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Masterthesis / Review

Procedural sedation in the elderly: a narrative review

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Abstract

Background: **There is a growing need for anaesthesia care tailored to elderly patients, particularly as more elderly individuals undergo medical procedures requiring anaesthesia. However, clinical trials focused explicitly on this demographic remain limited, with many prospective studies excluding elderly patients, hindering progress in identifying optimal anaesthesia practices for this group.**
Objective: **This narrative review aims to consolidate recent evidence on procedural sedation in elderly patients, focusing on the safety and efficacy of new and existing anaesthetic agents.**
Method: **A systematic search of EMBASE and MEDLINE was conducted, covering studies published between January 2000 and March 2024. The review included randomized controlled trials (RCTs), systematic reviews, and meta-analyses examining various sedation strategies for patients over 65 years old, assessing outcomes such as recovery time, perioperative cardiopulmonary adverse events, delirium, and cognitive dysfunction.**
Results: **The review provides an overview of various sedation strategies and their impact on elderly patients. Propofol offers faster onset and higher sedation success but carries a risk of adverse effects. Newer agents like remimazolam and dexmedetomidine show promising safety profiles, particularly in reducing cardiopulmonary adverse events and cognitive dysfunction. The combination of lidocaine and propofol for sedation in endoscopic procedures has shown promising results, allowing for lower propofol doses while retaining sedative efficacy and reducing hypoxia. High-flow nasal cannula (HFNC) oxygen therapy consistently shows a positive impact on oxygenation during gastrointestinal endoscopy.**
Conclusion: **This narrative review provides an overview of recent trials on procedural sedation in elderly patients, highlighting the need for further research to validate outcomes and guide improvements in geriatric anaesthesia care.**

Keywords: **Conscious Sedation, Deep Sedation, Aged, Geriatric Anaesthesia.**

Introduction

Procedural sedation, also known as conscious sedation, is a medical technique used to induce a state of calm or sleep, alleviate anxiety, and provide analgesia during diagnostic or therapeutic procedures. This technique aims to achieve a lighter level of sedation than general anesthesia, allowing the patient to maintain protective reflexes, airway patency, and responsiveness to verbal commands or light stimulation. Procedural sedation is commonly used in settings such as endoscopy, minor surgical procedures, and various diagnostic imaging procedures, providing patients with comfort while ensuring their safety and cooperation.

The ageing global population is accompanied by an increasing demand for anaesthesia care tailored specifically to the elderly. As of early 2023, approximately 2.3 million Belgians were aged 65 or older, representing nearly 20% of the population. The Belgian Federal Planning Bureau projects this share to surpass 25% by 2050[1]. As life expectancy rises, more older patients are undergoing medical procedures requiring anaesthesia, presenting unique challenges due to their distinct physiological and pharmacological profiles. Geriatric patients, often defined as those 65 years and older, exhibit variations in drug metabolism and organ function, significantly affecting the dynamics of anaesthesia[2].

The growing prevalence of comorbid conditions in this demographic amplifies these challenges, influencing anaesthesia's effectiveness and safety.

Despite the well-documented physiological changes associated with ageing, there is a scarcity of clinical trials focused explicitly on the elderly, often excluding them from prospective studies that could provide valuable insights into optimal anaesthesia practices for this group[3]. Research has shown that elderly patients are more susceptible to the adverse effects of anaesthetic drugs, such as increased risk of hypotension during sedation and a higher incidence of postoperative delirium and cognitive dysfunction[4]. Retrospective studies also suggest that short-term mortality rates are elevated in elderly patients undergoing procedural sedation compared to younger individuals, yet the direct impact of anaesthesia on this mortality is not fully understood[5].

Age-related physiological changes significantly influence how elderly patients respond to sedation. These changes include a decline in cardiac output, reduced renal and hepatic function, decreased respiratory reserve, and altered body composition, all of which affect the pharmacokinetics and pharmacodynamics of anesthetic drugs. As a result, careful consideration and adjustment of anesthetic dosages are necessary to avoid adverse effects like prolonged sedation and increased drug sensitivity.

Several pharmacological agents are commonly used for sedation in elderly patients, each with specific considerations. Midazolam is a benzodiazepine known for its anxiolytic, amnestic, and sedative properties, but elderly patients are more susceptible to its sedative effects, which can lead to prolonged sedation and a higher risk of postoperative cognitive dysfunction (POCD). Propofol is widely used for its rapid onset and short duration of action, but elderly patients require lower doses due to increased sensitivity, and careful monitoring is needed to prevent hypotension and respiratory depression. Dexmedetomidine, an alpha-2 adrenergic agonist, provides sedation without respiratory depression. It has a longer onset and recovery time, which can be beneficial for certain procedures but requires cautious use in elderly patients due to potential bradycardia and hypotension. Remimazolam, a new ultra-short-acting benzodiazepine that acts as a GABA-A receptor agonist, offers rapid onset and swift recovery. Its recent development calls for thorough evaluation of its safety in sedating elderly patients, particularly for short-term medical procedures.

