

Disputes & Debates: Editors' Choice

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Editors' Note: Cause of Death in Spontaneous Intracerebral Hemorrhage Survivors: Multistate Longitudinal Study

Using administrative claims data from 3 US states, Dr. Kuohn et al. report the long-term mortality rate of survivors with spontaneous intracerebral hemorrhage (ICH). Using an original population of 104,000 patients who were screened for eligibility, 72,432 survivors of the index hospitalization were followed for a median of 4 years. The 1-year risk of death or discharge to hospice was 9.5% (95% CI 9.2%–9.7%), with the most common proximate causes of death being infection (34%) or subsequent intracranial hemorrhage (13%). The median time from ICH to death was 10 months (IQR 2–31 months). Dr. Llamas-Nieves and colleagues highlight the importance of confounders such as diabetes, which was independently associated with death as shown in the multivariable regression model (HR 1.22, 95% CI 1.17–1.27), as this may be an important mediator of death because of infectious causes. The investigators acknowledge that diabetes contributes to death in the overall population; however, it was not independently associated with death due to infection (OR 1.16, 95% CI 0.86–1.55). The authors posit that diabetes (as well as age, post-ICH disability, and other comorbidities) are important contributors to the development of later infection, but it remains unclear why diabetes is not an independent modifier of death risk among patients who develop infection.

James E. Siegler, MD, and Steven Galetta, MD
Neurology® 2021;97:148. doi:10.1212/WNL.00000000000012281

Reader Response: Cause of Death in Spontaneous Intracerebral Hemorrhage Survivors: Multistate Longitudinal Study

Andrés E. Llamas-Nieves (Cartagena, Colombia), Ivan D. Lozada-Martinez (Cartagena, Colombia), Daniela M. Torres-Llinás (Cartagena, Colombia), and Luis R. Moscote-Salazar (Cartagena, Colombia)
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We read with great interest the recent article by Kuohn et al.¹ The authors conducted a comprehensive review on the factors associated with mortality in patients who survived spontaneous intracerebral hemorrhage, where they showed that the infection was the main cause of death in such a group with a value of 34%. However, they do not emphasize other comorbidities that could have influenced the morbidity and mortality of patients in the infection group, such as diabetes. Diabetes is a disease that increases susceptibility to infections such as those involving the skin, urinary tract, or lungs.² Lau et al. performed a systematic review and meta-analysis, where they found that isolated diabetes is strongly associated with poor prognosis after stroke, including increased morbidity, mortality, and disability.³ For this reason, it is very important to know the factors that underlie and really impact on the subject of study, to obtain certainty in the

results of the research, and to avoid underestimations as what likely happened in the study of Kuohn et al. We suggest separate future study groups to avoid this type of bias during data analysis.

1. Kuohn LR, Leasure AC, Acosta JN, et al. Cause of death in spontaneous intracerebral hemorrhage survivors Multistate longitudinal study. *Neurology*. 2020;95(20):e2736-e2745.
2. Pannu AK, Saroch A, Singla V, et al. Clinical spectrum, etiology and outcome of infectious disease emergencies in adult diabetic patients in northern India. *Diabetes Metab Syndr*. 2020;14(5):921-925.
3. Lau L-H, Lew J, Borschmann K, Thijs V, Ekinici EI. Prevalence of diabetes and its effects on stroke outcomes: a meta-analysis and literature review. *J Diabetes Investig*. 2019;10(3):780-792.

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Author Response: Cause of Death in Spontaneous Intracerebral Hemorrhage Survivors: Multistate Longitudinal Study

Lindsey Kuohn (New York) and Kevin Sheth (New Haven, CT)
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We thank Dr. Llamas-Nieves et al. for their interest in our article¹ and recognize that coexisting diabetes, among other comorbidities, may influence infection-related mortality in ICH survivors. We hypothesized that the high proportion of deaths caused by infections may be due to the burden of disability in this population. Intracerebral hemorrhage (ICH) survivors often require chronic hospitalization and are prone to infections such as *Clostridium difficile*, urinary tract infections, and aspiration pneumonia. Our finding that older age was an independent risk factor for death caused by infection supports this hypothesis. However, we agree that increased susceptibility to infection in patients with diabetes should be considered as a potential driver of infection-related deaths in patients with ICH.² Diabetes was included as a covariate in the adjusted multinomial logistic regression model of causes of death during follow-up in our study (table 3). Diabetes was not associated with increased odds of death caused by infection (odds ratio 1.16, 95% confidence interval 0.86–1.55), although diabetes did correlate with increased risk for death overall (hazard ratio 1.22, 95% confidence interval 1.17–1.27). The cause of elevated mortality after ICH in patients with diabetes is not clear, and our results are not conclusive regarding the potential association with infection. As Dr. Llama-Nieves et al. point out, future studies of the specific causes of infection-related morbidity and mortality are warranted and necessary to improve long-term outcomes after ICH.

1. Kuohn LR, Leasure AC, Acosta JN, et al. Cause of death in spontaneous intracerebral hemorrhage survivors: multistate longitudinal study. *Neurology*. 2020;95(20):e2736-e2745.
2. Moutschen MP, Scheen AJ, Lefebvre PJ. Impaired immune responses in diabetes mellitus: analysis of the factors and mechanisms involved. Relevance to the increased susceptibility of diabetic patients to specific infections. *Diabete Metab*. 1992;18(3):187-201.

