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Review Article

The Fragile Brain: Understanding Frailty in Neuroanesthesia

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Abstract

Frailty is a multidimensional geriatric syndrome characterized by decreased physiological reserve, making patients more vulnerable to stressors, such as surgery and anesthesia. In neuroanesthesia, frailty is particularly relevant due to the high-risk nature of neurosurgical procedures and the potential for significant perioperative stress. Although there are several studies on the implications of frailty in spine surgery, there are lacunae in the knowledge understanding and frailty risk assessment in the cranial cohort of neurosurgical patients. A systemic review process with a qualitative data analysis of the available literature was used to extract data for this review. By identifying, acknowledging, and addressing the knowledge gaps in our understanding of frailty, specifically the cranial cohort, and developing a neuroanesthesia-specific frailty risk index, along with establishing best practice strategy guidelines and institutional protocols, neuroanesthesiologists will enhance and optimize outcomes.

Keywords
- frailty
- neuroanesthesia
- risk assessment

Introduction

Aging is complex and intricate. The world's population is living longer and growing older. Embracing and planning for this massive demographic transition is one of the greatest social challenges of the 21st century. As per the World Health Organization (WHO) data, people aged ≥50 years are increasing in number. The hexagenerians and older population was 1 billion in number in 2019. It is expected to rise at a staggering pace, reaching 1.4 billion by 2030 and 2.1 billion by 2050. While India has the highest number of young people, aging is rapidly progressing. Currently, India hosts 153 million people above 60 years of age, which is only expected to rise further, reaching a staggering 347 million by 2050. This demographic shift is not merely a statistic; it is a societal transformation and a health care challenge of unparalleled magnitude with far-reaching implications. There has been a paradigm shift in the past 20 years, as many studies have shown that age as an independent risk factor should not be used as a contraindication to neurosurgical procedures.[1,2]

With the advancement of newer neurosurgical and medical techniques, safety and neurological outcomes have improved progressively. Neurosurgeries that were once considered risky for frail elderly patients now form an essential part of the treatment protocol. With intraoperative functional neurological testing modalities in place, the surgical goals in contemporary practice have moved away from disease elimination to achieving an acceptable quality of life. This increases the responsibility of the perioperative physician to evaluate and optimize, to minimize the effects of patient-related trespasses on the overall outcome.

Frailty is defined as an age-accelerated decline across multiple organ systems leading to vulnerability to poor resolution of homeostasis after a stressor event.[3] In a broad sense, the term "frail" refers to a physiologic state of vulnerability. Although not solely associated with advanced age, a recent systematic review and meta-analysis reported that the prevalence of frailty in a general surgical population of 61- to 77-year-olds ranged from 10.4 to 37%, and frailty was associated with an eightfold increase in 30-day mortality.[4]

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Frailty is a multidimensional geriatric syndrome characterized by decreased physiological reserve, making patients more vulnerable to stressors, such as surgery and anesthesia. In neuroanesthesia, frailty is particularly relevant due to the high-risk nature of neurosurgical procedures and the potential for significant perioperative stress. Frailty has been progressively shown to be a critical index for predicting postoperative complications and thus weighing in the risk of surgery against the likely benefit.

Fried, who studied frailty for the first time, described a community prevalence of 6.9%, with an increased incidence seen with increasing age, and female gender. It reportedly had a higher association with incident falls, accumulated disabilities, hospitalization, and death.[5] Fried and colleagues proposed "frailty" for the first time as an age-related syndrome of physiological decline.[5,6]

As experts in perioperative medicine, the time has similarly come for anesthesiologists to play a more active role in supporting the healthy aging of older adults who require some form of anesthesia care. An initial step toward improving perioperative care of older adults requires a better appreciation of how clinical outcomes are impacted by frailty so that anesthesiologists will fear less and understand more of the complexities and risks of frailty in neuroanesthesia.[7] Frailty is different from comorbidity, so it has lagged in the quest for an objective assessment score. However, many studies are underway to define and quantify frailty in a reliable, reproducible, and practically feasible manner.

This review aims to improve the understanding of the growing concern and the magnitude of the issue of frailty in neuroanesthesia, and describe the tools available to measure frailty and the prevalence of frailty in the intracranial and spine surgical populations. It also intends to present the current evidence on the relationship of frailty with postoperative outcomes and interventions to improve outcomes and discuss the scope of future directions to formulate best practices through prospective research.

