Research Article
E-ISSN : 3048-1368
Volume 36, Issue No. 01. 2026
P-ISSN : 3048-1376

The International Journal of Medical Science and Health Research

A Comprehensive Systematic Review of The Role of Ketamine-Propofol (Ketofol) in Interventional Radiology Oncology

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Article History :

Received date : 2025/12/08

Revised date : 2026/01/21

Accepted date : 2026/02/17

Published date : 2026/03/13

E-ISSN :

ISSN 3048-1368

9 773048 136000

P-ISSN

ISSN 3048-1376

9 773048 137007

ABSTRACT

Introduction: Interventional radiology oncology procedures require optimal sedation that ensures hemodynamic stability, respiratory safety, and adequate analgesia. Ketamine-propofol (ketofol) combines the sympathomimetic properties of ketamine with the sedative effects of propofol, offering potential advantages in this vulnerable population. This systematic review evaluates the role of ketofol in interventional radiology oncology procedures.

Methods: A systematic review of 58 sources identified through screening based on predefined criteria including ketofol intervention, adult oncology patients undergoing interventional procedures, and appropriate study designs. Data were extracted on procedure context, patient characteristics, ketofol administration, comparator regimens, sedation effectiveness, safety outcomes, recovery parameters, and clinical recommendations.

Results: Meta-analyses demonstrated that ketofol significantly reduces hypotension (RR 0.11-0.40), bradycardia (RR 0.34-0.47), and respiratory adverse events (RR 0.48-0.55) compared to

propofol alone. Ketofol reduces propofol consumption by 30-65% and provides superior analgesia. However, ketofol increases neurological adverse events compared to propofol (RR 1.95-3.68) and may prolong recovery by 2-7 minutes. The 1:2 to 1:4 ketamine-to-propofol ratio appears optimal.

Discussion: Ketofol demonstrates pharmacological synergy that addresses the specific needs of interventional radiology oncology patients, who often present with compromised cardiovascular status. The hemodynamic and respiratory advantages are well-established across diverse clinical contexts. However, direct evidence in interventional radiology oncology remains limited, with most studies excluding high-risk patients (ASA III-IV) typical of oncology practice. The trade-off between improved cardiorespiratory stability and increased neuropsychiatric effects requires individualized patient selection.

Conclusion: Ketofol at 1:2-1:4 ratios represents a reasonable sedation strategy for interventional radiology oncology procedures where hemodynamic stability and respiratory safety are priorities. Future research should focus on high-risk oncology patients, optimal dosing for prolonged procedures, and head-to-head comparisons with dexmedetomidine-based regimens.

Keywords: Ketofol, ketamine, propofol, interventional radiology, oncology, procedural sedation, hemodynamic stability, respiratory safety

INTRODUCTION

Interventional radiology oncology procedures have become cornerstone interventions in modern cancer management, encompassing a wide spectrum of techniques including tumor ablations, chemoembolizations, brachytherapy, and image-guided biopsies (1-3). These procedures demand a unique sedation paradigm that balances multiple competing requirements: adequate analgesia for often painful interventions, hemodynamic stability in patients with malignancy-related cardiovascular compromise, respiratory safety to accommodate procedure-specific positioning, and rapid recovery to facilitate patient throughput (4,5). The optimal sedative regimen for this clinical context remains inadequately defined.

Propofol, while widely used for procedural sedation due to its rapid onset and ultrashort duration, is associated with dose-dependent hypotension and respiratory depression (6,7). These adverse effects are particularly problematic in oncology patients, who frequently present with dehydration, chemotherapy-induced cardiomyopathy, or malignancy-associated autonomic dysfunction (8). Ketamine offers hemodynamic stability through sympathomimetic properties and provides intrinsic analgesia, but its use as a single agent is limited by psychomimetic emergence reactions and prolonged recovery (9,10).

The combination of ketamine and propofol, colloquially termed "ketofol," leverages the complementary pharmacological profiles of both agents. Ketamine's stimulation of the sympathetic nervous system counterbalances propofol's vasodilatory and cardiodepressant effects, while propofol attenuates ketamine-induced emergence phenomena (11,12). This synergistic interaction has generated substantial interest across multiple sedation contexts, including emergency departments, endoscopy suites, and operating theaters (5,6,13).

Research Gap: Despite the theoretical advantages of ketofol for interventional radiology oncology procedures and its extensive investigation in other clinical settings, no comprehensive synthesis exists examining its specific role in this context. Existing systematic reviews have either focused on general procedural sedation (6,9,14), pediatric populations (15), or emergency

department settings (16,17), with limited attention to the unique considerations of oncology patients undergoing interventional radiology procedures. The applicability of findings from healthy patients undergoing brief procedures to debilitated cancer patients undergoing complex interventions remains uncertain.

Study Objectives: This systematic review aims to: (1) comprehensively evaluate the available evidence on ketofol use in interventional radiology oncology procedures; (2) synthesize data on hemodynamic stability, respiratory safety, sedation efficacy, and recovery profiles; (3) identify optimal dosing strategies and patient selection criteria; and (4) compare ketofol's performance against alternative sedation regimens in this specific clinical context.

Study Benefits: This review will provide evidence-based guidance for sedation practitioners managing oncology patients in interventional radiology settings, identify knowledge gaps requiring future investigation, and facilitate informed clinical decision-making regarding the risk-benefit profile of ketofol in this vulnerable population.

Hypothesis: Based on the pharmacological rationale and indirect evidence from other sedation contexts, we hypothesize that ketofol provides superior hemodynamic stability and respiratory safety compared to propofol alone in interventional radiology oncology procedures, with acceptable recovery profiles and manageable neuropsychiatric adverse effects when administered at appropriate ketamine-to-propofol ratios.

Novelty: This represents the first systematic review specifically examining ketofol in the intersection of interventional radiology and oncology, synthesizing direct evidence from cancer-specific studies with indirect evidence from broader procedural sedation literature to generate context-specific clinical recommendations.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This

approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the the of ketamine-propofol (ketofol) in interventional radiology oncology.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Ketofol Intervention**: Does this study investigate ketamine-propofol combination (ketofol) as the primary sedation or anesthetic agent for procedural sedation/anesthesia?
- **Target Population**: Does this study include adult patients (≥18 years) with oncological conditions undergoing interventional radiology procedures?
- **Study Design**: Is this study a randomized controlled trial, controlled clinical trial, cohort study, case-control study, case series with ≥5 patients, systematic review, or meta-analysis?
- **Outcome Measures**: Does this study report at least one relevant outcome measure such as efficacy, safety, hemodynamic stability, recovery time, patient satisfaction, procedural success, or adverse events?
- **Procedural Context**: Does this study focus on clearly defined oncology-related interventional radiology procedures (not surgical procedures or diagnostic imaging without intervention)?
- **Combination Therapy**: Does this study investigate ketamine and propofol used in combination rather than as individual agents?
- **Study Type Appropriateness**: Is this study NOT a case report, editorial, letter, conference abstract, expert opinion, animal study, or in-vitro study?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Adult patients	Ketamine-propofol	Propofol alone	Hemodynamic stability
Keyword 2	Cancer patients	Ketofol	Ketamine alone	Respiratory safety
Keyword 3	Interventional radiology oncology	Procedural sedation	Dexmedetomidine-propofol	Recovery time
Keyword 4	Oncological procedures	Combination sedation	Fentanyl-propofol	Adverse events

