Time Trends and Characteristics of Prevalent Dementia among Patients Hospitalized for Stroke in the United States

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Background: Little is known about how prevalent dementia rates among patients with stroke have evolved over the last decade or how this relationship varies by gender, race ethnicity, stroke type, or dementia type. We assessed time trends and demographic predictors of coexisting dementia in a large cohort of patients hospitalized for stroke. *Materials and Methods:* Patient admission data between 1999 and 2012 were sourced from the National Inpatient Sample. Patient admission records were included in the retrospective analysis if they were diagnosed with ischemic or hemorrhagic stroke during admission. Predictors of dementia subtype were analyzed using unadjusted and adjusted multinomial logistic regression. *Results:* Of 1,170,051 patients hospitalized for stroke between 1999 and 2012, 66,703 (5.7%) had a coexisting diagnosis of dementia. Female gender was associated with increased odds of Alzheimer's dementia (AD) (adjusted odds ratio [aOR] 1.15, 95% confidence interval [CI] 1.11-1.19) but decreased odds of both vascular dementia (VaD) (aOR .50, 95% CI .44-.58) and non-Alzheimer's–nonvascular dementia (aOR .79, 95% CI .79, 95% CI .74-.83). Relative to whites, African-Americans had higher odds of AD (aOR 1.25, 95% CI 1.18-1.32) and VaD (aOR 1.51, 95% CI 1.40-1.64). Similarly, Hispanics had increased odds of AD (aOR 1.40, 95% CI 1.30-1.50). *Conclusions:* Rates of coexisting dementia among patients hospitalized for stroke in the United States have risen over the last decade. Prevalence of dementia among these patients varies by gender and race-ethnicity. Key demographic groups may need to be targeted to reduce disparities in dementia occurrence. **Key Words:** Stroke—dementia—dementia subtype—nationwide—hospitalization.

Introduction

Stroke is a major cause of disability among the elderly, and the progression from stroke to cognitive impairment and dementia is common. Recent estimates of the prevalence of cognitive impairment among patients with stroke range from 20% to 80%, depending upon the setting and appear to be increasing in parallel to improvements in poststroke survival.[1] Although the neurovascular mechanisms underlying the pathogenesis of vascular dementia (VaD) in patients with stroke have been well described, less is known around the relationship between stroke and Alzheimer's disease.[2] These include well-documented vascular risk factors such as hypertension, dyslipidemia, diabetes mellitus, previous infarct history, and alcohol intake in addition to more lifestyle and clinical predictors such as diet, physical activity, cerebral magnetic resonance imaging markers, peripheral arterial disease, and heart failure.[3-7] There is a considerable overlap between risk factors for stroke and both vascular cognitive impairment and Alzheimer's disease.[8] Although previous studies have suggested a synergistic interaction of such risk factors in the clinical manifestation

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of both dementia and cerebrovascular disease,[9-11] isolating the independent influence of any 1 risk factor has been proven to be difficult, particularly with regard to relatively heterogeneous diseases such as VaD. Of the comparatively limited studies on dementia risk factor studies explicitly in a stroke cohort setting, results are mixed. This is particularly the case with less well-established demographic risk factors including gender and ethnicity. The 14-year longitudinal ARIC magnetic resonance imaging confirmed hypertension, insulin resistance, and previous stroke as correlates of increased risk of cognitive decline in the stroke cohort, but was unable to isolate any demographic risk factors such as gender or ethnicity.[12] Conversely, a meta-analysis of 30 stroke cohorts across 59 years observed that the female gender was associated with a higher risk of a dementia diagnosis before stroke relative to the male gender, although this correlation was not replicated for poststroke dementia.[13]

The objective of the present study was primarily to explore the clinical and demographic predictors of dementia type, and secondarily to also elucidate trends of disease association and prevalence in a large cohort of patients with stroke sourced from the Nationwide Inpatient Sample (NIS) administrative admission database and describe trends in dementia subtype over time.

Materials and Methods

Data Source

All data used in this analysis were sourced from the NIS, a database of hospital inpatient admissions derived from hospital-level administrative data from across the United States, administered as part of the broader Health Cost and Utilization Project (HCUP).[14] Because this was an analysis of publicly available deidentified data, the study was exempted by the institutional review board. Patient records included in the NIS represent a 20% sample of discharges from hospitals participating in the HCUP. Patient records were stratified as per the sampling methodology employed by NIS. Prevalence trend data were further weighted in accordance with NIS guidelines.