To extract data for this review, a qualitative data analysis of the available literature was done using the search terms "frailty," "surgery," and "neurosurgery."

Preoperative Identification of Frailty

Studies on frailty have assigned it a fair share of relevance in prognostication and outcome prediction. Furthermore, this puts the onus on the developing research and literature to go one step further and evaluate frailty in a way that would reasonably affect clinical decision-making. The evolving concept of frailty and the emerging knowledge of its impact on outcomes and recovery after illness or surgery has made it imperative to develop tools for its simple, dependable, precise, and objective assessment.

Clinical Evaluation

Often, features of frailty are overlooked and passed on as a normal aging process. This is mainly due to a lack of standard criteria for assessment. Invariably clinical evaluation of all elderly patients must include comorbidities, medications, activities of daily living (ADLs), memory, vision, hearing, cognition, and risk of falls. A thorough neurological assessment is important as the disease-specific focal deficits may strongly contribute to the above factors and thus confound the clinical assessment of frailty.

Sarcopenia and Inflammation

Sarcopenia refers to the progressive loss of muscle mass and strength, attributable to the natural process of aging and associated with chronic diseases that affect the musculoskeletal system like chronic obstructive pulmonary disease (COPD), chronic kidney disease, diabetes mellitus (DM), human immunodeficiency virus, and cancer. A progressive decline in type II muscle fibers is observed in sarcopenic patients.

The International Clinical Practice Guidelines for Sarcopenia recommend annual screening to be performed in all individuals aged $\geq$60 years.[8] Such annual screening will contribute to the frailty assessment with preexisting data, which may be possibly unaffected by recent functional impairment.

SARC-F was a simple questionnaire-based screening tool developed for sarcopenia assessment, involving five questions: Strength, Assessment in walking, Rising from a chair, Climbing stairs, and Falls. Owing to its lower predictive value, several modifications have been made, like SARC-CalF + AC (adding arm and calf circumference) and SARC-F + EMB (adding body mass index).[8]

Frailty Scoring Systems

Various scoring systems exist for measuring frailty (►**Table 1**), based on deficit accumulation or phenotypic models. The deficit accumulation model works on the principle that deficits accumulate as age progresses, and the higher the deficits, the higher the risk. Contrarily, the phenotypic model states that comorbidities form the cause, and disabilities result from frailty, but frailty is synonymous with neither.

The *Clinical Frailty Scale*, developed by the Canadian Society of Health and Ageing in 2005, was a 7-point scale at its inception, namely very fit, well, managing well, very mildly frail, mildly frail, moderately frail, and severely frail, with very severely frail and terminally ill being added in the 2007 amendment.[9] It considers the functional status and ability to perform ADLs. Its use in the emergency department has been shown to help in the triage of patients and aid clinical decision-making.[10] However, this score is susceptible to an "ableism" bias, that is, it quantifies a physiological inability as the same in all cases, disregarding its cause and factors surrounding it.[11]

The *Risk Analysis Index* (RAI) is a 14-point index to measure frailty. It can be used prospectively (RAI-C) with the help of a questionnaire and retrospectively (RAI-A) using variables from surgical quality improvement databases. Its development and initial validation were done by Hall et al in 2017 and was found to have good predictive value for postoperative morbidity and mortality.[12] However, the study did not assess its predictability for patient-related outcome factors like level of independence, disability accumulation, etc.

Table 1 Frailty Risk Indices:Advantages and Disadvantages

Sl. no.	Frailty risk indices	Advantages	Disadvantages
1	Fried's frailty index	• Widely used and validated • Easy to calculate • Identifies physical frailty	• Does not account for cognitive or social frailty • Requires clinical assessment • Not neurosurgery specific
2	Rockwood's frailty index	• Comprehensive, including 92 variables • Accounts for cognitive and social frailty	• Complex and time-consuming • Requires extensive clinical data • Not neurosurgery specific
3	Edmonton frailty scale	• Quick and easy to administer • Accounts for cognitive and social frailty	• Less widely validated • Physical frailty may be missed • Not neurosurgery specific
4	Clinical frailty scale	• Simple/easy to use • Accounts for physical, cognitive, and social frailty	• Subjective • Less accurate • "Ableism" bias • Not neurosurgery specific
5	FRAIL scale	• Quick/easy to administer • Accounts for physical, cognitive, and social frailty	• Less widely validated • May not capture frailty as comprehensively • Not neurosurgery specific
6	Risk Analysis Index	• Prospective (RAI-C) and retrospective (RAI-A) scores available • Good predictability of morbidity and mortality	• Cannot predict the level of independence and disability accumulation • Not neurosurgery specific
7	Modified 11-Item Frailty Index	• Comprehensive • Accurate	• Exhaustive in practice • Not neurosurgery specific
8	Modified 5-Item Frailty Index	• Easy to calculate • Accurate	• Factors outside the 5 comorbidities scored are missed • Not neurosurgery specific