Given the complexities and potential risks associated with sedating elderly patients, a narrative review is essential to consolidate current evidence and evaluate the safety and efficacy of new and existing anesthetic agents like remimazolam. This review aims to enhance understanding and guide improvements in procedural outcomes and quality of care for these patients by focusing on the safety and efficacy of commonly used pharmacological agents, including the newly developed remimazolam. By evaluating the existing literature, this review seeks to provide insights into best practices and guide improvements in the management of sedation in elderly patients, ultimately enhancing procedural outcomes and quality of care.

Methods

The literature search was conducted using EMBASE and MEDLINE. We used the following search term: ('geriatric anesthesia' OR 'frail elderly' OR 'aged' OR 'geriatric') AND ('conscious sedation' OR sedation OR 'procedural sedation' OR 'monitored anesthesia care').

The study selection was conducted by a single reviewer over a period spanning December 2023 to March 2024. The review included only RCTs, systematic reviews, and meta-analyses published between January 2000 and March 2024, assessing sedation strategies in patients over 65 years, with outcomes such as recovery time, perioperative cardiopulmonary adverse events, delirium, and cognitive dysfunction. Studies involving painless procedures or where sufficient analgesia was provided through topical, loco-regional, or neuraxial methods were considered. Studies focusing on patients under general anaesthesia, including participants younger than 60 years, or concerning postoperative sedation and mechanical ventilation were excluded.

Results

A systematic search of the literature was conducted. A detailed flowchart of the study selection, aligned with PRISMA criteria, is presented in Figure 1. A total of 127 studies were initially identified as potentially relevant based on title and abstract screening. Following a full-text review, most studies (n = 29) were excluded due to a lack of specific focus on elderly patients, as they included participants younger than 60 years. An additional substantial group of studies (n = 25) was excluded because their primary focus was on surgical outcomes and complications, rather than sedation practices or cognitive effects in the elderly and lacked available anesthesiologic data. The 41 included studies comprised 40 randomized controlled trials (RCTs) and one meta-analysis. No systematic reviews were identified.

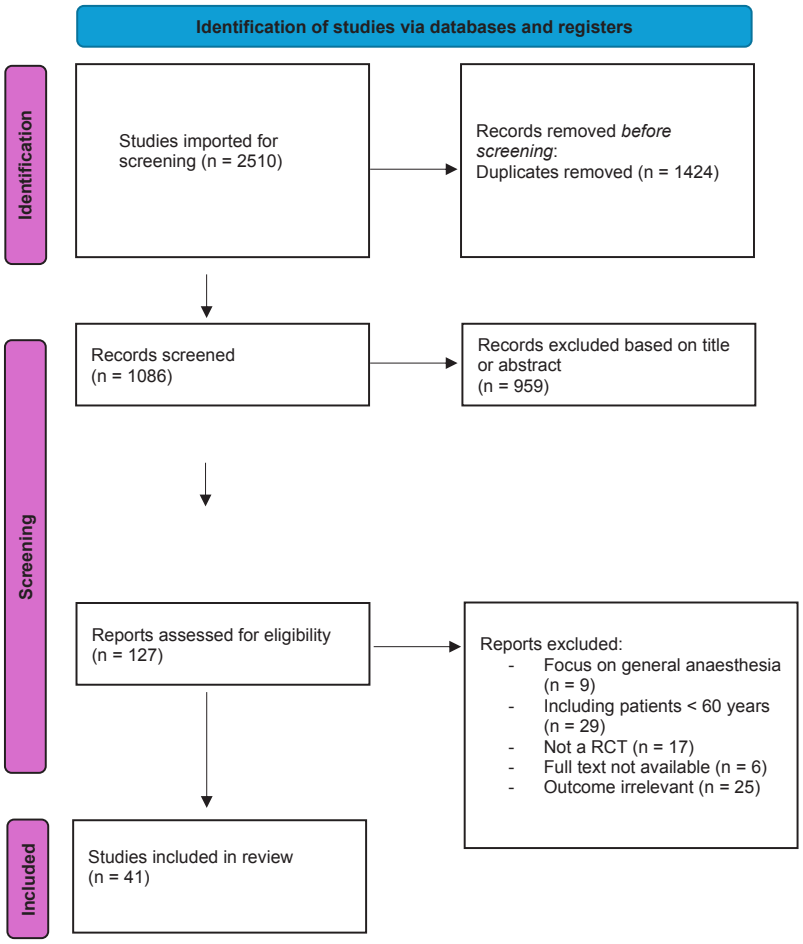

Fig. 1 — PRISMA Flow chart.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Procedural Adjuncts and Techniques

1. Lidocaine

Several studies have demonstrated that adding intravenous lidocaine (1.5 mg kg^{-1}) to propofol-based sedation during gastroscopic procedures can effectively reduce the required propofol dose (Table I)[6–10]. Four studies showed that the total propofol dose needed to maintain adequate sedation was significantly lower in the lidocaine group[6,8–10]. Regarding respiratory outcomes, two studies reported a reduced risk of desaturation in the lidocaine group, although three studies found no significant differences in hypoxia rates[6,8]. Hypotension was generally similar between groups, with only one study indicating a notable difference[10].