Inclusions

Patient admission records were included in the analysis if they recorded any of the following International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes for any admission available from NIS within the observation years of 1999 through 2012 inclusive: "431" for hemorrhagic stroke, and "434.01," "434.11," or "434.91" for ischemic stroke. Records where both hemorrhagic and ischemic strokes were recorded concurrently for the same admission were excluded from the analysis. This process identified 1,170,051 eligible discharge records, which were then screened for the following primary dementia type codes: "331.0" for Alzheimer's dementia (AD), and 290.4X VaD and "331.11," 331.19," or "331.82" for non-Alzheimer's–nonvascular dementia (NAVD). Both primary and secondary diagnosis codes were included. This resulted in a total of 66,703 eligible patient admission records used for the primary analysis.

Outcomes and Definitions

The primary outcome of the analysis was dementia subtype, defined over 3 levels: (1) AD, (2) VaD, and (3) NAVD.

Statistical Analyses

Categorical variables were summarized using frequency and percentage and were compared across dementia types using a chi-square test. Continuous variables were summarized using mean, standard deviation, and standard error (SE) or median and interquartile range, and were compared by dementia type using an analysis of variance or Kruskal–Wallis test as appropriate. A chi-square test of trend was used to assess prevalence trends for significance. Demographic, socioeconomic, and comorbidity factors potentially associated with dementia type were analyzed using unadjusted and adjusted multinomial logistic regressions. The multinomial approach describes an extension of traditional binary outcome logistic regression and is appropriate for outcome variables defined on 3 or more levels. For this analysis, the 3 dementia subtypes were compared against a reference group comprising nondementia stroke admissions. Comorbidity factors included in the modeling were identified using ICD-9-CM codes as summarized in Supplementary Table S1. Subgroup analysis was performed disaggregating the models on age (<85 years, 85+) and stroke type (hemorrhagic or ischemic). An Akaike Information Criterion (AIC) was used to compare goodness of fit across models. For all analyses, a P value less than .05 was considered significant. All analyses were conducted in SAS version XX (SAS Institute Inc, Cary, NC).

Results

Admission Characteristics

Of the 1,170,051 admission records identified between 1999 and 2012 recording a stroke diagnosis, 1,003,218 (85.7%) were ischemic strokes and 166,833 (14.3%) were hemorrhagic strokes. Of these admissions, 66,703 (5.7%) also recorded a dementia diagnosis, of which 43,524 (65.3%) were AD, 20,321 (30.5%) were VaD, and the remaining 2858 (4.3%) were NAVD. The mean (SE) age at stroke admission was highest in the AD group at 83.3 years (.03) compared with 81.4 years (.13) for NAVD and 79.7 years (.06) for VaD (Table 1). The mean (SE) length of stay was longest for patients with VaD (7.1 days, SE .06), marginally greater than both NAVD (6.4 days) and AD (6.1 days).

Table 1. *Summary of admission and baseline characteristics*

Characteristic	Level	Dementia subgroup: Alzheimer's (n = 43,524)		Vascular (n = 20,321)		Non-Alzheimer's–nonvascular (n = 2,858)		Nondementia (n = 1,103,348)	
Patient characteristics		n	%	n	%	n	%	n	%
Age (y)—mean (SE)		83.26 (.03)		79.71 (.06)		81.42 (.13)		76.87 (.01)	
Gender—n (%)	Female	29,312	67.3	11,593	57.0	1,318	46.1	623,288	56.5
	Male	14,209	32.6	8,728	43.0	1,540	53.9	479,955	43.5
	Not reported	3	.0	0	.0	0	.0	105	.0
Ethnicity—n (%)	White	27,180	62.4	11,985	59.0	1,977	69.2	666,663	60.4
	African-American	4,210	9.7	2,833	13.9	201	7.0	111,943	10.1
	Hispanic	2,394	5.5	897	4.4	141	4.9	57,176	5.2
	Other	1,562	3.6	745	3.7	112	3.9	48,634	4.4
	Not reported	8,178	18.8	3,861	19.0	427	14.9	218,922	19.8
Income quartile ($U.S.)—n (%)	1-38,999	9,618	22.1	4,251	20.9	604	21.1	226,365	20.5
	39k-47.9k	8,251	19.0	3,730	18.4	634	22.2	211,865	19.2
	48-62.9k	7,994	18.4	3,450	17.0	770	26.9	192,914	17.5
	63k or higher	7,640	17.6	3,035	14.9	796	27.9	172,296	15.6
	Not reported	10,021	23.0	5,855	28.8	54	1.9	299,908	27.2
Comorbidity—n (%)	Hypertension	25,479	58.5	12,006	59.1	1,609	56.3	674,394	61.1
	Diabetes (type 2)	9,407	21.6	6,142	30.2	6,993	24.7	309,296	28.0
	Hyperlipidemia	7,434	17.1	3,987	19.6	649	22.7	256,096	23.2
	Chronic heart failure	6,300	14.5	3,089	15.2	382	13.4	176,954	16.0
	Atrial fibrillation	10,851	24.9	15,455	76.1	693	24.2	285,872	25.9
	Hypercholesterolemia	2,570	5.9	1,282	6.3	171	6.0	95,721	8.7
	CAD	2,758	6.3	1,514	7.5	221	7.7	1,103,348	100.0
	Depression	4,202	9.7	2,085	10.3	393	13.8	69,457	6.3
Admission characteristics		n	%	n	%	n	%	n	%
Length of stay (d)—mean (SE)		6.11 (.03)		7.12 (.06)		6.38 (.12)		7.03 (.01)	
Hospital location—n (%)	Rural	5,105	11.7	2,261	11.1	166	5.8	113,574	10.3
	Urban	24,780	56.9	12,123	59.7	1,239	43.4	644,331	58.4
Discharge	Routine	5,439	12.5	2,931	14.4	277	9.7	289,063	26.2
	Transfer	838	1.9	412	2.0	51	1.8	37,112	3.4
	Intermediate or other	26,732	61.4	12,836	63.2	1,838	64.3	506,079	45.9
	Death	4,990	11.5	1,328	6.5	304	10.6	133,655	12.1
	Not reported	5,525	12.7	2,814	13.8	388	13.6	137,439	12.5
Insurance	Medicare	39,932	91.7	17,945	88.3	2,598	90.9	895,049	81.1
	Medicaid	544	1.2	561	2.8	40	1.4	34,508	3.1
	Private	2,439	5.6	1,426	7.0	180	6.3	137,465	12.5
	Self-pay	171	.4	154	.8	8	.3	18,104	1.6
	No charge	22	.1	22	.1	1	.0	1,731	.2
	Other	356	.8	179	.9	24	.8	14,725	1.3
	Not reported	60	.1	34	.2	7	.2	1,766	.2

