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Frailty in Trauma Patients: An Emerging Geriatric Syndrome

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Abstract
Purpose of Review In contrast to their younger counterparts, geriatric patients have a decreased physiological reserve. This age-related vulnerability poses unique challenges for clinical decision-making. Additionally, as the population of the United States (U.S.) continues to age at a rapid pace, an increasing number of elderly patients need trauma care. Accordingly, this review examines the relevance of the concept of frailty in trauma cases, as well as its role in identifying vulnerable trauma patients and improving patient care. Moreover, through a process of simplification, we made the fundamental concepts of frailty and Frailty Index clearer and more useful.
Recent Findings Frailty is a state of decline in many physiological systems. It increases vulnerability to a poor resolution after a stressor event. More precisely, this cumulative depletion of the body's reserves makes it more likely, that a stressor will trigger disproportionate changes in health. This being the case, investigators have developed several validated models of frailty that show the association between frailty and health outcomes in trauma.
Summary Frailty can decisively impact a wide spectrum of a trauma patient care, including morbidity, mortality, hospital stay, discharge disposition from the hospital, and informed clinical decision-making. Therefore, especially given the increasing number of aging individuals in the U.S., the frailty of such patients must be considered to improve outcomes.

Keywords Frailty · Geriatric trauma · Geriatric syndrome · Frailty Index · Trauma outcomes

Introduction

Generally, trauma is thought to be a disease of the young because it is assumed that the elderly are sedentary and less active [1]. However, this outdated stereotype is changing as greater numbers of older adults maintain an active lifestyle that, in turn, puts them at risk for trauma. Along with falls, burns, and motor vehicle crashes, this trend makes trauma one of the leading causes of morbidity and mortality in the geriatric population. There is an ongoing debate about the exact age of a "geriatric" trauma patient (e.g., some argue that it includes 50-year old, others say it does not start until 70 years old). Despite this, however, it is estimated that over 500,000 geriatric trauma patients (over the age of 65 years) are admitted to the hospital annually, accounting for one-quarter of all trauma admissions in the U.S. [2].

Aging is a process characterized by progressive and unavoidable physiological and biological changes. Gradually, such changes accumulate and result in a decrease in performance as well as an increase in impaired physiological function, resulting in a diminished ability to tolerate the pathological process. Indeed, the most devastating consequences of traumatic injuries occur in the geriatric population, which, in the U.S., has significantly increased by 21% since 1980 [3•]. This fastest growing subgroup

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accounts for 14.5% of the total population (46.3 million), and is expected to grow to 98 million or 23.5% of the population by 2060 [4]. And, because trauma is one of the most significant causes of death and disability amongst the elderly, this is a major public health concern. The growing number of geriatric trauma patients is already having a significant impact on our healthcare system. Elderly trauma patients pose a unique challenge to their care; the mechanism of injury is different: distinct physiological reserve, along with multiple comorbidities, multiple medications, and functional impairments contributes to this uniqueness. As a group, they experience higher mortality, higher complication rates, and slower recovery [5•]. In addition, operative intervention after trauma exposes them to a wide variety of stress that further increases morbidity and mortality [6].

Physiological changes secondary to aging, combined with comorbidities, significantly increase trauma-related morbidity and mortality [7]. Still, variability exists among elderly patients regarding their individual physiological reserve, which is the consolidation of individual biological factors, such as age, sex, functional capacity, hormonal and immunological balance, and nutritional status. Additionally, any preexisting condition might increase their morbidity and mortality after a stressful event. Indubitably, trauma surgeons must be in sync with multidisciplinary teams to provide high-quality and cost-effective geriatric-specific trauma care for these older adults. Such service lines should be tailored to the geriatric trauma patient within the trauma bay, intensive care units, and the general ward. This kind of infrastructure will improve the transition between in-hospital and outpatient care as well as overall patient outcomes.

Therefore, the purpose of this article is to assess the usefulness of the concept of frailty for identifying high-risk vulnerable trauma patients, improving patient care, and decreasing morbidity and mortality.