2. High-Flow Nasal Cannula (HFNC) Oxygen Therapy

HFNC showed positive effects on oxygenation in elderly patients undergoing endoscopic procedures with propofol sedation. Two studies examined this approach[11,12]. Zhang et al. compared HFNC with standard nasal cannula (NC) during gastroscopy, reporting significantly lower hypoxia rates in the HFNC group: 12.2% for FiO_2 100% and 14.6% for FiO_2 50%, versus 30.1% with NC ($P < 0.05$). Similarly, Lee et al. found that HFNC at FiO_2 50% reduced hypoxia incidence during ERCP compared to NC (4% vs. 13%, $P = 0.031$).

2. Nebulized Lidocaine

In the single study identified, Watts et al. found that using nebulized lidocaine with alfentanil in elderly bronchoscopy patients reduced coughing and the need for additional oral lidocaine sprays, improving comfort and procedural tolerance without affecting respiratory stability[13].

4. Magnesium

The addition of magnesium sulfate (40 mg kg^{-1} IV) to propofol-based sedation for endoscopic retrograde cholangiopancreatography (ERCP), has been shown to significantly reduce the total propofol dose needed. In a study by Chen J. et al., magnesium reduced the propofol dose by 21.4% compared to saline, with a notably lower risk of respiratory depression (0% vs. 15% in the control group) and no increase in bradycardia or hypotension[14].

Table I. — Lidocaine vs. placebo added to propofol sedation.

Study	Type	Year	N	Age (years)	Surgery	All patients	Lidocaine Bolus	Lidocaine infusion	Total propofol Dose (mg)	Results in the Lidocaine group vs control
Breazu et al. [6]	RCT	2022	83	C: 72.6 L: 74.7	ERCP	Propofol 1mg kg^{-1} 10-20 mg boluses	1.5 mg kg^{-1}	None	C: 214.9 L: 135.4 P=0.001	* Lower incidence of hypoxia (<94%) (0% vs 33.3%; P=0.001) * Shorter recovery time (6.3 vs 11.3 min; P=0.001)
Chen M. et al. [47]	RCT	2020	79	C: 71.4 L: 70.4	Colonoscopy	Propofol 1.2 mg kg^{-1} Sufentanil 2.5 µg	1.5 mg kg^{-1}	4 mg kg^{-1} h^{-1}	NS C: 136.8 L: 122.4 P=0.06	* Lower additional dose (69.9 vs 51.5 mg; P=0.039) * Less additional boluses (2.1 vs 1.4; P=0.003) * NS difference in total propofol dose, oxygenation and MAP
Hu S. et al.[8]	RCT	2022	140	C: 70.7 L: 71.5	Gastroscopy	Propofol 1.5 mg kg^{-1} 20-30 mg boluses	1.5 mg kg^{-1}	4 mg kg^{-1} h^{-1}	C: 127.0 L: 107.3 P<0.001	* Lower incidence of hypoxia (12.9% vs 27.1%; P=0.035) * Shorter recovery time (1.9 vs 2.8 min; P<0.05)
Li et al. [9]	RCT	2022	87	C: 69.0 P: 69.0	Colonoscopy	Propofol 1 mg kg^{-1} 0.5 mg kg^{-1} boluses Sufentanil 0.1 µg kg^{-1}	1.5 mg kg^{-1}	2 mg kg^{-1} h^{-1}	C: 115.6 L: 100.3 P=0.008	* Faster loss of consciousness (40 vs 55 s; P<0.0001) * NS difference in airway modifications, time to awakening, pain, endoscopists' and patients' satisfaction scores, awareness and adverse events.
Tang et al. [10]	RCT	2024	64	C: 68.1 L: 69.1	Gastroscopy	Propofol 1.5 mg kg^{-1} 0.5–1.0 mg kg^{-1} boluses Sufentanil 0.1 µg kg^{-1}	1.5 mg kg^{-1}	None	C: 77.3 L: 56.6 P<0.001	* Less hypotension (<80% baseline MAP) (19.4% vs 42.4%; P=0.047)

/: not reported, C: Control group, L: Lidocaine group, NS: No significant difference, P: Propofol.

Propofol

Propofol, commonly used as the standard hypnotic agent, also served as the control in most studies reviewed. While propofol's dosing effects on cognitive outcomes like postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) have been examined, research on propofol dosing and its cardiopulmonary effects specifically in elderly patients is currently limited. Sieber et al. reported no significant difference in POD between light and deep propofol sedation during hip fracture repair (39% vs. 34%, P = 0.46), suggesting sedation depth may not strongly influence delirium[15]. Similarly, Mayr et al. found no significant differences in POCD between general anesthesia and propofol-based sedation in TAVI patients, highlighting comparable cognitive safety[16]. These findings suggest that propofol's impact on cognitive function may depend more on procedural context than on sedation depth, yet further research on cardiopulmonary safety is needed.

