



Perioperative frailty: lessons learned and future directions

Ibukunoluwa Adeleke^a and Jeanna Blitz^b

Purpose of review

As the surgical population ages, preoperative diagnosis and optimization of frailty becomes increasingly important. Various concepts are used to define frailty, and several tools have been validated for use in the perioperative period. This article reviews current conceptual frameworks of frailty, references current literature and provides a practical approach to the preoperative frailty assessment with a focus on potential interventions.

Recent findings

A multipronged approach toward preoperative optimization should be used in patients with frailty syndrome. Oral protein supplementation and immunonutrition therapy can reduce complications in patients with malnutrition. Initiating a preoperative physical exercise regimen may mitigate frailty. Nonpharmacologic interventions to reduce preoperative anxiety and improve mood are effective, low-cost adjuncts associated with improvement in postoperative outcomes. Engaging in shared decision making is a critical component of the preoperative evaluation of frail patients.

Summary

Emerging evidence suggests that frailty may be mitigated with patient-specific, multidimensional preoperative interventions, thus potentially improving postoperative outcomes in this vulnerable patient population.

Keywords

cognitive screening, frailty, nutritional supplementation, prehabilitation, psychological preparation

INTRODUCTION

Healthcare spending in the United States is evolving towards a value-based model of care [1]. The goal of this evolution is to achieve the triple aim: improving health of the population, enhancing patient experience and reducing cost of care [2]. Achievement of the triple aim becomes critical in the context of providing perioperative care for our most vulnerable patients, including the elderly and frail. In order to define the standard of quality care delivery for the geriatric surgery population, the American College of Surgeons (ACS) has established the geriatric surgical verification [3].

The potential impact of the Geriatric Surgical Verification Program is large, representing a national scale of millions of lives [4]. Although ageing is associated with physiologic changes that increase risk from anaesthesia and surgery, more than 95% of geriatric patients survive even emergency surgery and more than 75% survive without major complications [5]. Thus, identification of patients at greatest risk of poor postoperative

outcomes is imperative to allow targeted application of scarce healthcare resources and to achieve value from perioperative enhanced care pathways and processes [6^{***}]. One approach to determining high-risk patients centres on the concept of frailty syndrome. Frailty represents a state of diminished reserves and increased vulnerability to stressors in the perioperative period. It predisposes patients to an increased risk of postoperative complications and results in higher resource utilization. Frailty is not solely a geriatric syndrome, nor the presence of comorbidities, although these patients are commonly frail [7]. Frailty not only allows for improved risk prediction, but it informs our approach to

^aNorthwestern University, Feinberg School of Medicine, Chicago, Illinois and ^bDuke University School of Medicine, Durham, North Carolina, USA

Correspondence to Jeanna Blitz, MD, Duke University School of Medicine, Department of Anesthesiology, DUMC 3094, Durham, NC 27710, USA. Tel: +1 919 684 2025; e-mail: jeanna.blitz@duke.edu

Curr Opin Anesthesiol 2021, 34:373–380

DOI:10.1097/ACO.0000000000001006

KEY POINTS

- A multipronged approach towards preoperative optimization should be used in patients with frailty syndrome.
- Oral protein supplementation and immunonutrition therapy may reduce complications in patients with malnutrition.
- Initiating a preoperative physical exercise regimen may mitigate frailty.
- Nonpharmacologic interventions to reduce preoperative anxiety and improve mood are effective, low-cost adjuncts associated with improvement in postoperative outcomes.
- Engaging in shared decision making is a critical component of the preoperative evaluation of frail patients.

preoperative optimization, guides shared decision-making conversations, and may potentially be modifiable, resulting in reduced postoperative complications.