Frailty

While there are competing definitions of frailty in the literature [8–11], at its most basic, frailty is a clinically recognizable state of increased vulnerability resulting from age-associated declines in physiological reserve and function across multiple organ systems. It entails loss of cognitive, social, physical, and psychological functioning. Frailty status rest on two competing conceptualizations of frailty: "physical/phenotypic" frailty vs. "deficit accumulation" frailty; the latter is also known as "index" frailty. The Canadian Study of Health and Aging (CHSA) defines frailty based on deficit accumulation, a multidimensional syndrome of loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability [8, 9]. In contrast, Fried et al. define frailty as a clinical syndrome comprising unintentional weight loss (>10 lb in the last year), self-reported exhaustion, weakness (assessed by grip strength), slow walking speed, and low physical activity [10, 11]. Others define it as a phenotype of an inflammatory state or a biological syndrome that decreases tolerance to stressors [12, 13]. Besides a lack of consensus on a concise and accurate definition of frailty, there is also a lack of a clinically acceptable definition [14].

Pathophysiology

The pathophysiology of frailty is complex and involves multisystem dysregulation, which ultimately leads to a decreased physiological reserve, loss of dynamic homeostasis, and increased vulnerability for morbidity and mortality [7, 15, 16]. The key mechanism contributing to the frailty syndrome is chronic inflammation, directly or indirectly through other pathophysiological pathways. Potential etiological factors include metabolic factors, genetic/epigenetic causes, diseases, and environmental and lifestyle stressors [17]. Although the role of molecular and cellular inflammatory mediators in the pathogenesis of frailty is clearly established, the critical question remains whether acute inflammation plays a role as well. Because frailty involves multisystem physiological dysregulation, it is plausible that chronic inflammation contributes to frailty through the triggering of anemia as well as its detrimental effects on the musculoskeletal system, the endocrine system, and nutritional dysregulation [16, 18]. However, thus far, studies have failed to demonstrate any association of IL-6 and frailty, which suggests the presence of other factors involved in the pathogenesis of frailty [19, 20]. Trauma itself initiates pro-inflammatory response and has been correlated with high morbidity and mortality [21].

Growth hormone, insulin-like growth factor (IGF-1), and sex steroids are essential for skeletal muscle metabolic function [22]. Given that impaired motor performance and weakness are cardinal features of the frailty syndrome, sarcopenia is likely a pathophysiological contributor to frailty [17]. Sarcopenia can be accelerated by chronic inflammation and other chronic diseases, and is a major contributor to disability among frail patients. A decrease in anabolic hormones, malnutrition, and decreased physical activity also contribute to sarcopenia [23]. Skeletal muscle contributes to the strengthening of bones, but its diminishment is associated with the development of osteopenia and osteoporosis [24]. At the same time, some pathophysiological changes associated with frailty overlap with normal aging, such as a decreased physiologic reserve, decreased organ function, a decreased functional reserve,

and a loss of complexity. Therefore, it might be difficult to distinguish between frailty and advanced stages of aging [25].

Frailty Assessment Tools

Accurately assessing frailty in trauma patients is the important first step in implementing the concept of frailty in clinical practice. Frailty status can be captured on numerous scales comprising various characteristics. The Trauma-Specific Frailty Index (TSFI) has been extensively utilized in the trauma literature, while Frailty Index (FI) and the frailty scale are the most widely utilized generally.

Trauma-Specific Frailty Index

In keeping with the deficit accumulation model, we devised an FI comprising 50 standard preadmission variables derived from the CSHA Frailty Index regarding the development of an unfavorable discharge disposition. These variables reflect a patient's demographics, comorbidities, medication history, social history, activities of daily living, and patient general mood. Most of the variables are dichotomized (yes/no). This FI is calculated as the ratio of the total number of deficits present in a patient divided by 50 [26•]. However, because this 50-variable FI is extensive, time consuming, and difficult to implement in a trauma setting, the same team developed a 15-variable Trauma-Specific Frailty Index (TSFI) based on the 50-variable FI. We chose the 15 variables most closely associated with the development of an unfavorable discharge disposition. Based on a sensitivity and specificity analysis, an FI of 0.27 was selected as the cutoff for either frail or robust patient [27•]. A higher FI represents a higher frailty status. The variables that make up the TSFI are demonstrated in Table 1. The TSFI was then prospectively validated in 100 trauma geriatric trauma patients [27•].

