## GERIATRIC ANESTHESIA: EVALUATING THE IMPACT OF AGE-RELATED PHYSIOLOGICAL CHANGES ON ANAESTHETIC PRACTICES

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#### **ABSTRACT**

**Introduction:** As the global population ages, the number of elderly patients undergoing surgical procedures increases, posing unique challenges for anesthetic management. Agerelated physiological changes affect multiple organ systems, impacting the pharmacokinetics and pharmacodynamics of anesthetic agents. Understanding these changes is crucial for optimizing perioperative care in geriatric patients. **Objective:** This literature review aims to comprehensively evaluate the impact of age-related physiological changes on anesthetic practices and outcomes in geriatric patients. By synthesizing current research, the review seeks to provide insights into tailored approaches for anesthesia in the elderly population, encompassing hemodynamic management, ventilation strategies, drug selection and dosing, and postoperative care. **Method:** A comprehensive literature search was conducted to identify studies on the impact of age-related physiological changes on anesthetic practices in geriatric patients. Electronic databases were searched using specific keywords. Inclusion criteria encompassed peer-reviewed articles focusing on anesthesia in patients aged 65 and older, while exclusion criteria eliminated studies not published in English or those focusing solely on pediatric or adult populations under 65. Data extraction and synthesis involved organizing findings on cardiovascular, respiratory, renal, hepatic, and central nervous system changes, anesthetic implications, and strategies for perioperative management. Result: Age-related physiological changes significantly influence anesthetic practices in geriatric patients. These changes necessitate tailored approaches to hemodynamic management, ventilation strategies, drug selection and dosing, and postoperative care. Anesthetic techniques such as regional anesthesia and multimodal analgesia mitigate risks and improve outcomes. Collaborative multidisciplinary care is essential for optimizing perioperative management in elderly patients. Conclusion: Optimizing anesthetic care in geriatric patients requires a comprehensive understanding of age-related physiological changes and their implications for perioperative management. Tailored approaches that consider these changes, utilize appropriate anesthetic techniques, and implement multidisciplinary care strategies are crucial for improving surgical outcomes and enhancing the quality of life in elderly patients. Ongoing research and education are essential for advancing geriatric anesthesia practice and addressing the evolving needs of this growing patient population.

**Keywords**: Geriatric anesthesia, age-related physiological changes, perioperative care, anesthetic managemen

#### INTRODUCTION

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As the world's population ages, so too does the number of elderly patients undergoing surgical procedures. Projections suggest that the number of people aged 65 and over will double by 2050, reaching approximately 1.6 billion people worldwide. This demographic shift significant presents challenges healthcare systems, particularly in the field of anesthesiology, where the management of geriatric patients requires specialized knowledge and tailored approaches.<sup>1-3</sup>

## **Physiological Changes with Aging**

Aging is associated with a multitude of physiological changes that significantly affect the pharmacokinetics pharmacodynamics of anesthetic agents. These changes occur across various organ systems, including the cardiovascular, respiratory, renal, hepatic, and central nervous systems. Each of these systems undergoes structural and functional modifications that can influence the response to anesthesia and the risk of perioperative complications.<sup>4–6</sup>

#### Cardiovascular System

With advancing age, there is increased arterial stiffness, reduced elasticity of the vascular system, and a decline in myocardial function. These changes result in higher systolic blood pressure, decreased cardiac output, and an

increased risk of arrhythmias. Anesthetic agents that cause vasodilation or myocardial depression can exacerbate these issues, necessitating careful hemodynamic monitoring.<sup>7–9</sup>

#### **Respiratory System**

Age-related changes the respiratory system include decreased chest wall compliance, weakened respiratory muscles, and reduced alveolar surface area. These changes impair gas exchange, reduce responses to hypoxia and hypercapnia, and increase the risk of postoperative respiratory complications such as hypoxemia and pneumonia..<sup>10–12</sup>

#### **Renal System**

Renal function declines with age, evidenced by decreased renal blood flow and glomerular filtration rate (GFR).<sup>13</sup> These changes affect the excretion of drugs and the body's ability to maintain fluid and electrolyte balance.<sup>14</sup> Anesthetic management in elderly patients must account for these factors to avoid drug toxicity and fluid overload. <sup>13,15</sup>

#### **Hepatic System**

Aging is also associated with a reduction in liver mass and hepatic blood flow, leading to decreased metabolism of

drugs. <sup>16</sup>This necessitates adjustments in dosing and careful selection of anesthetic agents to prevent prolonged drug effects and potential toxicity. <sup>16,17</sup>

#### **Central Nervous System**

The central nervous system undergoes significant changes with age, including neuronal loss and alterations in neurotransmitter levels. 18 These changes increase the sensitivity of elderly patients to anesthetics and their susceptibility to postoperative cognitive dysfunction and delirium. 19,20