HISTORICAL MODELS: FRAILTY PHENOTYPE AND FRAILTY INDEX

Historically, a lack of consensus existed on the definition of frailty syndrome. The frailty phenotype model hypothesizes frailty has a biological basis consistent with energy depletion [8,9]. Fried *et al.* [8] defined frailty in a prospective cohort study as unintentional weight loss, self-reported exhaustion, weakness (grip strength), slow walking speed and low physical activity. In this study, frailty was correlated with adverse outcomes measured 3 and 7 years after the initial assessment [8]. This standardized approach demonstrated predictive value for adverse outcomes [8]. By contrast, the deficit accumulation model uses the frailty index to describe the vulnerability associated with medical, social and functional deficits [10]. The frailty index is derived from less than 30 to 70 variables. Rockwood showed decreased function in multiple domains, quantified by frailty index, correlates to increased risk for adverse events [10]. Although variables are selected randomly to calculate frailty index, results remain comparable for risk of adverse outcomes [9,11]. Although studies show incomplete agreement between both approaches to frailty, both are predictive in identifying preoperative frailty [12,13]. In a recent prospective study among Transcatheter Aortic Valve Replacement (TAVR) and Surgical Aortic Valve Replacement (SAVR) patients, the

frailty phenotype and frailty index were recorded. Frailty index was shown to have better prediction of death or poor recovery than frailty phenotype in the TAVR and SAVR population [12]. In another prospective study measuring frailty in orthopaedic surgery patients, both tools were shown to be strong, independent predictors of surgical outcomes with moderate correlation [13]. Recently, the concept of frailty centres on a framework wherein deficits in multiple domains contribute to an increase in vulnerability to perioperative stress [7].

FRAILTY SCREENING

Multiple frailty screening tools were derived from both the energy depletion and deficit accumulation models, and a good amount of literature exists regarding their use in the preoperative assessment [14[■]]. Commonly, an age threshold of 65 or 75 years is used to determine eligibility for frailty screening in a preoperative clinic and preference is given to an in-person evaluation whenever possible [15[■]]. A common preoperative screening tool is the Clinical Frailty Scale (CFS), derived from the frailty index model. This tool was established as a feasible and accurate predictor of adverse postoperative outcomes, including mortality, new disability diagnosis and discharge to location other than home [14[■]]. Studies comparing predictive abilities of other screening tools derived from both the deficit accumulation and energy depletion models have performed less well [16,17]. CFS is subject to heuristic biases, thus each provider should review the CFS training module before screening patients (Fig. 1): <https://rise.articulate.com/share/deb4rT02lvONb-q4AfcMNRUudcd6QMts3>

The FRAIL scale is a screening tool derived from the frailty phenotype concept, which uses a short questionnaire to assess patients in five major domains; Fatigue, Resistance (inability to climb stairs), Ambulation (inability to walk a certain distance), Illnesses and weight Loss [18]. This tool has been validated in different populations and showed to correlate with mortality risk [19,20]. Another is the Edmonton Frailty Scale (EFS), a 17-point questionnaire that assesses patients in nine domains: general health status, social support, cognition, functional independence, medication use, mood, nutrition, continence and functional performance, then classifies them as not frail, vulnerable or mild to severe frailty [21]. EFS effectively predicts mortality and postoperative complications. Compared with CFS, it is a broader assessment tool and incorporates non-physical elements of patient's status such as cognitive decline and social support [22].