Upper Extremity Frailty Assessment

The real limitation in the assessment and application of frailty is the lack of objective tools, as all the currently available frailty tools rely on subjective variables. Recently, there has been an increasing focus on identifying objective measures for frailty measurement; one of them is the concept of kinesiology. It refers to the study of mechanics of human movements. It has been used to assess the physiological state of elderly individuals based on their velocity of movement. More specifically, body motion in the form of upper and lower extremity movements has been extensively studied in elderly patients, and it is an independent predictor of outcomes [28, 29]. Lower extremity motion sensors have also been shown to predict risks of fall and disease states. However, they cannot be used in geriatric trauma patients who are unable to walk [30, 31]. This being the case, upper extremity sensors have been utilized to assess frailty status. Toosizadeh et al. utilized the concept of kinesiology and devised an upper extremity motion sensor that assesses frailty status based on the TSFI and Fried's scale [32•]. While algorithms based on motion sensors have been developed to predict outcomes, their role in trauma patients is still unclear.

Other Scales

Several other scales have been utilized to measure frailty status in trauma patients. Maxwell et al. utilized three validated tools that included the Vulnerable Elders Survey (VES-13), the modified Barthel Index (BI), and the Life Space Assessment (LSA) [33–35]. The aVES-13 is a 13-item tool that assigns a score to four domains: age, self-rated health, common physical tasks, and activities of daily living (ADL) [36]. The modified BI is a 10-item tool that assesses 10 ADL, focusing on physical disability and mobility of the patient [37]. Similarly, the LSA mainly assesses the mobility function of a patient within a community, and is associated with impaired physical function [38]. American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) in collaboration with American Geriatric Society (AGS) has devised best practice guidelines for geriatric patients and recommends using frailty scale for the assessment of frailty status [39].

Some studies have also suggested that sarcopenia can be an objective way to predict the frailty status of a patient [40]. The gold standard for measuring sarcopenia is computed tomography. Using a questionnaire to measure frailty can be time consuming, especially in an acute setting where the patient might be sedated or disoriented. Besides, most geriatric trauma patients get a CT scan of the abdomen and pelvis, which can then be used to assess the degree of sarcopenia (measuring psoas muscle mass) and frailty [41]. However, poor functional capacity, the hallmark of frailty, results from multiple other causes, not all of which are related to skeletal muscle amount or function. Hence, it would be difficult to measure frailty status based on the level of sarcopenia alone.

Outcomes Assessment Tools

Several different assessment tools are routinely used to predict outcomes after trauma. They include the physiological, anatomical, and combined trauma scoring systems: the Injury Severity Score (ISS); the Trauma and Injury Severity

Table 1 Variables in Trauma-Specific Frailty Index (TSFI)

Fifteen variable Trauma-Specific Frailty Index			
Comorbidities			
Cancer history	Yes (1)	No (0)	
Coronary heart disease	MI (1)	CABG (0.75)	PCI (0.5)
	Medication (0.25)	None (0)	
Dementia	Severe (1)	Moderate (0.5)	Mild (0.25)
	No (0)		
Daily activities			
Help with grooming	Yes (1)	No (0)	
Help managing money	Yes (1)	No (0)	
Help doing housework	Yes (1)	No (0)	
Help toileting	Yes (1)	No (0)	
Help walking	Wheelchair (1)	Walker (0.75)	Cane (0.5)
	No (0)		
Health attitude			
Feel less useful	Most time (1)	Sometimes (0.5)	Never (0)
Feel sad	Most time (1)	Sometimes (0.5)	Never (0)
Feel effort to do everything	Most time (1)	Sometimes (0.5)	Never (0)
Falls	Within last month (1)	Present not in last month (0.5)	None (0)
Feel lonely	Most time (1)	Sometimes (0.5)	Never (0)
Function			
Sexual active	Yes (0)	No (1)	
Nutrition			
Albumin	<3 (1)	>3 (0)	

