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Letter to the Editor

Declining in-hospital mortality in vasculitis: A 17-year US national study

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Vasculitis is a serious systemic autoimmune disease. Antineutrophil cytoplasmic autoantibody-associated vasculitis (AAV) was associated with 2.7-fold higher mortality rate than the general population.[1] Age-adjusted mortality rate for the AAV declined by 2% per year from 1999 to 2017 in the United States.[2] Most of the excess mortality in vasculitis occurred in people who are young.[3] This indicates that comparisons should be age-adjusted and benchmarked to the general population. To our knowledge, only a few population-based studies for vasculitis exist, and most are limited to vasculitis subtypes. Therefore, our study objective was to assess time-trends in in-hospital mortality in vasculitis and compare it to the general population, using the US National Inpatient Sample (NIS).

We included the data from the healthcare cost and utilization project (HCUP) NIS from 1998 to 2014. The NIS is a deidentified national all-payer in-patient healthcare database that has a 20% stratified sample of hospital discharges. NIS is used frequently for creating US national estimates. The NIS changed design from a 20% sample of hospitals to a 20% sample of discharges in 2012. We used the provided set of trend weights to allow analyses across multiple years which included the period of design change. Cases of hospitalized vasculitis were defined based on the listing of 446.xx or 447.6 as the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes in the primary diagnosis position. A previous study showed sensitivity of 93% and specificity of 95% using this approach.[4] We limited our study to 2014; the last year ICD-9-CM codes were used in the United States before switching to ICD-10-CM in 2015.

We calculated the unadjusted in-hospital mortality rates per 1,000 hospitalizations for people with versus without primary vasculitis hospitalizations, with the respective denominators. We calculated age-adjusted rates by grouping age in quintiles (<20, 20-39, 40-59, 60-79, >79) and age- and sex-adjusted rates. We analyzed in-hospital mortality rate time-trends using the Cochran Armitage test, weighted by the number of hospitalizations in each year.

There were 266,461 primary vasculitis hospitalizations in 1998-2014 with 7,215 in-hospital deaths (2.7%). Mean age was 42.9 years, 57% were men, 50% were white, 30% had a Deyo-Charlson comorbidity score of ≥2, and 18% had a Medicaid payer (Appendix 1).

Unadjusted in-hospital mortality in primary vasculitis hospitalizations decreased by 43% from 32.8 per 1,000 in 1998 to 18.7 per 1,000 in 2014 ($P < .01$), compared to a 24.5% reduction in deaths for all NIS claims without vasculitis (28.1-21.2 per 1,000; $P < .01$; Figure 1).

Age- and sex-adjusted in-hospital mortality decreased both in primary vasculitis hospitalizations from 27.3 per 1,000 claims in 1998 to 19.1 in 2014 and nonvasculitis hospitalizations from 15.1 to 13.2 per 1,000 in 2014, respectively ($P < .01$; Figure 1 and Appendix 2). The age- and sex-adjusted mortality rate gap between those with versus without vasculitis narrowed (Figure 1) vasculitis to nonvasculitis in-hospital mortality ratio was 1.81 in 1998-2000 and 1.45 in 2013-2014 (Appendix 2). Primary vasculitis hospitalizations per year remained fairly constant from 1998 to 2014 at 14-18,000 per year; rate was 43 per 100,000 NIS claims in 1998-2000 versus 43.2 in 2013-2014, i.e., 0.05% of claims per year (Appendix 3).

We made several important observations in our US national study. The key study findings were that adjusted in-hospital mortality decreased significantly over time in both the general US population and primary vasculitis hospitalization cohorts, and the absolute and relative reductions were larger for vasculitis hospitalizations. Unadjusted in-hospital mortality was higher in primary vasculitis hospitalizations compared to the general population in 1998 but was lower in 2014. Age- and sex-adjusted in-hospital mortality was higher in vasculitis compared to the general population in both 1998 and 2014, but the gap narrowed over time. This may be related to an increasing awareness of vasculitis, an earlier diagnosis, and more frequent