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) dataset was used to assess frailty using an 11-point scoring system, the *modified 11-Item Frailty Index* (mFI-11). It categorized patients into low-frailty ($\leq$1 comorbidities) and high-frailty ($\geq$2 comorbidities) groups. Overall, higher mortality (3 vs 0.6%) and increased hospital length of stay (LOS) were seen in the high-frailty group.[13]

With progressive research, few of the variables in the mFI-11 were removed. By 2015, a filtered-out derivative of the original scale remained, modified 5-Item Frailty Index (mFI-5). The mFI-5 is a concise comorbidity-related assessment tool for frailty. It stratifies risk based on the presence or absence of five comorbidities, namely hypertension requiring medication, congestive heart failure less than 30 days before surgery, insulin- or non-insulin-dependent DM, COPD or pneumonia, and partially or totally dependent health status at the time of surgery.[14] Higher mFI-5 scores were associated with a higher risk of adverse postoperative outcomes. A comparative study between the mFI-5 and the mFI-11 showed an equal predictive ability of both scores in terms of postoperative outcomes.[15] The mFI-5 shows promise as an effective frailty measure within the NSQIP database. Even in patients with neurotrauma, higher mFI-5 scores were evidently associated with increased risk of hospital-acquired infections and, subsequently, increased length of hospital stay and health care cost.[16]

In a study conducted by Huq et al on 1,692 patients, every point increase in the mFI-5 was associated with a 0.32- and 1.38-day increase in intensive care unit (ICU) stay and total LOS, respectively, along with increased incidences of pulmonary embolism, physiological derangement, respiratory failure, and sepsis, and an overall increase in total charges.[17]

In 2020, Sastry et al conducted a similar analysis on data collected from the NSQIP database of 25,386 patients undergoing elective craniotomy for tumor and showed a striking association with major postoperative complications, non–home discharge, and 30-day morbidity and mortality.[18]

The Fried Frailty Phenotype (FFP) considers five criteria to assess the presence and level of frailty: unintentional weight loss, weakness or poor handgrip strength, self-reported exhaustion, slow walking speed, and low physical activity.[19] Validated in several surgical populations, especially cardiovascular and spine, the FFP shows promising value as a predictor of postoperative outcomes. While assessing FFP, one needs to be mindful of neurological deficits like power loss or imbalance if present. Measuring the grip strength of the nonpathological hand in case of paresis of the dominant side and relying on the subjective implication of slowed speed compared to peers are possible modifications to apply this index in neurosurgical patients successfully. Contrary to what may seem, these will not dilute the index's essence of being objective, as one patient rarely has multiple confounding neurological deficits. However, more studies and randomized controlled trials are required for their validation.

The *Rockwood Frailty Score* measures the proportion of accumulated deficits, out of 40 potential deficits, and the

index is calculated by adding the score of each deficit and dividing the total by the total number of variables.[20]

In 2022, Le Pogam et al validated FFP with an electronic knowledge-based tool using 1 year of hospital discharge data. The *electronic Frailty Score* (eFS) was developed using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). It identifies 18 organs/systems as critical and calculates eFS based on the number of deficient ones.[19] The eFS was an inexpensive way to categorize patients and prioritize more extensive frailty assessment in a select group, thus saving time and manpower among health care workers.

Frailty is rapidly growing as an outcome modulator; hence, objectifying it has become a matter of interest in contemporary medical research. However, we still lack a standardized assessment tool for frailty, especially in the neurosurgical setting, specifically in the cranial surgery cohort, an ideal tool with optimum statistical value and effortlessness in clinical practice. While modifying the current scores is one way of adapting them to suit these patients, a score specifically designed to work around these confounders and still hold an acceptable level of accuracy would be helpful. It is essential to acknowledge this definite lacuna among the available frailty scores and develop an index specifically designed to assess frailty in cranial and spinal surgeries.

Implications of Frailty in Neuroanesthesia

Frailty has been established as a factor affecting postoperative mortality and morbidity including surgical complications, prolonged hospital stays, and non–home discharge in other surgical populations.[21,22] There are relatively few studies in the neurosurgical population. They have been tabulated and presented in ►**Table 2**.