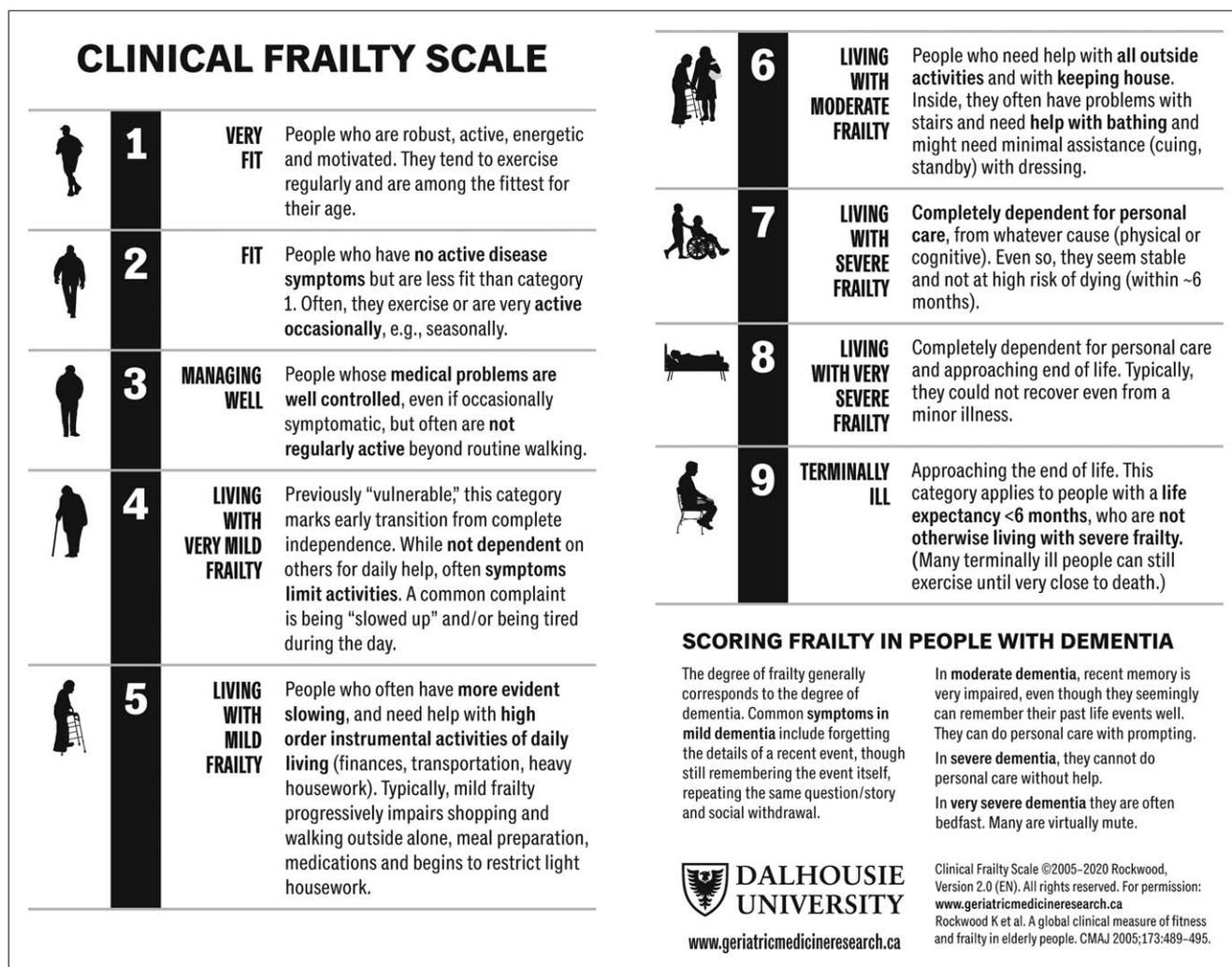


FIGURE 1. The Rockwood Clinical Frailty Scale version 2.0, as presented by The Geriatric Medicine Research, Dalhousie University, Halifax, Nova Scotia, Canada. Reproduced with permission.

Screening for frailty identifies patients who may benefit from a Comprehensive Geriatric Assessment (CGA), a multidisciplinary diagnostic process that evaluates social, functional, psychological and medical abilities identifying various geriatric syndromes and degree of frailty. Outcomes of this assessment are useful in risk stratification and identifying opportunities for frailty targeted interventions [23]. Use of CGA as a frailty tool is limited by its comprehensive and time-consuming nature, need for skilled clinician administrators and lack of standardization of components used to identify frailty [15]. Identification of severely frail patients correlates with clinically significant factors such as increased operative time, increased risk of major complications and worse health related quality of life outcomes up to 3 years postspinal fusion [24]. Long-term increase in disability and neurocognitive disorders occurs in frail patients postoperatively

[25,26]. Preoperative multimodal interventions focused on improving functionality, nutrition and overall health function; known as prehabilitation, reduces these postoperative risks, mortality and improves long-term outcomes [27]. Despite the importance and documented preoperative application of this screening, use remains limited by uncertainty regarding which tool to use, lack of clarity on interventions when frailty is diagnosed and feasibility of screening and prehabilitation in the preoperative setting [27,28]. Although debate persists on the optimal screening tool, both the CFS and FRAIL scale are simple and efficient tools. Although they focus on physical strength evaluation, they can identify patients who may benefit from referral to a geriatrician for CGA assessment to identify more global aspects of frailty such as cognition and nutrition and elective surgery delay for prehabilitation [22,29].

