Review Article

Pain control in older adults undergoing video-assisted thoracoscopic surgery

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Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: The older adult patient population is growing, composing a significant portion of those undergoing video-assisted thoracoscopic surgery (VATS). The physiological changes experienced by this population impact every organ system and require advanced understanding and prioritization as they impact pain presentation and the pharmacokinetics of pain medicines. Optimizing preoperative functioning prior to surgical intervention may promote improved pain control in older adults. The approach to pain control perioperatively should be focused on a multimodal approach considering the patient's medical comorbidities. Focus should be placed on cognitive deficits which may act as barriers to recognizing and treating postoperative pain in older adult patients. Understanding the etiology of pain and the unique pain presentation in older adults will guide the assessment of and multimodal pain approach to pain control following VATS. A multimodal approach to postoperative pain control should include analgesics with diverse mechanisms of action such as acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and adjuvant medications. Additionally, pain regimens should consider utilizing regional anesthesia and non-pharmacological pain control approaches to decrease the use of opioids. Throughout the planning, treatment, and monitoring of older adults with postoperative pain following VATS, patients' physiology, and comorbidities must be considered to guide appropriate pain control and avoid unwanted complications.

Keywords: Pain; geriatric; adult; video-assisted thoracoscopic surgery (VATS)

Received: 09 January 2023; Accepted: 14 July 2023; Published online: 24 August 2023.

doi: 10.21037/vats-23-7

View this article at: https://dx.doi.org/10.21037/vats-23-7

Introduction

Background

With the advances in medical care, the standard of living, and education, the world's population is living longer and experiencing increasing rates of chronic disease. As of 2021, those aged 65+ make up 17.1% of the population of the US (1). Higher disease burden brings increased reliance on surgical care, necessitating pain management when compared with the younger population.

Rationale and knowledge gap

There remains a gap in the knowledge of pain control in older adult patients undergoing video-assisted thoracoscopic surgery (VATS) despite their increasing fraction of

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the medical population and increased use of the VATS approach in thoracic surgery. Much of the current practice and guidelines are drawn from studies of younger patients or expert opinions. The challenge is heightened when dealing with acute perioperative pain in a patient following VATS. Distinct from chronic pain in the older adult, the management of acute perioperative pain in the older adult is often met with confusion and misunderstanding.

Objective

The objective of this review is to inform the reader of the approach to pain control in the older adult patient undergoing VATS to avoid complications and undertreated pain and improve outcomes related to pain control. We will review pain control modalities and principles in the acutely hospitalized perioperative patient, emphasizing the older adult patient undergoing VATS. Developing an understanding of pain control in the perioperative patient and the unique physiological characteristic of older adults will frame the conversation to address pain in the older adult undergoing VATS. While chronic pain may impact patients who have undergone VATS, this is not the focus of our review.

Principles and approach to pain control in the older adult undergoing VATS

Preoperative optimization

An area of importance when considering the pain control of the older adult VATS patient, though often disregarded, is the preoperative assessment and optimization of functional status. While chronological age has historically been a focus when assessing perioperative risk, a patient's physiological or biological age, performance status, functional status, and frailty may better assess risk. Frailty, a term used to describe the decline of physiological function, is used as a measure of perioperative risk in older patients. Specifically, frail surgical patients carry an increased risk of adverse events and poor outcomes (2-4) and 68.8% of thoracic surgical patients are prefrail or frail (5). The preoperative performance status score, as defined by the Eastern Cooperative Oncology Group, correlates to the experience of postoperative pain in thoracic surgical patients (6). Patients with low preoperative functioning or frailty benefit from targeted preoperative therapy, a practice commonly seen in cardiac surgery. This therapy focuses on physiologically, psychologically, and physically optimizing patients prior to their surgical experience. In frail patients undergoing VATS, the pain benefit of prehabilitation is not clearly defined though benefits may be seen in the identification and optimization of patients with cognitive disorders to allow appropriate pain assessment perioperatively.