Remimazolam

In 2024, a meta-analysis by Ahmer et al. included seven out of nine studies we identified, focusing on remimazolam[17] (Table II). This study encompassed seven RCTs with a total of 1,466 patients comparing propofol and remimazolam sedation during gastroscopy and colonoscopy[18–24]. Both sedatives were administered as boluses: propofol at a dosage of 1-2 mg kg-1 and remimazolam at 0.10-0.20 mg kg-1.

The analysis revealed that propofol led to a quicker loss of consciousness and higher initial sedation success. Conversely, remimazolam was associated with a lower risk of bradycardia, hypoxemia, and injection site pain. There were no significant differences in the incidence of hypotension, postoperative nausea and vomiting (PONV), recovery time, or time to discharge.

There was only one trial involving remimazolam that did not compare it to propofol. In a study by Wu et al. sedation with remimazolam during bronchoscopy was compared to midazolam[25]. Adequate sedation was more likely after a single dose of remimazolam. Specifically, the midazolam group required additional doses of propofol to reach adequate sedation significantly more often (60.4% vs. 34.8%, P=0.013). There were no statistically significant differences between the two groups regarding adverse events, induction times, or recovery durations.

Remifentanil

Two studies comparing dexmedetomidine and remifentanil for perioperative sedation suggest that dexmedetomidine may provide respiratory advantages (Table III). Kaya et al. found that during cataract surgery with a peribulbar block, dexmedetomidine led to fewer respiratory side effects and higher oxygen saturation levels than remifentanil, without significant differences in hemodynamic stability[26]. Lee et al. similarly observed higher oxygen desaturation rates in the remifentanil group during vertebroplasty (35.1% vs. 13.2%, P = 0.026), while blood pressure and PACU stay durations were comparable[27]. These findings indicate that dexmedetomidine may offer improved respiratory stability over remifentanil, with similar hemodynamic profiles.

Dexmedetomidine

Evidence suggests that incorporating a dexmedetomidine loading dose during propofol sedation in elderly patients can reduce propofol requirements and improve sedation quality, though effects on hemodynamic stability and recovery times vary across studies.

In all three studies examining the addition of a dexmedetomidine loading dose (0.4–0.5 $\mu g\ kg^{-1}$) during propofol sedation, a consistent finding was a reduction in the total propofol dose needed to reach target sedation levels, indicating dexmedetomidine's sedative-sparing effect (Table IV)[28–30]. Chen et al. reported that adding dexmedetomidine in ERCP reduced hypotension and hypoxia requiring airway intervention, without affecting emergence time, which highlights its potential benefit for respiratory stability[28]. However, Yin et al., in a gastroscopy study, noted that although dexmedetomidine lowered hypoxia risk, it increased the incidence of bradycardia and hypotension and led to prolonged recovery time[30]. Meanwhile, Ergenoglu et al. observed faster recovery with dexmedetomidine in elderly patients with end-stage renal disease (ESRD) undergoing hip fracture surgery, suggesting that patient-specific factors, such as comorbidities, may influence dexmedetomidine's effects on recovery times[31].

When directly compared with propofol in studies across different surgical contexts, dexmedetomidine consistently demonstrated cognitive advantages. Three studies involving patients under locoregional or neuraxial anesthesia found that dexmedetomidine not only reduced the incidence of postoperative delirium (POD) but also supported quicker ambulation and earlier discharge, suggesting a favorable recovery profile (Table V)[32–34]. Mei et al. highlighted that dexmedetomidine-sedated patients had higher Mini-Mental State Examination (MMSE) scores on postoperative days

Table II. — Remimazolam vs. propofol sedation in gastrointestinal endoscopy.