PREHABILITATION STRATEGIES

As frailty is a multidimensional syndrome, a multi-pronged optimization regimen is often required. Prehabilitation addresses three domains: **nutritional optimization, physical exercise and psychological preparation** [27^{***},30].

NUTRITIONAL OPTIMIZATION

Malnutrition is common preoperatively, particularly in frail patients, and is associated with poor postoperative outcomes, including wound infection, prolonged hospitalization and mortality [31]. Approximately 50% of surgical patients are at risk, yet less than 10% are identified and treated preoperatively [31]. Malnutrition is reversible with proper screening and focused preoperative interventions. One screening tool recently validated in the preoperative population is the Perioperative Nutrition Screen (PONS) score [31,32]. **The PONS score consists of these screening questions and laboratory values:**

- (1) Does the patient have a BMI less than 18.5 kg/m² (<20 kg/m² if more than 65 years)?
- (2) Has the patient experienced unintentional weight loss of more than 10% in the past 6 months?
- (3) Has the patient had reduced oral intake by more than 50% in the past week?
- (4) Does the patient have a preoperative serum albumin less than 3.0 g/dl?

A score of at least 1 is considered 'at risk' for malnutrition; further evaluation of nutritional status is indicated and interventions to improve the patient's nutritional state should be provided before surgery. **Nutritional intervention recommendations for at-risk patients include use of high protein oral nutritional supplementation (ONS) as well as immunonutrition (IMN). Ideally, high-protein ONS should be initiated 2–4 weeks before surgery. Guidance on dietary choices to ensure adequate protein intake of more than 1.5 g/kg/day should be provided and additional oral protein supplementation may be recommended [32]. Immunonutrition supplements include a combination of arginine, omega-3 fatty acids, glutamine and nucleotides. Current guidelines recommend 7 days of IMN before surgery; however, benefits from as few as 3 days have been demonstrated in patients with malnutrition and gastrointestinal cancer [33]. Patients receiving IMN before surgery for gastrointestinal cancer were less likely to develop postoperative surgical site infections than patients on a normal diet without supplementation [33]. Both high protein ONS and IMN are available without a prescription, but barriers to implementation**

of nutritional supplementation include lack of knowledge or cost. In the absence of preoperative nutrition consultation with a registered dietician and/or oral nutritional supplementation, frail patients should be educated on dietary options to improve nutrition and protein intake before surgery [32].

NUTRITIONAL DEFICIENCY AND ANAEMIA

Identification of undiagnosed anaemia during preoperative evaluation frequently occurs. The prevalence ranges from 5 to 75% depending on the surgery type and patient's comorbidities with greater incidence in elderly and frail patients [34^{***}]. Anaemia multiplies risk, increasing mortality risk by 16-fold, and doubling the risk of perioperative complications such as acute kidney injury, major adverse cardiac events and length of hospitalization [35]. Thus, preoperative anaemia of any degree should be addressed before surgery.

Approximately 60% of preoperative anaemia is due to iron deficiency. Furthermore, treatment of iron deficiency anaemia (IDA) even in the immediate preoperative period (1–3 days before surgery) improves outcomes by reducing blood transfusion, infection and length of hospitalization [36]. IDA is confirmed by low transferrin saturation (<20%), ferritin (<100 µg/l) and/or reticulocyte haemoglobin content (<30%). Other laboratory studies commonly included in a comprehensive anaemia workup panel include tests to determine other nutritional causes of anaemia such as levels of folate and B12.

Iron replacement may be administered orally or intravenously (i.v.). Route of administration is decided by the patient's preferences, degree of anaemia and time-window before surgery. **Oral iron replacement therapy may be effective in cases of mild anaemia if initiated 4 weeks before surgery. Oral replacement therapy is inexpensive, readily accessible and well tolerated. Main limitations of oral iron therapy include lack of compliance due to gastrointestinal side effects, lack of absorption in patients with gastrointestinal diseases or inflammation, and the need for a one-month interval before surgery for effectiveness [34^{***}]. Recommendations suggest alternate day dosing of 80–100 mg of oral iron to increase the amount absorbed, decrease gastrointestinal side effects and improve patient compliance. Vitamin D supplementation in patients with vitamin D deficiency improves iron absorption by reducing hepcidin levels related to anaemia of inflammation [37].**