Physiological changes with aging and impact on pain management

The physiological changes in the older adult population impact the pharmacokinetics and pharmacodynamics of analgesic medications, necessitating adjustments to pain control regimens (*Table 1*). Specifically, declining hepatic and renal function results in fewer hepatocytes and a decreased glomerular filtration rate, respectfully. In turn, there is reduced renal reserve to recover from nephrotoxic medications, decreased renal clearance of medications, and impaired hepatic metabolism of drugs (7). From a cardiac standpoint, a decreased cardiac output slows the distribution of drugs throughout the body (8). The slower distribution of the medication to the tissues and organs may be misconstrued as a failure of the medication to work, leading to incorrect redosing or overdosing. Neuropsychologically, this patient population is prone to cognitive impairment, decreased autonomic responses, and a higher risk of delirium (9). Additionally, nerve fibers associated with pain have been shown to decrease and alter with age resulting in varied neuropsychological responses (10,11). Older adults have a diminished respiratory reserve, making them sensitive to the adverse effects of respiratory depressing medications and increasing the risk of respiratory decompensation from pain (8). Lastly, many elderly are frail and have decreased muscular mass, leading to decreased drug volume distribution and absorption of medications given via the transdermal route (8). A heightened understanding of the physiological changes seen with aging is imperative to effectively treating pain in the physiologically compromised patient.

Clinical manifestations of pain in the elderly

The assessment of pain should involve consideration of medical, psychological, cognitive, neuropsychologic, and behavioral factors (12). Understanding the pathophysiological mechanisms of pain is imperative to adequately treating the pain. The three main types of pain include nociceptive, neuropathic, and mixed/undetermined.

Table 1 Physiologic changes and pharmacologic considerations with aging (7-9)

Organ system	Age-related physiologic change	Impact on pain management and pharmacologic considerations
Neurological	Increased prevalence and risk of confusion, delirium, dementia-related disorders	Altered sensation of pain
	Diminished proprioception and autonomic responses	Poor sympathetic response to pain
		Varying pain presentations
Cardiovascular	Decreased cardiac output	Slower distribution of drugs
Pulmonary	Diminished respiratory reserve	Increased risk of respiratory decompensation due to untreated pain
Renal	Decreased glomerular filtration and renal blood flow	Increased of half-life and decreased clearance of drugs renally cleared
		Reduced renal reserve to recover from renally toxic drugs
Gastrointestinal	Slowed gastrointestinal transit time	Lengthen effect of continuous release enteral agents
		Opioid related bowel dysmotility
Hepatic	Decreased arterial hepatic blood flow	Decreased hepatic metabolism
	Fewer hepatocytes	Bioavailability of medications with high first-pass metabolism will be increased
	Oxidation is variable	
	Conjugation usually preserved	
Musculoskeletal	Increased body fat to lean body weight ratio	Increased volume of distribution for fat-soluble drugs, prolonged effective drug half life
	Muscular atrophy	Decreased overall drug volume of distribution to muscular atrophy (higher risk of drug toxicity)

Nociceptive pain may be somatic (i.e., incisional pain) or visceral (i.e., pleuritic pain from pneumonia) and arises from tissue damage or inflammation, stimulating pain receptors (13). Somatic pain is typically described as well localized, constant, aching, and throbbing. Visceral pain is typically diffuse, poorly localized, dull, associated with cramping, and often accompanied by nausea, vomiting, or diaphoresis (14). Neuropathic pain arises from injury or inflammation of the peripheral (i.e., diabetic neuropathy) or central (i.e., cervical radiculopathy) nervous system. Neuropathic pain is typically described as sharp, burning, prickling, tingling, or a "pins and needles" sensation (14). Lastly, pain syndromes classified as mixed and undetermined include fibromyalgia, rheumatic pain, and myofascial pain syndromes (14). This pain syndrome is poorly understood, with no identifiable organ pathology.

The clinical manifestations of pain symptoms in the elderly are multifaceted and require a focused assessment to characterize. The physiological changes seen in aging, such as the decrease in pain fibers, may impact the degree to which pain is perceived, further challenging the pain assessment (10,11). When experiencing pain, the older adult population often does not present with similar complaints as their younger counterparts. Because of common neurocognitive disorders such as delirium and dementia, self-reporting pain can be diminished (15). Rather than reporting pain, cognitively impaired older adults may manifest pain through changes in their mental status or in routine daily activities, such as refusing food or exhibiting socially inappropriate behavior. In addition, they may display pain vocalizations or nonvocal manifestations of pain, such as grimaced facial expressions, body movements pointing to the pain, tense body postures, guarding, or fidgeting.

Older adult patients may underreport the presence of pain despite its actual physical and psychological effect, often believing it is part of the normal aging process (16,17). The fear of additional diagnostic tests, diagnoses,

and polypharmacy all play into patients' reluctance to report pain-related symptoms (17). Many times, this leads to a downplay of symptoms and the use of pain synonyms such as "discomfort" or "aching" versus describing it as pain (University of Iowa Acute Pain Management Guidelines, page 17) (18). Due to the unique presentation and description of this population, soliciting family and caregivers in the care of these individuals is imperative. The complexities of pain manifestation in the older adult necessitate a meticulous assessment and individualized plan for pain management.