Score (TRISS); Revised Trauma Score (RTS); Abbreviated Injury Scale (AIS); the Geriatric Trauma Outcomes Score (GTOS); Trauma Mortality prediction Model (TMPM); and the Glasgow Coma Scale-Age Prognosis (GAP) score. Each assessment tool has its own pros and cons. The ISS and AIS are associated with higher morbidity and mortality; however, they cannot be calculated at the time of hospital admission. Based on age as well as vital and injury parameters, the TRISS scoring system and GTOS predict the probability of survival [42]. Although it is simple and easy to calculate, it is not readily available after admission. Similarly, the GAP score is simple and easy to calculate, it is only limited to patients with traumatic brain injury [43]. In contrast to these other types of assessments, the TSFI integrates all the facets of a patient's health that are recognized as contributing factors to morbidity and mortality. It integrates the individual's age, comorbidities, nutritional status, daily activities, functional status, and physiological health.

Frailty and Trauma Outcomes

Frailty is associated with an increased risk of morbidity, mortality, adverse discharge disposition, diminished quality of life, and disability [1, 44–51]. Any morbidity during the hospital course can be detrimental to a patient's recovery, as well as increase the hospital stay and total cost.

Frailty and Complications

Frailty, a cumulative decline across several organ systems, often leads to clinical deterioration and adverse events in response to stressors, such as trauma and surgery. It is linked to post-operative complications in geriatric patients undergoing general surgery [52], urological procedures [53], vascular surgery [54], spine surgery [55], and neurosurgery [56]. This is also the case for trauma surgery. We prospectively calculated frailty status using the TSFI. Frail patients were more likely to develop sepsis, a urinary tract infection (UTI), deep venous thrombosis, and pneumonia [57•]. Interestingly enough, an FI $\geq$ 0.25 was independently associated with in-hospital complications, irrespective of increasing age. In another prospective analysis using the TSFI, frail patients were more likely to develop in-hospital complications, particularly acute kidney injury and anemia [58•]. Likewise, frail patients were 5 times more likely than non-frail patients to develop complications. A more recent prospective analysis also shows that frail patients were more likely to develop in-hospital complications, especially a UTI and pneumonia [59•].

Frailty and Hospital Stay

The average hospital stay is often used as an indicator of efficiency. A shorter hospital length of stay will shift the care from an expensive inpatient to less expensive post-acute settings resulting in a reduction in the cost per discharge. Recent literature demonstrates the association of frailty and the FI with hospital length of stay [60–63]. Kasotakis et al. found that frail patients usually require additional care and support, which results in an increase in ICU and hospital length of stay [63]. In trauma, we used the TSFI to analyze the impact of frailty on hospital and ICU length of stay. In our prospective analysis, frail patients had a higher hospital and ICU length of stay compared to non-frail patients. However, there was no difference in time spent on mechanical ventilation [57•]. Contrary to the previous study, another prospective analysis showed no difference in the hospital and ICU length of stay between frail and non-frail [58•]. Higher complications rate usually requires more in-hospital support and care resulting in a prolonged stay.

