

# Underestimated factors may also precipitate delirium and can lead to the misinterpretation of frailty in these patients

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## Dear editor

We have read the article entitled “Association between frailty and delirium in older adult patients discharged from hospital” by Verloo et al<sup>1</sup> with great interest. In their study, the authors observed that frailty is strongly associated with delirium in older patients at hospital discharge. Consequently, they concluded that assessing frailty gives health care professionals the opportunity to improve the effectiveness of primary prevention strategies for delirium, by promptly ascertaining which discharged older adults are at a higher risk of presenting with that syndrome.

We would like to give comments on a few points of this study. In the methodology section, the authors stated that frailty was assessed using the Edmonton Frailty Scale, which includes nine domains as two of cognitive impairment and functional dependency by using the Mini-Mental State Examination (MMSE) and Lawton Index of instrumental activities of daily life, respectively, at hospital discharge. According to these MMSE scores, patients have been divided into categories with regard to cognitive impairment. We would like to ask the authors about how they distinguished the impact of delirium on MMSE scores; because delirium itself may lead to lower MMSE scores independent of basal cognitive state. And this may cause misinterpretation of the patients as frail. Also, no information was given if the patients have had dementia diagnosis, which is known as one of the important risk factors for delirium.<sup>2</sup>

Regarding the assessment of functional dependency, the authors stated that a score of <16 indicates that the patient is independent, which is not in accordance with the original Lawton Index of instrumental activities of daily life article.<sup>3</sup> Can the authors clarify this point?

Another point is that, the authors compared only a number of daily medications between delirium and nondelirium groups both of which used a similar number of medications. However, certain medications may play a role in the risk of delirium. Anticholinergic agents, fluoroquinolones, and benzodiazepines are among those reported to precipitate delirium. We suggest that the data regarding the use of such medications may provide relevant information.<sup>4</sup>

Regarding the number of delirious patients, there is conflicting data in this study. It was stated as n=22 in the abstract, n=94 in Table 2, and n=20 in the result’s section. Thus, clarification of this confusion would be beneficial.

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## Disclosure

The authors report no conflicts of interest in this communication.

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## Author's reply

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## Dear editor

We thank Dr İlhan and his colleagues for their interest and comments on the recent published paper, "Association between frailty and delirium in older adult patients discharged from hospital". The following paragraphs aim to respond to their questions.

A previous published primary study distinguished the impact of delirium on the Mini-Mental State Examination scores, using appropriate statistical analysis methods.<sup>1</sup> However, as documented in other papers, delirium is a fluctuant state of attention and consciousness including unpredictable clinical manifestations during a delirium episode.<sup>2</sup> Obviously, the assessment of the mental state (Mini-Mental State Examination, Geriatric Depression Scale) could be influenced by the occurrence of a prodromal or a subsyndromal delirium episode.<sup>3,4</sup> Nurses must know the clinical and early prodromal signs. However, studies in the hospital environment show that they do not recognize the signs of delirium. To encounter this issue, a threefold strategy was adopted in our study. First, we standardized the mental state assessment procedure. Second, we trained the research nurse in delirium/mental state assessment to minimize measure bias. Of course to detect prodromal or subsyndromal delirium symptoms, appropriate knowledge and clinical observation skills are needed.<sup>4</sup> Consequently, we recruited an experienced research nurse with recognized competencies in geriatric clinical assessment. Nevertheless, it has been documented that depression and dementia are substantial confounders in relationship to the detection of the different types of delirium (hypoactive and subsyndromal delirium),

confirmed in well-documented reviews of Inouye et al<sup>5</sup> and Siddiqi et al;<sup>6</sup> although, the comment of the authors is pertinent. Cognitive impairment is a substantial confounding factor in relationship to the assessment of delirium, but also delirium influences the assessment of cognitive impairment.<sup>7</sup> This highlights the importance to integrate comprehensive geriatric assessment at the hospital admission of older inpatients including instrumental activities of daily live (IADL) and the Mini-Mental State Examination.<sup>8,9</sup>

To respond to the question of the IADL cutoff point dependency versus independency in our study, the following answer is proposed. Since the development of the IADL scale in 1969 by Lawton and Brody,<sup>9</sup> multiple linguistic translations and cultural adaptations were realized. These versions are not always corresponding with the cutoff points proposed in the original scale. Our study employed the French-IADL-validated 4-level-Likert ordinal scale for the home-dwelling older adults of Israel and Weintraub.<sup>10</sup> The scale presents a score variation from 9 to 36 (1= completely independent versus 36= completely dependent). A receiver operating characteristic analysis revealed 16 points as the optimal cutoff value in our study between independent versus dependent.<sup>10,11</sup>

In answer to the relationship between delirium and frailty, we propose the following reflections. For more than 20 years, clinical researchers have been trying to progress in the early detection of delirium. Even with well-established delirium guidelines<sup>12</sup> proposing multiple delirium detection tools, listing pharmacological and nonpharmacological risk factors, poor progress has been observed in delirium prevention and detection in daily practice.<sup>13</sup> The challenge is even worse among home-dwelling older adults after hospitalization. A huge number of hospitalized elderly adults are prematurely discharged and return home. In approximately half of the elderly patients leaving hospital, an episode of delirium is not detected. Undoubtedly, delirium is likely to develop among this frail population, as it is documented in several studies that hospitalization provokes physical and cognitive decline.<sup>14,15</sup> To assess the severity of frailty, we used the French version Edmonton Frailty Scale including physical and cognitive dysfunction, considered as a major risk factor for delirium.<sup>15</sup> The majority of the frailty instruments do not look for cognitive dysfunction. Despite the association between frailty and cognitive dysfunction, a minority of frailty instruments assesses cognition, and the type of assessment varies substantially. However, some indicators of frailty have been shown to better predict cognitive impairment decline than others. Timed walk and grip strength

were significant predictors of subsequent diagnosis of Mild Cognitive Impairment.<sup>16,17</sup> O'Halloran et al<sup>18</sup> documented the link between frailty and poorer sustained attention. Although, there is significant epidemiological evidence linking elements of frailty and cognitive decline, little work has directly explored the mechanism underlying this link. Several publications have suggested frailty components as mediators or possible pathways for cognitive decline but actually there is a lack of experimental evidence to support these suggestions. However, cognition and frailty are both assessed together more frequently during the last 5 years.<sup>19</sup>

Dr İlhan and colleagues discussed the variable “poly-medication” and proposed a more exhaustive exploration to document this variable’s impact on delirium. We agree that a more detailed analysis could offer more information; however, three major reasons can be evoked explaining why we limited our analysis. First, our study did not focus on medication risk factors. Second, due to a lack of resources, we were not able to integrate this variable into our study. Third, many medications have been associated with the development of delirium, but the strength of the associations is uncertain and it is unclear which medications should be avoided in people at risk of delirium.<sup>20,21</sup> Few studies examined different types of medications together in different doses, and most studies assessed the effects in small heterogeneous samples.

Finally, we apologize for the conflicting data, considered as a typing error in the abstract and we will discuss adapting this error with the journal editor.

## Disclosure

The authors report no conflicts of interest in this communication.

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