*Southern African Journal of Anaesthesia and Analgesia.* 2021;27(6 Suppl 1):S162-166
https://doi.org/10.36303/SAJAA.2021.27.6.S1.2740


South Afr J Anaesth Analg
ISSN 2220-1181 EISSN 2220-1173

FCA REFRESHER COURSE

# Frailty and anaesthesia

**Z Jooma**

*Department of Anaesthesia, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, South Africa*
*Charlotte Maxeke Johannesburg Academic Hospital, South Africa*
***Corresponding author, email:*** *zainub.jooma@gmail.com*

Frailty is defined as a state of vulnerability due to reduced physiological reserve that predisposes patients to adverse outcomes from a stressor. It is a multidimensional state where reduced biological reserves interplays with cognitive factors, psychosocial factors and the external environment, resulting in reduced resilience and adaptive capacity. This clinical syndrome confers a higher risk for falls, hospitalisation, readmission, disability, loss of functional independence and death. Preoperative frailty screening assesses domains outside traditional risk measures and can add prognostic value. Identifying frail patients allows the opportunity for optimisation and prehabilitation, risk prediction, shared decision making, implementation of enhanced care pathways and appropriate intensive care resource allocation in an attempt to mitigate risk, thereby improving outcomes. Anaesthetists need to be familiar with the unique challenges in this patient group in order to offer high quality perioperative care.

**Keywords:** anaesthesia, frailty, outcomes, perioperative, clinical frailty scale, risk

## Introduction

Increased longevity has resulted in an increase in the aged population globally. The trend is no different in low-middle income countries.[1] In South Africa, the proportion of population aged 60 and above is expected to increase from 9.3% to 15.4% between 2022 and 2050; in Africa it is expected to triple by 2030.[1] The aged population has implications for the provision of health care.[1] Ageing increases the risk of developing multiple comorbidities and disability which may result in frailty, conferring a higher risk for adverse perioperative outcomes.[2,3] Improvement in surgical techniques and perioperative care has resulted in more elderly patients presenting for surgery, imposing a burden on healthcare systems in terms of intensive care facility admission and longer length of hospital stay.[2] There is a need for anaesthetists to be familiar with the unique challenges in this patient group[1] in order to offer high quality perioperative care.[2]

## Definition

The concept of frailty was first described by Fried et al.[3] in the context of geriatric medicine and has now gained attention in the anaesthesia[2,4] and critical care[5] fields. Frailty is defined as a state of vulnerability due to reduced physiological reserve that predisposes patients to adverse outcomes from a physiological, physical or psychosocial stressor.[6] It is a multidimensional state where reduced biological reserves interplays with cognitive factors, psychosocial factors and the external environment, resulting in reduced resilience and adaptive capacity.[7] This clinical syndrome confers a higher risk for falls, hospitalisation, readmission, disability, loss of functional independence and death.[3,5,8] While it occurs more commonly in geriatric patients and those with comorbidities, it is not limited to this age group.[9] Younger patients presenting with advanced oncological disease or with severe immunodeficiencies may easily fit the criteria for frailty.[10,11]

Frailty assessment is regarded as a better prognosticator for outcomes than biological age and it is recommended as part of routine preoperative assessment by the American College of Surgeons (ACS) and the American Geriatric Society (AGS).[2,12] It allows for the assessment of domains outside traditional perioperative risk measures which do not account for the increased vulnerability in the elderly patient[8,13] and can add prognostic value.[14]

## Biological mechanism

The biological mechanism of frailty is not known and its clinical manifestations present as a consequence of disturbed physiological processes associated with ageing, resulting in molecular, cellular and tissue damage.[4,5] Mechanisms proposed include oxidative stress, dysregulation of inflammation, cellular senescence, genomic instability and endothelial dysfunction.[4,5]

While not causative, genetic, epigenetic and environmental factors play a role.[13,15] Genetic findings in frail patients indicate changes in the function of β receptors, mitochondrial DNA and muscle along with a state of chronic inflammation.[5] Comorbid disease, nutritional factors, limited physical activity and smoking interplay with socioeconomic factors on the backdrop of the biological changes, resulting in the development of the frailty syndrome. No biomarkers have been specifically associated with frailty, although many may be implicated based on the pathophysiology.[5,7,10]

Notable pathophysiological changes occur in the brain, endocrine, immune and skeletal systems of frail patients.