Kazim et al performed an NSQIP analysis of 4,662 patients with spine tumors to compare age with frailty as measured using mFI-5, with respect to 30-day mortality, major complications, unplanned reoperation, unplanned readmission, and hospital LOS.[23]

Zhu et al conducted the first systematic review of the implications of frailty in neurosurgical patients. They reviewed 13 studies, and frailty was shown to be an independent predictor of mortality, postoperative complications, nonroutine discharge disposition, LOS, and hospitalization costs.[24]

Mitchell and Flexman conducted a systematic review of the implications of frailty in neuroanesthesia and found frailty to be overall useful to predict postoperative outcomes, and help in surgical decision-making, preoperative counseling, and prehabilitation. A further subgroup analysis showed that the association of frailty with adverse outcomes was pathology specific, being stronger in cases of meningiomas while requiring further validation in other pathologies like glioblastoma, chronic subdural hemorrhage, intracranial aneurysms, and spine surgery.[25]

In certain conditions, where brain or spine pathologies are the primary cause of functional derangements, surgical intervention is indicated despite the functional status of the patient and may even help reduce frailty by treating the neurodeficit.

The literature consists of only one study that fails to demonstrate the usefulness of the mFI score in outcome predictability in patients with spontaneous intracranial hemorrhage.[26] However, this was a retrospective study based on limited data, done on a nonsurgical patient group.

Pazniokas et al conducted a systemic review of 25 studies related to frailty in neurosurgery. They observed the definite heterogeneity of frailty studies in this patient group that lack the quality to design a practicing protocol. At the same time, their analysis demonstrated a strong association between complications of any type and preoperative frailty.[27]

Table 2 Implications of Frailty in Neuroanesthesia

Sl. no.	Study	Scale measured	Impact of frailty			
			Mortality	Postoperative outcome[a]	Non–home discharge	Hospital length of stay
1	Sastry et al[1]	mFI-5	+	+	+	
2	Kazim et al[23]	mFI-5	+	+	+	+
3	Do we need a neurosurgical frailty index?[3] Oluwaseyi Adebola, Department of Neurosurgery, The Walton Centre, Liverpool, United Kingdom.	mFi-5	+	+		
4	Frailty as a predictor of neurosurgical outcomes in brain tumor patients[4] Tessa A. Harland, Mary Wang, Dicle Gunaydin, Anthony Fringuello, Jacob Freeman, Patrick W. Hosokawa, D. Ryan Ormond	?FFP		+	+	+
5	Cole et al[16]	mFI-5		+		+
6	Kim et al[26]	mFI-5	–	–	–	–

Abbreviations: FFP, Fried Frailty Phenotype; mFI-5, modified 5-Item Frailty Index.
[a]Complications/reoperation.

Thus, frailty evaluation is imperative, at least in patients prone to be frail. However, the literature on the intracranial surgical population lacks the required research material to form a standard protocol for its objective assessment. Frailty has been established as a reliable predictor of an eventful perioperative and postoperative course.

Strategies for Managing Frailty in Neuroanesthesia

With advancing age and frailty, there is an overall redistribution of body mass proportions. Increased proportions of fat mass lead to prolonged accumulation of lipid-soluble drugs. Senile degeneration in kidneys is reflected in the delayed elimination of certain drugs even before reaching the stage of renal replacement therapy. Thus, fine titration of anesthetic agents is essential while dealing with these patients.[28]

Postoperative delirium (POD) is defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), as a mental state disturbance that occurs in the hospital up to a week after surgery and meets the following criteria: a disturbance in attention, awareness, and cognition; a fluctuating course; a change in brain function that differs from patient's baseline. Among others, increasing age is an important risk factor for POD. The ABCDEF bundle used in the ICU is also useful for the treatment of POD. It includes pain Assessment and management, daily Breathing trials, Choice of sedation, Delirium assessment and intervention, Early mobility, and Family involvement.[29] There is a growing concern about POD, and postoperative cognitive dysfunction (POCD), with a prevalence of 1% at 1 year, affecting the level of independence and ADLs.[30] It becomes more challenging to tackle physiologic derangements and achieve the best possible homeostasis as age and frailty advance. Strategies for managing frailty (►**Fig. 1**) start in the preoperative period. Preoperative patient visits well ahead of an elective surgery to thoroughly assess and optimize are essential. A good preoperative assessment, including frailty and sarcopenia scoring followed by optimization with adequate nutrition and prehabilitation, goes a long way in these patients.