Pain assessment

During the initial evaluation of a patient, obtaining a thorough patient history is key to developing a targeted approach to pain control. Focus is placed on the patient's pain symptoms, management history, and past medical history. Understanding chronic pain symptoms will help differentiate between acute and chronic pain symptoms. The medication history will play an integral factor in medication selection. For example, avoiding meperidine or fentanyl use may be prudent in a patient on multiple serotonergic-modulating medications to decrease the risk of serotonin syndrome. Moreover, the patient's past medical history will guide the thought process on the patient's current pain symptomology. The past medical history will provide insight into medical conditions that may be contributing to their pain symptoms and manifestations, ultimately influencing medication management (12).

An initial pain assessment is ideally completed in a controlled setting to allow a thorough review of the patient's medical history. However, in the setting of acute pain, a more abbreviated review may be required to address severe pain rapidly. In this situation, there may not be adequate time to perform a thorough medical and medication review to avoid sequelae associated with untreated pain. The Acute Pain Management Guidelines, outlined by the University of Iowa (18), provide a concise, evidence-based approach to this initial assessment. This initial assessment, at the minimum, should include the following (guideline page 11) (18):

(I) Patients' level of consciousness, including orientation to person/self, time, and location.
(II) Characteristics of pain, including intensity, location, duration, onset, pattern, and quality of pain.
(III) Changes in vital signs, including respiratory status, heart rate, blood pressure, and temperature.

Following the initial assessment, pain history will include patients' current and past pain experiences. For cognitively intact patients, the most accurate pain assessment is the patient's own report. A verbally administered numerical rating scale is the most validated assessment tool to quantify the level of pain (9,12). If a numeric scale is unsuccessful, verbal descriptive scales, pain thermometers, and facial pain scales have been determined to be reliable (guideline pages 12–13) (18). The comprehensive examination includes a thorough physical examination and assessment of functional status. Guided by the history, painful regions should be inspected for inflammation, atrophy, or autonomic signs. The functional evaluation will assess the ability of the patient to perform activities of daily living and post-operative routines (turn, take deep breaths, sleep). A functional pain scale has been shown to be reliable in assessing functional activities (19). Functional pain scales may evaluate changes in pain more appropriately than other tests available (12).

Central to the management of acute pain in the elderly is a cognitive assessment. A self-report may be used in patients with mild to moderate cognitive impairment (20). A brief cognitive screen, such as the 3-minute mini-cog or family/caregiver involvement, can be used to quickly assess cognitive status (21). Verbal patients may be able to prompt pain statements which can be used to identify pain. In patients who can't provide verbal clues to pain, family or caregivers can be a reliable source of information on variations from baseline functioning. Patients can also be observed for unusual behavior such as posturing, resisting care, changing moods, or crying (12). It is important to use clinical judgment to assess potential causes of pain such as infection, incision, or fracture and empirically treat based on assumed pain. Recommendations for patients with severe cognitive impairment include validated pain assessment tools based on behavior, such as The Checklist of Nonverbal Pain Indicators (22) and The Pain Assessment in Advanced Dementia Scale (23). In the critically ill, the Critical Care Pain Observation Tool (CPOT) and Behavioral Pain Scale (BPS) have the highest level of validity and reliability for assessing pain in the cognitively impaired (24).

Medication management

Guiding principles to pain management

Pharmacologically treating pain in older adults is fraught with challenges due to the complexity of considerations in this population. Several evidence-based guidelines have

addressed the complexity in this population and guide the core principles of management (9,18,25). These principles include selecting analgesics based on patient history, utilizing the least invasive route of administration, timing and dose matter, and using a multimodal approach.

First, as discussed in the initial assessment, the patient's past medical history, medication history, and pain history should guide drug selection. Second, the least invasive route of medication administration should be used. Generally, these will be medications administered via the oral route (9). However, due to the onset of most oral medications being 30 minutes to 1 hour, this route may not be adequate for acute, severe pain requiring immediate treatment. When the intravenous (IV) route is used, it should be used as short as possible until pain control is achieved and an oral route can be tolerated. Patient controlled analgesia (PCA) may be selectively used in patients needing prolonged parenteral administration who are cognitively intact. However, routine use of basal dosing should be avoided in opioid naïve patients due to an increased risk of accumulation and toxicity (26,27). Intramuscular and subcutaneous administration are generally avoided due to increased variance in rate and extent of absorption. Transdermal, sublingual, and rectal analgesics are safe alternatives for patients unable to take oral medications, but medication selection via these routes is limited.