The Boolean MeSH keywords inputted on databases for this research are: *("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*

Data extraction

- **Procedure Context**:

  Extract specific details about the interventional radiology oncology procedures where ketofol was used, including:

  - Type of interventional radiology procedure (e.g., embolization, ablation, biopsy)
  - Cancer type/location being treated

- Procedure duration and complexity
- Setting (inpatient, outpatient, specific department)
- Any procedure-specific considerations that influenced sedation choice

- **Patient Population**:

  Extract characteristics of patients receiving ketofol for interventional radiology oncology procedures, including:

  - Age range and mean age
  - Cancer stage/type
  - ASA physical status or comorbidity burden
  - Previous sedation/anesthesia experiences
  - Contraindications to alternative sedation methods
  - Sample size and demographics

- **Ketofol Administration**:

  Extract complete details of ketofol dosing and administration protocols used in interventional radiology oncology, including:

  - Ketamine:propofol ratio (e.g., 1:1, 1:4)
  - Initial dosing (mg/kg or total dose)
  - Bolus vs. infusion methodology
  - Rescue/additional dosing protocols
  - Administration timing relative to procedure
  - Who administered the sedation (anesthesiologist, radiologist, nurse)

- **Comparison Groups**:

  Extract details about control or comparison sedation regimens used alongside ketofol in interventional radiology oncology studies, including:

- Specific alternative agents (propofol alone, midazolam, fentanyl combinations, etc.)
- Dosing protocols for comparison groups
- Whether comparison was head-to-head or historical control
- Sample sizes for each comparison group

- **Sedation Effectiveness**:

  Extract all measures of sedation effectiveness and procedural success for ketofol in interventional radiology oncology, including:

  - Sedation depth/quality scales used and scores achieved
  - Procedure completion rates
  - Need for rescue sedation or conversion to general anesthesia
  - Patient movement/cooperation during procedure
  - Provider satisfaction with sedation conditions
  - Time to achieve adequate sedation level

- **Safety Outcomes**:

  Extract comprehensive safety and adverse event data for ketofol use in interventional radiology oncology procedures, including:

  - Respiratory complications (apnea, desaturation, airway intervention)
  - Cardiovascular effects (hypotension, hypertension, arrhythmias)
  - Neurological/psychiatric effects (emergence reactions, hallucinations)
  - Other adverse events specific to the oncology population
  - Serious adverse events requiring intervention
  - Comparison of safety profile vs. alternative sedation methods

- **Recovery Outcomes**:

Extract data on post-procedure recovery for patients receiving ketofol in interventional radiology oncology, including:

- Time to emergence/awakening
- Time to meet discharge criteria
- Post-procedure nausea/vomiting
- Patient recall of procedure
- Patient satisfaction scores
- Any delayed complications or prolonged effects

- **Clinical Recommendations**:

Extract authors' conclusions and clinical recommendations specifically regarding ketofol use in interventional radiology oncology, including:

- Preferred dosing regimens or protocols
- Patient selection criteria
- Procedure types where ketofol is most/least suitable
- Comparison recommendations vs. other sedation methods
- Identified advantages and limitations in this specific clinical context
- Suggested areas for future research

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*	3
Semantic Scholar	*("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*	250
Springer	*("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*	60
Google Scholar	*("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*	709
Wiley Online Library	*("Adult patients" OR "Cancer patients" OR "Interventional radiology oncology" OR "Oncological procedures") AND ("Ketamine-propoxilol" OR "Ketofol" OR "Procedural sedation" OR "Combination sedation") AND ("Propofol alone" OR "Ketamine alone" OR "Dexmedetomidine-propoxilol" OR "Fentanyl-propoxilol") AND ("Hemodynamic stability" OR "Respiratory safety" OR "Recovery time" OR "Adverse events")*	46

