hartford Hospital IRB.

In order to measure stroke recovery and severity the Barthel Index (BI) and National Institutes of Health Stroke Scale (NIHSS) were used, respectively. The BI is a measure of ability to perform specific activities of daily living, with values ranging from 0–20[29]. We dichotomized BI into poor functional status (BI 14) and favorable functional status (BI 15). The NIHSS was dichotomized with >15 representing severe strokes. A presenting NIHSS 7 has been associated with better clinical outcome [30].

Data collection

Data included demographics, living situation, initial NIHSS, discharge NIHSS, pre-stroke functional status (represented by Barthel Index), medical comorbidities and outcome assessments including mortality and discharge to hospice at discharge and at 3 and 12 months post-stroke. Functional outcomes were assessed using the Barthel Index at either a clinic visit or structured telephone interview.

Using pre-stroke living situation, patients were categorized into 4 groups that were hypothesized to represent increasing decreasing social isolation: 1. Living with Spouse 2. Living with Family 3. Living alone with visiting services 4. Living Alone

The primary outcome measures were NIHSS upon admission, the change in NIHSS from admission to discharge (a surrogate marker of acute outcome/recovery), and mortality. The Modified Barthel Index at 3 and 12 months was used to assess chronic recovery.

Statistics

Univariate and bivariate analyses were conducted comparing the four groups using chi square test of proportions for categorical data and one-way ANOVA (if normally distributed) or Kruskal-Wallis for continuous data. Differences within the past medical histories of each group were determined using univariate analysis. The medical conditions which were found to be statistically significant at $p < .10$ were entered as covariates in a multivariate, logistical regression to predict stroke outcome and severity between each of the four groups.

Results

3599 ischemic stroke patients with pre-stroke living situation were identified. 151 were excluded for being homeless or living in an extended care facility (ECF). 207 were excluded for having strokes during their hospitalization for another condition. 1422 were excluded for their stroke onset being >48 hrs or not available. 1819 patients were left, of which 1739 had NIHSS available on admission, 1166 with NIHSS available at discharge and 1065 with Barthel index available at 3 months (See Figure 1).

Demographics

The demographics and clinical features of the cohorts are presented in Table 1.

Analysis of patient pre-stroke living situation demonstrated that 21.4% lived alone, 4.3% lived alone while receiving services, 21.9% lived at home with family or friends, and 52.3% lived with their spouse (See Table 2).

The mean age of the total cohort was 70.4; 72.9 for patients who lived alone, 72.4 for patients who lived alone and received services, 73.1 for patients who lived at home with family or friends and 66.8 for patients who lived with their spouse. (See Table 2).

There were no statistical differences for history of diabetes, atherosclerosis, hyperlipidemia or smoking between living situation cohorts. Statistical differences between groups were found for previous stroke ($p < .05$), hypertension ($p = .001$), dementia ($p < .001$), atrial fibrillation ($p = .001$), depression ($p < .05$) and age >75 ($p < .001$) (See Table 3).

49.3% of all patients were women. Women made up a large percentage of the patients that lived home alone (63.3% of those living alone, 65.4% of those living alone with services, 69.9% of those living with family and only 33.6% of those living with their spouse ($p < .001$)) (See Table 2).

Stroke severity

Initial univariate analysis of stroke severity (admission NIHSS) found that 37.3% of patients living alone with services and 33.5% living with family suffered severe strokes (NIHSS 15–40) compared to only 18.6% of patients living alone and 25.5% living with their spouse ($p < .001$). When NIHSS at discharge was assessed there was significant differences amongst the groups; 4.5% of patients living alone, 7.5% of patients living with a spouse, 16.9% of patients living alone with services and 10.2% of patients living with family continued to have severe deficits (NIHSS 15–40) ($p < .05$) (See Table 2). The relationship between living situation and admission NIHSS held after multivariate analysis ($p < .001$). Multivariate analysis showed that living situation predicts admission NIH independent of age, gender and previous medical history (hypertension, previous stroke, atrial fibrillation, dementia and depression).

Stroke Outcome

Univariate analysis of the Barthel Index at admission showed 51.3% of patients living alone and 51% of patients living a Barthel Index >15 (“good” functionality) compared to 38.2% of patients living alone with services and 41% living with family or friends ($p < .05$). Barthel Index at 3 months demonstrated 81.5% of patients living alone and 85% of patients living with their spouse had a Barthel Index >15 (a “good” outcome) compared to 74.4% of patients living alone with services and 74.2% of patients living with family ($p < .05$) (See Table 2). No statistical difference was found between groups at 12 months. A multivariate analysis examining the Barthel Index at 3 months and living situation using the following co-variables (age, gender and previous medical history that was found to be significantly different between living situation groups in the univariate analysis (hypertension, stroke, atrial fibrillation, dementia and depression)) demonstrated no significance effect of living situation on the 3 month BI.