Structural and physiological changes in the ageing brain include loss of neurons, importantly in the hippocampal region, which is a key area for cognition and for relaying messages to the hypothalamus as part of the stress response.[15] Microglial cells are the immune cells of the brain that become activated by brain injury and inflammation, and this can result in neuronal injury and death in response to stimuli.[15] Aberrant oxidative metabolism results in neurotransmitter imbalance in the brain.[16] These mechanisms result in neuroinflammation[16] that may contribute to the cognitive decline and delirium seen in frail patients.[5,8]

Changes in hormone production occur with ageing: serum Vitamin D, oestradiol and testosterone levels decrease; decrease in growth hormone causes a reduction in insulin-like growth factor-1 (IGF-1); and a decrease in the steroid precursors, dehydroepiandrosterone and dehydroepiandrosterone sulphate occurs with a concurrent increase in cortisol.[5,7,15] An imbalance between anabolic and catabolic hormones results.[5] Peripheral insulin resistance and reduction in sirtuins contribute to metabolic dysregulation.[5,7]

Immune senescence results in decreased function of all components of the immune system.[15] It is characterised by a state of low grade inflammation that is hyperresponsive and persists long after the initiating stimulus is removed.[15] An imbalance between pro- and anti-inflammatory cytokines[7] results in the formation of advanced glycated end products from protein and lipid metabolism, which perpetuate an ongoing inflammatory process resulting in cell damage.[5,15]

Sarcopenia is a key component of the frailty syndrome which results from loss of power and strength from decreased muscle mass.[15] This is postulated to occur due to decreased muscle formation and increased breakdown driven by the catabolic, inflammatory state.[15]

## Models for frailty assessment

Three models can be used to assess frailty, namely: the phenotype, accumulated deficits and the multidimensional models.[5]

The phenotype model was first described by Fried et al.[3] and hypothesises energy depletion as the basis for frailty. The presence of any three of the following features indicates frailty: self-reported exhaustion, slow gait, low physical activity, weak grip strength and unintentional weight loss; presence of one or two of the features signifies a pre-frail state. This model neglects the cognitive and psychosocial components of the frailty syndrome[2,15] and requires specialised equipment for diagnosis in clinical practice.[2]

The accumulated deficits model was developed by Rockwood and Mitnitski and assesses for clinical deficits in a number predefined domains (generally more than 30)[5] including functional status, nutrition, cognition, mood disorders and comorbidities.[2] The Frailty Index is expressed as the number of deficits present as a fraction of all deficits measured, generating a number between 0 and 1 with values greater than 0.25 indicating frailty.[10] Values above 0.4 indicate severe frailty.[13] This model recognises frailty as a multidimensional risk state[13] and suggests the more the deficits, the greater the likelihood of an adverse outcome.[2,6,10] The extensive nature of the assessment limits use in clinical practice.[2] The modified Frailty Index is a shorter version of the original index for ease of use.[4,13]

The multidimensional model recognises both the physical basis and age-related deficits that contribute to frailty.[5] The decline in functionality is attributed to an interplay between the biological mechanisms and psychological, social, cognitive and physical factors.[5]

## Frailty screening tools

A standard approach to assess frailty is lacking[10] and more than 75 scales have been derived using the above models.[7] Commonly, an age cut-off of 65 is applied to screen for frailty.[9]

The comprehensive geriatric assessment is an established gold standard[17] for the assessment and optimisation of elderly patients in the functional, physical and psychosocial domains.[2] A multidisciplinary team is needed and it is a resource-intensive assessment but it has shown benefit in the perioperative setting.[2] It can be used selectively for frail patients who may benefit from more holistic assessment and optimisation.[9]

The FRAIL scale is a simple, validated questionnaire based on the phenotype model assessing fatigue, stair climbing, ambulation, weight loss and illness and has been found to correlate with mortality.[9] It does not assess cognition or psychosocial factors.[7]

The Clinical Frailty Scale (CFS) is based on the frailty index model that uses simple clinical descriptors to score patients from 1 (robust) to 9 (terminally ill).[2] A score of five or more indicates frailty.[11] It is the most clinically utilised screening tool for frailty.[5] It is a feasible method of assessment in the preoperative clinic environment[6,9] and can be used as a predictor for adverse postoperative outcomes and mortality.[9]

The Edmonton Frail Scale is a 17-point questionnaire based on the frailty index model assessing nine domains: functional independence, functional performance, general health condition, social support, cognition, mood, medication, nutrition and continence. It includes both self-reported answers and activities to assess cognition, gait and balance.[7] It has been shown to correlate with postoperative complications as well as mortality, and can be used in the emergency surgical setting.[7,9]