Healthy outcomes for frail patients can result from active interventions in four distinct aspects: exercises, nutritional intervention, multicomponent interventions, and individually tailored geriatric care models.[31] Studies have shown that endurance building and exercise training of frail patients preoperatively are beneficial. Concerning nutrition, even though the literature gives mixed data, nutritional education, daily food fortification with proteins, and micronutrient supplements are wise choices. The third prong consisting of multicomponent intervention targeting multifactorial etiology of frailty consists of combination strategies, for example, nutrition along with resistance training. These have shown promise not only in preventing progress from prefrail to frail state but also in prehabilitating patients before major surgeries. Patient-specific prehabilitation measures tailored to the existing impairments form the fourth prong and potentially result in functional improvement and reduced hospital LOS. These four-pronged frailty interventions, however, best work when applied at optimal stage of functional progress and modified to suit each patient's physiological and pathological characteristics. This is especially worth considering in patients with progressive neurological impairment. In such cases, modifying the prehabilitative measures by down titrating the exercising part, focusing more on the other aspects, while also pairing it with measures to facilitate enhanced recovery after surgery in whichever neurosurgical cases possible, may turn out to be more beneficial than formulating and following a strict protocol-based management strategy.

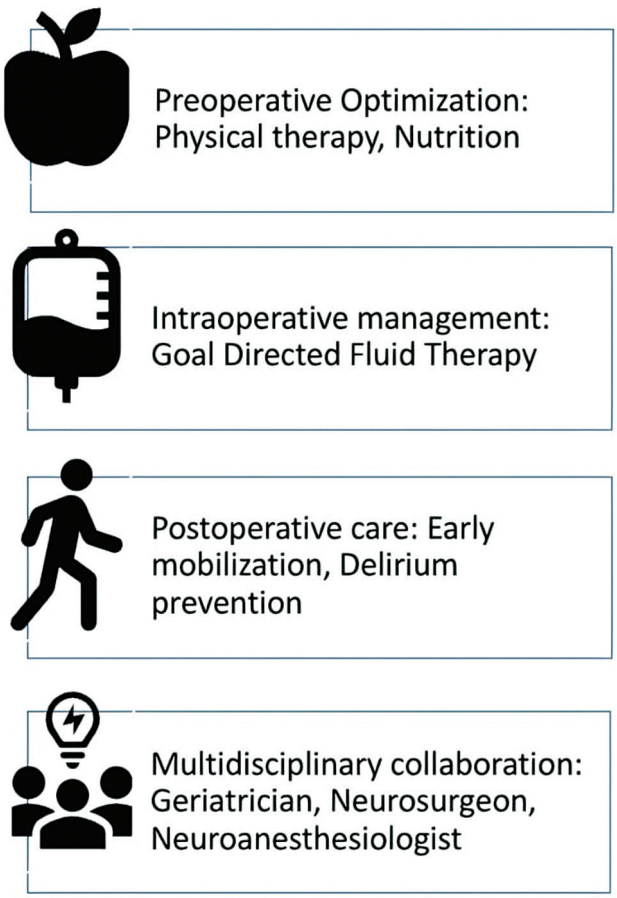

Fig. 1 Strategies for managing frailty in neuroanesthesia.

Intraoperative maintenance of stable physiology using the available advanced tools like pulse pressure variation guided goal-directed fluid therapy helps in better management. Early mobilization is especially useful in frail patients prone to getting bedridden in the absence of such efforts. Active measures need to be taken to prevent POCD, like active reversal to preoperative habits, providing medical aids in the immediate postoperative period, and early social rehabilitation.

There is a need for early identification of frailty and delirium in an emergency setting, and the presence of geriatric emergency management service with trained interprofessional members is ideal.[32]

Finally, a multidisciplinary collaboration employing expert professionals in handling every aspect of case

management helps reach the goal of minimal potential physiological insults, leading to a good patient outcome.

Conclusion

Frailty is a growing critical consideration in neuroanesthesia, requiring preoperative identification, tailored anesthetic management, and postoperative care. Developing a neuroanesthesia-specific frailty risk index, and establishing best practice strategy guidelines, with institutional protocols is essential. Cross-collaboration among disciplines with multicentric trials will help collect robust data for an iterative approach to evolve patient care and enhance and optimize outcomes.

Conflict of Interest
None declared.

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