Abbreviations: CAD, coronary artery disease; SE, standard error.

The highest proportion of female patients was observed in the AD group (67.3%) followed by VaD (57.0%) and a minority of NAVD dementia (46.1%). The majority of admissions were to urban hospitals across all 3 dementia types (56.9%, 59.7%, and 43.4% of admissions reporting a location for AD, VaD, and NAVD, respectively), whereas the majority of discharges were to an intermediate care service (61.4%, 63.2%, and 64.3% of AD, VaD, and NAVD admissions, respectively). Across all stroke admissions for patients with dementia, a total of 6622 (9.9%) deaths were recorded with the highest percentage recorded in patients with AD (11.5% of AD admissions) followed by NAVD (n = 304 deaths, 10.6%) and VD (n = 1328 deaths, 6.5%). Depression was recorded as a comorbidity in 6680

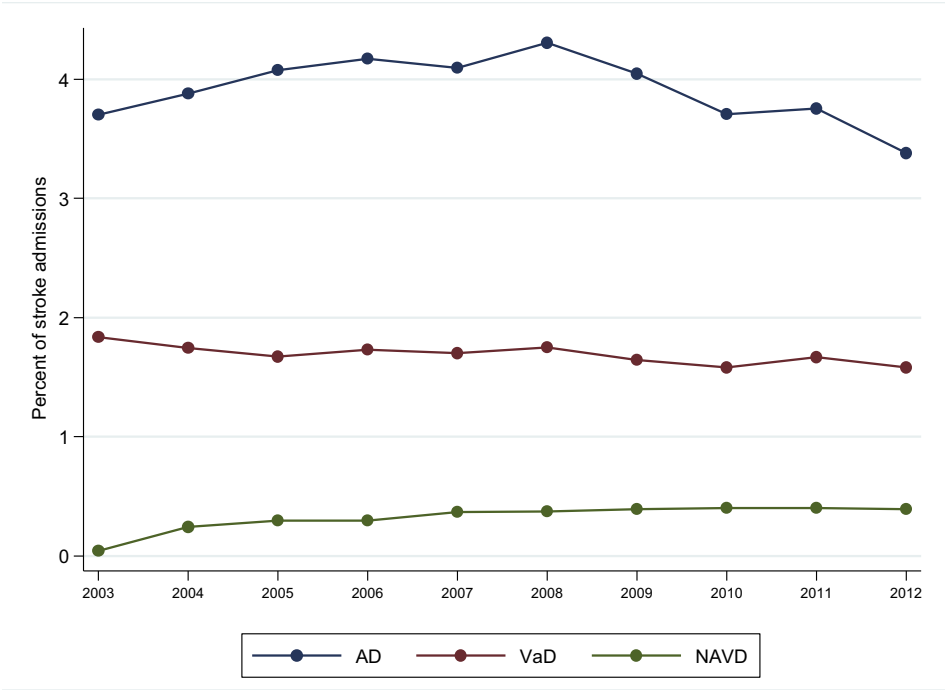

Figure 1. *(Point) prevalence by year by dementia type. Abbreviations: AD, Alzheimer's dementia; NAVD, non-Alzheimer's–nonvascular dementia; VaD, vascular dementia.*

(10.0%) of all dementia admissions, with the highest proportion recorded in NAVD (13.8%). The distributions of other comorbidities are further summarized in Table 1.