Clinical impression of a patient based on physician "gut instinct" has been described and can correctly identify patients as frail with a higher mortality risk.[8] Single assessments of function using gait speed alone or the timed up-and-go test (TUGT) are more objective tests for frailty.[7] The TUGT is performed with the patient rising from a chair of standardised height, walking three metres, turning and returning to sit on the chair again.[7] Completion of the test in >12 seconds identifies patients with impaired mobility.[9]

Radiological imaging using ultrasound or computed tomography can demonstrate sarcopenia and this has been associated with adverse perioperative outcomes.[7] However, these assessment methods neglect the multifactorial nature of the frailty syndrome. Digital systems allow for automatic assessment of frailty using hospital records; the electronic Frailty Index and Hospital Frailty Risk Score are two such tools in development.[10]

## Perioperative implications of frailty

The incidence of frailty has been found to be higher in the surgical population compared to community-based assessments.[6,11] In the elective setting, between 30–50 % of patients will be assessed as frail using a multidimensional assessment tool[6,8] as compared to 10–15% in the community setting.[6] In a South African study, 45% of patients above 65 years presenting for elective surgery were classified as frail.[11] Higher incidences are found in patients presenting for oncology and emergency surgery.[6]

Frailty in the perioperative period is associated with major morbidity and mortality.[4,6,13] Delirium,[6] prolonged length of stay, readmissions, impaired quality of life and discharge to institutional care have also been found to occur in frail patients.[6,8,14]

Screening for frailty and subsequent implementation of targeted interventions in elective surgical patients have shown a reduction in mortality in both frail and robust patients at 30 days, and this beneficial impact persisted to one year postoperatively.[18] Assessment for frailty in the perioperative period allows the opportunity for optimisation and prehabilitation, risk prediction, shared decision making, implementation of enhanced care pathways and appropriate resource allocation for intensive care in an attempt to mitigate risk, thereby improving outcomes and maintaining functional independence.[6,8-10]

## Perioperative care of the frail patient

A key component in the care of frail patients is routine inclusion of a frailty screening tool in the preoperative assessment.[6,13] This flags a high-risk patient and allows a systematic approach to the assessment and optimisation of the various domains. The CFS is a simple, feasible tool[6,9] that shows value from a patient- and system-outcome perspective.[9]

Physical activity, nutritional deficiencies, comorbidities, polypharmacy, psychosocial and cognitive factors are areas for optimisation.[17] The ACS and AGS recommend discontinuation of non-essential medication preoperatively.[17] Polypharmacy can be addressed using a tool such as the AGS Beers Criteria® for inappropriate medication in elderly patients.[19]

Prehabilitation is described as the enhancement of a patient's preoperative status[4] and traditionally includes exercise, nutritional and psychological interventions.[9,13,17,20] The evidence for improved outcomes with interventions in frail patients has shown low or very low evidence[4,17] and positive outcomes were seen with multiple rather than single interventions.[10] Despite this, prehabilitation strategies are advocated.[2,9,13,17,20]

### *Exercise*

Assessment of physical vulnerability preoperatively can identify patients who may benefit from exercise prehabilitation.[6] The Duke Activity State Index, although not validated in frailty, has been shown to predict adverse postoperative events and new disability and can be considered.[6,20] Gait speed assessment and the TUGT can be used to identify patients at risk for impaired mobility and falls; these patients would benefit from exercise interventions.[9] Preoperative home-based exercise programmes include: aerobic activity, strength training as well as exercises to promote balance and flexibility[9,17,20] and ideally are initiated at least two weeks prior to surgery.[6] Programmes should be personalised for maximum benefit without harm.[20] Exercise prehabilitation has shown only moderate benefits.[6,17] Further well designed studies in this field are required.[4]

### *Nutrition*

Malnutrition occurs in 10–20% of frail patients presenting for surgery[6] and it is considered an independent predictor of adverse perioperative outcomes.[6,17] Nutritional screening and interventions addressing both macro- and micronutrient deficiencies are recommended.[2,6,9] The Perioperative Nutrition Screen (PONS) score is validated for use in the preoperative population.[9] It assesses the following: BMI < 18.5 kg/m$^2$ (< 20 kg/m$^2$ if more than 65 years), unintentional weight loss > 10% in the last six months, reduced oral intake > 50% in the past week and preoperative albumin < 3 g/dl; a score of one or more indicates an "at-risk" patient.[2,9]