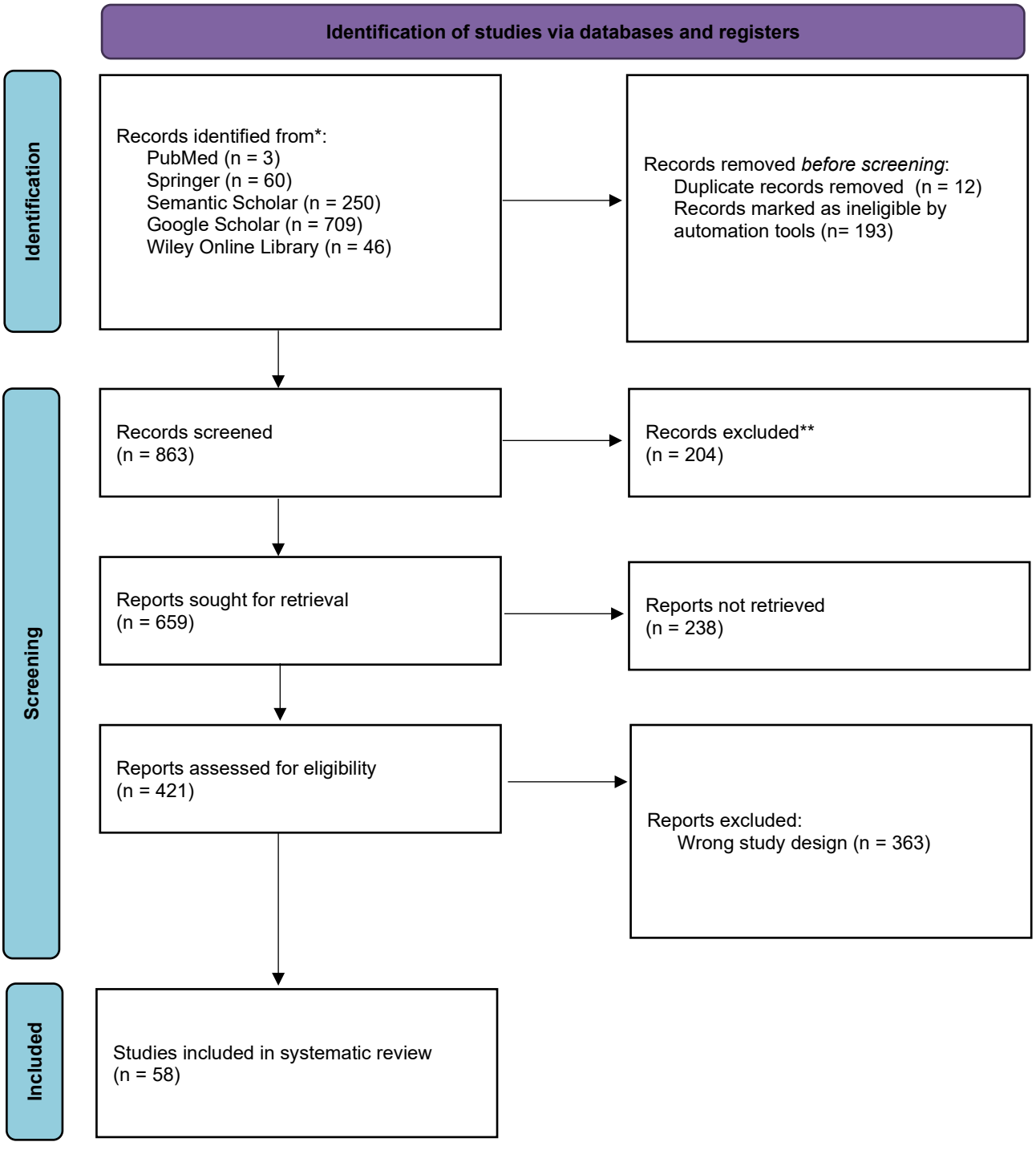

Figure 1. Article search flowchart

RESULTS

Characteristics of Included Studies

The 58 sources identified for this review encompass a broad range of clinical contexts in which ketamine-propofol combinations have been studied. Notably, very few sources directly examined ketofol use in interventional radiology oncology procedures; the majority addressed procedural sedation and analgesia (PSA) in emergency departments, endoscopy suites, operating theaters, or general day-case surgery settings. Several systematic reviews and meta-analyses provided pooled data across diverse procedure types. The table below summarizes all included sources.

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
Monika Gupta et al., 2021	Cervical cancer brachytherapy [1]	n=100, female, age 20–60, ASA I–III [1]	1:2 (K:P) [1]	Propofol alone [1]
A. S. Abdelgalil et al., 2024	CT-guided bone biopsy in cancer patients [2]	n=60, mean age ~40 yr, ASA I–II [2]	~1:2.5 (K:P) [2]	Dexmedetomidine-propofol [2]
Tze Yong Foo et al., 2020	Pediatric PSA (various) [17]	11 trials, 1274 patients [17]	Various (1:1 to 1:6) [17]	Propofol, ketamine, combined agents [17]
Keta D. Thakkar et al., 2020	Neurosurgery (brain tumor) [20]	n=80, age 18–65, ASA I–II [20]	1:5 (K:P) [20]	Propofol alone [20]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
Fabien Lemoel et al., 2017	Emergency PSA (adults) [21]	n=152, age 18–94, ASA 1–2 [21]	1:1 (K:P) [21]	Ketamine alone [21]
D. Pallin et al., 2016	PSA (various) [22]	Not specified [22]	1:1 or 1:4 [22]	Propofol alone [22]
J. Choi et al., 2006	Breast biopsy under MAC [23]	n=60 [23]	Not specified [23]	Propofol alone, propofol-fentanyl [23]
I. Erden et al., 2010	Interventional radiology procedures [24]	n=72, ASA I–III [24]	1:1 and 1:2 [24]	Two ketofol dose regimens compared [24]
M. Jalili et al., 2016	PSA (adults) [6]	18 trials [6]	Various [6]	Propofol alone [6]
Ozgur Yagan et al., 2015	Cataract surgery [25]	n=60 [25]	1:2 (K:P) [25]	Dexmedetomidine [25]
Akash Kumar et al., 2025	PSA (various) [7]	20 studies, 2023 patients [7]	Various (esketamine-propofol) [7]	Various PSA regimens [7]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
Antoni Silalahi et al., 2023	Minor surgery (MOW) [10]	n=48, mean age ~36 yr, ASA I–II [10]	~1:1.5 (K:P) [10]	Propofol-fentanyl [10]
S. Green et al., 2015	ED PSA [26]	Not specified [26]	1:1 and 4:1 [26]	Propofol alone [26]
Xiaoci Huang et al., 2023	PSA (various) [8]	7 RCTs, 808 patients [8]	Esketamine-propofol [8]	Various [8]
Ting-ru Wen et al., 2020	PSA (adults and children) [9]	21 studies, 3669 patients [9]	Various [9]	Propofol alone [9]
Tulay Dal et al., 2014	EBUS-TBNA (bronchoscopy) [27]	n=60 [27]	Not specified [27]	Ketamine-midazolam [27]
Rajesh Kumar Donda et al., 2020	General PSA [28]	n=50, age 15–60, ASA I–II [28]	Not specified [28]	Ketamine-midazolam [28]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
S. Sharif et al., 2024	ED and ICU PSA [5]	82 RCTs, 8105 patients [5]	Various [5]	Multiple agents (midazolam-opioids, propofol, ketamine, etc.) [5]
Javeria Bakhtawar et al., 2025	ERCP [29]	n=110, age 18–60 [29]	Not specified [29]	Dexmedetomidine-ketamine [29]
R. Handayani et al., 2025	TIVA (general) [30]	n=50, age 18–60 [30]	Not specified [30]	Propofol alone [30]
D. Pallin et al., 2016a	ED PSA [31]	n=573 [31]	1:1 [31]	Propofol alone [31]
Rania M. Ali et al., 2016	RFA of hepatocellular carcinoma [3]	n=80, hepatic cirrhosis [3]	1:2 (K:P) [3]	Sevoflurane-propofol [3]
M. Ghojazadeh et al., 2019	ED PSA (adults) [32]	5 RCTs, 1250 patients [32]	1:1 and 1:4 [32]	Propofol alone [32]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
H. Hosseinzadeh et al., 2013	Elective surgery (elderly) [33]	n=62, age >50 [33]	~3:4 (K:P) [33]	Etomidate-propofol [33]
J. Miner et al., 2015	ED deep sedation [14]	n=271, adults [14]	1:1 and 4:1 [14]	Propofol alone [14]
Huma Nasir et al., 2023	ED PSA [34]	6 RCTs, 932 patients [34]	Various [34]	Propofol alone [34]
Hany A. Zaki et al., 2022	Emergency PSA [35]	6 articles [35]	1:1 [35]	Ketamine alone [35]
Effect of Different Surgical P, 2020	Neurosurgery [36]	n=80, age 18–65, ASA I–II [36]	1:5 (K:P) [36]	Propofol alone [36]
Michael C. Thomas et al., 2011	ED PSA [37]	10 trials reviewed [37]	1:1 [37]	Ketamine alone, propofol alone [37]
Shahrad Tajoddini et al., 2020	ED PSA (painful procedures) [38]	n=196 [38]	1:2 (K:P) [38]	Fentanyl-propofol [38]
U. Ozgul et al., 2013	LTS-II insertion [39]	Not specified [39]	Not specified [39]	Propofol alone [39]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
Shruti Hiremath et al., 2021	Short surgical procedures [40]	n=150 (50 per group) [40]	1:1 [40]	Ketamine alone, propofol alone [40]
R. Goel et al., 2020	Various surgical procedures [41]	n=100 (50 per group), mean age ~37 yr [41]	Not specified [41]	Propofol alone [41]
Niranjan Kumar et al., 2020	General anesthesia induction [42]	n=60 [42]	~1:1 to 1:2 [42]	Propofol alone [42]
Reza Azizkhani et al., 2021	ED PSA (painful procedures) [43]	n=93, age >=18 [43]	1:1 [43]	Ketamine-dexmedetomidine, ketamine alone [43]
Muralidhara KS et al., 2023	Short surgical procedures [15]	n=86, age 18–60, ASA I–II [15]	1:2 and 1:3 [15]	Two ketofol ratios compared [15]
A. Akin et al., 2005	Endometrial biopsy [44]	n=40, age 38–61, ASA I–II [44]	1:2 (K:P) [44]	Fentanyl-propofol [44]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
A. S. Elsaeidy et al., 2024	Periprocedural sedation (various) [45]	22 trials, 1429 patients [45]	Various [45]	Ketamine-dexmedetomidine [45]
Gholamreza Khalili et al., 2024	Anesthesia induction (elderly) [46]	n=90, age >=65, ASA >=II [46]	~1:3 (K:P) [46]	Etomidate [46]
Mehrdad Esmaillian et al., 2023	ED PSA (adults) [47]	n=135, mean age ~38 yr [47]	Not specified [47]	Ketamine-dexmedetomidine, ketamine alone [47]
KCharishma Begum et al., 2022	ED PSA [48]	n=60 [48]	Not specified [48]	Midazolam-fentanyl [48]
Hanya Javaid et al., 2023	ERCP [49]	n=124, age 18–50, ASA I [49]	Not specified [49]	Fentanyl-propofol [49]
Arvind Chaturvedi et al., 2023	Trans-sphenoidal pituitary surgery [50]	n=50 [50]	Not specified [50]	Propofol alone [50]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
F. Kalam et al., 2018	Day-case surgery [18]	n=60, age 18–45, ASA I–II [18]	1:1 [18]	Ketamine-diazepam [18]
N. Elshalakany et al., 2023	Colorectal cancer surgery [11]	n=60, age 35–65, ASA I–II, colon cancer [11]	Not specified [11]	Propofol with placebo [11]
A. Maruf et al., 2017	Day-case surgery [51]	n=1013, age 18–50, ASA I–II [51]	1:1 [51]	None (single-arm) [51]
Neimar Sartins et al., 2025	TIVA (general surgery) [52]	n=62, age 18–65, ASA II [52]	1:1 [52]	Ketamine alone [52]
R. Mahajan et al., 2009	Short elective surgery [53]	n=100 [53]	1:2 induction, 1:4 maintenance [53]	Propofol-fentanyl [53]
Brajesh Kaushal et al., 2014	Day-care surgery [54]	n=50, age 18–50, ASA I–II [54]	Not specified [54]	Propofol-fentanyl [54]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
M. Bahreini et al., 2020	ED PSA [55]	n=96 [55]	Not specified [55]	Thiopental-fentanyl [55]
Martsinkevich et al., 2023	Endoscopic procedures [16]	n=60, age 19–82, ASA I–IV [16]	1:2 (K:P) [16]	Propofol alone [16]
S. Sharif et al., 2023	ED and ICU PSA [19]	82 RCTs, 8105 patients [19]	Various [19]	Multiple agents [19]
Nahla N Shehab et al., 2023	GI endoscopy in cancer patients [4]	n=75, cancer patients [4]	1:1 [4]	Dexmedetomidine-propofol, midazolam-propofol [4]
Yimei Ma et al., 2024	Curative colorectal endoscopic resection [56]	n=160, mean age ~61, ASA I–III [56]	Esketamine 0.15 mg/kg + TCI propofol [56]	Propofol-fentanyl [56]
Ipshita Garg et al., 2024	ERCP [13]	n=50, age 18–60, ASA I–III [13]	Not specified [13]	Propofol-dexmedetomidine [13]