Study	Type	Year	N	Age (Years)	Surgery	Both groups	Propofol Dose (mg)	Remimazolam dose (mg)	Results RT group
Ahmer et al. [17]	meta-analysis	2024	1466	/	Gastroscopy Colonoscopy	/	Study-specific	Study-specific	* Less bradycardia, hypoxemia, and injection pain * Slower onset and lower sedation success * NS difference: Sedation time, supplemental doses, procedure time, time to discharge and time to recovery
Guo J. et al. [18]	RCT	2022	82	RT: 70.4 P: 69.1	Gastroscopy Colonoscopy	Alfentanil 5 μg kg^{-1}	1.5 mg kg^{-1} 0.5 mg kg^{-1} boluses	0.15 mg kg^{-1} +0.05 mg kg^{-1} boluses	* Less respiratory depression (2/39 vs 9/38, P=0.026) * Less hypotension (6/39 vs 17/38, P=0.005) * Slower onset (time to LOC 20.7 ±6.1s vs 13.2 ±5.2s, P<0.001) * NS difference in recovery time
Hu B. et al. [19]	RCT	2022	346	P: 69.9 RT: 70.1	Gastrocopy	Sufentanil 0.1 μg kg^{-1}	1.5 mg kg^{-1} 0.5 mg kg^{-1} boluses	0.20 mg kg^{-1} + 0.07 mg kg^{-1} boluses	* Less respiratory depression (9.8% vs 17.9%, P=0.042) * Less hypotension (32.4% vs 50.9%, P=0.001) * Slower onset, longer recovery
Liu X. et al. [20]	RCT	2021	260	RT: 68.9 EP: 69.1	Colonoscopy	Fentanyl 0.5 μg kg^{-1}	0.1 ml kg^{-1} Etomidate-Propofol (20mg/10ml etomidate +100 mg/10ml propofol)	0.15 mg kg^{-1}	* Faster recovery * Slower onset * NS difference in hypotension or respiratory depression
Liu F. et al. [21]	RCT	2023	216	RT: 67.6 P: 67.5	Gastroscopy Colonoscopy	Sufentanil 5 μg	1.5 mg kg^{-1}	0.10 mg kg^{-1}	* Less moderate hypoxemia (2.8% vs 17.4%, P<0.001) * Higher median SpO_2 (98% vs 96%, P<0.001) * Less hypotension (2.8% vs 12.8%, P=0.006) * More supplemental doses (P=0.014) * NS difference in severe hypoxemia, mild hypoxemia, PONV or prolonged sedation
Lu et al. [22]	RCT	2022	400	RT: 70.6 P: 70.1	Gastroscopy	Fentanyl 50 μg	3000 mg h^{-1}	300 mg h^{-1}	* Less Respiratory Depression (4.5% vs 10.0%, P=0.034) * Less hypotension (36.5% vs 69.6%, P<0.001) * NS difference in onset or recovery time
Tan et al. [23]	RCT	2022	99	RT: 66.4 P: 66.2	Gastroscopy	Lidocaine 200 mg Butorphanol 0.01 mg kg^{-1}	1.0–1.5 mg kg^{-1}	RT 1: 0.10 mg kg^{-1} RT 2: 0.20 mg kg^{-1}	* Less hypotension (R1 3.0%, R2 21.2% vs P 48.5%, P<0.05) * Cognitive functions: R1 similar to P, worse in the R2 group
Ye et al. [24]	RCT	2023	129	RT: 68 P: 68	Gastroscopy	Remifentanil 0.2 μg kg^{-1}	2.0 mg kg^{-1}	0.20 mg kg^{-1}	* Less Hypoxia (1.6% vs 16.9%, P=0.0043) * Less Hypotension (14.1% vs 55.4%, P<0.0001) * Shorter time to Eye-opening (8 vs 9 min, P<0.0001)

/: not reported, C: Control group, LOC: Time to Loss of Consciousness, NS: No significant difference, P: Propofol, RT: remimazolam tosilate.

Table III. — Studies comparing remifentanil and dexmedetomidine sedation.

Study	Type	Year	N	Age (Years)	Surgery	Anaesthesia	Dexmedetomidine	Remifentanil	Heart Rate	Hypotension	Hypoxia
Kaya et al. [26]	RCT	2022	80	D: 68.0 RF: 67.0	Cataract	Peribulbar block + Propofol bolus 0.5 mg kg^{-1}	1 µg kg^{-1} 0.4 µg kg^{-1} h^{-1}	0.05 µg kg^{-1} min^{-1}	NS	NS	Favors dexmedetomidine (0 vs 25%, P=0.02)
Lee et al. [27]	RCT	2016	75	D: 75.4 RF: 77.1	Vertebroplasty	Lidocaine infiltration Midazolam 0.02 mg kg^{-1} Propofol 0.3 mg kg^{-1}	0.3–0.4 µg kg^{-1} 0.2–1 µg kg^{-1} h^{-1}	0.02-0.08 µg kg^{-1} min^{-1}	/	NS	Favors dexmedetomidine (13.2% vs 35.1%, P=0.026)

/: not reported, NS: No significant difference, Dex: Dexmedetomidine, P: Propofol, RF: remifentanil.

Table IV. — Comparison of Propofol Sedation with and without Dexmedetomidine Loading Dose.

