

Anesthesia and perioperative pain relief in the frail elderly patient

ABSTRACT

Demand for anesthesia and analgesia for the frail elderly is continuously increasing as the likelihood of encountering very elderly, very vulnerable, and very compromised patients has, ever so subtly, increased over the last three decades. The anesthesiologist has, increasingly, been obliged to offer professional services to frail patients. Fortunately, there has been a dramatic improvement in medications, methods of drug delivery, critical monitoring, and anesthesia techniques. Specific methodologies peculiar to the frail are now taught and practiced across all anesthesia subspecialties. However, administering anesthesia for the frail elderly is vastly different to giving an anesthetic to the older patient. Frail patients are increasingly cared for in specialized units—geriatric intensive therapy units, post-acute care services, palliative, hospices, and supportive care and aged care facilities. Several medications (e.g., morphine-sparing analgesics) more suited to the frail have become universally available in most centers worldwide so that best-practice, evidence-based anesthesia combinations of drugs and techniques are now increasingly employed. Every anesthetic and pain management techniques in the frail elderly patient are going to be discussed in this review.

Key words: Elderly, emergency surgery, frailty, general anesthesia, geriatric anesthesia, geriatric medicine, perioperative pain in the frail, regional anesthesia, surgical pain in the elderly

The Geriatric Patient Population—The Fastest Growing Group in our Society

Life expectancy at birth is continuously increasing worldwide, with the elderly population increasing at a fast rate. Members of the elderly generation routinely undergo—often complex—surgical interventions with high levels of postoperative pain, necessitating aggressive pain relief treatment.

Because of complex multi-morbidity, multi-pharmacy use and limited physical reserves, elderly patients more commonly have (long-lasting) adverse events, related to pain therapy and complications related to inadequately treated pain.^[1-11] The perioperative—opioid-sparing—pain management strategy for elderly patients is rather unique and requires a comprehensive and collaborative interdisciplinary approach.^[12]

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Frail elderly patients, post-surgical outcomes, and pain relief

Historically, age has been a variable, linked to predict negative post-surgical outcomes. Aging is characterized by cumulative declines across multiple physiologic systems. Frailty is the intermediate between normal and pathological ageing.^[13]

Frailty is a much faster decline than expected based on age alone. Its prevalence increases with age and is estimated to be 26% in the patient group above 85 years.^[14] Frailty is a multisystem and multidimensional physiologic decline in, for example, limited physical performance, reduced gait speed/mobility, impaired nutrition, sarcopenia (loss of muscle mass and coordination), cognitive disorders, and mental well-being. Frailty is extremely relevant to the general surgical practice, with 10% of patients displaying frailty characteristics, especially in the geriatric group.^[1] This decreased reserve and resistance to (surgical) stressors results in an increased vulnerability to adverse outcomes, that is, a higher likelihood of accidental falls, pressure ulcers, hospitalization, an increased length of stay, morbidity, complications, and disability (impairment to undertake daily activities), which ultimately result in inferior clinical outcomes, readmission, dependency, discharge to another facility, and a higher risk of mortality.^[11,14-22] The pathogenesis of frailty is related to chronic inflammation, immune activation, age-related changes to the endocrine systems, lower production of sex hormones, vitamin D deficiency and higher levels of cortisol, interacting with (epi) genetic factors, and environmental and lifestyle stressors.^[14] Apart from the hospitalization and surgery, unfamiliar hospital environment, fasting, immobility and use of anesthetic drugs and opioids, intraoperative blood loss, use of intraoperative catheters (e.g., urinary catheter), and postoperative side effects (pain, nausea, and vomiting) can all be triggers that may cause a previously balanced but frail body system to fail. In a very frail patient, a minor insult may be sufficient to lead to permanent functional decline.

Frailty increases with age, from 4% (65–69 age group) to 26% (85 and older group), and is a predictor for postoperative complications.^[14,15,23] Increased frailty can translate in a fourfold greater risk of postoperative complications. The high rates of postoperative complications and mortality do occur in (very) frail patients even at the lowest-stress procedures, for example, a cystoscopy. Therefore, using “frailty flags” in the preoperative frailty assessment helps the surgical team to predict postoperative adverse events, to adapt the treatment approach, implement preoperative rehabilitation, implement adjustments to the medication taken by the patient and nutritional support. Evaluation of frailty may initiate a discussion whether the intervention makes sense, whether a non-operative treatment

strategy is a reliable option. The extremely frail patient may accept the high risk of morbidity and mortality while undergoing palliative surgery with the goal of improved quality of life. However, these frail patients may also wish to opt out for curative surgery, which may treat a disease but not necessarily improve the quality of life after surgery. It is important that the frail elderly patient (and family) is involved in this decision to make an informed choice about their surgery.^[14,24]