Third, medication dosing and timing should be considered. The geriatric medication adage "start low and go slow" should be employed here. Outside of drug-specific dose reductions for hepatic and renal dysfunction, there are few dosing recommendations for older adult patients. Thus, for most scenarios, starting with the lowest effective dose and titrating slowly will help avoid adverse effects of medication dosing. When considering the timing of medication administration, rapid, short-acting medications may be used for episodic pain (guideline page 26) (18). As-needed pain medication, based on an objective pain assessment tool, is appropriate for patients with intermittent pain. Alternatively, around-the-clock administration, with careful monitoring, can be utilized for patients experiencing persistent and predictable pain (guideline page 25) (18). For patients scheduled for known painful procedures or activity, pre-medication should be employed (guideline page 25) (18,27). It is crucial to consider the administration time of scheduled medication as administration can impact daily wake/sleep cycles and be interrupted by scheduled tests or procedures. Consideration of waking patients up while sleeping at night should be discussed to balance the risk of pain versus sleep disturbances which may promote delirium.

Lastly, a multimodal approach will afford the best pain control for patients with moderate to severe pain. For patients with mild-moderate pain, non-opioid analgesics alone are recommended to manage symptoms (guideline page 14) (18). However, in patients with severe pain, the combination of non-opioid or adjuvant with opioid medication may decrease the overall opioid exposure and improve overall pain status (guideline page 31) (9,18,25). A recent retrospective review by Shafeeq and colleagues revealed a significant decrease in postoperative opioid use in older adults, with no difference in mean pain scores, when employing a multimodal approach using IV acetaminophen (28). Multimodal combination analgesia may be initiated pre-operatively to reduce post-operative analgesia requirements in older adults. Several studies have seen this benefit with a single-dose initiation of acetaminophen, gabapentin, celecoxib, and local anesthetic agents (guideline page 25) (18).

Pharmacologic management

Analgesic medications can be categorized into non-opioid medication, opioid medication, and adjuvant therapy. With effective acute pain management, especially in the perioperative setting, older adults experience decreased morbidity and mortality, faster recovery, shorter hospital stays, and decreased healthcare costs (8). The most frequently used medication agents for perioperative pain management in older adults are included in *Table 2*.

Acetaminophen

Acetaminophen is the cornerstone of analgesic therapy. Although not fully understood, analgesic effects are believed to be due to the activation of descending serotonergic inhibitory pathways in the central nervous system (CNS). Acetaminophen is the preferred first-line agent for mild to moderate pain in the elderly. Acetaminophen is especially useful post-operatively as it has fewer side effects than non-steroidal anti-inflammatory drugs (NSAIDs) and does not have antiplatelet effects. There is sufficient evidence that including acetaminophen as part of a multimodal approach reduces opioid consumption (9,28). The maximum daily dose is 4 g per day in most adults, with experts recommending reduced dosing of 3 g per day (9). A maximum weight-based dosing of 75 mg/kg/day should be considered in frail older adults who weigh less than 50 kg (24). Doses exceeding the maximum dose have been associated with acute liver failure. It is imperative to account for all sources of acetaminophen a patient receives, as many