Nutritional intervention includes high protein oral nutritional supplementation of 1.2–1.5 g/kg/day[2,9,17] at least 2–4 weeks prior to surgery.[9] Immunonutrition supplements including arginine, omega-3 fatty acids, glutamine, nucleotides and antioxidants are recommended[2,9,17] at minimum for 3–7 days before surgery.[9]

Diagnosis and treatment of anaemia preoperatively is recommended.[6,9] The majority of anaemia is due to iron deficiency and is characterised by low transferrin saturation (< 20%) and ferritin levels (< 100 ug/l).[9] Intravenous iron supplementation is preferred to oral supplementation even in the immediate preoperative period.[9]

Fasting guidelines should be strictly adhered to and preoperative carbohydrate loading is recommended in major surgery.[2]

### *Psychological*

Anxiety and depression are common in older surgical patients[6,9,17] and can be compounded by loss of functional capacity from the disease process and fear of further loss of independence in the perioperative period.[9] Psychological factors may hamper participation in prehabilitation interventions and are associated with adverse postoperative outcomes.[17]

The Personal Health Questionnaire consists of two questions that can be used to screen for depression preoperatively, although intervention in this regard has not been well researched.[6]

Psychological prehabilitation includes non-pharmacological strategies such as deep breathing, meditation, music therapy, cognitive behavioural therapy and educational interventions.[9] Social support after discharge can be addressed.[6] Benefits from these outcomes are variable and further research is needed.[9,17]

### *Cognitive*

"Cognitive frailty" was described in 2013 as the co-existence of physical frailty with cognitive impairment.[8] Mild cognitive dysfunction occurs frequently in frail patients and may predispose to postoperative delirium (POD)[6,9,16] and other perioperative cognitive disorders (PCD).[8] PCD is a new nomenclature encompassing POD, delayed neurocognitive recovery and either mild or major neurocognitive disorders.[8,16]

The ACS and AGS recommend the Mini-Cog test as a cognitive screening method preoperatively.[6] It involves a three word recall and clock drawing exercise; scores less than three indicate an increased risk for POD.[9] POD is the commonest complication postoperatively and may result in further longer term PCD.[8] Patients at risk should be informed and appropriately counselled.[2,8,9] Non-pharmacological strategies for POD prevention are preferred and the use of care bundles such as the Hospital Elder Life Program[6] or ABCDEF ICU care bundle are two such multifaceted approaches.[6,16] These strategies include: avoidance of delirogenic medication, use of sensory aids, good sleep hygiene, cognitive orientation, noise reduction, early mobilisation, resumption of early oral intake and management of pain perioperatively via multimodal techniques.[2,6,9]

### *Decision making*

Cognitive impairment, either apparent or occult, occurs commonly in frail patients and this has implications for a patient's capacity for decision making and obtaining informed consent.[8] A number of elderly patients wish to have autonomy regarding medical decisions, but the majority lack the capacity to do so.[2] Psychological tools can be used to assess a patient's medical decision-making capacity and competence.[8]

Shared decision making is important in this context and entails reaching a consensus between the patients preferences and the available treatment options.[8] Family members and carers may be included while supporting the patient's autonomy.[8] There is a tendency to treat frail patients in a paternalistic manner which will limit patient self-determination.[8]

The ACS and AGS guideline recommend preoperative counselling of elderly and frail patients by a multidisciplinary team.[2,13] The informed consent process should explore the patient's goal of treatment and patient-specific outcomes of importance, and provide realistic information regarding the material risk for PCD and loss of functional independence.[2,5,8,13] It should be ascertained that the patient understands the disease and treatment options (usually by recall), comprehends the consequences of their choice and is able to rationalise their decision.[8] Designated health proxies should be identified and the option for advanced directives discussed.[2] Assent from the patient when a proxy is used is encouraged if cognitive capacity allows.[8]

Identifying frailty in patients assists in recognising vulnerable patients where alternative forms of non-operative management or palliation may be more appropriate.[13]

## Intraoperative strategies

Intraoperative complications that occur more commonly in frail patients include hypotension, desaturation and the need for vasopressors or blood transfusion.[11] The literature on intraoperative techniques to improve outcomes in frail patients in particular is limited.[6,13] Recommendations are taken from the literature pertaining to elderly patients in general. An important principle is to individualise the anaesthetic technique to the patient and the procedure.