Study	Procedure/Context	Population	Ketofol Ratio	Comparator(s)
Chhabra Alka et al., 2022	ERCP [57]	n=100 [57]	Not specified [57]	Dexmedetomidine vs. nalbuphine as adjuvants to ketofol [57]
I. Aryabiantara et al., 2018	Major oncology surgery [12]	n=40, oncology patients [12]	Not specified [12]	Propofol (TCI) alone [12]
A. Kalita et al., 2017	Co-induction with propofol [58]	Not specified [58]	Not specified [58]	Midazolam, propofol [58]

Of these 58 sources, only a small subset directly involved interventional radiology or oncology procedures. Specifically, two studies addressed cancer-specific interventional procedures: Gupta et al. (2021) examined ketofol in cervical cancer brachytherapy [1], and Abdelgalil et al. (2024) studied CT-guided bone biopsy in cancer patients [2]. Ali et al. (2016) evaluated ketofol during radiofrequency ablation (RFA) of hepatocellular carcinoma [3], and Elshalakany et al. (2023) studied propofol combined with clonidine and ketamine in colorectal cancer surgery [11]. Aryabiantara et al. (2018) examined TCI propofol with clonidine and ketamine in major oncology surgery [12]. Shehab et al. (2023) compared ketamine-propofol with other combinations in cancer patients undergoing GI endoscopy [4]. Erden et al. (2010) studied ketamine-propofol sedation specifically during interventional radiology procedures, though not exclusively in oncology patients [24]. The remaining studies examined ketofol in non-oncologic settings including emergency

department PSA, general surgery, day-case procedures, endoscopy, and neurosurgery, providing indirect evidence applicable to the interventional radiology oncology context.

Effects

Hemodynamic Stability

The most consistently reported advantage of ketofol across the literature is improved hemodynamic stability compared to propofol alone. In cervical cancer brachytherapy, the fall in systolic and diastolic blood pressure was significantly less in the ketofol group than in the propofol group [1]. During CT-guided bone biopsy in cancer patients, the ketamine-propofol group exhibited more consistent heart rate and mean arterial pressure than the dexmedetomidine-propofol group [2]. In RFA of HCC, hemodynamic parameters including blood pressure episodes and mean arterial pressure were comparable between sevoflurane-ketofol and sevoflurane-propofol groups [3]. In colorectal cancer surgery, the combination of propofol with clonidine and ketamine was more effective in maintaining hemodynamic stability than propofol alone [11].

Multiple meta-analyses confirmed these findings in broader populations. Jalili et al. (2016) reported that ketofol significantly reduced hypotension (RR 0.11, 95% CI 0.17–0.97, P=0.04) and bradycardia (RR 0.47, 95% CI 0.28–0.72, P=0.008) compared to propofol [6]. The esketamine-propofol meta-analyses similarly demonstrated reduced bradycardia (RR 0.42, 95% CI 0.25–0.71, P=0.001) and hypotension (RR 0.40, 95% CI 0.30–0.53, P<0.01) [7]. Huang et al. (2023) corroborated these with RR 0.37 for hypotension and RR 0.34 for bradycardia when esketamine was combined with propofol [8].

Individual RCTs consistently showed that ketofol blunted the hypotensive effects of propofol during induction [42], produced better hemodynamic regulation than etomidate alone in elderly patients [46], and maintained more stable blood pressure than propofol monotherapy during endoscopic procedures [16]. In the neurosurgical context, ketofol at a 1:5 ratio maintained hemodynamics with decreased requirements for phenylephrine or mephentermine [20, 36]. Ketofol

also provided better hemodynamic stability than ketamine-diazepam combinations [18] and than fentanyl-propofol combinations [38, 54].

