WriteClick®
Editor's Choice

Editors' Note: In the American Academy of Neurology and the American Epilepsy Society practice guideline on sudden unexpected death in epilepsy (SUDEP) incidence rates and risk factors, Harden et al. made recommendations to clinicians caring for people with epilepsy including the need to inform their patients about SUDEP, the most common cause of epilepsy-related death. Commenting on the guideline, Stanton et al. note that certain pediatric populations (children with Dravet syndrome, Dup15q syndrome) face a significantly higher risk of SUDEP. They also suggest accurate surveillance data and expanded research to understand the mechanisms of SUDEP. The authors of the guideline agree. In "Dementia risk in renal dysfunction: A systematic review and meta-analysis of prospective studies," Deckers et al. conducted random effects meta-analyses on the prospective association between potential markers of renal dysfunction and development of cognitive impairment or dementia. The authors concluded that albuminuria was a useful marker of renal dysfunction for screening the development of cognitive impairment or dementia. Prof. Kawada raises 2 concerns about the study. He cites another systematic review that evaluated the relationship between chronic kidney disease and physical frailty and cognitive impairment. In that study, the mechanism of chronic kidney disease–induced physical frailty and cognitive impairment was also unclear. He suggests multidimensional therapeutic interventions to study the effect of chronic kidney disease on subsequent physical frailty and cognitive impairment. Second, he suggests also studying the effect of cognitive impairment on subsequent kidney dysfunction. Deckers et al. agree that there is a need for additional studies on shared biological pathways between albuminuria and cognitive impairment or investigating the effect of multidimensional therapeutic interventions. They also agree that more mechanistic studies are needed to evaluate the bidirectional relationship between renal dysfunction and cognitive impairment or dementia.

—Chafic Karam, MD, and Robert C. Griggs, MD

LETTER RE: PRACTICE GUIDELINE SUMMARY: SUDDEN UNEXPECTED DEATH IN EPILEPSY INCIDENCE RATES AND RISK FACTORS: REPORT OF THE GUIDELINE DEVELOPMENT, DISSEMINATION, AND IMPLEMENTATION SUBCOMMITTEE OF THE AMERICAN ACADEMY OF NEUROLOGY AND THE AMERICAN EPILEPSY SOCIETY

Tom Stanton, Robin Harding, Chicago; Phil Gattone, Landover, MD; Daniel Friedman, Angela Geiger, Orrin Devinsky, New York; Kari Luther Rosbeck, Silver Spring, MD; Vanessa Vogel-Farley, Highland Park, IL; Mary Anne Meskis, Cherry Hill, NJ; Alison Singer, New York; Amy Brin Miller, Minneapolis; Ilene Miller, Bethesda, MD:

The new guideline by the American Academy of Neurology (AAN) and the American Epilepsy Society (AES) on sudden unexpected death in epilepsy (SUDEP) is a landmark.[1] The communication between medical professionals and patients about SUDEP risk remains unacceptably low. Tragically, family members often first learn about SUDEP after their loved one's death. Every patient and parent deserves to know the risks of epilepsy. For the first time, the AAN and AES recommend that neurologists inform them about SUDEP, the most common cause of epilepsy-related death.[1]

Generalized tonic-clonic seizures increase SUDEP risk; the greater their frequency, the greater the risk.[2,3] Minimizing seizures through specialized medical care and strategies to reduce breakthrough seizures can reduce risk.[2,3] Since SUDEP happens more often in sleep,[2] nighttime supervision or monitoring may help and should be part of the patient/provider conversation. While the report assigns a blanket SUDEP risk ratio to children,[1] certain pediatric populations (children with Dravet syndrome, Dup15q syndrome) face a significantly higher risk.[4,5]

All medical professionals should use these recommendations to initiate an honest and ongoing conversation tailored to their patient's risk. We urgently need accurate surveillance data and expanded research to understand the mechanisms and save lives.

1. Harden C, Tomson T, Gloss D, et al. Practice guideline summary: sudden unexpected death in epilepsy incidence rates and risk factors: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

© 2017 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

and the American Epilepsy Society. Neurology 2017;88:1674–1680.
2. Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. Lancet Neurol 2016;15:1075–1088.
3. Tomson T, Surges R, Delamont R, Haywood S, Hesdorffer DC. Who to target in sudden unexpected death in epilepsy prevention and how? Risk factors, biomarkers, and intervention study designs. Epilepsia 2016;57(suppl 1):4–16.
4. Cooper MS, Mcintosh A, Crompton DE, et al. Mortality in Dravet syndrome. Epilepsy Res 2016;128:43–47.
5. Friedman D, Thaler A, Thaler J, et al. Mortality in isodicentric chromosome 15 syndrome: the role of SUDEP. Epilepsy Behav 2016;61:1–5.

© 2017 American Academy of Neurology

AUTHOR RESPONSE: PRACTICE GUIDELINE SUMMARY: SUDDEN UNEXPECTED DEATH IN EPILEPSY INCIDENCE RATES AND RISK FACTORS: REPORT OF THE GUIDELINE DEVELOPMENT, DISSEMINATION, AND IMPLEMENTATION SUBCOMMITTEE OF THE AMERICAN ACADEMY OF NEUROLOGY AND THE AMERICAN EPILEPSY SOCIETY

David Gloss, Charleston, WV; Jacqueline A. French, Dale C. Hesdorffer, New York; W. Henry Smithson, Cork, Ireland; Cynthia Harden, New York: We wholeheartedly agree with the comments of Stanton et al. on our sudden unexpected death in epilepsy guideline article.[1]

1. Harden C, Tomson T, Gloss D, et al. Practice guideline summary: sudden unexpected death in epilepsy incidence rates and risk factors: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2017;88:1674–1680.