Frailty and Discharge Disposition

Discharge disposition plays an important role in limiting excess hospital readmissions. Early assessment and identification of frail patients are critical in predicting likely outcomes and tailoring the proper management of elderly trauma patients. An appropriate discharge disposition can be worrisome for trauma clinicians. Discharge to home is the most favorable disposition. In some cases, like traumatic brain injuries, discharge to rehabilitation facilities is associated with improved outcomes. Interestingly, frailty has also been shown to predict discharge disposition in various surgical specialties [64–67]. The first study ever done in trauma patients to evaluate the role of frailty in discharge disposition utilized a modified version of Rockwood's 50-variable FI. They concluded that frail patients were more likely to be discharged to a skilled nursing facility (SNF) compared to the non-frail [26•]. Recently we analyzed the impact on frailty on discharge disposition using the TSFI [59•]. We prospectively enrolled 350 patients. In our analysis, frail patients were more likely to be discharged to a SNF, while non-frail patients were more likely to be discharged to home or a rehabilitation center. Frailty has been shown to predict short-term as well long-term mortality in geriatric trauma patients [26•, 35, 58•].

Frailty and Failure-to-Rescue

Failure-to-rescue (FTR), defined as death after developing a major complication, is a well-studied indicator of patient safety and quality of care within a healthcare organization [68]. Complications after injury are relatively common among trauma patients, and emerging literature indicates that most of these complications may be independent of a hospital's quality of care. Recent evidence suggests that reducing FTR events might be the most appropriate target for quality improvement in the geriatric population. Research shows, however, that patient-level factors are equally important in determining the quality of a patient's recovery from post-operative complications [69]. The impact of hospital care on FTR is well-documented in the surgical literature [70–72]. However, the concept is novel in trauma surgery. In fact, we were the first ones to analyze the impact of frailty on FTR in trauma [58•]. We enrolled a total of 368 geriatric trauma patients. Frail patients had a higher FTR rate compared to non-frail patients. Even after controlling for demographics as well as vital and injury parameters, frailty status was independently associated with FTR. The ability to effectively rescue a patient from a complication relies on several factors. To successfully manage this at-risk population, intensivists need to recognize the frailty status of geriatric patients. Moreover, a multidisciplinary collaborative approach by physicians and nurses is required for more effective interventions, diagnosis, and management of geriatric trauma patients who experience complications [72]. By identifying potential contributing factors that include frailty, we can significantly modify adverse outcomes for these patients. This should occur early within a trauma patient's hospital stay to reduce FTR rates.

Frailty and Long-Term Outcomes

Frail patients are less likely to tolerate the stressor event acutely and develop adverse outcomes short term. In addition, frailty has an association of developing long-term adverse outcomes in various fields of medicine [73–75]. It was hypothesized that frail patients are less likely to fully recover from acute trauma and will have long-term consequences. Trauma patients were prospectively evaluated to assess the association of frailty and long-term outcomes [59•]. Frailty status was calculated utilizing the TSFI and then all patients were followed until 6 months post discharge. Frail patients were more likely to have a trauma-related readmission, recurrent falls, as well as were more likely to die compared to non-frail patients. Maxwell et al. analyzed the impact of frailty on long-term mortality after trauma by utilizing the VES-13, BI, and LSA [35]. They prospectively analyzed a total of 188 trauma patients and concluded that preinjury frailty was independently associated with 6 months and 1-year mortality.

Frailty and Health-Related Quality of Life

The recent era has witnessed a change of focus in health care from complications and mortality to a novel metric "qualify of life." Health-Related Quality of life (HRQoL) is an important outcome measure; however, its understanding among trauma patients is still evolving. Masel et al. and Chang et al. found that being frail or pre-frail was strongly associated with diminished HRQOL in the elderly population [76, 77]. Therefore, we aimed to assess the impact of frailty on HRQoL in trauma population. We found that frail patients had an inferior quality of life at discharge and 30-day post discharge compared to non-frail. In addition, the quality of life did not improve significantly for frail patients even after discharge. The most significant difference was found to be in the physical functioning and limitations due to physical health domains. Similarly, Maxwell et al. also analyzed the association of preinjury frailty with functional status at 6 months and 1 year post-injury [35]. They concluded that preinjury frail status was associated with a decrease in functional status as well as mobility at 6 months and 1-year post-injury.