#### **Anesthetic Implications**

Given these physiological changes, the anesthetic management of geriatric patients requires a nuanced approach.21 Anesthetic techniques and agents must be carefully chosen and dosed to minimize adverse effects while ensuring effective perioperative care.21,22 General anesthesia, while commonly used, poses a higher risk cardiovascular and respiratory complications in the elderly.<sup>23</sup> Regional anesthesia, such as spinal or epidural anesthesia, can often be preferable as it reduces the likelihood of respiratory depression and cognitive impairment. 24 Furthermore, a multimodal approach to pain management, incorporating nonopioid analgesics, local anesthetics, and adjunctive therapies, can help minimize opioid-related side effects and enhance recovery. The goal is to provide effective analgesia while reducing the risk of delirium and other cognitive disturbances. 18–22,24,25

#### **Postoperative Considerations**

Postoperative care for elderly patients involves vigilant monitoring complications such as delirium, cognitive dysfunction, respiratory failure, cardiovascular instability $^{26-29}$ . **Early** mobilization and rehabilitation are critical to reducing the risk of deep thrombosis, pulmonary embolism, and prolonged immobility.<sup>30</sup>

#### **Research Objectives**

This literature review aims to provide a comprehensive evaluation of the impact of age-related physiological changes on anesthetic practices and outcomes in geriatric patients. By synthesizing current research, the review seeks to offer insights into optimizing anesthetic care for the elderly, addressing both intraoperative management and postoperative recovery.

#### **Importance of the Study**

Understanding the complex interplay between aging physiology and anesthesia is essential for improving surgical outcomes and quality of life for elderly patients. As the population ages, the demand for geriatric anesthesiology expertise will continue to grow. <sup>31</sup>. This review contributes to the body of knowledge necessary for developing best practices and guiding future research in this critical area of healthcare.

By examining the latest evidence on age-related physiological changes and their anesthetic implications, this review underscores the importance of tailored anesthetic management in the geriatric population, ultimately aiming to enhance patient safety and outcomes in this vulnerable group.

#### **METHOD**

#### **Literature Search Strategy**

A systematic literature search was conducted to gather relevant studies on the impact of age-related physiological changes on anesthetic practices in geriatric patients. Electronic databases searched included PubMed, MEDLINE, Scopus, and the Cochrane Library. Keywords and search terms used were "geriatric anesthesia," "elderly patients," "age-related physiological changes," "cardiovascular system," "respiratory system," "renal system," "hepatic system," "central nervous

system," "pharmacokinetics," and "pharmacodynamics."

#### **Inclusion and Exclusion Criteria**

Studies were included if they met the following criteria:

- Peer-reviewed articles published in English.
- 2. Studies focusing on anesthetic management in patients aged 65 years and older.
- Research discussing physiological changes due to aging and their impact on anesthetic practices.
- 4. Types of studies considered: clinical trials, observational studies, reviews, and meta-analyses.

Studies were excluded if:

- 1. Not published in English.
- 2. Involved non-human subjects.
- 3. Focused exclusively on pediatric or adult populations under 65 years.
- 4. Consisted of case reports or editorials without substantial data.

#### **Data Extraction and Synthesis**

Data from eligible studies were extracted and organized according to:

- 1. Study characteristics (authors, publication year, study design).
- 2. Population characteristics (age range, sample size).

- 3. Key findings on age-related physiological changes in the cardiovascular, respiratory, renal, hepatic, and central nervous systems.
- 4. Specific anaesthetic techniques and pharmacological considerations for elderly patients.
- 5. Postoperative outcomes and complications.

The extracted data were synthesized to create a comprehensive overview of how physiological changes in elderly patients affect anaesthetic practices. Key themes were identified and categorized based on the physiological systems involved and their anaesthetic implications.

#### **Quality Assessment**

The quality of included studies was assessed using a standardized tool.

- Randomized controlled trials (RCTs) were assessed using the Cochrane risk of bias tool.
- 2. Observational studies were assessed using the Newcastle-Ottawa scale.
- Reviews and meta-analyses were assessed using the AMSTAR (Measurement Tool for Appraising Systematic Reviews) criteria.

#### **Data Analysis**

A qualitative synthesis approach was employed to integrate findings from diverse study designs. Quantitative data were summarized using descriptive statistics where applicable. Due to the heterogeneity of study designs and outcomes, a formal meta-analysis was not performed. Instead, key patterns and themes were identified and discussed

#### **Ethical Considerations**

As this study was a review of existing literature, ethical approval was not required. However, ethical considerations in the included studies, particularly those involving the management of elderly patients, were noted and discussed.

This methodical approach ensures a comprehensive understanding of the interplay between aging physiology and anaesthetic management, aiming to improve anaesthetic care and outcomes for geriatric surgical patients.