Table 2 Medication considerations in older adults

Medication	Considerations
Acetaminophen	Maximum dose is 4 g daily
	Max dose of 3 g daily in frail older adults (<50 kg)
	Reduce maximum dose 50% to 75% in patients with hepatic insufficiency or history of alcohol abuse
NSAIDs	Avoid use in patients with history of PUD and renal impairment
	Do not use COX-2 inhibitors (celecoxib, meloxicam) in patients with cardiovascular disease or post-op pain management following a CABG
	Ibuprofen and naproxen are preferred nonselective NSAIDs due to lower side effects
	Ketorolac: high potential for adverse gastrointestinal and renal toxicity, do not exceed 5 days of use
Hydrocodone	Manufactured in fixed combination with acetaminophen/NSAIDs
	Consider amount of non-opioid drug in each preparation
Tramadol (IR)	Less potent than many opioids in class
	Less risk of respiratory depression and constipation
	High incidence of nausea/vomiting
	Caution in patients with hepatic and renal disorders
	Avoid in those with risk of seizures
	May enhance the serotonergic effect of serotonergic agents
Oxycodone (IR)	Reduce dose in patients with severe hepatic dysfunction
	Available as preparation with acetaminophen
	Consider total amount of acetaminophen patient is receiving
Morphine (IR)	PO options include tablet and oral solutions
	Avoid in renal dysfunction due to active metabolite, which accumulates in renal dysfunction
	Use with caution with hepatic dysfunction
Hydromorphone (IR)	Use with caution in renal/hepatic impairment
Methadone	Avoid use of long-acting opioid agents in opioid naïve or acute pain
	Use recommended only by practitioners knowledgeable in its pharmacology and experienced in its use
Fentanyl IV	Short duration of action and half-life compared to morphine or hydromorphone
	Avoid in hepatic dysfunction (99% metabolized in liver)
	Safe in renal impairment
	May enhance the serotonergic effect of serotonergic agents
Antidepressants-TCAs, SSRIs, SNRIs	Used for neuropathic pain
	TCAs: significant risk of adverse effects in older patients. Anticholinergic effects (visual, urinary, gastrointestinal); cardiovascular effects (orthostasis, atrioventricular blockade). Avoid use
	Avoid in combination with tramadol or fentanyl
Gabapentinoids	Monitor sedation, ataxia, edema. Recent studies of use in older adults show increasing risk of adverse events. Use with extreme caution
Muscle relaxants	Associated dizziness and somnolence may increase risk for falls in older persons

Table 2 (*continued*)

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Medication	Considerations
Benzodiazepines	Very high risk of delirium and respiratory depression. Avoid use
Lidocaine	Topical (lidoderm 5%): monitor for rash or skin irritation
	IV: monitor for signs of systemic toxicity, metabolized in liver by cytochrome P450
Ketamine	Use cautiously in patients who are opioid dependent or have contraindications to other alternatives
	High rates of psychoperceptual adverse effects
	Slower infusion rates decrease the incidence of adverse events
	Avoid IV push bolus dosing

NSAIDs, non-steroidal anti-inflammatory drugs; PUD, peptic ulcer disease; CABG, coronary artery bypass graft; IR, immediate release; PO, per os; IV, intravenous; SSRI, selective serotonin reuptake inhibitors; SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

combination analgesic products contain acetaminophen. In hospitalized patients, consider dosing every 6 to 8 hours rather than every 4 hours to avoid waking the patient at night.

NSAIDs

Twenty different NSAIDs are commercially available which work by inhibiting cyclooxygenase (COX) and decreasing prostaglandin precursors formation, leading to antipyretic, analgesic, and anti-inflammatory effects. NSAIDs are categorized by their non-selective inhibition of COX-1 and COX-2 receptors or selective COX-2 inhibition. For nonselective NSAIDs, caution must be considered in patients with acute or chronic kidney disease, cardiovascular disease, and patients with a history of peptic ulcer disease or gastrointestinal (GI) bleeding. Hematologic effects associated with prolonged bleeding time and increased risk of hemorrhage also limit the use of nonselective NSAIDs post-operatively. COX-2 inhibitors overcome some of the limitations of NSAIDs in the elderly as they have reduced GI toxicity and hematologic effects. However, COX-2 selective inhibitors maintain renal and cardiovascular side effects, such as acute kidney failure, hyperkalemia, hypertension, heart failure, and peripheral edema. Ibuprofen and naproxen are preferred nonselective NSAIDs with older adults due to their lower side effect profile compared to nonselective NSAIDs (guideline page 30) (18). Ketorolac, a potent IV NSAID, should be used at 50% of the recommended dose in the older adult and for no longer than 5 days. There is some evidence that doses as low as 7.5 mg provide effective pain management (29). Topical NSAIDs have been recommended over systemic NSAIDs by numerous guidelines for managing osteoarthritis and rheumatic disease in the elderly (9,30,31). Despite their use in these disease processes, NSAIDs side effect profile create significant barriers to their use in the perioperative patient. However, with a careful selection of patients, this class of drugs can be very useful.

Opioids

Opioids, administered alongside non-opioid medication in a multimodal approach, are accepted as the first-line therapy for the treatment of acute severe pain. The American Geriatric Society and the University of Iowa treatment guidelines both recommend the use of opioids in both persistent and acute pain management in the elderly population (guideline page 31) (9,18). Opioids exert their effect by binding to mu opiate receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception and response of pain, and producing a generalized CNS depression. For acute pain management, opioids with shorter half-lives are the best choices for older adults (i.e., hydromorphone, oxycodone, or fentanyl). Long-acting preparations should be avoided for the treatment of acute pain. In opiate-naive patients, a dose decrease of 25% to 50% from normal adult dosing is recommended (guideline page 31) (18). In opioid-tolerant patients, an increase in their baseline regimen will be required to treat acute on chronic pain.