Study	Type	Year	N	Age (years)	Surgery	All patients	Propofol (Bolus, Infusion rate)	Dexmedetomidine	Control	Onset (min)	Recovery time (min)	Cumulative dose of propofol (mg)	Results dexmedetomidine group
Chen M. et al. [28]	RCT	2022	49	P: 73.0 D: 72.0	ERCP	Sufentanil 0.1 µg kg^{-1}	1-2 mg kg^{-1} TCI 2-4 µg ml^{-1}	0.5 µg kg^{-1}10 min^{-1}	Saline	NA	NS	P: 143.7 D: 111.0 P<0.001	* More bradycardia (58.3% vs 12%, P<0.001) * Less hypotension (16.7% vs 60%, P=0.003) * Less hypoxemia (4.2% vs 36%, P=0.011) * NS difference in recovery time
Ergenoglu et al. [31]	RCT	2015	60	P: 71.7 D: 70.8	Hip fracture	Spinal + Midazolam 0.02 mg kg^{-1}	No initial bolus 3 mg kg^{-1} h^{-1} + bolus 0.5mg kg^{-1} if needed	0.5 µg kg^{-1}10 min^{-1}	Saline	P: 4.03 D: 5.28 P<0.001	P: 16.73 D: 7.30 P<0.001	P: 197.0 D: 82.0 P<0.001	* NS difference in bradycardia, hypotension or hypoxemia
Yin et al. [30]	RCT	2019	120	P: 69.8 D: 70.9	Gastroscopy	Oral Lidocaine spray + Lidocaine 0.5 mg kg^{-1} IV	1 mg kg^{-1} 3-5 mg kg^{-1} h^{-1}	0.4 µg kg^{-1}10 min^{-1}	Saline	P: 7.3 D: 10.9 P<0.05	P: 11.7 D: 17.4 P<0.05	P: 228.0 D: 169.0 P<0.05	* More bradycardia (60% vs 20%, P<0.05) * More hypotension (57% vs 30%, P<0.05) * Less hypoxemia (7% vs 40%, P<0.05)

NA: not reported, C: Control group, NS: No significant difference, P: Propofol.

Table V. — Studies comparing dexmedetomidine and propofol sedation.

Study	Type	Year	N	Age (Years)	Surgery	Anaesthesia	Dexmedetomidine dose (Loading, infusion rate)	Propofol infusion	Results dexmedetomidine group
Khalil et al. [35]	RCT	2016	50	P: 75.4 D: 74.7	TAVI	Lidocaine 1% femoral infiltration	1 μg kg^{-1} 0.5 μg kg^{-1} h^{-1}	0.5 mg kg^{-1} bolus, 30-50 μg $kg^{-1}min^{-1}$	* Lower heart rates (67.3 vs 78.0 bpm; P<0.001) * Lower MAP 58.1 vs 68.2 mmHg; P<0.001 * NS difference in oxygen saturation, recovery time, sedation, pain, satisfaction and postoperative complications.
Mei et al. [32]	RCT	2018	296	P: 74.0 D: 76.0	Total hip arthroplasty	Lumbosacral plexus + T12 paravertebral block	0.8-1.0 μg kg^{-1} 0.1-0.5 μg kg^{-1} h^{-1}	TCI: 0.8-1.0 μg ml^{-1}	* Less delirium (7% vs 16%; P=0.030) * Faster ambulation and discharge * NS difference in heart rate, hypotension
Shin et al.[33]	RCT	2023	748	P: 71.0 D: 72.0	elective lower extremity orthopedic surgery	Spinal	1 μg kg^{-1} 0.1-0.5 μg kg^{-1} h^{-1}	TCI 1.0-2.0 μg ml^{-1}	* Lower heart rates during sedation (60 vs 63 bpm) and in the PACU (64 vs 68; P<0.001) * Higher MAP during sedation (77 vs 74; P<0.001) * Lower MAP in the PACU (74 vs 80; P<0.001) * Less delirium (11% vs 24%; P=0.036) * Longer PACU stay (37 vs 27 min; P<0.001) * NS difference in vasopressor use, hospital length of stay,
Zhu et al. [34]	RCT	2023	219	P: 75.0 D: 80.0	Hip Surgery	Spinal	0.3 μg kg^{-1} 0.2–0.7 μg kg^{-1} h^{-1}	0.5–3.0 mg kg^{-1} h^{-1}	* Less delirium (11.9% vs 23.6%; P=0.024) * NS difference in heart rate, blood pressure, hypoxemia

not reported, C: Control group, M: Midazolam, NS: No significant difference, P: Propofol.

Table VI. — Studies comparing etomidate and propofol sedation.

Study	Type	Year	N	Age (Years)	Surgery	Anaesthesia	Etomidate group	Propofol Group	Propofol+Etomidate group	Results Etomidate group
Meng et al. [37]	RCT	2016	200	P: 68.4 E: 69.7 P+E: 72.3 E+P: 71.8	Gastroscopy	Fentanyl 1 μg kg^{-1}	0.150.2 mg kg^{-1} + 0.4 μg kg^{-1} h^{-1}	1.52.0 mg kg^{-1} + 4 mg kg^{-1} h^{-1}	P 0.75[1] mg kg^{-1} + E 0.0750.1 mg kg^{-1} P 1-2 mg kg^{-1} h^{-1} + E 0.2 μg kg^{-1} h^{-1}	* Less hypotension 12% vs 88%; P<0.05 * Less hypoxia 4% (E) and 6% (EP) vs 24%; P<0.05 * NS difference in heart rate
Shen et al. [38]	RCT	2015	715	P: 66.3 E: 66.6	Gastroscopy	Remifentanil 0.4-0.6 μg kg^{-1}	0.1-0.15 mg kg^{-1} + 4–6 mg boluses	1-2 mg kg^{-1} + 20-40 mg boluses	/	* Faster onset (78.2 vs 85.1 s; P<0.001) * Less hypoxia (12.7% vs 21.4%; P=0.002) * NS difference in heart rate, hypotension, recovery time

/: not reported, C: Control group, E: Etomidate, EP: etomidate propofol, NS: No significant difference, P: Propofol.