## **DISCUSSION**

#### **Overview of Findings**

The literature review highlights the profound impact of age-related physiological changes on the anesthetic management of geriatric patients. These changes affect multiple organ systems,

necessitating specialized approaches to anesthesia to mitigate risks and optimize perioperative outcomes. This discussion delves deeper into these physiological changes, their anesthetic implications, and strategies for effective management.<sup>32,33</sup>

#### Cardiovascular System

Aging brings significant changes to the cardiovascular system, including increased arterial stiffness, reduced vascular compliance, and diminished myocardial function. These alterations result in higher systolic blood pressure, decreased cardiac output, and an increased propensity for arrhythmias and myocardial ischemia. <sup>34–36</sup>These changes require anaesthesiologists to adopt a cautious approach to hemodynamic management during anaesthesia.33

#### **Anaesthetic Implications:**

- **Hemodynamic Monitoring:**Continuous monitoring of blood pressure, heart rate, and cardiac output is crucial.<sup>37,38</sup> Invasive monitoring, such as arterial lines, may be necessary for high-risk patients. <sup>39</sup>
- Agent Selection: Agents with minimal cardiovascular depression, such as etomidate for induction, are often preferred. The use of volatile anaesthetics should be carefully titrated, as agents like sevoflurane can

- cause vasodilation and myocardial depression.<sup>40–42</sup>
- **Fluid Management:** Elderly patients often have a reduced capacity to handle fluid overload. <sup>43</sup>Fluid administration should be carefully balanced to avoid both hypovolemia and fluid overload. The use of goal-directed fluid therapy can help optimize fluid status and improve outcomes. <sup>44,45</sup>

## **Respiratory System**

Age-related changes in the respiratory system include decreased chest wall compliance, weakened respiratory muscles, reduced alveolar surface area, and diminished response to hypoxia and hypercapnia.46 These changes increase the risk of perioperative respiratory complications such hypoxemia, as atelectasis, and pneumonia.46,47

## **Anesthetic Implications:**

- Ventilation Strategies: Lungprotective ventilation strategies,
  including low tidal volumes (6-8
  mL/kg) and appropriate levels of
  positive end-expiratory pressure
  (PEEP), should be employed to reduce
  the risk of ventilator-associated lung
  injury.<sup>48–50</sup>
- Regional Anesthesia: Where feasible, regional anesthesia techniques (e.g., spinal, epidural, and peripheral nerve blocks) are preferable as they maintain

spontaneous respiration and reduce the risk of postoperative respiratory complications.<sup>51,52</sup>

• Postoperative Care: Early mobilization, pulmonary rehabilitation, and incentive spirometry are critical components of postoperative care to prevent respiratory complications. 53–55

## **Renal System**

The decline in renal function with age, characterized by reduced renal blood flow and glomerular filtration rate (GFR), affects the pharmacokinetics of many anesthetic agents and increases the risk of perioperative renal complications.<sup>56,57</sup>

## **Anesthetic Implications:**

- **Drug Selection and Dosing:**Anesthetic agents and adjuncts that are renally excreted should be dosed cautiously. Agents with extra-renal clearance pathways, such as remifentanil, are advantageous.<sup>58,59</sup>
- Fluid Management: Maintaining adequate renal perfusion through careful fluid management and avoiding nephrotoxic agents (e.g., NSAIDs and certain antibiotics) is critical.<sup>60–62</sup>
- Monitoring: Perioperative monitoring of renal function, including urine output and serum creatinine levels, is

essential to detect and manage acute kidney injury promptly. 63-65

#### **Hepatic System**

Aging affects the hepatic system through decreased liver mass, reduced hepatic blood flow, and diminished metabolic capacity. These changes alter the metabolism of anesthetic agents and increase the risk of drug accumulation and toxicity. 66,67

## **Anesthetic Implications:**

- Agent Selection: Anesthetic agents
  with minimal hepatic metabolism,
  such as propofol and remifentanil,
  should be considered to avoid
  prolonged drug effects.<sup>68–70</sup>
- **Dosing Adjustments:** Dosages of anesthetic agents and adjuncts should be adjusted based on the patient's hepatic function to prevent toxicity.<sup>71,72</sup>
- **Monitoring:** Liver function tests and monitoring for signs of hepatic dysfunction are important in the perioperative period.<sup>73–75</sup>

#### **Central Nervous System**

The central nervous system undergoes significant changes with aging, including neuronal loss, reduced neurotransmitter levels, and increased sensitivity to anesthetics. These changes contribute to a

higher risk of postoperative cognitive dysfunction (POCD) and delirium.<sup>76,77</sup>

#### **Anesthetic Implications:**

- **Dose Reduction:** Elderly patients typically require lower doses of anesthetic agents to achieve the desired effect, reducing the risk of over-sedation and cognitive side effects.<sup>78–80</sup>
- Multimodal Analgesia: Utilizing a combination of analgesic modalities, including local anaesthetics, nonopioid analgesics, and adjuncts like gabapentinoids, can reduce the reliance on opioids and their associated cognitive risks.<sup>81–83</sup>
- Regional Anaesthesia: Regional anaesthesia techniques are beneficial as they are associated with a lower incidence of POCD and delirium compared to general anaesthesia.<sup>84–86</sup>
- Postoperative Strategies: Measures such as maintaining normothermia, ensuring adequate pain control, promoting early ambulation, and minimizing the use of psychoactive drugs are critical in preventing and managing POCD and delirium. 85,87