The use of opioid medication comes with notable risks. Patients should be monitored closely for respiratory depression, delirium, central nervous system depression, and constipation. A prophylactic bowel regimen to reduce the risk of constipation should be initiated on all patients on opioid therapy unless medically contraindicated. It is important to consider specific contraindications

to individual opioid medications based on patient comorbidities. In patients with renal impairment, morphine should be used cautiously, and meperidine should be avoided due to the accumulation of active metabolites. Tramadol is less potent relative to other available opioids in the class and causes less respiratory depression and GI motor dysfunction. Partial or mixed agonist-antagonist opioids should be avoided due to neuropsychiatric adverse effect profiles (hallucinations, delirium, and agitation) in older adults (guideline page 35) (18).

Adjuvant medications

Several medications have been studied as a part of a multimodal approach in acutely ill patients. Drug classes include gabapentinoids, antidepressants, muscle relaxants, benzodiazepines, corticosteroids, topical analgesics, and ketamine. However, with the exception of ketamine and topical analgesics, all are considered potentially inappropriate in the America Geriatric Society Beers Criteria (32).

Gabapentenoids are among the most studied drugs, with recommendations from major guidelines (guideline page 39) for pre-operative use, multimodal use in opioid-tolerant patients, and neuropathic pain (9,18,27). However, mounting evidence is questioning their effectiveness. Recent studies show no difference in postoperative pain and an increased risk of dizziness and visual disturbances when used as part of a multimodal approach (33). Similarly, Park and colleagues performed a propensity-matched study looking at the association of perioperative gabapentin with in-hospital adverse clinical events in over 967,547 older adults after major surgery and found gabapentin use was associated with an increased risk of delirium, new antipsychotic use, and pneumonia among older patients after major surgery (34).

Topical local anesthetic analgesics (ex: lidocaine 5% patch) are effective and recommended in neuropathic pain symptoms, procedural symptoms, and rib fractures (9,18,28,35). When administered for the treatment of rib fractures, lidocaine patches and opioid medication decrease the overall opioid requirement in admitted patients with rib fractures compared to patients who only receive opioid pain medication (35).

Ketamine is a non-competitive N-methyl-d-aspartate (NMDA)/glutamate receptor complex antagonist that decreases pain by diminishing central sensitization. Ketamine is recommended to be considered as a component of multimodal analgesia in the general adult population for perioperative and opioid-tolerant patients (24,26,36). Notable short-term adverse effects of IV ketamine include hemodynamic instability, emergence reactions, respiratory depression, drug-induced liver injury and increased cerebrospinal fluid pressure (36,37). The most common and medication-limiting adverse effects are the neuropsychological manifestations, with labeled contraindications limited to patients who can not tolerate significant elevations in blood pressure and those with known hypersensitivity to ketamine (37). Few studies have evaluated ketamine for acute pain solely in the elderly population. In a prospective, randomized, double-blind trial, Motov and colleagues compared the analgesic efficacy and safety of sub-dissociative IV ketamine short infusion (0.3 mg/kg) with morphine (0.1 mg/kg), in patients aged 65 and older. Analgesic efficacy was comparable between the groups, though patients in the ketamine group had higher rates of psychoperceptual adverse effects (38). Reducing the infusion rate may decrease the incidence of these adverse events (36).

Interventional approaches in the perioperative patient

Interventional approaches to pain control are an important aspect of the multimodal pain regimen in the postoperative older adult patient. Local anesthetic-based therapy is the mainstay of interventional methods targeting acute pain control in the perioperative period. The location of administration of local anesthetic varies, targeting the epidural and paravertebral spaces, peripheral nerves, and peri-incisional tissues. Local anesthetic may be administered as a bolus or via continuous catheter administration to allow for PCA. In the patient undergoing a thoracotomy or VATS, thoracic epidural anesthesia (TEA) has historically been the standard of pain control in open procedures for its improved pain control with minimal systemic side effects (39,40). Both local anesthetic and opioid-based medication are used in TEA, creating an additive analgesic effect and avoiding the adverse effects seen with a singular medication. TEA is contraindicated in patients on anticoagulation or with systemic infection as they are at high risk for infection and spinal cord compressive neuraxial hematoma formation that can have devastating effects.