Frailty assessment before surgery is therefore recommended for all elderly patients as this may allow specific perioperative interventions to improve the patient’s outcomes and decrease the risk of mortality and dependency after surgery. The commonly used risk prediction tools such as, for example, age, American Society of Anesthesiologists (ASA) physical status, and exercise tolerance as measured by metabolic equivalent task scores (METs) are good at predicting organic-specific complications. However, these tools are unable to identify and measure vulnerability and decreased reserve and do not consider geriatric syndromes and frailty. Frailty is a better predictor of morbidity and mortality than age, ASA, and comorbidities alone.^[14] Frailty assessment is complimentary to the traditional surgical risk assessment tools.

Frailty often resides together with heart failure and respiratory failure.^[25-28] Clinical frailty ≥ 4 , as assessed according to the Clinical Frailty Scale, is considered the threshold representative of frailty, which has a robust impact on the incidence of postoperative severe complications as studied on elderly patients with colorectal surgery.^[11,15,27-30] Studies using the most commonly applied index in surgical cohorts across multiple surgical specialties, that is, the modified Frailty Index (mFI), showed that frailty is associated with a higher rate of all-cause complications and mortality.^[16] mFI is easy to calculate and uses characteristics extracted from the patient’s history and examination. As such, mFI is a prognostic indicator, which strongly correlates with higher risks of postoperative complications, longer hospitalization periods, greater rates of readmission and reoperations, and discharge to skilled special care institutions, and higher mortality rates.^[16] As not all older patients are frail, it suggests that frailty is not an inevitable consequence of aging and is potentially reversible, with return to prior homeostasis and functionality level. Multimodal Prehabilitation and Comprehensive Geriatric Assessment may improve perioperative functional capacity and decrease postoperative incidents and complications in elderly patients undergoing major abdominal surgery.^[20,23,31] Furthermore, the multidisciplinary structured approach of enhanced recovery after surgery (ERAS) has proven to provide useful guidelines and best available evidence for patients

undergoing abdominal surgery (both elective and emergency laparotomies).^[32]

Designing an ideal, customizable technique for the frail

In the frail patient, the safest anesthesia techniques are those combinations, which are the simplest, least invasive and which are made up of elements that are themselves minor “insults” of very short duration. Perturbations of the sensorium in the frail will often lead an independent individual into postoperative delirium (POD) and postoperative cognitive decline (POCD) from which the person never quite recovers and sends the patient into a dependent, supported environment.^[33]

Surgery must always be limited to the absolute minimum. Nevertheless, there will be emergency situations, which require intervention (e.g., common bile duct obstruction by stone). Also, there are minimally invasive surgeries performed under local anesthesia, e.g., phaco-emulsion of a cataract and insertion of intraocular lens for restoration of sight. With oncological surgeries in the frail, one must carefully measure whether the benefits justify the risk. Once a decision is reached to perform surgery, the anesthesiologist must be prepared to design the ideal anesthetic. Luckily, several “ideal” anesthesia and pain relief packages customizable in “mix and match” fashion for every surgery imaginable in the frail are now available [Figure 1]. Usually, the best anesthesia mixes in the frail are “complete hemodynamic, ventilatory, and vital parameters” techniques using short-acting drugs with minimal “hangover.”^[25] For example, the use of judicious, gradual regional anesthesia combined with controlled, carefully titratable total intravenous anesthesia (TIVA), general anesthesia, is best for emergency, major, and unavoidable surgery.

Many elegant techniques available to the elderly, for example, monitored light sedation, local or zonal anesthesia with

patient-controlled propofol intermittent sedation are not suitable for the frail who may have multi-organ impairment or severe systemic disease.