# **Anaesthetic Techniques and Multimodal Analgesia**

## Regional Anaesthesia:

 Regional anaesthesia, including spinal, epidural, and nerve blocks,

- offers several advantages for elderly patients. These techniques preserve respiratory function, reduce systemic drug exposure, and are associated with lower rates of POCD and delirium <sup>88–90</sup>
- Techniques like ultrasound-guided nerve blocks enhance the precision and efficacy of regional anaesthesia, potentially reducing the risk of complications and improving analgesic outcomes.<sup>91,92</sup>

#### **Multimodal Analgesia:**

- Multimodal analgesia involves using a combination of analgesic agents and techniques to achieve effective pain control with minimal side effects. Non-opioid analgesics (e.g., NSAIDs), acetaminophen, local anaesthetics, and adjunctive therapies gabapentinoids, **NMDA** (e.g., receptor antagonists) are integral components of this approach. 93-95
- This strategy minimizes opioid use, reducing the risk of opioid-related adverse effects such as respiratory depression, constipation, and delirium, which are particularly problematic in elderly patients. 96,97

## Postoperative Considerations Cognitive Function:

- Monitoring for signs of delirium and cognitive dysfunction is crucial. Implementing strategies to reduce the incidence of these complications, such as avoiding prolonged fasting, ensuring adequate hydration, and optimizing pain control, is essential.<sup>98–100</sup>
- Non-pharmacological interventions, including orientation protocols, early mobilization, and family involvement in care, can help mitigate cognitive decline.<sup>101</sup>

#### **Pain Management:**

- Adequate pain control is vital for preventing complications such as prolonged immobility, deep vein thrombosis, and pulmonary issues.
   Regional anaesthesia and multimodal analgesia play a significant role in achieving effective pain management.<sup>102,103</sup>
- Regular pain assessment using appropriate scales (e.g., Visual Analog Scale, Numeric Rating Scale) ensures timely and adequate pain relief.<sup>104</sup>

#### **Mobility and Rehabilitation:**

 Early mobilization and physical therapy are critical to reducing the risk of postoperative complications such as pressure ulcers, deep vein thrombosis, and muscle wasting.<sup>105,106</sup>  Multidisciplinary care teams, including anaesthesiologists, surgeons, geriatricians, physical therapists, and nurses, are essential for coordinating care and promoting optimal recovery.

## Implications for Practice and Future Research

The review underscores the need for tailored anaesthetic management protocols for elderly patients. Anaesthetic care should prioritize patient safety, minimize adverse effects, and enhance recovery through appropriate anaesthetic techniques and multimodal analgesia.

#### **Practice Implications:**

- Developing and implementing guidelines specific to geriatric anaesthesia can standardize care and improve outcomes.
- Training programs for anaesthesiologists should include comprehensive education on the physiological changes associated with aging and their anaesthetic implications.
- Collaboration between anaesthesiologists, surgeons, and geriatricians is vital for creating individualized perioperative care plans.

#### **Future Research:**

- Further research is needed to develop and validate specific guidelines for geriatric anaesthesia, exploring the efficacy and safety of different anaesthetic agents and techniques in elderly populations.
- Studies focusing on the prevention and 1.
   management of POCD and delirium in elderly patients are crucial for improving cognitive outcomes.
- Long-term outcome studies are necessary to understand the impact of various anaesthetic approaches on the 2. quality of life and functional status of elderly patients postoperatively.

#### **CONCLUSION**

The management of anesthesia in  $^{3}$ . geriatric patients unique presents challenges due to age-related physiological changes affecting various organ systems. A tailored approach that considers these changes and employs strategies such as and regional anesthesia multimodal improve <sup>4</sup>. analgesia can significantly perioperative outcomes. Ongoing research and education in geriatric anesthesia are essential to optimize care for this growing patient population, ultimately enhancing their surgical experience and recovery.

By understanding and addressing the <sup>5</sup>. complex interplay between aging physiology and anesthesia, healthcare

providers can improve the safety and effectiveness of anesthetic care for elderly patients, ensuring better surgical outcomes and enhanced quality of life.

#### REFERENCES

Oksuzyan, A., Höhn, A., Pedersen, J., Rau, R., Lindahl-Jacobsen, R., & Christensen K. Preparing for the future: the changing demographic composition of hospital patients in denmark between 2013 and 2050. *PLoS One*; 15.

M. M-AL and D-M. geriatric medicine in the medical curriculum: a must in the globally aging world. *Journal of Medicine University of Santo Tomas* 2022; 6: 944–951.

Heck V., Klug K., Prasse T., Oikonomidis S., Klug A. HB et al. rojections from surgical use models in germany suggest a rising number of spinal fusions in patients 75 years and older will challenge healthcare systems worldwide. *Clin Orthop Relat Res* 2023; 481: 1610–1619.