Prevalence and Trends

Across the 1999-2012 observation period, the proportion of patients admitted for stroke with concurrent AD steadily and significantly increased from 2.8% of studied stroke admissions in 2003 to a peak of 4.3% in 2008 ($P < .001$), after which prevalence has since decreased to 3.4% in 2012 ($P < .001$) (Fig 1). Prevalence of VaD in the stroke admissions studied has remained steady across the 14 years from 1.8% in 2003 to 1.6% in 2012 ($P < .001$). The prevalence of stroke admissions with NAVD dementia was nonexistent from 1999 to 2003 and has described a marginal increase from .04% in 2003 to .39% in 2012 ($P < .001$).

Patient and Admission Factors and Correlation with Dementia Subtype

On adjusted multinomial modeling, every year older at stroke admission was associated with a 1.08, 1.03, and 1.05 times the odds of having AD, VaD, and NAVD dementia, respectively (Table 2). Being female increased the risk of AD on stroke presentation (adjusted odds ratio [aOR] 1.15, 95% confidence interval [CI] 1.11-1.19) but appeared to be protective for both VaD (aOR .50, 95% CI .44-.58) and NAVD (aOR .79, 95% CI .74-.83). African-Americans were associated with 1.25 times the odds of having AD on admission (aOR 1.25, 95% CI 1.18-1.32) and 1.51 times the odds of VaD (aOR 1.51, 95% CI 1.40-1.64) relative to whites. Conversely, an inverse relationship was observed with regard to NAVD dementia with African-Americans associated with a 36% reduction in the odds of NAVD (aOR .64, 95% CI .49-.84). Similarly, Hispanics were associated with increased odds of having AD on admission relative to whites (aOR 1.40, 95% CI 1.30-1.50), although no such difference was observed in either the likelihood of VaD or NAVD. Increasing income appeared to correlate with increased odds of NAVD (aOR 1.37, 95% CI 1.13-1.66), although no such association was observed in either AD or VaD. Depression was strongly associated with increased odds of all 3 dementia types on stroke admission, when compared against nondementia stroke. The largest signal was observed in the NAVD group with depression associated with 2.37 times the odds of NAVD on admission (aOR 2.37, 95% CI 1.97-2.85), followed by VaD (aOR 1.76, 95% CI 1.97-2.85) and AD (aOR 1.67, 95% CI 1.57-1.77). Of the other comorbidities studied, hypertension, hyperlipidemia, atrial fibrillation, and chronic heart failure were all associated with significantly reduced odds of all 3 dementia subtypes (i.e., these patients were more likely to present with stroke without dementia). Patients with type 2 diabetes were more likely to have VaD on admission (aOR 1.22, 95% CI 1.15-1.29) but *less* likely to have either AD (aOR .90, 95% CI .86-.94) or NAVD (aOR .85, 95% CI .73-.99). Coronary artery disease decreased the odds of AD on admission for stroke (aOR .85; 95% CI .79-.92) but was not associated with either

Table 2. *Multinomial logistic regression—patient and admission correlates with dementia subtype*