Regional Analgesia in the Frail Elderly

In the frail elderly, a novel set of considerations and objectives come into force, and ideally, some form of neuraxial or regional anesthesia and analgesia should be at the heart of every anesthesia.^[14,31,32] Even when complete control “general anesthesia,” whether TIVA or inhalational, is used, a neuraxial, regional, peripheral nerve block, infiltration, topical, etc., local anesthesia should either be the main technique or employed as adjunct whenever possible, provided there are no contraindications (e.g., patients using anticoagulants). Because the frail patient decompensates rather quickly, the more vulnerable ones will not tolerate very poorly even short episodes of hypoxemia, hypercapnia, hypovolemia, electrolyte disturbance, cardiac output drops, and metabolic disturbance. This means that the airway should be secured, the patient ventilated, and the hemodynamic parameters controlled aggressively.^[25] Organ perfusion and oxygenation assume prime objective status. Frailty precludes spontaneously breathing techniques if any form of sedation is to be added.

While inhalational anesthesia is not to be excluded entirely, it is to be used for specific indications, for example, smoothing out a TIVA and TCI (target-controlled infusion) during syringe swaps. Many assume that POD/POCD are an effect of poor pharmaceutical choice in the perioperative period.^[31] This may be so in the geriatric medicine setting but, in the operating theatre/recovery room/PACU scenario, it could just as easily be due to hypoxemia or hypotension. Indeed, in the frail postoperatively, the differential diagnosis may have to include hypoglycemia, anemia, hypothermia, electrolyte disturbance,

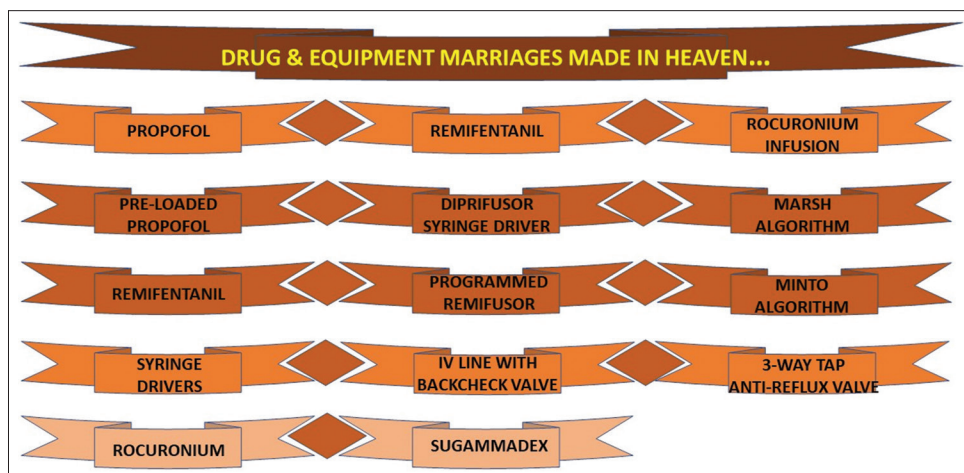


Figure 1: Combinations of drugs, algorithms, equipment, and disposables, which can produce the ideal anesthetic for surgery in the frail patient

hypercapnia, raised intracranial pressure, third space fluid losses, and many other abnormalities (e.g., myxedema and hypothyroidism, liver failure, uremia). In the anesthesia literature, there is increasing evidence that POD is due to neuroinflammation, related to surgery and patient-related factors with the effect of anesthesia *per se* being secondary.

Some regional anesthesia continuous infusion techniques are especially valuable in the frail, for example, the pain buster soaker where a multi-port catheter is placed within the surgical wound and attached to a flow-controlled (5 mL/hr.) high-pressure chamber loaded with local anesthetic, which removes wound pain for 72 hours postoperatively. Patient-controlled devices, so useful for pain relief in aged care, are not the technique of choice for the frail. A potential better solution for frail elderly patients undergoing certain abdominal or thoracic interventions is an operation under segmental thoracic spinal anesthesia,^[34-37] or using specific nerve blocks.^[38]

Postoperative care, even when regional anesthesia is used and the patient is seemingly recovered and stable, must extend for many days in monitored care and have extensive input from intensivists, geriatricians, endocrinologists, renal physicians, nutritionist, and rehabilitation team. The technique of doing an anesthetic and dumping the patient into the care of the surgical team in a standard surgical ward is a recipe for recurrent disaster. The postoperative conditions whether in a PACU, recovery room, ICU, and CCU should involve a monitored bed with competent staff covering both nursing and medical aspects of care. In general, patient-controlled devices, so useful for pain relief elsewhere in surgery for the elderly, are not always the technique of choice for the frail elderly.

Do we need a Standardized, Universal Anesthesia/Analgesia Template for the Frail?