Ginsberg G., Hattis D., Russ A. & SB. pharmacokinetic and pharmacodynamic factors that can affect sensitivity to neurotoxic sequelae in elderly individuals. *Environ Health Perspect* 2005; 113: 1243–1249.

C. HL and O. changes in pharmacokinetics and pharmacodynamics in the elderly patient. *J Pharm Pract* 2007; 20: 4–12.

- 6. T. ND and H. perioperative multimodal 14. anesthesia using regional techniques in the aging surgical patient. *Pain Res Treat* 2014; 15. 1–13.
- 7. Singam N., Fine C. & FJ. cardiac changes associated with vascular aging. *Clin* 16. *Cardiol* 2019; 43: 92–98.
- 8. Steppan J., Barodka V., Berkowitz D. & 17. ND. vascular stiffness and increased pulse pressure in the aging cardiovascular system. 18. *Cardiol Res Pract* 2011; 1–8.
- 9. Wang W., Chang W. & CH. the relationship of vascular aging to reduced cognitive function: pulsatile and steady state arterial hemodynamics. *Pulse* 2022; 10: 19–25.
- 10. Šprung J., Gajic O. & WD. Review article: age related alterations in respiratory function anesthetic considerations.

  Canadian Journal of Anesthesia/Journal 20.

  Canadien D Anesthésie 2006; 53: 1244—1257.
- 11. Patel N., Chong K. & BA. Methods and applications in respiratory physiology: respiratory mechanics, drive and muscle 21. function in neuromuscular and chest wall disorders. *Front Physiol*; 13.
- Sasaki N., Meyer M. & EM. postoperative 22.
   respiratory muscle dysfunction.
   Anesthesiology 2013; 118: 961–978.
- 13. Czarkowska–Pączek B., Mucha K. & PL. age-related decline in renal blood flow 23. could be a beneficial and compensatory mechanism. *Medical Science Monitor*; 26.

- A. L. fluid and electrolytes in the aged. *Archives of Surgery* 2003; 138: 1055.
- Musso C., Scibona P., Bellizzi V. & NJ. Impact of renal aging on drug therapy. *Postgrad Med* 2015; 127: 623–629.
- H. W. drug metabolism and ageing. *Menopause Int* 2005; 11: 51–56.
- D. ZJ and P. The aging liver. *Gerontology* 2002; 48: 121–127.
- Robinson T., Raeburn C., Angles E. & MM. Low tryptophan levels are associated with postoperative delirium in the elderly. *the American Journal of Surgery* 2008; 196: 670–674.
- La D., Am R., R Y., Marcantonio E., Xie Z. LK et al. postoperative delirium and postoperative cognitive dysfunction. *Anesthesiology* 2019; 131: 477–491.
- Xiao Q., Liu Q., Deng R., Gao Z. & ZY. postoperative cognitive dysfunction in elderly patients undergoing hip arthroplasty. *Psychogeriatrics* 2020; 20: 501–509.
- T. H. perioperative pain management in the elderly surgical patient. *Universal Journal of Medical Science* 2013; 1: 36–49.
- T. ND and H. perioperative multimodal anesthesia using regional techniques in the aging surgical patient. *Pain Res Treat* 2014; 2014: 1–13.
- Egan T. Are opioids indispensable for general anaesthesia? *Br J Anaesth* 2019; 122: e127–e135.

- 24. E. GÉ and T. anaesthesia and postoperative 32.
  analgesia in older patients with chronic obstructive pulmonary disease. *Drugs*Aging 2003; 20: 347–360.
  33.
- 25. M. JJ and J. perioperative regional anaesthesia and postoperative longer-term outcomes. *F1000Res*; 5.
- 26. Desai S., Law T. & ND. Long-term complications of critical care. *Crit Care* 34. *Med* 2011; 39: 371–379.
- 27. Mart M., Roberson S., Salas B., Pandharipande P. & EE. Prevention and 35. management of delirium in the intensive care unit. *Semin Respir Crit Care Med* 2020; 42: 112–126.
- 28. Jildenstål P., Rawal N., Hällén J., Berggren 36. L. & JJ. Perioperative management in order to minimise postoperative delirium and postoperative cognitive dysfunction: 37. results from a swedish web-based survey. Annals of Medicine and Surgery 2014; 3: 100–107.
- 29. K. GR and M. pulmonary complications in neurosurgical patients. *Indian Journal of Neurosurgery* 2012; 01: 175–180.
   38.
- 30. Jang M., Shin M. & SY. pulmonary and physical rehabilitation in critically ill patients. *Acute and critical care* 2019; 34: 39. 1–13.
- 31. Ogan, K., Master, V., & Canter D. Perioperative assessment of elderly surgical patients. *Curr Transl Geriatr Exp Gerontol Rep* 2013; 2: 45–50.