Outcome*	Characteristic	Adjusted odds ratio	95% Confidence interval	
			Lower limit	Upper limit
Patient factors				
No dementia	Age (continuous)		Reference	
AD		1.076	1.074	1.079
NAVD		1.053	1.045	1.061
VaD		1.034	1.031	1.037
No dementia	Female gender		Reference	
AD		1.149	1.105	1.194
NAVD		.504	.442	.575
VaD		.786	.744	.831
No dementia	Ethnicity		Reference	
AD	(African-American	1.246	1.175	1.321
NAVD	versus white)	.64	.49	.836
VaD		1.513	1.401	1.635
No dementia	Ethnicity		Reference	
AD	(Hispanic versus white)	1.398	1.299	1.504
NAVD		.959	.719	1.279
VaD		.976	.867	1.1
No dementia	Income quartile		Reference	
AD	(>63k versus 1-38,999)	1.02	.968	1.075
NAVD		1.372	1.134	1.661
VaD		1.027	.948	1.112
No dementia	Depression		Reference	
AD		1.669	1.573	1.772
NAVD		2.372	1.972	2.854
VaD		1.756	1.609	1.917
No dementia	Hypertension		Reference	
AD		.888	.856	.922
NAVD		.777	.681	.886
VaD		.911	.861	.964
No dementia	Type 2 diabetes		Reference	
AD		.899	.86	.939
NAVD		.853	.73	.996
VaD		1.215	1.146	1.29
No dementia	Hyperlipidemia		Reference	
AD		.788	.749	.829
NAVD		.729	.611	.869
VaD		.865	.805	.928
No dementia	Atrial fibrillation		Reference	
AD		.713	.683	.744
NAVD		.568	.484	.667
VaD		.77	.722	.822
No dementia	Chronic heart failure		Reference	
AD		.741	.704	.779
NAVD		.684	.565	.829
VaD		.849	.789	.915
No dementia	Coronary artery disease		Reference	
AD		.854	.793	.918
NAVD		.832	.651	1.062
VaD		.972	.881	1.074
Admission factors				
No dementia	Stroke type		Reference	
AD	(hemorrhagic	1.25	1.189	1.313
NAVD	versus ischemic)	.808	.662	.985
VaD		.563	.51	.622

(*continued on next page*)

Table 2 (*continued*)

Outcome*	Characteristic	Adjusted odds ratio	95% Confidence interval	
			Lower limit	Upper limit
No dementia	Hospital location		Reference	
AD	(urban versus rural)	.912	.865	.961
NAVD		1.324	1.064	1.648
VaD		1.008	.929	1.094
No dementia	Insurance		Reference	
AD	(private versus	.694	.638	.755
NAVD	Medicare)	.588	.436	.793
VaD		.618	.547	.698
No dementia	Insurance		Reference	
AD	(self-pay versus	.438	.326	.589
NAVD	Medicare)	.114	.016	.812
VaD		.623	.444	.874
No dementia	Discharge		Reference	
AD	(death versus routine)	1.293	1.204	1.388
NAVD		2.144	1.643	2.799
VaD		.984	.872	1.11

Abbreviations: AD, Alzheimer's dementia; NAVD, non-Alzheimer's–nonvascular dementia; VaD, vascular dementia.
*Adjusted for admission year.

VaD or NAVD. Of the admission factors studied, admission for hemorrhagic stroke was associated with 1.25 times the odds of concurrent AD (aOR 1.25, 95% CI 1.19-1.31) relative to ischemic stroke. Conversely, hemorrhagic strokes correlated with a *reduction* in the odds of both VaD (aOR .56, 95% CI .51-.62) and NAVD (aOR .81, 95% CI .66-.99). Urban hospitals were more likely to admit patients with stroke with NAVD (aOR 1.32, 95% CI 1.06-1.65) relative to rural sites but less likely to admit patients with AD (aOR .91, 95% CI .87-.96). Privately insured and self-pay patients were more likely to present with nondementia stroke relative to medicate patients. An admission resulting in patient death was more likely in patients with AD relative to patients with nondementia stroke (aOR 1.29, 95% CI 1.20-1.39) and NAVD patients (aOR 2.14, 95% CI 1.64-2.80).

Subgroup Analyses—Hemorrhagic versus Ischemic Stroke

Age and gender demonstrated similar associations with dementia type in both the hemorrhagic and ischemic admission subgroups (Table 3). However, some differences were observed with regard to ethnicity. African-Americans were associated with 1.29 times the odds of AD (aOR 1.29, 95% CI 1.08-1.18) relative to whites in the ischemic stroke group. However, no such association was observed in the hemorrhagic group (aOR 1.04, 95% CI .89-1.22). Similarly, the top income bracket (>63k) was associated with increased odds of NAVD in the ischemic group (aOR 1.42, 95% CI 1.16-1.74) but not in the hemorrhagic group (aOR 1.07, 95% CI .63-1.82). Depression was again more prevalent across all dementia groups relative to nondementia stroke in both hemorrhagic and ischemic groups. The reduction in the odds of dementia associated with hypertension, hyperlipidemia, and chronic heart failure observed across the full sample appears to be more localized to ischemic strokes rather than in hemorrhagic presentations.

Subgroup Analyses—Age 85+

Older patients (aged 85 years and older at admission) generally reported similar magnitudes and significance of associations between dementia type and most patient and admission factors studied relative to younger patients (Table 4). Younger patients with dementia at stroke admission generally reported larger odds of both depression and death for all 3 dementia types relative to older patients.