While different surgeries require differing sets of alternatives, a skeleton template for what may be “best practice” for a frail patient, a “coat-hanger” onto which to add or subtract customized, patient- or surgery-specific drugs, variants, modifiers, techniques, and agents, is achievable in much the way as we have ERAS (enhanced recovery after surgery) for other surgical types.^[32] With the frail, there is no “one-size-fits-all.” While the overall intervention should incorporate a vast multidisciplinary team, the anesthetic itself is a “solo activity” achieved by a small team of, at most, 2-3 people. The anesthesia team should assume the role in the perioperative period usually assigned to them but make sure that the pre- and post-interfaces interdigitate with the geriatric, surgical, and other subspecialty teams. Because frail

patients can decompensate very rapidly, the anesthesia and acute care may have to extend beyond the standard limits.^[31]

Monitoring and Drug Delivery Systems

Improvements in monitoring, especially in advanced hemodynamics; closed feedback delivery and highly accurate drug delivery systems; very short-acting, spontaneous molecular breakdown agents, which do not require metabolism by any organ; major neuraxial and regional anesthesia techniques; peripheral nerve or local nerve blocks; and effective reversal agents have made anesthesia safe for frail patients.^[31,32] These anesthesia and pain management techniques are geared to preserve stability or improve functional status; avoid POD and POCD; maintain or improve organ function; and have minimal adverse impacts.

Major neuraxial methods (spinal, combined spinal–epidural, and epidural) have to be accompanied by monitoring advanced hemodynamic beat-to-beat techniques (cardiac output, stroke volume, and stroke volume variation), oximetry, pressure measurements (central venous, arterial, capillary wedge, and pulmonary artery pressure), and ventilation parameters. Immediate action to ensure stability is to be taken for every aberration. Not only is the anesthesia technique itself to be slow, calculated, and smooth; vital parameters themselves are to be treated aggressively in their own right. Titrated, multimodal analgesia combined with sustained hydration, good oxygen delivery to tissues, exquisite augmentation of nutritional needs, and effective analgesia local anesthetic blocks are the ideal package for managing the postoperative period.

Which Drugs are Best in the Frail?

While all pain receptor antagonists are available intravenously, many are not suitable in the frail elderly patient. Our armamentarium provides several opioids for the opiate receptor, ketamine for the NMDA, paracetamol for central COX-3, ibuprofen for the COX, parecoxib for COX-2, and tramadol for the noradrenalin and 5-hydroxytryptamine receptor. Small doses of each agent used additively and synergistically can provide good analgesia with less side effects.^[31,32] Ultra-short-acting agents, which do not require organ metabolism, have short half-lives, and have no active metabolites, are ideal in the frail. Rapid onset and offset, high potency, adjustable duration of action, or reversible agents of 100% efficacy are available in every anesthesia toolkit.

Certain drugs have effect profiles beneficial to the frail and fall into four main groups: a) medications that terminate effect of a drug by having either antagonist vs agonist effect or full agonist vs partial agonist effect, for example, partial

agonist opiates; b) agonist with direct specific reversals, for example, non-depolarizing muscle relaxants (vecuronium–rocuronium) with a direct reversal (sugammadex) agent; c) agents that act on alternative receptors to reduce the need to rely on key receptors (e.g., opiate sparing by ibuprofen, tramadol, and paracetamol) by acting on alternate pain receptors (e.g., 5HT₃, Noradrenalin, COX-2, NMDA); and d) synergistic use of local anesthetics (LAs) in a variety of guises (e.g., intrathecal, epidural, intravenous, in LA local and regional blocks, intradermal, subcutaneous, by transcutaneous patches; or in combinations) to reduce pain while avoiding the use of intravenous, oral or rectal opiates, and other analgesics. There are some blanket exclusions in the frail—avoid benzodiazepines, phenothiazines, and anticholinergic drugs. On the other hand, while the benzodiazepine midazolam, which has widespread use as preoperative sedation adjunct, is undesirable in the frail because it exhibits enterohepatic cycling and has potent active metabolites, the new short-half-life remimazolam, which exhibits spontaneous breakdown without the need for liver or excretion by kidneys, is a superb choice in the frail [Table 1].