3 and 7, indicating a lower risk of postoperative cognitive dysfunction (POCD)[32]. Shin et al. and Zhu et al. also reported lower POD rates in dexmedetomidine groups, with Zhu noting that higher doses of propofol correlated with increased delirium, while dexmedetomidine doses did not appear to impact POD rates[34]. Collectively, these studies suggest dexmedetomidine may provide superior cognitive outcomes compared to propofol, especially in settings where early postoperative cognition and mobility are prioritized.

In the context of transcatheter aortic valve implantation (TAVI), Khalil et al. found that dexmedetomidine yielded lower blood pressure and heart rate compared to propofol, yet oxygen saturation, sedation duration, and procedural success rates were similar between the two agents, indicating comparable overall sedation efficacy[35].

Finally, Park et al. explored an alternative approach, comparing dexmedetomidine loading with a midazolam bolus in elderly patients undergoing total knee arthroplasty[36]. Midazolam provided a faster sedation onset without significant hemodynamic compromise, suggesting it as a practical alternative in patients at higher bradycardia risk or requiring rapid sedation onset.

Etomidate

Two trials compared the use of etomidate and propofol sedation during gastroscopy in elderly patients (Table VI)[37,38].

A 2016 RCT by Meng et al. involved 200 patients and compared four groups: propofol alone, etomidate alone, propofol followed by etomidate, and etomidate followed by propofol[37]. The study found that combining etomidate and propofol provided improved hemodynamic stability, minimal respiratory depression, and high levels of satisfaction among patients, anaesthetists, and endoscopists, with a rapid recovery to full activity.

A separate 2015 study by Shen et al. focused on comparing propofol-remifentanil and etomidate-remifentanil[38]. The RCT of 720 patients found that the etomidate-remifentanil combination resulted in more stable hemodynamic responses, fewer adverse events, and similar satisfaction levels compared to the propofol-remifentanil combination. Both studies underscore the benefits of etomidate in reducing cardiovascular risks in elderly patients and recommend its use, either alone or in combination with other anaesthetics, for maintaining hemodynamic stability during gastroscopy. However, Shen et al. conclude that etomidate-remifentanil is a preferable option, while Meng et al. emphasize the value of combining etomidate with propofol.

Midazolam

Several studies have explored the comparative efficacy and safety of midazolam and propofol for sedation in elderly patients undergoing various procedures. Christe et al. examined midazolam versus placebo for gastroscopy and found no significant difference in postoperative confusion or Mini-Mental State Examination (MMSE) scores at 2 and 24 hours postoperatively, suggesting limited cognitive impact of midazolam in this setting[39].

In studies comparing midazolam to propofol, results consistently showed that propofol offered faster recovery times. Riphaus et al. found that while recovery was quicker with propofol (22 ± 7 minutes) compared to midazolam/meperidine (31 ± 8 minutes), oxygen saturation declined more significantly with propofol, although severe desaturation rates were similar across groups[40]. Han et al. also reported that propofol led to shorter recovery times than midazolam/fentanyl during therapeutic ERCP in patients over 80, with no significant differences in cardiopulmonary adverse events, indicating comparable safety between the two agents[41].

Ersoy et al. focused on hypoalbuminemic geriatric patients undergoing elective hip surgery and found that propofol provided shorter recovery times and better hemodynamic stability compared to midazolam, which was associated with lower respiration rates at various points during surgery[42]. This study suggests that propofol may be a more suitable sedative for elderly patients with hypoalbuminemia due to its reliable recovery profile and hemodynamic stability.

Ketamine

Only trials focused on ketamine's effects on postoperative cognitive dysfunction (POCD) were identified, specifically in elderly patients undergoing ophthalmic surgery. Two randomized controlled trials (RCTs) explored ketamine's impact on POCD[43,44]. In both studies, ketamine was shown to reduce POCD rates when used as an adjunct to sedation, with common findings indicating improved cognitive outcomes post-surgery. Oriby et al. examined three groups of cataract surgery patients receiving either saline, ketamine (0.3 mg kg^{-1} h^{-1}), or dexmedetomidine (0.5 µg kg^{-1} h^{-1}) alongside midazolam and fentanyl[43]. Both the ketamine and dexmedetomidine groups had significantly lower incidences of POCD at 1 week and 3 months postoperatively compared to the control group, with no significant differences in hemodynamic stability or intraocular pressure among groups.

Similarly, Rascón-Martínez et al. focused on cognitive outcomes in elderly ophthalmic surgery patients receiving ketamine (0.3 mg kg^{-1}) versus saline[44]. Consistent with Oriby's findings, the ketamine group showed improved cognitive performance as assessed by the Short Portable Mental Status Questionnaire (SPMSQ), with no adverse effects on intraocular pressure or hemodynamic stability. Additionally, this group required less anesthesia overall, highlighting ketamine's potential to reduce sedative requirements.