Intravenous iron is preferred for most preoperative patients due to increased efficacy, efficiency and reduction of gastrointestinal side effects [34^{*}]. Response to i.v. iron occurs within 1 week (50%**

response) with maximum response 2–3 weeks post infusion [34[■]]. Rate and magnitude of response depends on the patient's bone marrow functional reserve and use of an erythropoiesis-stimulating agent [34[■]]. Total iron deficit, the iron repletion dose, is calculated using the Ganzoni equation [38]. Repletion strategy should be patient-specific and result in a clinically significant improvement in hemoglobin level to impact outcomes. Administration of a single, standardized preoperative dose of i.v. iron, without confirmation of the diagnosis of iron deficiency, does not effectively correct anaemia or reduce transfusions and postoperative complications [39[■]].

PHYSICAL PREHABILITATION

Frailty predisposes patients to autonomic dysregulation, which may result in an impaired response to haemodynamic changes [27[■]]. Frail patients should be assessed for orthostatic blood pressure changes preoperatively. Mobility and gait speed assessments are other important components of a CGA and several frailty screening tools [8,9,15[■],18,21]. Common tests of mobility and gait speed include Timed Up and Go (TUG) Test and 6-min walk test (6MWT). TUG requires a patient to rise from a seated position in an armchair, walk to a line 10 feet away, turn around and return to a seated position [40]. Patients who complete the test in over 12 s are considered at risk for impaired mobility and falls. 6MWT is performed by asking the patient to ambulate a 15-m stretch of level ground for 6 min at a tiring pace. Distance travelled is then compared with the average result for patients of the same age and sex. 6MWT is used as an assessment of functional exercise capacity and its results strongly correlate with maximal oxygen consumption on extensive exercise testing [41].

Patients with a slow gait speed or decreased balance may benefit from preoperative home-based or supervised exercise regimens. The main components of a prehabilitation-focused exercise regimen include aerobic activity for 30 min per day, strength training (one to two sets, 8–15 repetitions per set) and exercises to promote balance and flexibility. Deep breathing exercises or formal inspiratory muscle training is also a recommended component of the prehabilitation regimen in frail patients. Inspiratory muscle training is associated with decreased pulmonary complications if initiated within 6 weeks of surgery [42].

COGNITIVE SCREENING AND INTERVENTIONS

Screening for deficits in executive functioning or memory may be combined with abbreviated frailty

screening tools [43]. The goal of preoperative cognitive screening is to identify patients at increased risk of postoperative delirium or other complications. Screening results change management in approximately 40% of geriatric oncology cases [44]. A common instrument used in the preoperative evaluation clinic is the Mini-Cog, derived from the Montreal Cognitive Assessment (MOCA). Benefits of this tool include brevity and established reliability as a screening tool for increased risk of postoperative delirium [14[■],45–47]. The Mini-Cog involves three-word recall and a clock-drawing test. Scores of 0, 1 and 2 designate patients at high risk for postoperative delirium. For patients receiving virtual or telephone-based preoperative assessment, the telephone interview of cognitive status (TICS) may be employed. A low TICS score is associated with postoperative delirium and increased risk of postoperative complications [43]. In the absence of a distinct cognitive screening tool, frailty screening alone may predict postoperative delirium [48[■]].

Patients identified as high risk for delirium should be provided with information about delirium, potential prevention strategies and perioperative interventions. Communication with the patient's primary care physician or geriatrician is important to initiate investigation of reversible causes and ensure longitudinal follow up.

Deliriogenic medications should be weaned preoperatively whenever possible. Benzodiazepines, anticholinergic medications, muscle relaxers such as cyclobenzaprine, sleep aids such as zolpidem, opioids and multiple psychotropic medications can negatively affect cognition and increase risk of postoperative delirium [49]. Discontinuation of benzodiazepines improves cognitive function. Medication weans should be done in a stepwise fashion. Use of a validated framework for weaning is recommended.