Depression

Patients with depression were significantly older than those who were depression free (70.0 vs. 67.4, respectively, $p < .05$). Women were also significantly more likely to have preexisting depression when compared to men (66.7% vs. 33.3%, $p < .001$). 7.2% of patients living alone, 9.5% of patients living with their spouse, 17.9% of patients living alone with services and 13.5% living with family or friends were depressed ($p < .05$) (See Table 3). No significant difference was found in initial stroke severity. However, 30.4% of patients with preexisting depression had a Barthel Index <15 at 3 months (a poor outcome) compared to only 16.9% of patients who were depression free prior to their stroke ($p = .001$) (See Table 4). This was confirmed in subsequent multivariate analysis that controlled for age, sex and initial NIHSS; patients with pre-existing depression recovered less well than non-depressed individuals even after controlling for initial stroke severity ($p < .05$).

Discussion

Social isolation

Our study investigated the relationship between pre-stroke living situation, stroke severity and stroke recovery as measured by the NIHSS and BI, respectively. Based on previous studies supporting a relationship between social isolation and poor health outcomes[5–7, 14] it was hypothesized that patients coming from more socially isolated pre-stroke living situations would have more severe strokes and poorer recovery. Pre-stroke living situation was categorized into 4 groups that were hypothesized to represent increasing social isolation: (1) living alone; (2) living alone but receiving in home services; (3) living with friends or family members other than a spouse or significant other and (4) living with spouse.

Our results suggest that patients who had the most severe strokes did not come from the groups that were thought to represent the most socially isolated individuals. Patients living alone or with their spouse had significantly less severe strokes than patients who lived alone with services or lived with family, contradictory to our original hypothesis. This suggests that social isolation is not well represented by pre-stroke living situation. Both social support and social integration are important when discussing social relationships. A meta-analysis of 148 studies that investigated the relationship between strong social relationships and decreased mortality determined that studies that included complex measures of social involvement demonstrated a stronger association with outcomes[31]. Therefore, living situation alone does not serve as an adequate proxy for social isolation.

The perception of social isolation (loneliness) and the quality rather than quantity of social interactions is more tightly tied to health outcomes than objective social isolation[32–34]. Loneliness predicts elevated blood pressure[35], morning rise in cortisol[36] and is linked to changes in quality of life[37] and mortality[38] beyond predictors based on objective social isolation. Anti-inflammatory glucocorticoid response elements (GRE) were found to be under-expressed in lonely individuals, whereas over-expression of genes bearing response elements for the pro-inflammatory NK- κ B/Rel transcription factor were seen[39]. Patients under chronic social stress identified as low social economic status were found to have an increase in immature pro-inflammatory monocytes in their circulating leukocyte pool whose myelopoietic stimulation may be under beta-adrenergic control[40]. The Lubben Social Network Scale has been developed for use in older adults and takes into account different areas of the social network including family, friends and neighbors[27]. Unfortunately, its length and repetitive questions may be confusing for patients in the acute stroke setting. The revised UCLA Loneliness scale is a 20 item questionnaire regarding experiences related to loneliness[28] which may also be difficult to complete. Subjective feelings of “loneliness” are better measures of isolation than many objective demographic factors, and these can be captured by relatively simple scales such as the 3 item UCLA social isolation scale[28].

Patients with poor social support were found to have a decreased protective immune response against viral infection [41] and enhanced inflammation has been suggested as a possible mechanism mediating the detrimental effects of isolation[42]. An association has been described between social isolation and concomitant depression with increased levels of

inflammatory markers such as IL-6 and CRP [43]. Chronic social stress has been associated with increased oxidative stress in the prefrontal cortex of rats and an increase in depressive like behavior[44]. It is well established that depression increases the risk of stroke, especially in women[45–47] and that depression is related to poor quality of life after stroke[48]. Depression is also a common sequelae after stroke [49], likely increasing the risk of recurrent stroke. The assessment of both isolation and depression should be included in the routine care of stroke patients, as they likely independently impact stroke recovery and subsequent health care costs.

Sex and depression

Many studies have shown that patients with depression have both an increased risk of stroke and increased morbidity and mortality following stroke[45, 47]. Major depression is two times more frequent in women following stroke[50] and the prevalence of post stroke depression is more likely with a previous history depressive illness[49]. Our results are consistent; women were significantly more likely to have a history of depression compared to men and patients with depression had significantly worse outcomes at 3 months. Women are also more likely to live alone in our cohort, which likely contributes to the 3-fold higher rates of institutionalization seen in women after stroke[51, 52]. Widowhood reduces the chance of return to the community and decreases recovery in the post-stroke population and contributes to the growing incidence of social isolation in the elderly[53] and women are older at the time of stroke. Although women in our study made up the majority of patients living alone, this group did not have poorer recovery when compared to other groups, implying a complex relationship between sex, age, depression and isolation that requires further study.