- A. T. Anaesthesia in the geriatric patient a case study. *Veterinary Nursing Journal* 2014; 29: 52–53.
- Hu F., O'Mara L., Tulebaev S., Orkaby A., Cooper Z. & BR. geriatric surgical service interventions in older emergency general surgery patients: preliminary results. *J Am Geriatr Soc* 2022; 70: 404–2414.
- Singam N., Fine C. & FJ. cardiac changes associated with vascular aging. *Clin Cardiol* 2019; 43: 92–98.
- Steppan J., Barodka V., Berkowitz D. & ND. vascular stiffness and increased pulse pressure in the aging cardiovascular system. *Cardiol Res Pract* 2011; 2011: 1–8.
- M. A. aging-related changes of the cardiovascular system. *Journal of Health and Environmental Research* 2017; 3: 27. Hill B., Rakocz N., Rudas Á., Chiang J.,
- Wang S. HI et al. Imputation of the continuous arterial line blood pressure waveform from non-invasive measurements using deep learning. *Sci Rep*; 11.
- M. B. Noninvasive and minimally invasive cardiac output monitoring. *Dimensions of Critical Care Nursing* 2022; 41: 121–123. Stens J., Oeben J., Dusseldorp A. & BC. Non-invasive measurements of pulse pressure variation and stroke volume variation in anesthetized patients using the nexfin blood pressure monitor. *J Clin Monit Comput* 2015; 30: 587–594.

- 40. Bogari A., Aldakhil I., Alsuwaidan M., Alhassani N., Alroudan D. AO et al. Inhalation anaesthetics: types, mechanism of action and adverse effects. *Int J Community Med Public Health* 2022; 9: 47. 4684.
- 41. Ghatge S., Lee J. & SI. sevoflurane: an ideal agent for adult day-case anesthesia? *Acta Anaesthesiol Scand* 2003; 47: 917–931.
- 42. Sivanna U., Joshi S., Babu B. JA. A comparative study of pharmacological 48. myocardial protection between sevoflurane and desflurane at anaesthestic doses in patients undergoing off pump coronary artery bypass grafting surgery. *Indian J* 49. *Anaesth* 2015; 59: 282.
- 43. Yin K., Ding J., Wu Y. & PM. Goal-directed fluid therapy based on noninvasive cardiac output monitor reduces postoperative complications in elderly 50. patients after gastrointestinal surgery: a randomized controlled trial. *Pak J Med Sci*; 34.
- D. U-S. optimal perioperative fluid management: what is the strategy? Serbian
   Journal of Anesthesia and Intensive therapy 51.
   2016; 38: 75–81.
- 45. J. L. Vascular endothelial growth factor-d plasma levels in fluid overload and cardiac function evaluation of elderly patients with cardiovascular disease. *Medicine* 2023; 52. 102: e36062.
- 46. Yanagi S., Tsubouchi H., Miura A., Matsuo A., Matsumoto N. & NM. the impacts of

cellular senescence in elderly pneumonia and in age-related lung diseases that increase the risk of respiratory infections. *Int J Mol Sci* 2017; 18: 503.

Šprung J., Gajic O. & WD. Review article: age related alterations in respiratory function — anesthetic considerations. Canadian Journal of Anesthesia/Journal Canadien D Anesthésie 2006; 53: 1244–1257.

Sato H., Nakamura K., Baba Y., Terada S., Goto T. & KK. low tidal volume ventilation with low peep during surgery may induce lung inflammation. *BMC Anesthesiol*; 16.

P. Perioperative S. lung-protective ventilation strategy reduces postoperative pulmonary complications in patients undergoing thoracic and major abdominal surgery. Korean J Anesthesiol 2016; 69: 3. Sinclair S., Polissar N. & AW. Spatial distribution of sequential ventilation during mechanical ventilation of the uninjured lung: an argument for cyclical airway collapse and expansion. BMC Pulm Med; 10.

Neal J., Bernards C., Hadžić A., Hebl J., Hogan Q. HT et al. ASRA practice advisory on neurologic complications in regional anesthesia and pain medicine. *Reg Anesth Pain Med* 2008; 33: 404–415.

Chen J., Lin J., Chen X. & LC. Efficacy of an intercostal nerve block administered with general anesthesia in elderly patients

- undergoing distal gastrectomy. *Clinical & Investigative Medicine* 2015; 38: 351.
- Hassanzadeh H., Jain A., Tan E., Stein B.,Hoy M. SN et al. postoperative incentive spirometry use. *Orthopedics*; 35.60.
- 54. Yamana I., Takeno S., Hashimoto T., Maki K., Shibata R. SH et al. Randomized 61. controlled study to evaluate the efficacy of a preoperative respiratory rehabilitation program to prevent postoperative 62. pulmonary complications after esophagectomy. *Dig Surg* 2015; 32: 331–337.
- 55. S. FJ, AL-Fayyadh. Preoperative incentive spirometer to prevent postoperative pulmonary complications following open 64. heart surgeries: a randomized single blinded multi-centric clinical trial. *Journal of Contemporary Medical Sciences*; 8.
- 56. Czarkowska–Pączek B., Mucha K. & PL. 65. age-related decline in renal blood flow could be a beneficial and compensatory mechanism. *Medical Science Monitor*: 26.
- 57. Verhave J., Fesler P., Cailar G., Ribstein J., Safar M. & MA. Elevated pulse pressure is associated with low renal function in 66. elderly patients with isolated systolic hypertension. *Hypertension* 2005; 45: 586–591.
- 58. P. M. Anaesthesia for the patient with impaired renal function. *Anaesth Intensive Care* 1983; 11: 321-332.67.
- 59. Keßler U., Bjorke-Bertheussen J., Søreide E., Hunderi P., Bache-Mathiesen L. OK et