© 2017 American Academy of Neurology

LETTER RE: DEMENTIA RISK IN RENAL DYSFUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PROSPECTIVE STUDIES

Tomoyuki Kawada, Tokyo: Deckers et al.[1] conducted random effects meta-analyses on the prospective association between potential markers of renal dysfunction and development of cognitive impairment or dementia. Pooled odds ratios (95% confidence intervals) of albuminuria and estimated glomerular filtration rate <60 mL/min/1.73 m^2 for cognitive impairment or dementia were 1.35 (1.06–1.73) and 1.28 (0.99–1.65), respectively.[1] As the number of studies was not sufficient, meta-analyses could not be done for serum creatinine, creatinine clearance, or cystatin C.[1] The authors concluded that albuminuria was a useful marker of renal dysfunction for screening the development of cognitive impairment or dementia.[1] I have 2 concerns about their study.

First, Shen et al.[2] also conducted a systematic review to evaluate the relationship between chronic kidney disease and physical frailty and cognitive impairment. They concluded that chronic kidney disease was a potential cause of frailty and cognitive impairment.[2] The mechanism of chronic kidney disease–induced physical frailty and cognitive impairment has not been confirmed, and multidimensional therapeutic interventions would be useful to know the effect of chronic kidney disease on subsequent physical frailty and cognitive impairment.

Second, the effect of cognitive impairment on subsequent kidney dysfunction should also be evaluated by a meta-analysis on prospective studies.[3] Worsening of albuminuria is speculated by the progression of cognitive impairment or dementia, and the bidirectional association between renal dysfunction and cognitive impairment or dementia should be comprehensively evaluated.

1. Deckers K, Camerino I, van Boxtel MP, et al. Dementia risk in renal dysfunction: a systematic review and meta-analysis of prospective studies. Neurology 2017;88:198–208.
2. Shen Z, Ruan Q, Yu Z, Sun Z. Chronic kidney disease-related physical frailty and cognitive impairment: a systemic review. Geriatr Gerontol Int 2017;17:529–544.
3. Kurella Tamura M, Yaffe K, Hsu CY, et al. Cognitive impairment and progression of CKD. Am J Kidney Dis 2016;68:77–83.

© 2017 American Academy of Neurology

AUTHOR RESPONSE: DEMENTIA RISK IN RENAL DYSFUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PROSPECTIVE STUDIES

Kay Deckers, Maastricht, the Netherlands; Ileana Camerino, Nijmegen, the Netherlands; Martin P.J. van Boxtel, Frans R.J. Verhey, Maastricht, the Netherlands; Kate Irving, Dublin, Ireland; Carol Brayne, Cambridge, UK; Miia Kivipelto, Stockholm, Sweden; John M. Starr, Edinburgh, UK; Kristine Yaffe, San Francisco; Peter W. de Leeuw, Sebastian Köhler, Maastricht, the Netherlands: We thank Prof. Kawada for the interest in our article,[1] and agree that the exact mechanisms underlying the relationship between renal dysfunction and cognitive impairment or dementia are not fully understood. In our article, we discussed several suggested potential mechanisms.[1] These might work additively, or synergistically, and include shared vascular risk factors or a direct effect of uremic toxins.[1,2]

A recent meta-analysis on the association between albuminuria and cognitive impairment or dementia stresses the point that albuminuria is a marker of microvascular damage that precedes the onset of renal disease[3]; hence, the debate on whether renal dysfunction is a causal risk factor or a risk state

© 2017 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

marking microvascular changes is not settled. Therefore, we embrace Prof. Kawada's suggestion for future studies on shared biological pathways or investigating the effect of multidimensional therapeutic interventions.

Prof. Kawada's second concern is about the effect of cognitive impairment on subsequent renal dysfunction. We agree that more mechanistic studies are needed that focus on the bidirectional relationship between renal dysfunction and cognitive impairment or dementia. These studies should include repeated assessment of both cognitive and kidney function, apply consistent methodology (e.g., neuropsychological test battery or formula/equation for estimating kidney function), and incorporate information on important confounders and mediators.

1. Deckers K, Camerino I, van Boxtel MP, et al. Dementia risk in renal dysfunction: a systematic review and meta-analysis of prospective studies. Neurology 2017;88:198–208.
2. Bugnicourt JM, Godefroy O, Chillon JM, Choukroun G, Massy ZA. Cognitive disorders and dementia in CKD: the neglected kidney-brain axis. J Am Soc Nephrol 2013;24:353–363.
3. Georgakis MK, Dimitriou NG, Karalexi MA, et al. Albuminuria in association with cognitive function and dementia: a systematic review and meta-analysis. J Am Geriatr Soc 2017;65:1190–1198.

© 2017 American Academy of Neurology

WriteClick® rapid online correspondence

Have a comment on a recent *Neurology*® article you would like to share? Now it is easier and more convenient. *Neurology.org* has launched WriteClick on the home page and sidebars of each article to encourage remarks and debate among users.

WriteClick is restricted to comments about studies published in *Neurology* within the last eight weeks.

Learn more at *Neurology.org/letters*

Visit the *Neurology*® Resident & Fellow Website

Click on Residents & Fellows tab at Neurology.org.

Now offering:

- *Neurology*® Resident & Fellow Editorial team information
- "Search by subcategory" option
- E-pearl of the Week
- RSS Feeds
- Direct links to Continuum®, Career Planning, and AAN Resident & Fellow pages
- Recently published Resident & Fellow articles
- Podcast descriptions

Find *Neurology*® Residents & Fellows Section on Facebook: http://tinyurl.com/o8ahsys

Follow *Neurology*® on Twitter: http://twitter.com/GreenJournal

Author disclosures are available upon request (journal@neurology.org).

© 2017 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.