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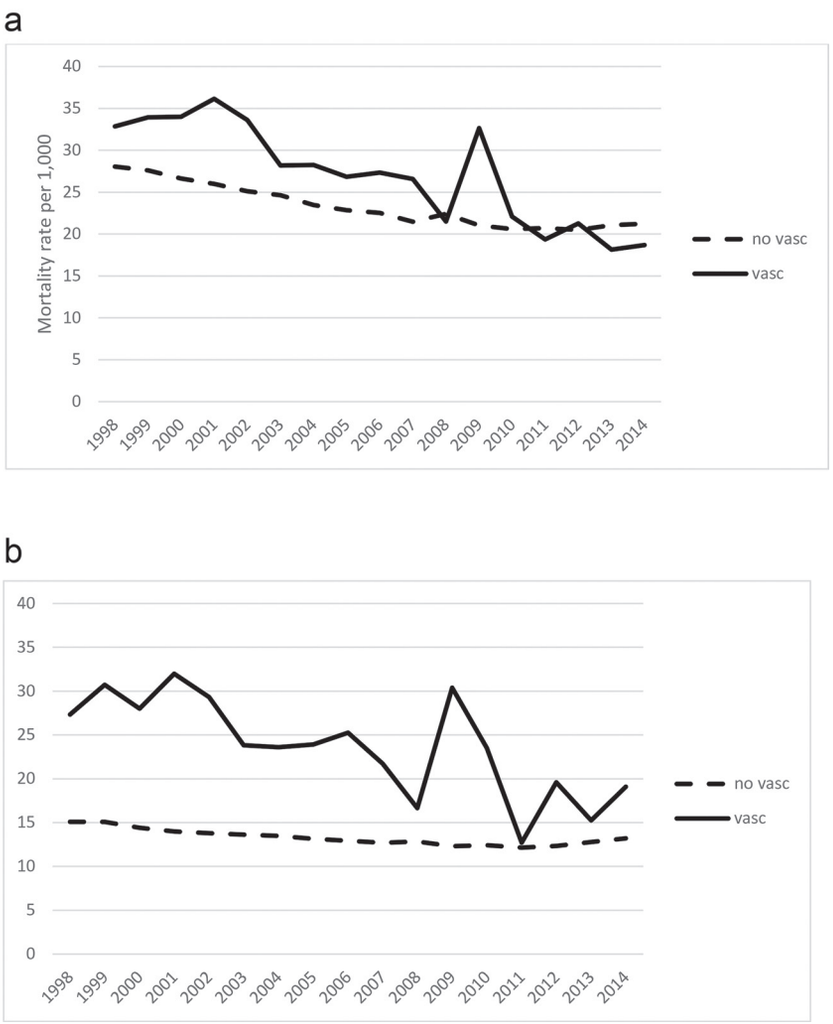

Figure 1. Time-trends in (b) unadjusted and (b) age- and sex-adjusted in-hospital mortality rates per 1,000 population of hospitalizations in people with vasculitis compared with people without vasculitis. The y-axis shows rate per 1,000 hospitalization claims with each respective denominator.

use of immunosuppressives/glucocorticoids (and biologics).[5–8] A much younger age and a higher proportion of females in primary vasculitis hospitalizations (both associated with lower mortality) as compared to the general population, explain the differences between unadjusted versus adjusted rates. Our study extends the time-trends of reduction in the standardized mortality ratio in granulomatosis with polyangiitis, a subtype of vasculitis, in Sweden[9] and Germany[10] to all vasculitis hospitalizations in the United States.

Study limitations included the misclassification bias due to the use of diagnostic code for vasculitis (both over- and under-reporting), the lack of medication, and laboratory data. We only assessed in-hospital mortality, not total mortality. Study strengths included the use of a national database and a large sample size.

In conclusion, our study is among the few time-trend studies that described the decreasing mortality gap between vasculitis and nonvasculitis hospitalizations over time from 1998 to 2014 in the United States. Future studies should focus on interventions that can further narrow the mortality gap between vasculitis and nonvasculitis hospitalizations.

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Conflict of Interest: There are no financial conflicts related directly to this study. JAS has received consultant fees from Crealta/Horizon, Medisys, Fidia, UBM LLC, Trio health, Medscape, WebMD, Clinical Care options, Clearview healthcare partners, Putnam associates, Focus forward, Navigant consulting, Spherix, Practice Point communications, the National Institutes of Health and the American College of Rheumatology. JAS owns stock options in Amarin pharmaceuticals and Viking therapeutics. JAS is on the speaker's bureau of Simply Speaking. JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 12 companies. JAS serves on the FDA Arthritis Advisory Committee. JAS is the chair of the Veterans Affairs Rheumatology Field Advisory Committee. JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis. JAS previously served as a member of the following committees: member, the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC) and Quality of Care Committees, the Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee and the co-chair of the ACR Criteria and Response Criteria subcommittee. JDC has no conflicts. There are no non-financial competing interests for either author.

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Appendix 1. Demographic and clinical characteristics of people hospitalized with vasculitis in the United States.