- al. remifentanil as an adjunct to anaesthesia for electroconvulsive therapy fails to confer long-term benefits. *Br J Anaesth* 2018; 121: 1282–1289.
- M. O. Preventing renal failure in the critically ill. *BMJ* 2001; 322: 1437–1439.
- M. P. Drug use and nephrotoxicity in the intensive care unit. *Kidney Int* 2012; 81: 1172–1178.
- A S-GK and Z. Perioperative renal protection. *Curr Opin Crit Care* 2021; 27: 676–685.
- Wu. The duration of postoperative acute kidney injury predicts in-hospital mortality in surgical patients. *World J Nephrol Urol*. Gumbert S., Kork F., Jackson M., Vanga N., Ghebremichael S. WC et al. perioperative acute kidney injury. *Anesthesiology* 2020; 132: 180–204.
- B D., PADHY S., Girijavani D. & LP. Role of serum creatinine in forecasting the outcome after cardiac surgery beyond acute kidney injury-a cross sectional study. *Asian Journal of Pharmaceutical and Clinical Research* 2021; 105–108.
- S. A. Effect of changes in metabolic enzymes and transporters on drug metabolism in the context of liver disease: impact on pharmacokinetics and drug–drug interactions. *Br J Clin Pharmacol* 2024; 90: 942–958.
- E. Eld. Pharmacokinetic-pharmacodynamic crisis in the elderly. *Am J Ther* 2007; 14: 488–498.

- 68. Nucera M., Marsili M., Malyan M. & BC. Ketamine, propofol and low dose remifentanil versus propofol and 75. remifentanil for ercp outside the operating room: is ketamine not only a "rescue drug"?

  Medical Science Monitor 2012; 18: CR575–CR580.
- 69. Ahn J., Kim D., Chung I., Lee J., Lee E. & 76. JJ. Pre-administration of remifentanil in target-controlled propofol and remifentanil anesthesia prolongs anesthesia induction in neurosurgical patients. *Medicine* 2019; 98: e14144.
- 70. Jahanbakhsh S., Bameshki A. & KP. remifentanil-induced abdominal pain: a randomised clinical trial. *Anaesth Intensive Care* 2009; 37: 447–449.
- 71. E. C. toxicity of inhalation anaesthetic 78. agents. *Br J Anaesth* 1978; 50: 665–675.
- 72. Barrington M., Weinberg G. & NJ. A call to all readers: educating all surgeons on preventing and treatment of local anaesthetic systemic toxicity. *Australian* 79. *and New Zealand Journal of Surgery* 2016; 86: 636–637.
- 73. Vogt J., Radermacher P. & GM. 13co2 breath tests, a tool to assess intestinal and liver function in the icu? *Curr Opin Crit* 80. *Care* 2010; 16: 169–175.
- 74. Tralhão J., Hoti E., Oliveiros B., Abrantes A., Botelho M. & C-SF. Intermittent pringle maneuver and hepatic function: perioperative monitoring by noninvasive 81.

- icg-clearance. *World J Surg* 2009; 33: 2627–2634.
- Simegn A., Melesse D., Bizuneh Y. & AW. perioperative management of patients with liver disease for non-hepatic surgery: a systematic review. *Annals of Medicine and Surgery*; 75.
- Xiao Q., Liu Q., Deng R., Gao Z. & ZY. postoperative cognitive dysfunction in elderly patients undergoing hip arthroplasty. *Psychogeriatrics* 2020; 20: 501–509.
- Urits I., Orhurhu V., Jones M., Hoyt D., Seats A. & VO. Current perspectives on postoperative cognitive dysfunction in the ageing population. *Turk J Anaesthesiol Reanim* 2019; 47: 439–447.
- Y. Z. Safety and efficacy of a low-dose combination of midazolam, alfentanil, and propofol for deep sedation of elderly patients undergoing ercp. *BMC Gastroenterol*; 24.
- Erdoğan M., Demirbilek S., Erdil F., Aydoğan M., Öztürk E. TT et al. the effects of cognitive impairment on anaesthetic requirement in the elderly. *Eur J Anaesthesiol* 2012; 29: 326–331.
- Y. L. Impact of sedation protocols on elderly patients undergoing mechanical ventilation and off-line weaning. *Journal of Clinical and Nursing Research* 2024; 8: 322–333.
- J. P. Exploring the combination of gabapentinoids and opioids for

