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Shades of Gray Matter in Severe Traumatic Brain Injury

Traumatic brain injury (TBI) is a critical public health problem throughout the world. As the leading global cause of death in persons under the age of 40 years, trauma classically affects young, healthy individuals, but it is also one of the main causes of death across all ages and locations, ranging from low- to high-income countries. In higher-income countries, as a result of improved life expectancy and increased mobility in the elderly, the incidence of TBI in individuals over the age of 65 years is rising exponentially (1). The epidemiologic patterns of severe TBI are in fact shifting toward a more balanced bimodal distribution. The management of older patients with severe TBI presents a significant challenge owing to their complex health status, including aspects such as chronic medical conditions, polypharmacy, and premorbid disabilities. Although the predominant mechanism of injury is falling from a height (2), the anticoagulant agents and platelet aggregation inhibitors that are often prescribed to these patients predispose them to a greater risk of bleeding and the development of subdural hematomas and hemorrhagic contusions (3). Furthermore, differences in the medical and surgical management of older patients with severe TBI compared with younger patients with the same brain injuries have been observed (4). More importantly, overall, older patients are more likely to die from their brain injuries than any other age group (1).

Given this changing epidemiology and lack of informative data on longer-term functional outcomes in older patients, the study by Maiden and colleagues (pp. 167–177) published in this issue of the *Journal* is an important and timely addition to our evolving knowledge in this domain (5). This registry-based cohort study, which included data from older adults (≥65 yr old) with severe TBI who had been admitted to hospitals in Victoria, Australia, showed a very high mortality rate and incidence of unfavorable neurologic outcomes. At 6 months, 85% of the patients (456/536) had died, 9% were dependent on others to live (Glasgow outcome score extended [GOSe] 2–4), and 6% were functionally independent (GOSe 5–8). A particular strength of the study by Maiden and colleagues is the inclusion of outcome assessments for up to 2 years, which had been collected as part of the comprehensive state trauma registry. Importantly, the proportion of patients in each functional status category did not change from 6 months up to 24 months after injury. These results are comparable to those obtained by Haller and colleagues in a study in which they examined the trajectory of disability (GOSe) after severe TBI (6). They observed no functional improvement in a subgroup of older patients (>65 yr) at 3–12 months after hospital discharge and also found no significant improvement in quality of life using the physical and mental components of the Short Form-12 Health Survey.

The majority of patients who are admitted to a hospital after a severe TBI die after a decision for withdrawal of life-sustaining therapy (WLST) is made (7–9). Such decisions appear to be variable across centers and are often made in the very early phase of acute care despite clinicians' limited ability to determine a long-term prognosis after a severe TBI (8, 10). These observations have generated concern within the neurological critical care community that a decision for very early WLST may not always be well informed. The very high in-hospital mortality rate (93% in the non-ICU admission cohort), the short lengths of stay, and the low rate of transfer to neurosurgical centers in the current study by Maiden and colleagues suggest that a large proportion of the patients experienced early limitation of interventions or WLST (5). Considering the historically very high mortality rate among elderly patients, there may be a tendency to withdraw or withhold life-sustaining therapies at an earlier stage in this age group owing to a perceived overly poor prognosis, resulting in a higher likelihood of self-fulfilling prophecies and potentially excess mortality (11, 12). In the case of young, otherwise healthy individuals, level-of-care decisions involving surrogate decision-makers are mainly guided by the neuroprognostic implications of the TBI; however, in elderly patients with a severe TBI, previous health conditions, existing disabilities, and quality of life must also be considered. Yes, there is

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uncertainty about prognosis in elderly patients, and most likely there are center-level differences in the rates of early WLST, but unfortunately the registry data used by Maiden and colleagues cannot address these important points (5). Nevertheless, physicians are faced daily with managing this uncertainty and communicating prognoses to families and other surrogate decision-makers. Of course, these early treatment decisions must take a patient's previously expressed wishes into account, and in many situations it is ethically justified to consider WLST as soon as it is appropriate, to respect the patient's wishes.

Outstanding clinical issues regarding this patient population also include the applicability of so-called "aggressive" interventions aimed at improving clinically significant outcomes and the scarcity of accurate tools for making reliable long-term prognoses in older patient groups. In the current study, the majority of patients admitted to the ICU were <80 years of age, whereas most of those admitted to the ward were >80 years old (5). Level-of-care decisions are sometimes already made before ICU admission, most often in a very appropriate manner and in accordance with the patient's prior wishes, to determine whether the patient should undergo intensive care. Because of this referral bias, it is difficult to assess the effect of ICU interventions on clinically significant and patient-oriented outcomes for very elderly patients with severe TBI. Nevertheless, considering only patients who were admitted to the ICU, for every 20 patients managed in the ICU, 2 recovered to functional independence by 6 months, 3 remained functionally dependent, and 15 died. The only independent factors associated with a good functional outcome (GOSe 5–8) were an injury severity score of <25 and age of <70 years. Although pupillary reactivity, one of the strongest prognostic factors, was not considered in the analyses, these findings suggest that age plays an important role, most likely secondary to less optimistic prognostic assessments in the elderly.

Considering the current limitations of the literature, it is likely that a paradigm shift in our approach to the resuscitation, critical care, and rehabilitation of older patients with TBI is necessary as the global population continues to age. The current study is a step forward, providing important insights for clinicians and patients' families seeking to make level-of-care decisions and administrators looking to adapt healthcare systems to meet the specific needs of older patients with TBI (5). Given the aging population, especially in high-income countries, we believe that further research is needed to understand how early decisions about administering intensive care to older patients are made, and whether delaying limitations of interventions in this population has any effect on quality of care, patient and family satisfaction, and overall patient-oriented outcomes. In future endeavors, researchers should also investigate whether intensified and specialized inpatient rehabilitation in older patients with severe TBI improves longer-term functional disability. ■

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