Disputes & Debates: Editors' Choice

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Editors' Note: Systolic Blood Pressure Postural Changes Variability is Associated With Greater Dementia Risk

In "Systolic Blood Pressure Postural Changes Variability is Associated With Greater Dementia Risk," Rouch et al. reported that systolic orthostatic hypotension (OHYPO, defined as a fall of ≥15 mm Hg in systolic blood pressure after standing from a sitting position on ≥1/3 visits) and visit-to-visit systolic blood pressure postural changes variability were associated with an increased risk of dementia. There was no association between diastolic OHYPO (a fall of ≥7 mm Hg in diastolic blood pressure) and risk of dementia. Soysal noted that the criteria used differed from those published by the 1996 Consensus Committee of the American Autonomic Society and American Academy of Neurology, which defined OHYPO as a fall of ≥20 mm Hg in systolic blood pressure and/or ≥10 mm Hg in diastolic blood pressure. Soysal further pointed out that systolic OHYPO is associated with frailty, fear of falling, malnutrition, and sarcopenia, all of which are associated with dementia. Rouch et al. responded that they did not use the criteria Soysal cited because they are applicable to the transition from supine-to-standing, which is more hazardous than standing from a sitting position. Instead, they selected their thresholds based on previous large studies and recent literature that these values were associated with 80% sensitivity and 89% specificity.

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Reader Response: Systolic Blood Pressure Postural Changes Variability is Associated With Greater Dementia Risk

Pinar Soysal (Istanbul, Turkey)
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I read with interest the study by Rouch et al.,[1] investigating whether orthostatic hypotension (OHYPO) and visit-to-visit blood pressure (BP) postural changes were associated with the incidence of dementia in the elderly, and they found systolic OHYPO and BP postural changes were associated with greater dementia risk. In the study, OHYPO was defined as a fall of ≥15 mm Hg in systolic or ≥7 mm Hg in diastolic BP after standing from a sitting position. However, according to the consensus on the detection of OH published in 1996, the diagnosis of OH is made in the event of ≥20 mm Hg decrease in systolic and/or ≥10 mm Hg decrease in diastolic BP after standing.[2] Moreover, in many recent published studies using the criteria of this consensus, in the elderly, systolic OHYPO has been associated with frailty, fear of falling, malnutrition, and sarcopenia, all of which are actually known to be predictive for dementia development.[3-5]

Therefore, if the authors had accepted the drop of ≥20 mm Hg—rather than ≥15 mm Hg for the diagnosis of systolic OHYPO—they could have achieved more accurate and significant results. On the other hand, if the reduction of ≥10 mm Hg was taken as a cutoff for diastolic OHYPO, maybe diastolic OHYPO would also be significant for the risk of dementia.

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

1. Rouch L, Vidal JS, Hoang T, et al. Systolic blood pressure postural changes variability is associated with greater dementia risk. *Neurology.* 2020 Epub July 20.
2. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. *Neurology.* 1996;46(5):1470.
3. Soysal P, Kocyigit SE, Dokuzlar O, et al. Relationship between sarcopenia and orthostatic hypotension. *Age Ageing.* 2020;49(6):959-965.
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Author Response: Systolic Blood Pressure Postural Changes Variability is Associated With Greater Dementia Risk

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The authors thank Dr. Pinar Soysal for this comment on our article.[1] We agree that the original standard diagnostic criteria of orthostatic hypotension (OHYPO), commonly based on supine-to-stand BP, are a reduction in systolic blood pressure (SBP) of at least 20 mm Hg or DBP of at least 10 mm Hg.[2] The studies Dr. Pinar Soysal mentions assessed orthostatic BP response from a supine-to-standing position, which is not the case of the Health ABC Study. Indeed, given that the prevalence of OHYPO is higher in older adults and many of whom have comorbidities that may affect mobility, a sit-to-stand testing often offers a safer method to transfer a patient into an upright position without triggering an acute fall or syncopal event. Because of the reduced acute change in gravitational stress, the sit-to-stand test makes conventional BP cutoffs to diagnose OHYPO challenging to reach. An insignificant number of participants in the Health ABC Study had baseline OHYPO using that definition. Very recently, optimal diagnostic thresholds for the diagnosis of OHYPO with a sit-to-stand test have been proposed by Shaw et al.[3] A sit-to-stand SBP drop of ≥15 mm Hg had optimal test characteristics (sensitivity = 80%; specificity = 89%), as did a DBP drop of ≥7 mm Hg (sensitivity and specificity both = 87%).[3] We, therefore, used this threshold—consistent with previous large studies—including the Hypertension in the Very Elderly Trial (HYVET).[4,5]