Discussion

This retrospective analysis of a large inpatient sample of stroke admissions with or without concurrent dementia observed several key distinctions within the distribution of potential prognostic correlates of both stroke and dementia between the 3 different dementia subtypes. Although many of the patient and admission factors studied described a similar *direction* of effect across the 3 dementia subtypes (differing only in the effect magnitude), ethnicity, gender, stroke type, type 2 diabetes, and hospital location were notable for their differences in the direction of their respective associations with the different

Table 3. *Subgroup analysis: hemorrhagic versus ischemic stroke*

		Hemorrhagic stroke			Ischemic stroke		
			95% Confidence interval			95% Confidence interval	
Outcome*	Characteristic	Adjusted odds ratio	Lower limit	Upper limit	Adjusted odds ratio	Lower limit	Upper limit
Patient factors							
No dementia	Age (continuous)		Reference			Reference	
AD		1.073	1.068	1.078	1.077	1.075	1.079
NAVD		1.058	1.036	1.081	1.052	1.044	1.06
VaD		1.047	1.035	1.059	1.033	1.029	1.037
No dementia	Female gender		Reference			Reference	
AD		1.233	1.123	1.354	1.129	1.082	1.179
NAVD		.546	.379	.787	.499	.433	.574
VaD		.85	.701	1.031	.78	.736	.827
No dementia	Ethnicity		Reference			Reference	
AD	(African-American	1.043	.891	1.221	1.285	1.206	1.368
NAVD	versus white)	.453	.174	1.18	.664	.503	.876
VaD		1.631	1.231	2.161	1.504	1.388	1.63
No dementia	Ethnicity (Hispanic		Reference			Reference	
AD	versus white)	1.221	1.025	1.455	1.439	1.327	1.559
NAVD		.907	.401	2.051	.967	.711	1.315
VaD		.883	.59	1.323	.988	.872	1.119
No dementia	Income quartile		Reference			Reference	
AD	(>63k versus 1-38,999)	.971	.855	1.103	1.03	.972	1.09
NAVD		1.072	.63	1.823	1.421	1.158	1.743
VaD		1.217	.922	1.605	1.013	.932	1.101
No dementia	Depression		Reference			Reference	
AD		1.935	1.672	2.239	1.625	1.522	1.735
NAVD		2.558	1.512	4.33	2.344	1.924	2.855
VaD		2.019	1.497	2.723	1.731	1.58	1.897
No dementia	Hypertension		Reference			Reference	
AD		.778	.71	.853	.913	.876	.951
NAVD		.823	.569	1.19	.774	.672	.891
VaD		.878	.72	1.071	.915	.863	.97
No dementia	Type 2 diabetes		Reference			Reference	
AD		.878	.781	.988	.904	.862	.948
NAVD		.784	.489	1.258	.86	.73	1.015
VaD		1.267	1.019	1.576	1.21	1.137	1.286
No dementia	Hyperlipidemia		Reference			Reference	
AD		.932	.815	1.065	.767	.726	.81
NAVD		1.451	.93	2.264	.659	.544	.798
VaD		1.058	.816	1.372	.851	.79	.916
No dementia	Atrial fibrillation		Reference			Reference	
AD		.663	.591	.744	.722	.69	.756
NAVD		.581	.355	.95	.567	.479	.672
VaD		.734	.577	.934	.774	.723	.828
No dementia	Chronic heart failure		Reference			Reference	
AD		.638	.547	.744	.755	.716	.796
NAVD		.797	.443	1.431	.672	.549	.822
VaD		.91	.676	1.224	.846	.783	.913
No dementia	Coronary artery disease		Reference			Reference	
AD		.81	.662	.99	.862	.797	.932
NAVD		.88	.436	1.778	.825	.635	1.071
VaD		.966	.664	1.404	.973	.878	1.078

(*continued on next page*)

Table 3 (*continued*)

		Hemorrhagic stroke			Ischemic stroke		
			95% Confidence interval			95% Confidence interval	
Outcome*	Characteristic	Adjusted odds ratio	Lower limit	Upper limit	Adjusted odds ratio	Lower limit	Upper limit
Admission factors							
No dementia	Hospital location		Reference			Reference	
AD	(urban versus rural)	.953	.816	1.113	.906	.857	.959
NAVD		.739	.413	1.324	1.421	1.124	1.797
VaD		.933	.668	1.303	1.015	.933	1.104
No dementia	Insurance (private versus		Reference			Reference	
AD	Medicare)	.658	.54	.802	.701	.639	.769
NAVD		.457	.178	1.17	.613	.447	.84
VaD		.597	.393	.906	.621	.547	.706
No dementia	Insurance (self-pay		Reference			Reference	
AD	versus Medicare)	.376	.192	.738	.458	.33	.637
NAVD		†	†	†	.139	.02	.987
VaD		.175	.024	1.266	.676	.479	.954
No dementia	Discharge (death versus		Reference			Reference	
AD	routine)	1.258	1.065	1.487	1.295	1.194	1.405
NAVD		3.064	1.19	7.89	2.152	1.613	2.872
VaD		.781	.555	1.1	1.001	.878	1.142