Discussion

This narrative review examined the efficacy and safety of various sedation agents in elderly patients, focusing on recent controlled trials. The findings indicate that while traditional agents like propofol offer rapid onset and high sedation success, newer agents such as remimazolam and dexmedetomidine demonstrate promising safety profiles, particularly in reducing cardiopulmonary adverse events and cognitive dysfunction.

Meta-analyses comparing remimazolam and propofol in elderly patients undergoing gastrointestinal endoscopy and colonoscopy highlight a balance between efficacy and safety[45]. Propofol provides faster induction and higher sedation success but is associated with increased adverse effects. Remimazolam, however, presents a superior safety profile, with reductions in bradycardia, hypoxemia, and injection site pain. Its reduced incidence of respiratory depression and hypotension is particularly advantageous in elderly patients undergoing sedation. Despite these benefits, remimazolam does not surpass propofol in terms of sedation efficiency metrics, such as onset, procedural duration, or recovery time, underscoring a critical trade-off in sedative selection for geriatric patients. Remimazolam's safety profile makes it an appealing alternative, especially for patients at risk of hemodynamic instability or respiratory compromise.

Although most studies report hemodynamic stability with remimazolam, variability exists, particularly at higher dosing levels, suggesting that further optimization of dosing strategies could enhance its safety and efficacy in the elderly. Lower doses (e.g., 0.10 mg kg^{-1}) have shown to maintain safety without significant hemodynamic effects, whereas higher doses may increase hemodynamic risks[23]. Further research into remimazolam's cognitive effects, dosing regimens, and broader application in elderly patients with diverse comorbidities is warranted to establish its potential as a primary sedative for this population.

Dexmedetomidine appears to offer cognitive and recovery benefits over propofol in elderly patients, with a lower risk of POD and potentially improved postoperative mobility. However, its impact on hemodynamic parameters and recovery times varies, underscoring the need for individualized dosing strategies and further studies to clarify its role in elderly procedural sedation.

Ketamine has demonstrated a favorable impact on reducing postoperative cognitive dysfunction (POCD) when used adjunctively, though its role as a primary hypnotic in elderly patients remains unclear due to limited data on cardiopulmonary safety and efficacy in this population. Further studies are required to establish ketamine's safety as a standalone sedative in elderly patients.

In elderly patients, midazolam is effective for procedural sedation with a favorable respiratory profile but is associated with prolonged recovery times compared to agents like propofol[40,42,46]. However, there is a notable lack of studies specifically addressing midazolam's effects on postoperative cognitive function (POCD) and delirium. Although limited evidence suggests midazolam may not significantly increase POCD risk compared to other agents, the data remain inconclusive, especially for elderly patients who are more susceptible to cognitive disturbances after sedation[39]. This gap highlights an urgent need for targeted research to better understand midazolam's impact on cognitive outcomes in the immediate postoperative period, ensuring that sedation practices are optimized for cognitive safety in the elderly.

The combination of lidocaine and propofol for endoscopic sedation shows promise, allowing for lower propofol doses while maintaining sedation efficacy and reducing hypoxia risk, although the mechanism by which lidocaine enhances propofol's effects is not fully understood. Limited studies on high-flow nasal cannula (HFNC) oxygen therapy during gastrointestinal endoscopy suggest a positive impact on oxygenation in elderly patients.

The studies reviewed reveal several limitations and common pitfalls. A notable issue is the frequent exclusion of very elderly patients and those with severe comorbidities (ASA III and IV), limiting the applicability of findings to frail elderly populations. Additionally, most studies involve mixed-age groups, with relatively few focusing exclusively on elderly patients. Heterogeneity in study design—particularly in methodologies, dosing regimens, outcome measures, and small sample sizes—is widespread, except in the case of remimazolam trials. This variability complicates the development of robust, evidence-based

recommendations for sedation practices tailored to frail elderly patients.

Given these limitations, it is challenging to make strong recommendations for the sedation of frail elderly patients. Future research should address these gaps by focusing specifically on elderly populations, including those with significant comorbidities, and by adopting standardized methodologies to improve comparability across studies.

Conclusion

This narrative review highlights the complexity and variability of sedation practices in elderly patients, particularly due to the heterogeneity across studies, including differences in dosing regimens, small sample sizes, and the frequent exclusion of elderly patients with severe comorbidities (ASA III and IV). Despite these limitations, certain agents like remimazolam and dexmedetomidine show promise for improving safety and cognitive outcomes, particularly by reducing cardiopulmonary adverse events and the risk of postoperative cognitive dysfunction (POCD).

Limitations: The review is limited by the diversity of studies analyzed, with significant variation in sedation protocols and outcome measures, as well as the exclusion of frail elderly patients with severe comorbid conditions. The lack of standardized trial designs complicates the development of definitive guidelines for this population.

Future Directions: Future research should expand clinical trials to include a broader range of elderly patients, particularly those with complex comorbidities, and assess long-term cognitive outcomes to establish optimal sedation practices.

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