The future is even brighter for general anesthesia in the frail, for example, specific antagonist using a propofol analogue, propofol, postsynaptic reversal agent flumazenil for the GABA_A receptor, or physostigmine and neostigmine at the acetylcholinesterase receptor being replaced by presynaptic reversal agents active on such proteins as kinesin and the SNARE complex. It has become easy to predict that the safest place for the poly-medicated, frail elderly with multi-disease will one day be the operating complex. Anesthesia pharmacology is built around potent, efficacious intravenous and inhalational agents, which have been developed over the last 100 years. Drug metabolism is typically altered in the frail elderly patient (reduction in hepatic blood flow and cytochrome P450 system).^[14] All agents must be 100% effective and safe over an infinitely broad range of conditions, disease states, and patient ages. The effectiveness of and ability to use these high-potency, high-efficacy, ultra-short duration drugs is highly dependent on very accurate, calibrated delivery systems dedicated to each individual drug. The operators are, like jet-fighter pilots, superbly trained specialists, multitasking people with intimate knowledge of the potentially deadly drugs and their specific delivery systems and able to deal with all contingencies including misadventure. The frail elderly patient presents the ultimate challenge.

Inhalation agents can be delivered using accurate, calibrated delivery systems

The classic combination of drug—machine—operator in anesthesia for the elderly is the inhalational agent (sevoflurane and isoflurane), the agent-specific vaporizer, and a geriatrics

anesthesiologist.^[32] Inhalational agents, which are also continuously administered drugs delivered and mostly excreted via the airway, especially shorter offset ones, have some applications, albeit limited, in anesthesia for the frail. Inhalational agents have been overtaken by more sophisticated alternatives, for example, propofol target-controlled infusions and TIVA. Because these agents are exceedingly potent and have deadly properties if used inappropriately, they require both accurate delivery equipment and extensive monitoring and measured corrective response systems. There are a number of “marriages made in heaven” when it comes to anesthesia for the frail [Table 2]. This milieu lies the best anesthesia technique for the frailest of our patients requiring unavoidable surgery. Also, this “world” lies the solution to avoidance of postoperative pain and POD/POCD.^[32] Many of the modern agents used for anesthesia are simply no longer there within minutes of cessation of surgery such that drug levels are no longer measurable and there are no by-products or metabolites left to metabolize or excrete.

Table 1: Desirable properties of drugs for the frail patient

- Ultra-short-acting, versatile, and flexible agents, which can be used by continuous, titratable, continuously adjustable intravenous infusion, and, if necessary, using closed-feedback loop technology, which can be terminated at any time with complete recovery with no active metabolites, within seconds, at the anesthesiologist’s discretion.
- Agents that do not require organ metabolism.
- Short half-life agents that break down or cleave spontaneously under normal body conditions.
- Medications without active or with very weak metabolites.
- Agents that can be rapidly cleared.
- Agents that do not need special enzyme systems for breakdown.
- Agents with very rapid onset and offset.
- Agents with adjustable duration of action.
- Agents that can be reversed immediately when combined with a second agent
- Agents whose potency is so high that few “molecules” will produce the desired effect.
- Efficacious drugs, which even when used in high dosage, produce minimal hemodynamic perturbation

Table 2: The ideal drug “marriages” include [Figure 1]

- Drugs with reversal agents to terminate their effect, e.G., Non-depolarizing muscle relaxants producing complete skeletal muscle paralysis (rocuronium, pancuronium) and the reversal agent sugammadex.
- The preloaded propofol syringe when combined with the pre-programmed diprifusor syringe driver loaded with the marsh algorithm.
- The ultra-short-acting, spontaneous breakdown remifentanyl used with the programmed remifusor using the minto algorithm.
- The combination of simultaneous exquisitely controlled infusions of propofol, remifentanyl, and rocuronium to produce total intravenous anesthesia (tiva), which is terminatable within minutes of the end of surgery.
- Multiple syringe drivers used in unison on the same iv line but with backcheck valves and 3-way taps and anti-reflux valves not only the tiva/tci anesthetic but also the multitude of drugs (antibiotics, anticoagulants, analgesics, antiemetics, pressor agents) and replacement and hydration fluids.

Multimodal, titratable analgesia in the frail elderly

In the frail, the debate on which is better: “Regional anesthesia or general anesthesia” is long dead because a combination of the two is usually the most appropriate especially for emergency, major, unavoidable surgery. Many elegant techniques available to the elderly, for example, monitored light sedation, local or regional anesthesia with patient-controlled propofol intermittent sedation, are best avoided in the frail. Instead, a very tightly controlled general anesthesia with advanced monitoring and continuous adjustment of virtually every organ function, plus some form of pain relief both intra- and postoperatively which has zero impact on mentation, mobility, and cognitive functions is best.