Abbreviations: AD, Alzheimer's dementia; NAVD, non-Alzheimer's–nonvascular dementia; VaD, vascular dementia.
*Adjusted for admission year.
†Insufficient numbers.

dementia groups. Of note, women were at a higher risk of AD while simultaneously being protected against VaD and NAVD. African-Americans admitted with stroke were at higher risk of both AD and VaD relative to white patients, but at lower risk of NAVD. The evidence base supporting a disproportionately high rate of dementia in African-Americans relative to other racial or ethnic groups is extensive[15-17]; however, relatively few studies have disaggregated this relationship by dementia type. The increased risk of AD and VaD in African-American patients was consistent across age subgroups and appeared more pronounced for ischemic stroke compared with hemorrhagic stroke. Our modeling also isolated type 2 diabetes as an independent risk factor for VaD while being nominally protective against both AD and NAVD. Interestingly, a recent analysis of the Kaiser Permanente Northern California Diabetes Registry reported that African-Americans with type 2 diabetes were at higher age-adjusted risk of dementia relative to whites with type 2 diabetes,[18] suggesting a possible interaction between these 2 risk factors, which may further vary differentially with dementia subtype. Women were more likely to present with concurrent AD and less likely to present with either VaD or NAVD. This observation was generally consistent across both age and stroke type subgroups. Gender, in the context of dementia subtypes, may act as a proxy for a range of genetic or protein expression interactions, notably as a potential effect modifier of the ApoE genotype-Alzheimer's association.[19,20] Stroke type was also associated with a markedly different pattern of risk across the 3 different dementia types. Hemorrhagic stroke was associated with a significant increase in the risk of AD compared with ischemic stroke, but a significant reduction in the risk of both VaD and NAVD. This association between VaD and ischemic stroke is consistent with the large U.K.-based General Practice Research Database 10-year follow-up study of 8745 patients with dementia, which reported that patients with VaD, but not Alzheimer's disease, were at considerably higher risk of subsequent ischemic stroke relative to nondementia subjects.[21] Across both the primary modeling and various subgroup analyses, depression was strongly and consistently associated with a markedly increased risk of any of the 3 dementia subtypes studied, relative to nondementia stroke admissions. A meta-analysis of 23 community-based cohort studies observed that late-onset depression (>50 years of age) was associated with an increase in the risk of all-cause dementia, with the risk of VaD being significantly higher than AD ($P = .03$).[22] This finding is consistent with our results, which likewise observed a slightly larger risk of VaD relative to Alzheimer's in patients reporting comorbid depression. However, an even larger association was observed

Table 4. *Subgroup analysis: age 85+ versus younger than 85 years*

		Age 85+			Age younger than 85		
			95% Confidence interval			95% Confidence interval	
Outcome*	Characteristic	Adjusted odds ratio	Lower limit	Upper limit	Adjusted odds ratio	Lower limit	Upper limit
Patient factors							
No dementia	Female gender		Reference			Reference	
AD		1.199	1.128	1.274	1.131	1.076	1.189
NAVD		.518	.417	.642	.509	.433	.6
VaD		.803	.726	.887	.784	.733	.837
No dementia	Ethnicity		Reference			Reference	
AD	(African-American	1.308	1.189	1.439	1.304	1.211	1.405
NAVD	versus white)	1.028	.664	1.59	.545	.391	.76
VaD		1.403	1.195	1.648	1.579	1.445	1.726
No dementia	Ethnicity (Hispanic		Reference			Reference	
AD	versus white)	1.522	1.352	1.713	1.344	1.224	1.477
NAVD		.998	.575	1.732	.947	.676	1.328
VaD		.929	.722	1.194	1.001	.874	1.146
No dementia	Income quartile		Reference			Reference	
AD	(>63k versus 1-38,999)	1.007	.932	1.088	1.02	.951	1.095
NAVD		1.518	1.096	2.103	1.298	1.023	1.646
VaD		.983	.857	1.128	1.038	.941	1.145
No dementia	Depression		Reference			Reference	
AD		1.592	1.453	1.745	1.699	1.571	1.838
NAVD		1.751	1.24	2.473	2.709	2.173	3.378
VaD		1.702	1.454	1.993	1.772	1.595	1.968
No dementia	Hypertension		Reference			Reference	
AD		.888	.84	.938	.89	.846	.936
NAVD		.757	.611	.938	.795	.673	.94
VaD		.968	.877	1.069	.887	.828	.95
No dementia	Type 2 diabetes		Reference			Reference	
AD		.917	.854	.984	.879	.832	.929
NAVD		.858	.646	1.139	.832	.692	1.001
VaD		1.117	.993	1.255	1.242	1.159	1.331
No dementia	Hyperlipidemia		Reference			Reference	
AD		.809	.745	.877	.75	.703	.8
NAVD		.83	.618	1.117	.664	.535	.825
VaD		.977	.855	1.118	.818	.752	.889
No dementia	Atrial fibrillation		Reference			Reference	
AD		.718	.677	.761	.682	.642	.725
NAVD		.556	.434	.711	.567	.461	.698
VaD		.747	.673	.828	.779	.717	.847
No dementia	Chronic heart failure		Reference			Reference	
AD		.793	.74	.85	.711	.661	.766
NAVD		.514	.374	.706	.845	.666	1.073
VaD		.809	.717	.912	.888	.809	.975
No dementia	Coronary artery disease		Reference			Reference	
AD		.77	.685	.865	.876	.798	.962
NAVD		.733	.469	1.146	.838	.625	1.124
VaD		.885	.735	1.067	.991	.882	1.115
Admission factors							
No dementia	Hospital location		Reference			Reference	
AD	(urban versus rural)	.972	.9	1.049	.85	.791	.913
NAVD		1.659	1.138	2.418	1.148	.878	1.502
VaD		1.127	.978	1.298	.942	.853	1.042