PSYCHOLOGICAL STATE: ASSESSMENT AND INTERVENTIONS

Anxiety and depression are common in patients facing a new diagnosis and preparing for surgery. Recovery from major surgery may represent a potential loss of independence for frail patients, which may exacerbate the patient's preoperative anxiety. Untreated anxiety or depression is a barrier to successful engagement and adherence to a prescribed prehabilitation programme, and is associated with increased postoperative pain, length of hospitalization, chronic post-surgical pain and prolonged opioid use [30,50]. Evidence of the mind-body connection in perioperative outcomes and frailty is emerging. A recent study on psychological components of the frailty phenotype noted an association between low resilience and

the development of frailty syndrome [51]. Most intriguing is the concept that resilience ability/level may be modifiable.

Examples of screening tools for psychological distress used in preoperative evaluation clinics include the Hospital Anxiety and Depression (HADS) Score, the Patient Health Questionnaire (PHQ) or the pain catastrophizing score (PCS) [60,50,52]. The 14-question HADS tool screens for both anxiety and depression, while the PHQ is specific to depression, and exists in both two and nine-question variations. The 13-item PCS is used to identify patients who employ catastrophization in response to pain or other stressors. In high-risk patients, like those with opioid use disorder, poorly controlled anxiety and a psychiatric condition, several preoperative assessment tools may be combined to attain a global preoperative risk assessment and an individualized preoperative optimization plan [50].

Psychological prehabilitation was originally developed with cancer patients, many of whom meet criteria for frailty. The most effective strategies for psychological preparation are nonpharmacologic, low-cost and tailored to the individual patient. Interventions range from time and resource intensive cognitive behavioural therapy (CBT) to low-resource interventions such as music therapy, relaxation techniques and nurse-administered educational interventions [50,53–55].

Results of CBT-based prehabilitation interventions are promising. Four to eight weeks of preoperative CBT is associated with faster recovery and improved postoperative pain control [50,52,56]. Despite demonstrating positive results, barriers exist in CBT's time-intensive nature, need for specially trained providers, cost and scalability of the programme [56].

Another well studied preoperative anxiety reduction technique is the use of music therapy. Music's effect is due to the emotional response it produces in the limbic system. Music tempo entrains heart rate, resulting in a calming effect from decreased sympathetic output, and regulation of endogenous opioids, oxytocin, cortisol and catecholamines [53]. The impact of music therapy is greatest when the patient selects the playlist. The Veteran's Administration has successfully implemented perioperative music therapy via a low-cost project that required several music players, earphones and playlists in several genres popular among veterans [54].

A meta-analysis of psychological preparation for surgery showed a positive impact upon postoperative outcomes. Interventions ranging from patient-centred procedural information and emotional validation, to relaxation techniques and cognitive interventions were associated with reduction in

postoperative pain severity, length of hospitalization and an improved quality of life [55].

SHARED DECISION MAKING

A key pillar of the Geriatric Surgical Verification programme is holding goals of care conversations and engaging in shared decision making with the patient [3]. Health literacy occurs when health information and services match the patient's ability to understand and use them. Patients at highest risk for surgical complications often have a poor understanding of their health status and overestimate their ability to manage their medical conditions. Low health literacy level is a risk factor independently associated with longer hospitalization after major surgery [57–59].

Template creation is a way to standardize the shared decision-making process and facilitate these discussions during the preoperative evaluation clinic visit. Elements to include in a standardized template include asking permission and introducing the topic, ascertaining the patient's understanding of his/her illness, exploring goals of care and fears, and identifying an alternate decision-maker.

FUTURE DIRECTIONS

The conceptual framework for frailty is evolving. Current models reflect an increased awareness of social and economic factors that contribute to poor health. Vulnerability to perioperative stress is often the result of physical, physiologic, psychologic and social factors.⁶ Without enhanced interventions in these domains, perioperative outcomes for our most vulnerable patients, such as those who are incarcerated or un-domiciled, are unlikely to improve [60]. Concerted efforts are needed to identify successful interventions aimed at reducing the impact of severe deficits in the patient's social, economic and physical environment.

CONCLUSION

Emerging evidence suggests that frailty may be mitigated with patient-specific, multidimensional preoperative interventions, thus potentially improving postoperative outcomes in this vulnerable patient population. Further research on optimal timing, duration and combination of interventions is warranted.

Acknowledgements

The authors would like to thank Dr Jordan N. Myers for her assistance with the manuscript.

Financial support and sponsorship

This work was supported by the Department of Anesthesiology, Duke University School of Medicine.

Conflicts of interest

There are no conflicts of interest.

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