A Cochrane review investigated the effects of volatile versus total intravenous anaesthesia on outcomes and PCD in elderly patients.[21] No differences were found in mortality or POD between the groups and there was low quality evidence of reduction in PCD in the total intravenous anaesthesia group.[21]

The debate on general versus regional anaesthesia is most well-studied in hip fracture patients. Neither technique has been found superior in terms of PCD[16] or other outcomes but studies are ongoing in this field.[13]

The effect of depth of anaesthesia monitoring by processed electroencephalogram (EEG) on mortality outcomes was investigated in the BALANCED study.[22] There was no difference in outcomes at one year when comparing light versus deep anaesthesia based on bispectral index (BIS) values, however a sub-analysis of this study found benefit from light anaesthesia in terms of POD.[22] Neuromonitoring for depth of anaesthesia is recommended for the prevention on POD by the European Society of Anaesthesiologists.[23] Higher incidences of burst suppression are seen in elderly patients at BIS values within the recommended target range, but it is unclear if this may contribute to PCD.[16] Raw EEG waveforms may provide more information and allow for tailored anaesthesia depth in the elderly; more research is needed in this field.[16]

The effect of hypotension in isolation on outcomes has not been well studied in this population group. Elderly patients may have altered cerebral auto-regulation curves[16] and blood pressure should be maintained within acceptable limits. Adverse postoperative outcomes were found with the "triple low state" where mean arterial pressure, BIS values and volatile minimum alveolar concentration are low.[13] Cerebral perfusion monitoring with near-infrared spectroscopy in combination with BIS monitoring has been shown to reduce PCD.[16]

Multimodal analgesic techniques utilising neuraxial anaesthesia and peripheral nerve blocks in conjunction with intravenous analgesics are recommended, thereby reducing opioid use.[13]

## Postoperative care

Screening for POD using an appropriate delirium-screening instrument in at risk patients should occur as early as the recovery room.[23,24] The 4A's test has been validated as a feasible and simple tool to use in this context.[24] Non-pharmacological measures are recommended for prevention and management of POD.[6,16] Ensuring that hearing aids, dentures and spectacles are with the patient before going to the ward are simple measures that can be instituted immediately postoperatively. Pharmacological intervention to treat POD should be used only if non-pharmacological measures fail and patient safety is compromised.[23]

Multidisciplinary teams should be involved for ongoing care.[13] Bundled care approaches allow for all facets of care in the postoperative period to be addressed.[6,13] This includes early resumption of oral nutrition, hydration, early mobilisation, rehabilitation and removal of catheters and drains which form part of enhanced recovery protocols. Improved surveillance postoperatively allows for prompt recognition and early intervention for surgical complications reducing the chance of failure to rescue in frail patients and can improve outcomes.[13]

## Future directions

Frailty is regarded as a clinical entity predisposing to adverse outcomes, but it has not been included in traditional risk assessments. Formal inclusion into risk stratification models will allow for better prognostication of elderly patients presenting for surgery.[5] Standardisation of a single frailty screening tool for use in the preoperative period will simplify assessment and enable better comparison of ongoing studies in this field.[4] Prehabilitation is a field of active research and robust trials assessing the benefits will allow for intervention strategies to be refined.[9] Intraoperative and postoperative interventions that would benefit this vulnerable group of patients requires further research.[6]

## Conclusion

Frailty has gained traction in the perioperative care setting as a predictor for adverse outcomes. Current guidelines recommend routine screening in the preoperative setting. This ensures identification of the frail patient, which allows for optimisation and targeted interventions to mitigate risk and improve outcomes.

### *Conflict of interest*

No conflicts of interest declared.


### *Funding source*

None.


### *Ethical approval*

Not required.