(*continued on next page*)

Table 4 (*continued*)

		Age 85+			Age younger than 85		
			95% Confidence interval			95% Confidence interval	
Outcome*	Characteristic	Adjusted odds ratio	Lower limit	Upper limit	Adjusted odds ratio	Lower limit	Upper limit
No dementia	Insurance (private versus		Reference			Reference	
AD	Medicare)	.869	.756	.998	.762	.685	.848
NAVD		1.009	.618	1.65	.587	.407	.847
VaD		.913	.714	1.167	.615	.534	.707
No dementia	Insurance (self-pay		Reference			Reference	
AD	versus Medicare)	.646	.399	1.047	.498	.341	.727
NAVD		†	†	†	.192	.027	1.365
VaD		.284	.07	1.147	.761	.535	1.082
No dementia	Discharge (death versus		Reference			Reference	
AD	routine)	1.104	.989	1.231	1.351	1.231	1.482
NAVD		1.695	1.078	2.664	2.209	1.594	3.063
VaD		.734	.598	.903	1.039	.895	1.205

Abbreviations: AD, Alzheimer's dementia; NAVD, non-Alzheimer's–nonvascular dementia; VaD, vascular dementia.
*Adjusted for admission year.
†Insufficient numbers.

between depression and NAVD, across all analyses. The present study has several limitations. The cross-sectional design and reliance upon diagnostic codes at admission meant the exact timing of dementia diagnosis and its temporal relationship with stroke was unclear. Further, individual patients potentially contributing to multiple stroke admissions to the analysis dataset could not be identified secondary to the deidentification used in the NIS data. However, the very large sample suggests that the effect of any violation of the independence assumed by the models is likely to be negligible. Another limitation of this database, as it pertains to diagnosis of dementia, is that hospital-based diagnosis of early stage dementia is often missed. Thus, our sample is probably slightly schemed toward moderate and advanced cases. In addition, patients with advanced dementia forgo hospitalization and often opt for hospice or palliative care and, therefore, in such severe cases of the disease. Using such a database has unavoidable limitations as well. Coding errors may either over or underestimate the true numbers. Certain cases of delirium and altered mental status could be misclassified as dementia. Despite these limitations, we believe that our large sample size gives us a robust representation of the disease and an accurate depiction of the relationship between the 2 conditions. Despite these limitations, we believe that the robustness of the data secondary to the large sample provides a unique ability to explore complex and important relationships between stroke and dementia, particularly with regard to distinct dementia subtypes. A common feature of previous studies exploring the overlap of risk factors for both stroke and dementia is that potential demographic factors, including age, gender, and ethnicity, are typically used as either matching or adjusting covariates to better isolate the influence of traditional biological or clinical risk factors, rather than being studied as independent risk factors in their own right. This finding may, in part, be secondary to the often prohibitively large sample sizes commonly required to detect such signals.

Conclusions

This retrospective analysis of a large inpatient admissions dataset observed that female gender was associated with an increased risk of AD, but a decreased risk of either VaD or NAVD dementia subtypes relative to males. Both African-Americans and Hispanics were associated with an increased risk of AD compared with whites. Better appreciation of the interaction and overlaps of risk factors for both stroke and dementia may lead to earlier identification of cognitive decline and improved risk factor management.

Appendix: Supplementary Material

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2017.12.029.

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