	Hospitalization with vasculitis N (%), unless specified otherwise
Age, mean (SE); median	42.98 (0.382); 48.4
Age category	
<50	134,837 (50.69%)
50-64	47,298 (17.78%)
65-79	55,283 (20.78%)
≥80	28,608 (10.75%)
Gender	
Female	114,360 (43.14%)
Male	150,715 (56.86%)
Race	
White	132,037 (49.55%)
Black	35,684 (13.39%)
Hispanic	26,693 (10.02%)
Other/missing	72,037 (27.04%)
Deyo-Charlson Index Score	
0	132,956 (49.90%)
1	52,121 (19.56%)
≥2	81,384 (30.54%)
Income category	
0-25th percentile	54,416 (20.86%)
25-50th percentile	65,186 (24.99%)
50-75th percentile	65,267 (25.02%)
75-100th percentile	75,968 (29.12%)
Hospital location/teaching	
Rural	21,259 (8.01%)
Urban	77,550 (29.21%)
Urban teaching	166,688 (62.78%)
Insurance	
Medicare	90,812 (34.16%)
Medicaid	48,056 (18.08%)
Private	105,338 (39.62%)
Self	12,122 (4.56%)
Other	9,515 (3.58%)
Hospital bed size	
Small	29,270 (11.02%)
Medium	64,854 (24.43%)
Large	171,374 (64.55%)
Hospital region	
Northeast	55,474 (20.82%)
Midwest	58,497 (21.95%)
South	101,008 (37.91%)
West	51,481 (19.32%)

Appendix 1. Demographic and clinical characteristics of people hospitalized with vasculitis in the United States. (continued)

	Hospitalization with vasculitis N (%), unless specified otherwise
Total charge, mean (SE); median	43,539 (570.3); 19,533
Discharge status	
Inpatient	31,810 (12.36%)
Home	225,593 (87.64%)
Length of stay (LOS), mean (SE); median	6.81 (0.048); 3.7
LOS cat	
≤3	136,575 (51.26%)
>3	129,886 (48.74%)
Died during hospitalization	7,214 (2.71%)

SE, standard error of the mean; hospitalization data from the NIS, 1998-2014

Appendix 2. Mortality rates per 1,000 population in people hospitalized without versus with vasculitis: unadjusted based on the NIS sample; age- and age- and sex-adjusted rates based on the NIS sample and the census data.

	No vasculitis			Vasculitis		
Year	Unadjusted	Age adjusted	Age and sex adjusted	Unadjusted	Age adjusted	Age and sex adjusted
1998	28.1	14.4	15.1	32.8	27.1	27.3
1999	27.6	14.5	15.1	33.9	31.9	30.7
2000	26.7	13.8	14.4	34.0	27.2	28.0
2001	26.0	13.4	14.0	36.1	30.3	32.0
2002	25.1	13.2	13.8	33.6	29.4	29.3
2003	24.6	13.0	13.6	28.2	23.5	23.8
2004	23.5	12.8	13.5	28.3	23.1	23.6
2005	22.9	12.5	13.2	26.8	23.7	23.9
2006	22.5	12.3	12.9	27.3	25.4	25.3
2007	21.5	12.1	12.7	26.6	23.8	21.7
2008	22.4	12.3	12.9	21.5	17.0	16.7
2009	21.0	11.8	12.3	32.6	29.4	30.4
2010	20.6	11.9	12.4	22.1	23.5	23.5
2011	20.7	11.7	12.2	19.4	12.8	12.7
2012	20.5	11.9	12.4	21.3	19.6	19.6
2013	21.1	12.3	12.8	18.2	15.8	15.2
2014	21.2	12.7	13.2	18.7	18.1	19.1
%Reduction—1998-2014	24.5%	11.8%	12.6%	43.0%	33.2%	30.0%

Appendix 3. Rate and frequency of primary vasculitis hospitalizations and associated in-hospital mortality in per 100,000 NIS claims.

	Vasculitis hospitalizations	Total NIS hospitalizations	Vasculitis hospitalization rate*	In-hospital deaths in vasculitis hospitalizations	In-hospital death rate* in vasculitis
1998-2000	44,694	103,665,051	43.11	1,500	1.45
2001-2002	31,329	72,617,381	43.14	1,091	1.5
2003-2004	32,160	74,571,583	43.13	906	1.21
2005-2006	33,706	75,919,595	44.4	912	1.2
2007-2008	30,033	76,366,797	39.33	722	0.95
2009-2010	32,895	75,086,597	43.81	891	1.19
2011-2012	30,957	73,447,261	42.15	628	0.86
2013-2014	30,685	70,956,610	43.24	565	0.8

*Both rates are per 100,000 total NIS claims.