1. Rouch L, Vidal JS, Hoang T, et al. Systolic blood pressure postural changes variability is associated with greater dementia risk. *Neurology.* 2020;95(14):e1932-e1940.
2. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. *Neurology.* 1996;46(5):1470.
3. Shaw BH, Garland EM, Black BK, et al. Optimal diagnostic thresholds for diagnosis of orthostatic hypotension with a "sit-to-stand test." *J Hypertens.* 2017;35(5):1019-1025.
4. Peters R, Anstey KJ, Booth A, et al. Orthostatic hypotension and symptomatic subclinical orthostatic hypotension increase risk of cognitive impairment: an integrated evidence review and analysis of a large older adult hypertensive cohort. *Eur Heart J.* 2018;39(33):3135-3143.
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Editors' Note: Temporal Trends and Autopsy Findings of SUDEP Based on Medicolegal Investigations in the United States

In "Temporal Trends and Autopsy Findings of SUDEP Based on Medicolegal Investigations in the United States," Cihan et al. reviewed medical examiner reports in 3 cities in the United States and found that although there was no correlation between sudden unexplained death in epilepsy (SUDEP) and diurnal patterns or time of year, there was a reduction in the incidence of SUDEP between 2009 and 2016. There was also no difference in autopsy findings between SUDEP- and non–SUDEP-related deaths associated with epilepsy. Bleasel was encouraged by these findings, which he attributed to increased awareness of SUDEP, access to affordable medical care, and prescribing antiseizure medications. However, he emphasized the importance of continued patient and family education about the risk of SUDEP, medication compliance, and treatment of comorbidities. He also noted that other studies have shown respiratory center neuronal cellular abnormalities in patients with SUDEP. Friedman et al. agreed that this positive trend is encouraging, but that it does not obviate the need to 1) counsel patients and families about SUDEP as part of general epilepsy care or 2) continue to pursue research to explain this reduction and minimize the risk of SUDEP as much as possible.

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Reader Response: Temporal Trends and Autopsy Findings of SUDEP Based on Medicolegal Investigations in the United States

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I read the article by Cihan et al.[1] with interest. Sudden unexpected death in epilepsy (SUDEP) is a dreadful event for families and physicians caring for patients with epilepsy. A case-control examination of SUDEP postmortems has shown no seasonal and diurnal patterns exist for SUDEP.[1] A downward trend in the incidence of SUDEP over 8 years is a welcome finding. Greater awareness, access to affordable medical care, and changes in antiseizure drug prescribing may have had positive effects on the incidence of SUDEP.

In observed cases during video EEG monitoring, the most common sequence of events appears to be a tonic-clonic seizure followed by prolonged postictal central apnea leading to a secondary hypoxic cardiac arrest.[2] The central apnea suggests thalamic and brainstem dysfunction. A study of the brainstem, ventrolateral medulla, and medullary raphe nuclei has shown alterations in specific neuronal populations of the respiratory control centers of the medulla in SUDEP patients' autopsy material.[3] These changes may predispose to dysfunctional respiratory control in the postictal state.

Recent work has shown the risk of SUDEP spans the whole spectrum of epilepsy from well-controlled to refractory cases.[4] Uncontrolled tonic-clonic seizures are consistently identified as an important risk factor.[5] Discussing this risk with patients and families early in our professional relationship is uncomfortable. However, as we establish trust, stress the expected good outcomes, and attempt to reduce stigma, we must also stress compliance and treat comorbidities.

1. Cihan E, Devinsky O, Hesdorffer DC, et al. Temporal trends and autopsy findings of SUDEP based on medicolegal investigations in the United States. *Neurology.* 2020;95(7):e867-e877.
2. Ryvlin P, Nashef L, Lhatoo SD, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. *Lancet Neurol.* 2013;12(10):966-977.

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3. Patodia S, Somani A, O'Hare M, et al. The ventrolateral medulla and medullary raphe in sudden unexpected death in epilepsy. *Brain*. 2018;141(6):1719-1733.
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Author Response: Temporal Trends and Autopsy Findings of SUDEP Based on Medicolegal Investigations in the United States

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We thank Dr. Bleasel for his interest in our study.[1] We, too, were encouraged to find that the incidence of SUDEP may be declining even in the absence of specific interventions. This confirms what many people caring for people with epilepsy suspected—we have many of the tools to reduce epilepsy mortality already at hand. The next steps are to understand the contribution of each of the measures that Dr. Bleasel highlights—awareness, clinician and patient behavior change, and access to treatment—to the reduction in SUDEP rates to maximize their effect. We also agree—as do people living with epilepsy and their caregivers,[2,3] those bereaved by SUDEP,[4] and professional societies[5]—that counseling about SUDEP should be part of general epilepsy education regardless of individual risk to help our patients make fully informed decisions.

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