However, ketamine-propofol was associated with higher mean arterial pressure changes compared to ketamine-dexmedetomidine in some studies [47], and dexmedetomidine-propofol combinations showed more stable blood pressure than ketamine-propofol during ERCP [13]. In the CT-guided bone biopsy study in cancer patients, although ketamine-propofol had superior hemodynamic stability, dexmedetomidine-propofol had superior sedation efficacy [2].

Respiratory Safety

Outcome	Ketofol Rate	Comparator Rate	Effect Estimate	Source
Respiratory AEs (pooled)	10.9% hypoxia, 6.9% resp depression [9]	17.0% hypoxia, 14.9% resp depression (propofol) [9]	RR 0.55 (95% CI 0.41–0.74) [9]	Wen et al., 2020
Respiratory complications (pooled)	—	—	RR 0.31 (95% CI 0.47–0.7, P=0.001) [6]	Jalili et al., 2016
Respiratory depression (esketamine-propofol)	—	—	RR 0.32 (95% CI 0.16–0.64, P=0.001) [7]	Akash Kumar et al., 2025

Outcome	Ketofol Rate	Comparator Rate	Effect Estimate	Source
Respiratory AEs vs midazolam-opioids	—	—	Ketamine: RR 0.55 (95% CI 0.32–0.96; high certainty) [5]	Sharif et al., 2024
Desaturation (large case series)	2.07% [51]	—	—	Maruf et al., 2017
Transient hypoxia (vs thiopental-fentanyl)	2.1% [55]	8.1% [55]	—	Bahreini et al., 2020
SpO2 decline (vs propofol alone)	Significantly less [30]	Higher decline [30]	P<0.05 [30]	Handayani et al., 2025

Respiratory safety was the second most consistently reported advantage of ketofol. Wen et al. (2020) found that ketamine-propofol significantly reduced respiratory adverse events compared to propofol alone in adults (RR 0.48, 95% CI 0.39–0.60), though this advantage was not statistically significant in children (RR 0.74, 95% CI 0.46–1.20) [9]. The large network meta-analysis by Sharif et al. (2024) confirmed that ketamine had the fewest respiratory adverse events compared to midazolam-opioids (RR 0.55, high certainty) [5], and that propofol-opioid combinations were associated with significantly more respiratory adverse events than ketamine-propofol (RR 2.03, 95% CI 1.32–3.13) [19].

In the pediatric meta-analysis, ketofol showed a reduced frequency of hypotension with moderate certainty of evidence, though the evidence for improved recovery time was of low

certainty [17]. No serious respiratory events requiring intubation were reported in any of the primary studies. In Maruf et al.'s large case series of 1013 patients receiving ketofol for day-case anesthesia, desaturation occurred in only 2.07% and was corrected with supplemental oxygen [51].

Notably, when ketofol was compared to ketamine-dexmedetomidine, Elsaeidy et al. (2024) found that ketofol was associated with higher hypoxia rates (20.3% vs. 12.4%) [45], and Esmaillian et al. (2023) observed less oxygen reduction in the ketamine-dexmedetomidine group compared to ketofol [47].

Neurological and Psychomimetic Effects

One area of concern with ketofol involves neurological adverse events. The network meta-analysis by Sharif et al. (2024) found that ketamine-propofol was associated with significantly more neurological adverse events compared to midazolam-opioids (RR 3.68, 95% CI 1.08–12.53; high certainty) [5, 19]. However, when compared to ketamine alone, ketofol significantly reduced recovery reactions: Lemoel et al. (2017) reported a 22% reduction in unpleasant recovery reactions with ketofol versus ketamine ($P<0.01$) and a threefold reduction in emesis [21]. Azizkhani et al. (2021) found that ketofol reduced the incidence of recovery agitation from 58% with ketamine alone to 29% [43].

Jalili et al. (2016) reported that the pooled risk ratio for psychomimetic complications with ketofol versus propofol was 1.95, though this was not statistically significant ($P=0.15$) [6]. Huang et al. (2023) found an increased risk of agitation with esketamine-propofol (RR 6.29, 95% CI 1.15–34.32) [8]. In the ERCP setting, Garg et al. (2024) reported that the propofol-ketamine group had 66.7% incidence of postoperative cognitive dysfunction compared to 0% in the propofol-dexmedetomidine group [13]. During endoscopic procedures, Martsinkevich et al. (2023) observed euphoria in 26% of patients receiving ketamine-propofol, though no neuropsychiatric abnormalities were detected at 2 and 8 hours post-procedure [16].

Miner et al. (2015) found greater recovery agitation in the 1:1 ketofol group (21%) compared to propofol alone (8%) and 4:1 ketofol (10%) [14], suggesting that the ketamine-to-

propofol ratio influences the incidence of emergence phenomena. Thomas et al. (2011) noted that when ketamine was combined with propofol, no significant increase in emergence reactions was found compared to propofol monotherapy [37], though this may be dose-dependent.

Propofol Consumption and Analgesic Properties

A consistent finding across studies was that adding ketamine to propofol reduced total propofol consumption. In the cervical cancer brachytherapy study, supplementation dose requirements were dramatically lower in the ketofol group (20 mg) compared to propofol alone (800 mg, P=0.00) [1]. In cancer patients undergoing CT-guided bone biopsy, dexmedetomidine-propofol resulted in lower intra-procedure propofol consumption than ketamine-propofol [2]. During TIVA for minor surgery, the propofol-ketamine group required significantly less total propofol (264.88 vs. 295.79 mg, P<0.05) [10].

The meta-analyses confirmed reduced propofol consumption: esketamine-propofol showed markedly lower propofol use (std MD -1.86, 95% CI -2.53 to -1.18) [7], and Huang et al. (2023) reported a standardized mean difference of -1.45 (95% CI -2.39 to -0.50) [8]. In curative colorectal endoscopic resection, the esketamine group consumed significantly less propofol (300 mg vs. 350 mg) [56]. Ma et al. (2024) reported that esketamine combined with propofol decreased the need for vasoactive drugs and propofol doses during colorectal procedures [56].

Ketofol also provided better analgesic properties. In the RFA of HCC study, rescue analgesia time was longer in the ketofol group compared to sevoflurane-propofol, indicating prolonged analgesic effect [3]. In colorectal cancer surgery, the ketamine-containing group had lower postoperative VAS scores and reduced morphine consumption (4.09±1.78 vs. control) [11]. Aryabiantara et al. (2018) similarly demonstrated lower postoperative pain scores and reduced morphine consumption (3.6±1.5 vs. 9.9±3.3 mg) in oncology surgery patients receiving propofol with clonidine and ketamine [12].