- postoperative analgesia. *JAMA Netw Open* 2020; 3: e2032139.
- 82. Lavin R., Liu C., Yuspeh L., Kalia N., 89. Leung N. TN et al. Trends in the utilization and dose of gabapentinoids in combination with opioids in an injured worker population between 2008 and 2018. *J Occup Environ Med* 2021; 63: e694–e700. 90.
- 83. Lee G., Berkowitz R., Hacker S. HJ, A. R. Htx-011 in combination with multimodal analgesic regimen minimized severe pain and opioid use after total knee arthroplasty 91. in an open-label study. *J Knee Surg* 2022; 36: 925–932.
- 84. L. SC and R. Challenges in anaesthesia for 92. elderly. *Singapore Dent J* 2014; 35: 23–29.
- 85. S. KD and M. Neurocognitive function monitoring. *J Neuroanaesth Crit Care* 2015; 2: 246–256.
- 86. Evered L., Silbert B. & SD. The impact of the peri-operative period on cognition in older individuals. *Journal of Pharmacy* 93. *Practice and Research* 2015; 45: 93–99.
- 87. Kakinuma K., Kakinuma T., Shinohara T.,
  Shimizu A., Okamoto R. KA et al. 94.
  management of giant ovarian tumors in
  elderly adults: preoperative evaluation
  using comprehensive geriatric assessment
  and estimation of physiologic ability and
  surgical stress and perioperative 95.
  management effectiveness using aron alpha
  method and enhance.
- 88. W. L, Y. F, W. C. Effects of combined spinal epidural anesthesia in orthopaedic

- surgery of elderly patients. *Comput Math Methods Med* 2022; 2022: 1–5.
- Chen J., Lin J., Chen X. & LC. Efficacy of an intercostal nerve block administered with general anesthesia in elderly patients undergoing distal gastrectomy. *Clinical & Investigative Medicine* 2015; 38: 351.
- T. ND and H. Perioperative multimodal anesthesia using regional techniques in the aging surgical patient. *Pain Res Treat* 2014; 1–13.
- Liu S., Ngeow J. & YJ. ultrasound-guided regional anesthesia and analgesia. *Reg Anesth Pain Med* 2009; 34: 47–59.
- J. F. Effects of ultrasound-guided lumbar plexus and sacral plexus block combined with general anesthesia on the anesthetic efficacy and surgical outcomes in elderly patients undergoing intertrochanteric fracture surgery: a randomized controlled trial. *J Orthop Surg Res*; 19.
- P. W, H. K. Improving postoperative pain management. *Anesthesiology* 2010; 112: 220–225.
- Girard P., Chauvin M. & VM. Nefopam analgesia and its role in multimodal analgesia: a review of preclinical and clinical studies. *Clin Exp Pharmacol Physiol* 2015; 43: 3–12.
- Yeo J., Park J., Choi G., Kim H., Kim J. OJ et al. Comparison of the analgesic efficacy of opioid-sparing multimodal analgesia and morphine-based patient-controlled analgesia in minimally invasive surgery for

- colorectal cancer. *World J Surg* 2022; 46: 1788–1795.
- 96. Z. DA and S. problematic opioid use among 104. older adults: epidemiology, adverse outcomes and treatment considerations. 105. *Drugs Aging* 2021; 38: 1043–1053.
- 97. Rekatsina M., Paladini A., Myrcik D., Viswanath O., Urits I. PJ et al. opioids in the elderly patients with cognitive impairment: a narrative review.
- 98. Wang H., Yi S., Wang H. & CM. Process management of analgesia and sedation can 106. reduce the incidence of delirium. *Surg Sci* 2019; 10: 405–411.
- 99. C. S, J. P. Evidence-based strategies to reduce the incidence of postoperative delirium: a narrative review. *Anaesthesia* 2022; 77: 92–101.
- 100. Huang P., Sun S. & LH. The effect of anesthesia depth monitoring on postoperative delirium and postoperative cognitive dysfunction in non-cardiac surgery patients---- a systematic review and meta-analysis.
- 101. L. SF and B. non-pharmacologic interventions for the prevention of delirium in the intensive care unit: an integrative review. *Nurs Crit Care* 2021; 26: 166–175.
- 102. Chitnis S., Tang R. & ME. The role of regional analgesia in personalized postoperative pain management. *Korean J Anesthesiol* 2020; 73: 363–371.
- 103. A. JR and S. Development of a multimodal analgesia protocol for perioperative acute

- pain management for lower limb amputation. *Pain Res Manag* 2018; 1–9.
- S. P. pain and sedation assessment. 2015; 749–753.
- Al-Dorzi H., AlQahtani S., Al-Dawood A., Al-Hameed F., Burns K. MS et al. Association of early mobility with the incidence of deep-vein thrombosis and mortality among critically ill patients: a post hoc analysis of prevent trial. *Crit Care*; 27.
- Walker N., Rodgers A., Birchall N., Norton R. & MS. Leg ulceration as a long-term complication of deep vein thrombosis. *J Vasc Surg* 2003; 38: 1331–1335.