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Editors' Note: Sex, Race, and Risk of Dementia Diagnosis After Traumatic Brain Injury Among Older Veterans

Traumatic brain injury (TBI) has a well-known association with cognitive impairment and dementia. Whether there is a differential risk of dementia after TBI based on sex, race, or ethnicity was the subject of the recently published retrospective cohort study by Dr. Kornblith et al. Using a 2% random sample of claims data from Veterans Health Administration systems databases (n = 999,640), investigators evaluated the cumulative incidence of all-cause dementia by age, sex, race, and ethnicity. They found a significant interaction between TBI and race for dementia, in which White veterans were at the highest risk for dementia diagnoses. Dr. Roberts affirms these findings are consistent with the literature on White vs Black NFL players, in which White athletes are diagnosed more frequently with postconcussion “dementia” and receive greater compensation for this disability. More importantly, Dr. Roberts emphasizes that this racial discrepancy in dementia diagnoses is not likely an indicator of differential disease burden between races but is more reflective of racial care inequality. Dr. Kornblith agrees that racial disparities in health care are ubiquitous and demand more than just our attention. They demand action.

James E. Siegler, MD, and Steven Galetta, MD
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Reader Response: Sex, Race, and Risk of Dementia Diagnosis After Traumatic Brain Injury Among Older Veterans

Jomar S. Roberts I (Matthews, NC)
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I read the article by Kornblith et al. with interest.¹ It seems this “trend” in diagnostic bias is not exclusive to veterans alone. As this article is being published, Black NFL and former NFL athletes are involved in litigation regarding the discrepancy in qualifying postconcussion dementia diagnoses applied to White athletes vs Black. White athletes are diagnosed with postconcussion dementia at higher rates and are thereby compensated for this at higher rates than Black athletes.²

In my experience as a veteran TBI neurologist, observing this bias is commonplace and not limited to concussion or any particular disease. The health care system is riddled with bias from the provider level on down. It manifests openly in less care being given to Black patients, less concern being given to their disease, and less resources allocated to deep diving into their illnesses. This is not a secret to Black neurologists or providers in any field and is openly discussed and hard fought against, daily.

To be perfectly honest, these authors are speaking softly about an issue that needs to be addressed much more openly. Racial bias in health care provision starts at the individual provider level. We need to further examine how providers' backgrounds affect their patterns of diagnosis, test ordering, and prescribing patterns. This should be prominently displayed in some metric for all patients to use when choosing a provider, a “bias report card” so to speak. Only with full transparency will patients be given the assurance their doctor/provider is giving full, ethically unbiased care to all.

1. Kornblith E, Peltz CB, Xia F, et al. Sex, race, and risk of dementia diagnosis after traumatic brain injury among older veterans. *Neurology*. 2020;95(13):e1768-e1775.
2. Radnofsky L, Beaton A. Lawsuit alleges NFL's concussion settlement discriminates against black players. In: *The Wall Street Journal*. Available at: [wsj.com/articles/lawsuit-alleges-nfls-concussion-settlement-discriminates-against-black-players-11598371843](https://www.wsj.com/articles/lawsuit-alleges-nfls-concussion-settlement-discriminates-against-black-players-11598371843).

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Author Response: Sex, Race, and Risk of Dementia Diagnosis After Traumatic Brain Injury Among Older Veterans

Erica S. Kornblith (San Francisco)

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Thank you for the thoughtful comment on our article,¹ Dr. Roberts. We agree that racial bias in health care is pervasive and must be addressed. We hope that our work draws attention to this issue and highlights the need for research aimed at identifying and mitigating disparities.

1. Kornblith E, Peltz CB, Xia F, et al. Sex, race, and risk of dementia diagnosis after traumatic brain injury among older veterans. *Neurology*. 2020;95(13):e1768-e1775.

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CORRECTIONS

Thrombolysis in Acute Ischemic Stroke in Patients With Dementia

A Swedish Registry Study

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In the article “Thrombolysis in Acute Ischemic Stroke in Patients With Dementia: A Swedish Registry Study” by Zupanic et al,¹ the affiliations for Drs. Zupanic and Kramberger should include “Faculty of Medicine, University of Ljubljana, Slovenia.” The authors regret the error.

Reference

1. Zupanic E, von Euler M, Kåreholt I, et al. Thrombolysis in acute ischemic stroke in patients with dementia: a Swedish registry study. *Neurology*. 2017;89(18):1860-1868.

ALS is a Multistep Process in South Korean, Japanese, and Australian Patients

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In the infographic corresponding with the article “ALS is a Multistep Process in South Korean, Japanese, and Australian Patients” by Vucic et al,¹ the labels for the pictures of South Korea and Japan should be switched so that South Korea reads as a 5-step process and Japan reads as a 6-step process. The editorial team regrets the error.

Reference

1. Vucic S, Higashihara M, Sobue G, et al. ALS is a multistep process in South Korean, Japanese, and Australian patients. *Neurology*. 2020; 94(15):e1657-e1663.

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