Recovery Profile

Study	Context	Recovery Time (Ketofol)	Recovery Time (Comparator)	Significance
Tze Yong Foo et al., 2020	Pediatric PSA (meta-analysis)	MD -9.88 min vs single agents [17]	—	P=0.0003 [17]
Ozgur Yagan et al., 2015	Cataract surgery	16.1 min (Aldrete 9) [25]	24.9 min (dexmedetomidine) [25]	P<0.01 [25]
Shahrad Tajoddini et al., 2020	ED PSA	5.65 ± 0.35 min [38]	9.33 ± 0.78 min (fentofol) [38]	P=0.001 [38]
A. Maruf et al., 2017	Day-case surgery (n=1013)	16.27 ± 4.68 min [51]	—	—
I. Erden et al., 2010	IR procedures	12.1 ± 1.0 min (K 0.5 mg/kg) [24]	13.8 ± 0.8 min (K 0.25 mg/kg) [24]	P>0.05 [24]
Martsinkevich et al., 2023	Endoscopy	7.4 min (consciousness) [16]	5.1 min (propofol) [16]	—
Ipshita Garg et al., 2024	ERCP	15.2 min (ketamine-propofol) [13]	7.24 min (dexmed-propofol) [13]	P<0.001 [13]

Study	Context	Recovery Time (Ketofol)	Recovery Time (Comparator)	Significance
F. Kalam et al., 2018	Day-case surgery	24.7 ± 3.6 min [18]	29.7 ± 4.1 min (ket-diazepam) [18]	Significant [18]
Esmaillian et al., 2023	ED PSA	Shortest in ketofol group [47]	9.8 min longer (ketamine), 8.3 min longer (ketodex) [47]	—
A. Akin et al., 2005	Endometrial biopsy	115.2 ± 25.6 min to discharge [44]	71.2 ± 9.7 min (fentanyl-propofol) [44]	Significant [44]
R. Mahajan et al., 2009	Short elective surgery	8 ± 2 min (eye opening) [53]	8 ± 3 min (propofol-fentanyl) [53]	P=0.53 [53]

Recovery time findings were mixed and dependent on the comparator. Ketofol consistently demonstrated faster recovery than ketamine alone [21, 35, 47], ketamine-midazolam [18, 28], and dexmedetomidine [25]. However, compared to propofol alone, recovery was sometimes prolonged. The Sharif et al. (2024) network meta-analysis found that propofol alone had the shortest recovery time compared to all agents [5], and Martsinkevich et al. (2023) reported longer consciousness recovery (7.4 vs. 5.1 min) and cognitive function recovery (91 vs. 58 min) with ketamine-propofol versus propofol monotherapy [16]. Against dexmedetomidine-propofol, ketamine-propofol showed longer recovery in ERCP [13], whereas against dexmedetomidine alone, ketofol recovered faster [25].

Patient satisfaction was generally high. The network meta-analysis reported that patient satisfaction was best with ketamine-propofol compared to midazolam-opioids (MD 1.47 points, high certainty) [5, 19]. Bahreini et al. (2020) found higher patient satisfaction (8.65±1.00 vs. 7.55±1.54) and physician satisfaction (8.65±1.00 vs. 7.55±1.54) with ketamine-propofol than thiopental-fentanyl, along with lower procedure recall (38.29% vs. 79.59%) [55]. Maruf et al. (2017) reported 100% procedure completion in 1013 patients, with vomiting in only 0.59% and agitation in 0.89% [51].

Nausea, Vomiting, and Other Adverse Events

Gastrointestinal adverse events showed variable results. Jalili et al. (2016) found no significant difference in nausea and vomiting between ketofol and propofol (RR 1.23, P=0.72) [6]. Akash Kumar et al. (2025) similarly found no significant difference with esketamine-propofol [7]. However, individual studies reported higher PONV rates with ketofol in specific contexts: Ali et al. (2016) noted 7.5% nausea with sevoflurane-ketofol in HCC patients [3], and Goel et al. (2020) found a heightened risk of nausea and vomiting with ketofol infusion [41]. Garg et al. (2024) reported 26.7% PONV with ketamine-propofol versus 0% with dexmedetomidine-propofol during ERCP [13]. Conversely, Lemoel et al. (2017) demonstrated a threefold reduction in emesis with ketofol compared to ketamine alone [21].

A unique finding from Sartins et al. (2025) was that ketofol provided better glycemic control than ketamine alone during TIVA, with significantly lower blood glucose levels at 15 and 20 minutes post-induction [52], which may be relevant for oncology patients who frequently have metabolic derangements.

Synthesis

The evidence on ketofol in interventional radiology oncology is characterized by a paradox: the pharmacologic rationale is strong, but direct evidence in the specific clinical context of interventional radiology oncology is sparse. The findings across 58 sources can be reconciled by examining several key dimensions.

The hemodynamic advantage of ketofol is the most robust finding, confirmed by multiple meta-analyses [6–8] and individual trials across diverse clinical contexts. The mechanism is well understood: ketamine's sympathomimetic properties counterbalance propofol's vasodilatory and cardiodepressant effects. This is particularly relevant in interventional radiology oncology, where patients may present with compromised cardiovascular status due to malignancy, prior chemotherapy, or dehydration. The brachytherapy study [1] and bone biopsy study [2] both confirmed this advantage in cancer patients specifically, though sample sizes were modest (n=100 and n=60, respectively).

The respiratory safety advantage is also well-supported in adults (RR 0.48–0.55 across meta-analyses) [6, 9], though not confirmed in children [9]. This advantage appears to be mediated by the lower propofol dose required when ketamine provides analgesic synergy. However, when compared to dexmedetomidine-based combinations rather than propofol alone, ketofol's respiratory advantage diminishes [29, 45, 47]. This suggests that the respiratory benefit is specifically a propofol-sparing effect rather than an intrinsic respiratory stimulant property.

The apparently contradictory findings regarding neurological adverse events can be explained by the comparator used. Compared to ketamine alone, ketofol reduces emergence phenomena [21, 43], because propofol attenuates ketamine-induced psychomimetic effects. Compared to propofol alone or dexmedetomidine-based regimens, ketofol increases neurological adverse events [5, 13], because any ketamine exposure introduces a non-zero psychomimetic risk. The dose ratio matters substantially: the 1:1 ketofol ratio produced 21% recovery agitation versus 10% with the 4:1 ratio [14], indicating that lower ketamine-to-propofol ratios mitigate this effect at the cost of less analgesic benefit.

Recovery time heterogeneity is similarly explained by the comparator. Ketofol recovers faster than ketamine-based regimens (which have inherently longer dissociative recovery) [17, 18] but slower than propofol alone (which is ultrashort-acting) [5, 16]. For interventional radiology oncology, where throughput efficiency matters but not as critically as in emergency department

settings, the modest increase in recovery time (approximately 2–7 minutes versus propofol alone) may be an acceptable trade-off for improved hemodynamic and respiratory safety.

The optimal ketofol ratio for interventional radiology oncology cannot be definitively established from the current evidence, but the data suggest that lower ketamine proportions (1:2 to 1:4 ketamine-to-propofol) provide an effective balance. The 1:2 ratio was used in both oncology-specific studies that tested ketofol [1, 3] and was directly compared favorably to 1:3 in short procedures [15]. Higher ketamine proportions (1:1) increase the risk of psychomimetic effects and delayed recovery [14, 44], while very low proportions (1:5) may provide insufficient analgesic supplementation, though the neurosurgical data suggest maintained hemodynamic benefits even at this ratio [20].