Thoracic paravertebral block (TPVB) has also been shown to decrease pain in patients undergoing thoracotomy and often is chosen over TEA for open and minimally invasive surgery due to the improved complication profile and similar acute pain control as TEA (41). The serratus anterior plane block has been shown to improve both subjective pain and performance on incentive spirometry in

the immediate perioperative period in patients undergoing VATS compared to IV and oral opioid medications alone (42) and improved pain alongside opioid PCA when compared to PCA alone (43). In the VATS Enhanced Recovery After Surgery (ERAS) protocol proposed by Piccioni *et al.*, TPVB is recommended as the first line for VATS procedures, with other peripheral interventional methods as the second line if TPVB is not feasible (44). As of 2019, the ERAS protocol after lung surgery reports a high level of evidence for regional anesthetic techniques during thoracic surgical procedures and provides a strong recommendation for their use (45). Finally, single-injection intercostal nerve blocks decrease opioid reliance postoperatively compared to systemic opioid-based pain regimens but are non-inferior to TEA and inferior to TPVB, according to a meta-analysis by Guerra-Londono and colleagues (46). While these approaches show improved outcomes and patient subjective pain scores, pain that is not covered in the dermatomal distribution covered by epidural, paravertebral, or peripheral blocks, such as referred pain from the diaphragm, or visceral pleural pain, will require additional systemic pain control or an interscalene block.

Despite the proposed benefit of regional anesthesia techniques on pain control in patients undergoing VATS, complications such as rebound pain, pneumothorax, and nerve injury should be recognized and considered. Rebound pain is a well-recognized but understudied complication of these techniques, especially in the VATS population. Rebound pain is the experience of severe acute pain following the resolution of a peripheral anesthetic block. While the underlying pathophysiology is poorly understood, up to half of patients who receive a peripheral nerve block in the ambulatory setting may experience rebound pain, with younger age being a risk factor for experiencing rebound pain (47). With the use of ultrasound guidance for paravertebral and peripheral blocks, the incidence of pneumothorax and nerve injury has plummeted. One prospective study of 1,427 thoracic paravertebral injections placed via ultrasound guidance showed no occurrences of pneumothorax or pleural injury (48). Despite the aforementioned considerations, local anesthesia and sedation have been shown to be safe in patients undergoing VATS (49).

Utilizing interventional approaches with local anesthetic medication can avoid complications seen with other methods of pain control in the perioperative patient and must be considered in the older adult population. Targeted pain management in the postoperative VATS patient can decrease the cardiopulmonary risk seen with general anesthesia in high-risk patients such as frail older adults. For example, thoracoscopic procedures using local anesthetic blocks and sedation allow the surgeon to perform procedures through less physiological stressing means for patients. These approaches are effective for patients undergoing VATS and are stable from a cardiopulmonary standpoint (50). In older adult patients requiring targeted peripheral pain control, a serratus anterior plane block is an appropriate adjunct to a multimodal pain regimen (51). When comparing TEA to opioids administered systematically via systemic IV, TEA provides improved pain control and postoperative pulmonary function (52) and improved quality of life scores (53) following lobectomy. The specific approach or choice of block requires consideration of the overlying anatomy. For instance, prior interventions, scars, or overlying infections should be considered when planning an interventional pain approach.

As the use of local anesthetics for pain prevention and control increases, an awareness of the adverse effects of interventional techniques and specific contraindications to their use is key. One of the most devastating adverse effects is local anesthetic systemic toxicity (LAST), which can lead to cardiac arrest. This iatrogenic complication may disproportionately impact the older adult patient as they are an increasing proportion of the surgical population. This population is also at increased risk of LAST, especially those with liver and cardiac disease (54) and those of low weight or with sarcopenia (55). Another consideration when choosing an invasive approach to pain control in the older perioperative patient is the use of therapeutic anticoagulation, which is a contraindication to epidural approaches due to the risk of neuraxial hematoma formation. A patient's hemodynamic status must be evaluated when using epidural anesthesia, as it can cause hypotension. Reducing potential complications of interventions and medications should be a priority when caring for older adult patients.