Prevention and Intervention

Reducing the severity and prevalence of frailty will clearly benefit the individual, their families, and society. Several interventions have been studied in clinical trials in non-trauma fields. These interventions in the form of primary and secondary prevention can be performed even after discharge and will improve short-term as well as long-term outcomes. Several types of therapeutic interventions include the following:

- Comprehensive geriatric assessment: Frail patients who receive a comprehensive geriatric assessment (CGA) are more likely to have improved outcomes. They tend to return to home, are less likely to have a functional or cognitive decline, and have lower mortality rates than those who do not receive a CGA [78]. By reducing the risk of falls, complex interventions based on an elderly patient's CGA can also increase the likelihood of such patients living at home because of a low risk for falls [79, 80].
- Exercise: Exercise exerts physiological effects on the brain, skeletal muscle, immune system, and endocrine system [81–84]. Several systemic reviews have shown that exercise intervention can improve mobility and functional ability in elderly frail patients [85–87]. Contrariwise, one meta-analysis does indicate that the effect of exercise might me inconsequential [85]. Nonetheless, the preponderance of the literature supports the assumption that exercise improves outcomes in frail patients, though the most effective type of exercise (i.e., intensity, frequency, duration, and kind of exercise) is still uncertain. A Cochrane review analyzed 49 randomized controlled trials of regarding the efficacy of exercise for long-term care residents [88]. They concluded that strength and balance training could successfully increase muscle strength as well as functional abilities.
- Nutrition: Elderly frail patients are more likely to have impaired nutrition and weight loss. Weight loss and low albumin levels are surrogate markers for impaired nutritional status, and are included in the deficit accumulation model of frailty. Nutritional intervention might be able to correct impaired nutrition and weight loss resulting in frailty. A randomized controlled trial investigated the impact of exercise and nutritional supplementation in 100 frail elderly patients. They concluded that nutritional supplementation along with exercise has no effect on muscle strength, gait speed, stair climbing, or physical activity [89]. A Cochrane review by Forster et al. concluded that nutritional supplementation in addition to exercise might lead to improved outcomes, but a firm conclusion cannot be made because of the absence of trials of a high methodological quality [88].
- Pharmacotherapy: Several pharmacological agents have been investigated that might have a potential role in frailty. These agents include angiotensin-converting enzyme inhibitors (ACEI), testosterone, and vitamin D. ACEI are thought to improve the structural and biochemical function of skeletal muscle. These agents could slow the decrease in muscle mass and possibly halt sarcopenia [45, 90], which improves the capacity to exercise and quality of life [91]. Testosterone supplementation improves muscle strength, but at the expense of cardiovascular and respiratory outcomes [92]. Low levels of vitamin D have been associated with frailty. Vitamins D supplementation results in improved neuromuscular function [93, 94]. In addition, such supplementation in frail patients deficient in vitamin D appears to reduce the number of falls [95]. Adding calcium to vitamin D supplementation can also reduce the risk of fractures [96].

The use of pharmacological agents for the prevention and treatment of frailty is a somewhat controversial and important topic for future research.

Conclusion

The growing elderly population is a major public health concern, and because geriatric patients have multisystem problems, healthcare systems can no longer mostly

function in terms of a single-system illness. Indeed, frailty, a state of increased vulnerability to stressors, is the only practical and unifying notion in the care of elderly patients that directs the attention from a single system-specific diagnosis to a more efficacious holistic approach. The distinction between frail elderly patients and non-frail patients should be an essential part of a healthcare assessment. Conversely, exclusion of non-frail patients merely based on age is unacceptable. As illustrated above, frailty has a decisive impact across the spectrum of patient care, including complications, mortality, and discharge disposition. Detecting and grading the severity of frailty would help researchers gain a deeper insight into more complex mechanisms of frailty as well as develop interventions to improve a patient's frailty status. This has considerable clinical merit because frailty would become the basis for a shift in the care of elderly patients towards more appropriate goal-directed care.

Compliance with Ethics Guidelines

Conflict of interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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