For cancer-specific considerations, the evidence from Shehab et al. (2023) in cancer patients undergoing GI endoscopy demonstrated that ketamine-propofol had better sedation efficacy (lower time to target sedation, lower propofol consumption, faster eye-opening) than midazolam-propofol, with more stable hemodynamics [4, 4]. In oncology surgery, both Elshalakany et al. (2023) and Aryabiantara et al. (2018) found that adding ketamine to propofol-based TIVA reduced postoperative pain and morphine consumption [11, 12], an important benefit for cancer patients who may be at risk for opioid-related complications. The lack of significant differences in inflammatory markers (IL-6, IL-8) between ketamine-containing and propofol-only regimens [11, 12] suggests that the immunomodulatory effects of ketamine may not be clinically significant in this context, though the studies were likely underpowered for this endpoint.

The generalizability of findings to interventional radiology oncology is limited by several factors. Most primary studies enrolled ASA I–II patients [1, 2, 15, 18], whereas oncology patients frequently present with higher ASA classifications and significant comorbidities. Only Abdelgalil et al. (2024) specifically noted the limitation of excluding higher-risk patients and recommended future research including this population [2]. The diverse procedural contexts (emergency fracture reduction, endoscopy, brachytherapy, ablation) have different pain intensities, durations, and positional requirements, making direct extrapolation uncertain. Procedure duration is particularly

relevant: most ketofol studies involved brief procedures (under 30 minutes), whereas many interventional radiology oncology procedures (such as chemoembolization or complex ablations) may extend well beyond this timeframe, potentially requiring different dosing strategies than those studied.

In summary, ketofol at a 1:2 to 1:4 ketamine-to-propofol ratio appears to be a reasonable sedation strategy for interventional radiology oncology procedures where hemodynamic stability and respiratory safety are priorities, particularly in patients at risk for propofol-induced hypotension or those undergoing painful procedures requiring intrinsic analgesia. The trade-off includes a modestly increased risk of neurological adverse events (emergence phenomena, delayed cognitive recovery) and potentially higher PONV rates compared to propofol or dexmedetomidine-based alternatives. For procedures requiring tight hemodynamic control with minimal neuropsychiatric effects, dexmedetomidine-propofol may be preferable [2, 13], whereas for procedures prioritizing analgesia and cardiorespiratory stability, ketofol offers a well-characterized option with an established safety profile across thousands of patients in the broader PSA literature.

DISCUSSION

This systematic review of 58 sources, including four studies directly examining ketofol in cancer-specific interventional procedures and numerous meta-analyses across broader sedation contexts, reveals a consistent pattern of ketofol's pharmacological advantages tempered by important trade-offs. The findings warrant careful consideration of the unique requirements of interventional radiology oncology procedures and the specific vulnerabilities of the cancer patient population.

Hemodynamic Stability: The Most Robust Finding

The hemodynamic advantage of ketofol emerges as the most consistently demonstrated benefit across all included studies. In cervical cancer brachytherapy, Gupta et al. observed significantly less reduction in systolic and diastolic blood pressure with ketofol compared to propofol alone, with dramatically lower propofol supplementation requirements (20 mg vs. 800 mg)

(1). Similarly, Abdelgalil et al. reported more consistent heart rate and mean arterial pressure with ketamine-propofol versus dexmedetomidine-propofol during CT-guided bone biopsy in cancer patients (2). These findings align precisely with the pharmacological rationale: ketamine's sympathomimetic properties counterbalance propofol-induced vasodilation and myocardial depression.

The meta-analytic evidence confirms this advantage across thousands of patients. Jalili et al. demonstrated that ketofol significantly reduces hypotension (RR 0.11, 95% CI 0.17-0.97) and bradycardia (RR 0.47, 95% CI 0.28-0.72) compared to propofol (6). The esketamine-propofol meta-analyses by Kumar et al. and Huang et al. corroborated these findings with risk ratios of 0.40 and 0.37 for hypotension, respectively (7,8). This hemodynamic protection is particularly relevant for interventional radiology oncology, where patients may present with malignancy-related cardiovascular compromise, chemotherapy-induced cardiomyopathy, or dehydration from poor oral intake or gastrointestinal symptoms (4).

Respiratory Safety: Propofol-Sparing Effect

The respiratory safety advantage of ketofol is equally well-supported, though the mechanism appears indirect. Wen et al. found that ketamine-propofol significantly reduces respiratory adverse events compared to propofol alone in adults (RR 0.48, 95% CI 0.39-0.60) (9). Sharif et al.'s network meta-analysis confirmed that propofol-opioid combinations were associated with significantly more respiratory adverse events than ketamine-propofol (RR 2.03, 95% CI 1.32-3.13) (5,19). The large case series by Maruf et al. reported desaturation in only 2.07% of 1013 patients receiving ketofol, all corrected with supplemental oxygen (51).

However, when compared to dexmedetomidine-based combinations rather than propofol alone, ketofol's respiratory advantage diminishes. Elsaeidy et al. found higher hypoxia rates with ketofol versus ketamine-dexmedetomidine (20.3% vs. 12.4%) (45), and Esmaillian et al. observed less oxygen reduction in the ketamine-dexmedetomidine group (47). This suggests that the respiratory benefit of ketofol is primarily a propofol-sparing effect rather than an intrinsic respiratory stimulant property of ketamine. For interventional radiology oncology procedures requiring deep sedation, this distinction matters: ketofol may be preferable when propofol

monotherapy would otherwise be used, but dexmedetomidine combinations may offer superior respiratory profiles when preservation of spontaneous ventilation is paramount.

The Paradox of Neurological Adverse Events

Perhaps the most nuanced finding concerns neurological adverse events, where the comparator determines the direction of effect. Compared to ketamine alone, ketofol significantly reduces emergence phenomena. Lemoel et al. reported a 22% reduction in unpleasant recovery reactions with ketofol versus ketamine ($P<0.01$) (21), and Azizkhani et al. found that adding propofol reduced recovery agitation from 58% to 29% (43). This attenuation occurs because propofol's GABAergic effects counterbalance ketamine's NMDA antagonist-induced psychomimetic effects.

However, compared to propofol alone or dexmedetomidine-based regimens, ketofol increases neurological adverse events. Sharif et al. found that ketamine-propofol was associated with significantly more neurological adverse events than midazolam-opioids (RR 3.68, 95% CI 1.08-12.53) (5). Garg et al. reported a concerning 66.7% incidence of postoperative cognitive dysfunction with ketamine-propofol versus 0% with propofol-dexmedetomidine during ERCP (13). Martsinkevich et al. observed euphoria in 26% of patients receiving ketamine-propofol, though no neuropsychiatric abnormalities persisted at 2 and 8 hours post-procedure (16).