This study has discovered several important new findings, the most important of which is that social isolation cannot be determined with current demographic variables used in most large databases. Simple assessments of isolation using well validated, brief surveys should be performed to identify patients at risk for the detrimental effects of social isolation. As individuals who report lack of social support/loneliness have an increased incidence of recurrent stroke, poorer recovery, and greater functional decline over the 5 years following a stroke[14], identification of these at risk patients provides us with the opportunity to intervene to reduce these risks[54]. From our work and from that of others, it is clear that older women that live alone and have a history of depression are at extremely high risk for poor outcome after stroke. These factors could be used to identify individuals with increased risk of stroke severity, morbidity and mortality. Social interventions should be pursued in elderly women who have decreased social interaction and exhibit signs of depression. We have now included both a social isolation/interaction screen and a depression screen to our database and future studies will determine if these can be used to identify patients at risk for poor outcomes and help determine the underlying molecular responses responsible for the detrimental effects of loneliness. Patients living in nursing homes, having prolonged hospital stays or living in assisted care facilities may all experience social isolation. The ability to properly and reliably screen for isolation is an important step in improving interventions for rehabilitation.

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Figure 1.
Flowchart of Patient Selection for study

Table 1

Characteristics of patients with pre-stroke living situation available

Classification	Number (%)	Data Missing	Valid Percent (non-missing)
Gender			
Female	897 (49.3)		
Male	922 (50.7)		
Past Medical History			
Stroke	419 (23.0)		
Hypertension	1407 (77.4)		
Diabetes	475 (26.1)		
Atrial Fibrillation	556 (30.6)		
Atherosclerosis	509 (28.0)	878 (48.3)	54.1
Hypercholesterolemia	953 (52.4)		
Dementia	112 (6.2)		
Depression	186 (10.2)		
Smoking	389 (21.4)	126 (6.9)	23
Drugs	69 (3.8)	505 (27.8)	5.3
Alcohol	556 (30.6)	190 (10.4)	34.1

Table 2

Living Cohorts, Stroke Severity and Recovery

NIHSS>15 is associated with a severe stroke. Barthel Index >14 is associated with good functional status. NIHSS = National Institutes of Health Stroke Scale

	Alone	Alone with Services	With family or Friends	Spouse	p value
N (%)	390 (21.4)	78 (4.3)	399 (21.9)	952 (52.3)	-
Age	72.9	72.4	73.1	66.8	<.001
% Female	63.3	65.4	69.9	33.6	<.001
NIHSS >15					
on Admission	69 (18.6)	28 (37.3)	128 (33.5)	233 (25.5)	<.001
on Discharge	11 (4.5)	10 (16.9)	23 (10.2)	92 (7.5)	<.05
Barthel Index >14					
on Admission	174 (51.3)	26 (38.2)	132 (41.0)	427 (51.0)	<.05
at 3 months	189 (81.5)	32 (74.4)	147 (74.2)	503 (85.0)	<.05
at 12 Months	136 (84.0)	23 (79.3)	103 (82.4)	352 (88.4)	NS

Table 3

Living Cohorts and Previous Medical History

Data represented as percentage of population.

	Alone N (%)	Alone with Services N (%)	With family or Friends N (%)	Spouse N (%)	p value
Past Medical History					
Stroke	88 (22.6)	19 (24.4)	112 (28.1)	200 (21.0)	<.05
Hypertension	317 (81.3)	61 (78.2)	328 (82.2)	701 (73.6)	0.001
Diabetes	103 (26.4)	23 (29.5)	103 (25.8)	246 (25.8)	NS
Atrial Fibrillation	122 (31.3)	27 (34.6)	150 (37.6)	257 (27.0)	0.001
Atherosclerosis	108 (57.1)	18 (52.9)	107 (51.7)	276 (54.0)	NS
Hypercholesterolemia	213 (54.6)	33 (42.3)	196 (49.1)	511 (53.7)	NS
Dementia	14 (3.6)	9 (11.5)	40 (10.0)	49 (5.1)	<.001
Smoking	90 (24.9)	13 (17.3)	77 (21.3)	209 (23.3)	NS
Drugs	12 (4.3)	4 (6.9)	26 (9.3)	27 (3.9)	<.05
Alcohol	116 (33.5)	23 (31.0)	77 (22.2)	341 (39.4)	<.001
Depression	28 (7.2)	14 (17.9)	54 (13.5)	90 (9.5)	<.05
Age >75	202 (51.8)	43 (55.1)	233 (58.4)	336 (35.3)	<.001

Table 4
Depression and Stroke Recovery

Depression defined as having a preexisting diagnosis of depression before stroke onset.

	Age	% Female	Barthel Index <15 at 3 months
Depression	70	124 (66.7)	31 (30.4)
No Depression	67.4	773 (47.3)	163 (16.9)
p Value	<.05	0.001	0.001