Non-pharmacological pain control in the perioperative patient

Non-pharmacological pain control benefits are well-documented for chronic pain and are recommended in the multimodal approach to acute pain control by multiple national societies (56). Multiple modalities have been used to manage postoperative pain and can act as adjuncts to a multimodal approach to pain control, including manual

therapy (osteopathic manipulative treatment, physical therapy, massage) and acupuncture-assisted anesthesia. Studies evaluating nonpharmacological/noninvasive approaches to pain control in older adult patients undergoing VATS are lacking, but these approaches show promise as another adjunct to decrease perioperative pain, as evidenced by initial studies on similar populations. A recent study of cardiac surgery patients suggests osteopathic manipulation may decrease pain (57). Similarly, acupuncture-related modalities have been implicated in improved pain control in the postoperative period for thoracic surgical patients. Recently, transcutaneous electrical acupuncture stimulation (TEAS) was compared to a sham TEAS group in patients with lung cancer undergoing general anesthesia for resection (58). The study found improved pain scores based on a visual analog scale and decreased postoperative nausea and vomiting (PONV) scores compared to the sham group (58). Additionally, TEAS has been shown to positively impact postoperative cognition in older adult patients undergoing single-port VATS (59). Similarly, TEAS with peripheral nerve blocks shows promise as an adjunct to pain control and reduction of PONV in older adults (60). As more prospective muti-center studies and metanalysis are completed, additional evaluation of incorporating this modality in the multimodal approach is required (61). While not all of the referenced literature targets the older adult population undergoing VATS, a large portion of the participants are adults greater than 65 years old. Further exploration into the impacts of non-pharmacological therapies on pain control in older adults undergoing VATS is required for stronger recommendations.

Strengths and limitations

The growing body of evidence on the impact of frailty in the surgical patient has brought awareness to the problem of pain control in older adult patients in the perioperative period. The use of preoperative frailty evaluation and functional optimization in conjunction with the development of ERAS protocols has promoted more thoughtful approaches to pain management, often benefiting the older adult surgical patient undergoing VATS. Additionally, improving knowledge of the physiology of aging allow for specific recommendations for the treatment of acute postoperative pain. The review of invasive approaches and non-pharmacological treatments promotes a multimodal approach to addressing pain. These aspects contribute to the strengths of this review. The relative paucity of scientific studies on pain control in the older adult surgical population, much less the older adult undergoing VATS, limits the strength of recommendations within this review. As described throughout the review, much of the pain control management in this population is guided by expert opinion, knowledge gained from other specialties, or by studies including a younger, healthier population without the degree of physiological burden. Further prospective, randomized studies comparing pain control regimens and approaches in older adult surgical patients and those undergoing VATS are required. While this review focused on acute postoperative pain control in older adults with an emphasis on patients undergoing VATS, we do not provide a comprehensive review of all aspects of pain control in the older adult, such as chronic pain, non-surgical pain, and pain from other surgical procedures.

Conclusions

The physiological changes and frailty observed in the aging person necessitate a specific approach to pain management in older adults who undergo VATS. This review can be summarized by four guiding principles for treating acute perioperative pain in older adults undergoing VATS.

(I) Frailty, commonly seen in older adults, decreases the ability to withstand adverse events and impacts drug pharmacokinetics, necessitating adjustment of drug dosing. Frailty should be identified preoperatively and addressed as needed through therapy and medical optimization prior to the procedure.

(II) Older adult patients often exhibit pain in non-classical ways when compared to younger patients but should be treated for pain as vigorously as younger populations.

(III) When choosing a pharmacological regimen for acute pain, select analgesics based on patient history, utilize the least invasive route of administration, adjust the timing and dose based on specific patient characteristics, and use a multimodal approach.

(IV) All options for pain control in the perioperative patient should be explored, including local anesthetic blocks and non-pharmacological pain control methods, as clinically appropriate.

Acknowledgments

We would like to recognize and thank Gregory Sinos, CRNA for evaluating this paper.
Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Video-Assisted Thoracic Surgery* for the series "VATS in Older Adults". The article has undergone external peer review.

Peer Review File: Available at https://vats.amegroups.com/article/view/10.21037/vats-23-7/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://vats.amegroups.com/article/view/10.21037/vats-23-7/coif). The series "VATS in Older Adults" was commissioned by the editorial office without any funding or sponsorship. MK served as the unpaid Guest Editor of the series and serves as an unpaid editorial board member of *Video-Assisted Thoracic Surgery* from April 2022 to March 2024. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/vats-23-7
Cite this article as: Amoateng R, Zeller M, Katlic M. Pain control in older adults undergoing video-assisted thoracoscopic surgery. Video-assist Thorac Surg 2023;8:32.