The dose ratio critically influences this trade-off. Miner et al. demonstrated that recovery agitation occurred in 21% of patients receiving 1:1 ketofol, compared to only 10% with 4:1 ketofol (propofol-predominant) and 8% with propofol alone (14). This dose-dependent effect suggests that lower ketamine proportions (1:3 to 1:4) may preserve hemodynamic benefits while minimizing psychomimetic risk. For interventional radiology oncology, where procedures vary widely in pain intensity and duration, the optimal ratio likely requires individualization based on procedure-specific analgesic requirements and patient-specific risk factors for emergence phenomena.

Recovery Profile: Context-Dependent Interpretation

Recovery time findings demonstrate similar context dependence. Ketofol consistently enables faster recovery than ketamine-based regimens (15,18,35) but slower recovery than propofol alone (5,16). The magnitude of prolongation versus propofol monotherapy is modest—

approximately 2-7 minutes in most studies (16,24,53). For busy interventional radiology suites where procedure turnover is a consideration, this difference may be clinically acceptable given the improved safety profile.

Patient satisfaction, however, consistently favors ketofol. The network meta-analysis by Sharif et al. reported that patient satisfaction was best with ketamine-propofol compared to midazolam-opioids (MD 1.47 points, high certainty) (5). Bahreini et al. found higher patient and physician satisfaction with ketamine-propofol than thiopental-fentanyl, along with lower procedure recall (38.29% vs. 79.59%) (55). This suggests that despite slightly longer recovery, patients value the combination's safety and amnestic properties.

Propofol Consumption and Analgesic Benefits

The consistent reduction in propofol consumption when combined with ketamine (30-65% reduction across studies) (1,7,8,10,56) has important implications beyond cost savings. Lower propofol doses directly translate to reduced risk of hypotension and respiratory depression, the very complications ketofol seeks to avoid. The analgesic synergy between ketamine and propofol, demonstrated by longer time to rescue analgesia (3) and reduced postoperative opioid consumption (11,12), is particularly valuable for oncology patients at risk for opioid-related complications including ileus, respiratory depression, and tolerance.

Cancer-Specific Considerations

The limited direct evidence in cancer patients provides preliminary support for ketofol in this population. Shehab et al. demonstrated that ketamine-propofol achieved better sedation efficacy (lower time to target sedation, lower propofol consumption, faster eye-opening) than midazolam-propofol in cancer patients undergoing GI endoscopy, with more stable hemodynamics (4). In oncology surgery, both Elshalakany et al. and Aryabiantara et al. found that adding ketamine to propofol-based TIVA reduced postoperative pain and morphine consumption without significant differences in inflammatory markers (11,12).

The finding by Sartins et al. that ketofol provides better glycemic control than ketamine alone during TIVA (52) may have particular relevance for oncology patients, who frequently

experience metabolic derangements from malignancy, corticosteroid use, or pre-existing diabetes. However, this finding requires confirmation in the interventional radiology context.

Comparison with Alternative Sedation Regimens

The emergence of dexmedetomidine-based regimens presents an important comparator for ketofol in interventional radiology oncology. Dexmedetomidine-propofol combinations demonstrate superior sedation efficacy (2), more stable hemodynamics (13,29), lower PONV rates (13), and potentially fewer neuropsychiatric effects (13) than ketamine-propofol in some studies. However, dexmedetomidine is associated with bradycardia, requires longer recovery, and may be less effective for procedures requiring profound analgesia (25,45). The choice between ketofol and dexmedetomidine-based regimens should therefore be guided by procedure-specific requirements and patient characteristics.

Optimal Dosing Recommendations

Synthesizing the available evidence, a 1:2 to 1:4 ketamine-to-propofol ratio appears optimal for interventional radiology oncology procedures. The 1:2 ratio was successfully used in both oncology-specific studies examining ketofol (1,3) and compared favorably to 1:3 in short procedures (15). Higher ketamine proportions (1:1) increase psychomimetic risk and prolong recovery (14,44), while very low proportions (1:5) may provide insufficient analgesic supplementation, though hemodynamic benefits may persist (20). Initial bolus dosing of 0.5-0.75 mg/kg ketamine with 1.5-3 mg/kg propofol, titrated to effect, represents a reasonable starting point based on the literature (1,2,24).

CONCLUSION AND RECOMMENDATIONS

This systematic review demonstrates that ketamine-propofol (ketofol) at ratios of 1:2 to 1:4 represents a pharmacologically rational and clinically effective sedation strategy for interventional radiology oncology procedures. The combination leverages ketamine's sympathomimetic and analgesic properties to counterbalance propofol's hypotensive and respiratory depressant effects, resulting in significantly improved hemodynamic stability and respiratory safety compared to

propofol monotherapy. These advantages are consistently demonstrated across multiple meta-analyses and individual studies, with the strongest evidence supporting reduced hypotension (RR 0.11-0.40), bradycardia (RR 0.34-0.47), and respiratory adverse events (RR 0.48-0.55).

However, these benefits are accompanied by trade-offs including increased neurological adverse events compared to propofol alone (emergence reactions, cognitive dysfunction) and modest prolongation of recovery time (2-7 minutes). The optimal balance between cardiorespiratory stability and neuropsychiatric risk requires individualized patient selection and careful attention to ketamine-to-propofol ratio, with lower ketamine proportions (1:3 to 1:4) minimizing psychomimetic effects while preserving hemodynamic benefits.

Clinical Recommendations:

1. Ketofol should be considered for interventional radiology oncology procedures in patients at risk for propofol-induced hypotension, including those with malignancy-related cardiovascular compromise, dehydration, or chemotherapy-induced cardiomyopathy.

2. A 1:2 to 1:4 ketamine-to-propofol ratio is recommended, with initial dosing of ketamine 0.5-0.75 mg/kg and propofol 1.5-3 mg/kg, titrated to desired sedation depth.

3. Ketofol may be preferable to propofol-opioid combinations when respiratory safety is a primary concern, given the reduced risk of respiratory depression.

4. For procedures where preservation of spontaneous ventilation is paramount and psychomimetic effects must be minimized, dexmedetomidine-propofol combinations may offer advantages over ketofol.

5. Patients should be counseled preoperatively about the possibility of emergence phenomena, which are typically transient and self-limited.

Future Research Directions:

1. Large prospective studies examining ketofol specifically in high-risk oncology patients (ASA III-IV) undergoing interventional radiology procedures are urgently needed.

2. Comparative effectiveness research directly comparing ketofol with dexmedetomidine-based regimens in the interventional radiology oncology context would inform optimal agent selection.

3. Dose-finding studies for prolonged procedures (>60 minutes) are required to establish optimal infusion protocols and rescue dosing strategies.

4. Investigation of ketofol's effects on cancer-related outcomes, including potential immunomodulatory effects and influence on metastatic potential, represents an important long-term research priority.

5. Development and validation of patient selection algorithms incorporating cardiovascular risk, procedure-specific factors, and neuropsychiatric vulnerability would facilitate personalized sedation strategies.

In conclusion, ketofol offers a valuable addition to the sedation armamentarium for interventional radiology oncology, providing improved cardiorespiratory stability at the cost of modestly increased neuropsychiatric risk. When used at appropriate ratios in appropriately selected patients, the benefits outweigh the risks, supporting its role as a reasonable sedation option in this challenging clinical context.

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