### *ORCID*

Z Jooma https://orcid.org/0000-0002-1036-8744


## References


1. Solanki G, Kelly G, Corneliv J, Daviaud E, Geffen L. Population ageing in South Africa: trends, impact, and challenges for the health sector. 2019. Available from: https://www.hst.org.za/publications/South%20African%20Health%20Reviews/16%20SAHR_2019_Population%20ageing%20in%20South%20Africa.pdf. Accessed 2 Sept 2021.
2. Chan S, Ip K, Irwin M. Peri-operative optimisation of elderly and frail patients: a narrative review. Anaes. 2019;74(Suppl 1):80-9. https://doi.org/10.1111/anae.14512.
3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56. https://doi.org/10.1093/gerona/56.3.M146.
4. Lior ST, Idit M. Frailty and anaesthesia. Curr Opin Anaesthesiol. 2017;30(3):409-17. https://doi.org/10.1097/ACO.0000000000000456.
5. De Biasio J, Mittel A, Mueller A, et al. Frailty in critical care medicine: a review. Anesth Analg. 2020;130(6). https://doi.org/10.1213/ANE.0000000000004665.
6. McIsaac D, MacDonald D, Aucoin S. Frailty for perioperative clinicians: a narrative review. Anes & Analg. 2020;130(6):1450-60. https://doi.org/10.1213/ANE.0000000000004602.
7. Lai JPC, So VC, Irwin MG. Assessment of frailty in the preoperative setting - is there an ideal tool? A practical perspective. Anaes Int Care Med. 2020;21(10):489-92. https://doi.org/10.1016/j.mpaic.2020.07.004.
8. Silbert B, Scott D. Informed consent in patients with frailty syndrome. Anesth & Analg. 2020;130(6):1474-81. https://doi.org/10.1213/ANE.0000000000004629.
9. Adeleke I, Blitz J. Perioperative frailty: lessons learned and future directions. Curr Opin Anaesthesiol. 2021;34:373-80. https://doi.org/10.1097/ACO.0000000000001006.
10. Derwall M, Coburn M. Safety and quality of perioperative anaesthesia care - Ensuring safe care for older people living with frailty. Best Prac Res Clin Anaes. 2021;35:3-9. https://doi.org/10.1016/j.bpa.2020.04.007.
11. Leopold-George NTN, Nethathe GD. Frailty in perioperative patients in three South African Academic hospitals. S Afr Med J. 2019;109(7):535-9. https://doi.org/10.7196/SAMJ.2019.v109i7.13439.
12. Alvarez-Nebreda ML, Bentov N, Urman RD, et al. Recommendations for preoperative management of frailty from the Society for Perioperative Assessment and Quality Improvement (SPAQI). J Clin Anes. 2018;47:33-42. https://doi.org/10.1016/j.jclinane.2018.02.011.
13. Lin H-S, McBride R, Hubbard R. Frailty and anesthesia - risks during and post-surgery. Local Reg Anesth. 2018;11:61-73. https://doi.org/10.2147/LRA.S142996.
14. Bose S, Telmor D. Who is a high-risk surgical patient? Curr Opin Crit Care. 2018;24(6):547-53. https://doi.org/10.1097/MCC.0000000000000556.
15. Clegg A, Young J, Iliffe S, Rikkert M, Rockwood K. Frailty in elderly people. Lancet. 2013;381:752-62. https://doi.org/10.1016/S0140-6736(12)62167-9.
16. Mahanna-Gabrielli E, Schenning KJ, Eriksson LI, et al. State of the clinical science of perioperative brain health: report from the American Society of Anesthesiologists Brain Health Initiative Summit 2018. Br J Anaes. 2019;123(4):464e-8. https://doi.org/10.1016/j.bja.2019.07.004.
17. Gritsenko K, Helander E, Webb MPK, et al. Preoperative frailty assessment combined with prehabilitation and nutrition strategies: emerging concepts and clinical importance. Best Prac Res Clin Anaes. 2020;34(2):199-212. https://doi.org/10.1016/j.bpa.2020.04.008.
18. Hall DE, Arya S, Schmid KK, et al. Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. JAMA Surg. 2017;152(3):233-40. https://doi.org/10.1001/jamasurg.2016.4219.
19. Croke L. Beers criteria for inappropriate medication use in older patients: an update from the AGS. Am Fam Physician. 2020;101(1):56-7.
20. Carli F, Baldini G. From preoperative assessment to preoperative optimization of frail older patients. Eur J Surg Oncol. 2021;47(3 Pt A):519-23. https://doi.org/10.1016/j.ejso.2020.06.011.
21. Miller D, Lewis S, Pritchard M, et al. Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery (Review). Cochrane Database Syst Rev. 2018;8:CD012317. https://doi.org/10.1002/14651858.CD012317.pub2.
22. Evered LA, Chan MTB, Han R, et al. Anaesthetic depth and delirium after major surgery: a randomised clinical trial. Br J Anaes. 2021;127(5):704-12. https://doi.org/10.1016/j.bja.2021.07.021.
23. Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol. 2017;34:192-214. https://doi.org/10.1097/EJA.0000000000000594.
24. Saller T, MacLullich AMJ, Schäfer ST, et al. Screening for delirium after surgery: validation of the 4 A's test (4AT) in the post-anaesthesia care unit. 2019;74(10):1260-6. https://doi.org/10.1111/anae.14682.