Two decades ago, this was not possible. The agents available to us were far too crude and delivery systems were too expensive as well as being clumsy and primitive. Vast improvements in (a) monitoring, especially advanced hemodynamic monitoring; (b) the development of closed feedback delivery and highly accurate drug delivery systems; (c) the emergence of very short-acting, spontaneous molecular breakdown agents, which do not require metabolism by any organ; (d) expansion of an array of major neuraxial and regional anesthesia techniques and peripheral nerve or local nerve blocks to the very limits of applicability; and (e) effective reversal agents such that potent drugs can be rapidly neutralized have ensured that the frail patient can be taken through the most complex surgeries in complete safety.

A brilliant anesthetic can be dismantled by poor management of postoperative pain. Adequate pain relief is vital for the frail elderly patient to recuperate and includes a variety of options, i.e., patient-controlled iv drugs, oral or intravenous paracetamol, COXIBs, NSAIDs, pregabalin, patient-controlled epidural analgesia, and newer techniques, such as extended-release epidural morphine and Pain Buster Soakers.^[39-43] Virtually, all μ -opioid receptor agonists are brilliant pain killers and very effective drugs during surgical interventions, especially the short-acting remifentanyl. These high-potent drugs may have several unwanted side effects and potentially result in severe complications in the postoperative period. Therefore, it is best to opt for non-opioid pain relief in frail elderly patients.

Pain Relief and Frail Elderly Patients

Elderly patients are often undertreated for pain. Pain assessment and treatment is challenging in the elderly, and especially the frail patient with physiological frailty, multi-medical comorbidities, polypharmacy, and cognitive

impairment. Paracetamol is safe to use as first-line pain therapy, whereas cautionary use of non-steroidal anti-inflammatory drugs should be practiced due to the gastric and renal damage it may cause. Morphine and opioids are effective pain killers, although cautious administration must be considered to the elderly (frail) patient with poor renal, respiratory, and cognitive function. However, systemic opioids are commonly prescribed for postoperative pain relief in elderly patients. Frail patients tend to use almost all opioids prescribed in the postoperative period, whereas non-frail patients tend to use much less of the opioids prescribed showing a unique pattern of opioid use after hospital discharge.^[44] This obviously comes with an increased risk for side effects and potentially even opioid misuse. In addition, frail patients are five times more likely to have intrusive pain compared to non-frail elderly, with chronic pain affecting 60-75% of elderly patients, significantly impacting recovery, quality of life, and physical activities. Intrusive pain is common, even three months after surgery, specifically after spine surgery.^[45,46]

Both general and regional anesthesia are useful techniques for frail elderly patients undergoing non-cardiac surgery, although adjustments to age and frailty are essential. However, in some procedures, regional anesthesia is the preferred techniques as general anesthesia showed to be associated with a higher risk of mortality and risk of deep vein thrombosis, whereas there is an association between epidural anesthesia and superior postoperative outcomes.^[31,47] With cardiac and respiratory frailties, loco-regional anesthesia techniques can be a major asset in the management of surgical patients with major medical problems, as it does not affect these organs.^[34,35] However, it is important that in frail patients with reduced adipose tissue and greater sensitivity to local anesthetics, the dose and concentration of local anesthetics need to be reduced, as toxicity depends not only on its total dose but also on its rate of absorption. On the other hand, surgeons may use large volumes (40 to 60 mL) of very diluted local anesthetics to infiltrate a large region of surgery.^[47] There is consistent evidence that the best course of action may be to avoid general anesthesia altogether. Without any doubt, epidural anesthesia is one of the most effective forms of pain relief and reduces opioid consumption. Regional anesthesia (central neuraxial and peripheral nerve blocks) may be supplemented with a variety of analgesic agents, sedatives, or general anesthesia. Theoretical advantages of regional anesthesia include the avoidance of exposure to general anesthesia, and a reduction in airway and pulmonary complications, although they too have specific side effects (e.g., hypotension, hematoma, infections and abscesses, post-dural puncture headache). Of course, the patient has to be willing to undergo regional

anesthesia. This requires adequate explanation and making the patient as comfortable as possible. Frail elderly patients undergoing surgery would benefit from early recognition and treatment of postoperative complications and infections, perioperative monitoring of adequate hydration, nutrition, mobilization and prehabilitation, preventing deconditioning, and improving outcomes.^[20] Neuraxial opioids and specifically spinal or epidural opioids may provide more effective pain relief than systemic opioids in the elderly population. However, intrathecal opioids may be complicated by sedation, pruritus, and respiratory depression, which may mean these patients need higher levels of monitoring.

Anesthesiologists, trained to manage the perioperative care, offer the best outcomes to frail patients, based on the best choice of anesthesia technique, which includes patient preferences, comorbidity, and potential postoperative complications. The preoperative assessment of the frail patient provides a timely opportunity for optimal medical management and optimization of polypharmacy. Drugs such as benzodiazepines, antihistamines, tricyclic antidepressants, and anti-cholinergic drugs have significant disadvantages and their potential benefits of continuing these drugs may need to be balanced against their risks. Optimization of the perioperative care of elderly patients requires a multidisciplinary approach. Multimodal drug therapy utilizes a variety of non-opioid analgesic medications, whereby adjusting the dose prevents adverse effects from opioids, while aiming for maximizing analgesic benefit.^[31] Comprehensive pain protocols adjusted to the frail elderly patients are essential, which includes ultrasound-guided loco-regional blocks and patient-controlled analgesia techniques where possible, providing satisfactory-quality effective anesthesia and postoperative analgesia in the elderly high-risk patient group. Emerging evidence demonstrates that Comprehensive Geriatric Assessment improves postoperative outcomes.^[14]

End-of-Life Discussion in the Frail Elderly Patient

Frail elderly patients, undergoing surgery, often end up in ICU due to prolonged disease, several comorbidities, serious sequelae, and issues with rehabilitation, requiring a long convalescence period. An ICU stay is only one of many steps in a patient's trajectory. Not every ICU stay contributes to improve the patient's quality of life and well-being, and not every patient has a reasonable chance of recovering a meaningful life after ICU stay. If the quality of life of a patient prior to the current acute episode was already very poor due to chronic disease and disability, the risks of survival are considerably reduced and ICU admission is unlikely to be

of benefit.^[4] In a Canadian multi-center prospective cohort study involving 1671 patients (average age 85), one-third of the cohort died in hospital, many after long hospital stays, while continuing to receive aggressive life-sustaining interventions.^[48] The deceased had a median time from ICU admission to death of 10 days, with approximately half dying with aggressive life-saving therapies including mechanical ventilation, renal replacement therapy, and vasopressors. These unfortunate outcomes raise questions about the appropriate use of critical care at the end of life for the very (frail) elderly. In a retrospective *post hoc* analysis of 7817 European critically ill patients (80 years and older), the overall ICU mortality was 27% and the 30-day mortality was 41%.^[49] Biston *et al.*^[50] studied the association between age and survival in the ICU following circulatory shock, treated with mechanical ventilation, vasopressor, and renal replacement therapy. These authors highlighted the poor outcomes of these elderly patients with very few of the old (75-84 years) and very old (≥ 85 years) surviving at six months (21% respectively 8%) and twelve months (8% respectively 3%).

End-of-life-care discussions in the elderly patient are complex and influenced by multiple socio-cultural-religious factors as discussed by intensivists Vincent and Creteur.^[51] Unfortunately, only 12.7% of patients over 80 years were asked if they wanted ICU care or not, demonstrating that elderly patients' wishes are rarely sought.^[52] We all should agree that a) medicine is all about a person's well-being, patient-centered care incorporating the patient's wishes, evaluation of the benefit/harm ratio of any intervention and the patient's condition; b) there is no ethical distinction between withholding and withdrawing life support; c) life support can be discontinued, but never patient care; d) the end of life for every patient should be as natural as possible, without suffering and with dignity; and d) that comfort measures are primordial, which never can be withdrawn.

In conclusion, providing adequate perioperative pain relief in anesthesia is a very important aspect that brings besides care also comfort to the patient. Good pain relief is a human right. Anesthesiologists are experts in pain relief and can apply multiple methods, each adjusted to patient-specific circumstances and needs. Pain relief using medication needs to be adjusted to the vulnerable elderly patient, especially to the frail elderly patient. Surgical interventions may not always be in the best interest of the patient and alternative options need to be discussed with the caring team and the patient. Sometimes, it is in the patient's interest not to operate and provide palliative care, concentrating on good pain relief, making it as comfortable as possible for these very vulnerable and compromised patients.

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