



Total intravenous anesthesia in kidney transplantation: A narrative review

Ervandy Rangganata, Juanita Castellanos De Brigard, Apostolos Prionas, Nagy Habib, Vassilios E Papalois

Peer review: Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific quality: Grade A, Grade B, Grade C

Novelty: Grade A, Grade B, Grade C

Creativity or innovation: Grade B, Grade B, Grade C

Scientific significance: Grade B, Grade B, Grade C

P-Reviewer: Lindner C, Associate Professor, MD, Chile; Patel K, MD, Senior Scientist, United States; Yang J, China

Received: March 31, 2026

Revised: June 30, 2026

Accepted: July 27, 2026

Published online: September 18, 2026

Processing time: 155 Days and 8.8 Hours

Copyright: ©Author(s) 2026. This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution-NonCommercial \(CC BY-NC 4.0\)](#) license. No commercial re-use. See [permissions](#). **Published by** Baishideng Publishing Group Inc.



Ervandy Rangganata, Juanita Castellanos De Brigard, Apostolos Prionas, Nagy Habib, Vassilios E Papalois, Department of Surgery and Cancer, Imperial College London, London W12 0HS, United Kingdom

ORCID number: Ervandy Rangganata [0000-0003-3273-3113](#); Juanita Castellanos De Brigard [0009-0006-2911-0395](#); Apostolos Prionas [0000-0002-7867-9266](#); Nagy Habib [0000-0003-4920-4154](#); Vassilios E Papalois [0000-0003-1645-8684](#).

Corresponding author: Ervandy Rangganata, MD, Department of Surgery and Cancer, Imperial College London, Du Cane Road, London W12 0HS, United Kingdom. e.rangganata24@imperial.ac.uk

Abstract

BACKGROUND

Kidney transplantation is the treatment of choice for end-stage renal disease. Whether propofol-based total intravenous anaesthesia (TIVA) confers advantages over volatile anaesthesia for perioperative stability, recovery, and graft outcomes remains debated.

AIM

To synthesise the currently available comparative evidence on propofol-based TIVA versus volatile anaesthesia in adult kidney transplantation—focusing on haemodynamic stability, renal injury biomarkers, early graft function, recovery, postoperative nausea and vomiting (PONV), immunologic outcomes, and safety—and to identify the key evidence gaps and priorities for future research.

METHODS

We performed a narrative review following the Scale for the Assessment of Narrative Review Articles framework, with structured search and selection consistent with PRISMA-S reporting. PubMed/MEDLINE, EMBASE, Cochrane CENTRAL, Scopus, and Web of Science were searched from inception to February 2026. Quality was appraised using Cochrane Risk of Bias 2 and ROBINS-I. Six studies were directly eligible in adult kidney transplant recipients; four supplementary mechanistic sources informed interpretation.

RESULTS

TIVA provided haemodynamic stability and immediate graft function equivalent to volatile anaesthesia. Urinary tubular biomarkers (kidney injury molecule-1, N-acetyl- β -D-glucosaminidase) were modestly lower with propofol in the VAPOR-1

trial ($n = 57$ living-donor pairs), but this did not translate into differences in delayed graft function, serum creatinine, or one-year graft survival. TIVA was associated with faster extubation and lower PONV, though recovery comparisons were confounded by opioid co-administration. Acute rejection rates did not differ significantly.

CONCLUSION

Propofol-based TIVA is a safe and effective alternative to volatile anaesthesia in kidney transplantation. Whether the cellular-level biomarker signal translates into clinically meaningful renoprotection in higher-risk grafts requires adequately powered multicentre trials with standardised perioperative protocols.

Key Words: Kidney transplantation; Total intravenous anesthesia; Propofol; Volatile anesthesia; Sevoflurane; Ischaemia-reperfusion injury; Delayed graft function; Postoperative recovery

Core Tip: This narrative review compares propofol-based total intravenous anaesthesia (TIVA) with volatile anaesthesia in adult kidney transplantation. Across six comparable studies, TIVA delivers haemodynamic stability and graft function equivalent to volatile maintenance, with reproducible advantages in extubation time and postoperative nausea and vomiting—the latter clinically important for reliable early enteral absorption of immunosuppressants. The biomarker signal of reduced tubular stress under propofol from the VAPOR-1 trial has not translated into measurable clinical benefit in low-risk living-donor cohorts. The next critical step is an adequately powered multicentre randomised trial in extended-criteria-donor and donation-after-circulatory-death recipients, with standardised opioid, fluid, and vasopressor protocols.

Citation: Rangganata E, Castellanos De Brigard J, Prionas A, Habib N, Papalois VE. Total intravenous anesthesia in kidney transplantation: A narrative review. *World J Transplant* 2026; 16(3): 121739

URL: <https://www.wjgnet.com/2220-3230/full/v16/i3/121739.htm>

DOI: <https://dx.doi.org/10.5500/wjt.121739>

INTRODUCTION

Kidney transplantation is the preferred renal replacement therapy for suitable patients with end-stage renal disease (ESRD), offering superior survival, improved quality of life, and lower long-term cost compared with dialysis. Yet the perioperative period remains physiologically hazardous. Recipients frequently present with longstanding hypertension, cardiomyopathy, endothelial dysfunction, and autonomic neuropathy; intraoperative management must bridge preload dependence, afterload sensitivity, and a propensity to vasoplegia while accommodating the abrupt haemodynamic shifts that accompany graft reperfusion. Anaesthetic technique is therefore not a neutral choice: It can influence systemic and renal haemodynamics, inflammatory signalling, ischaemia-reperfusion injury (IRI), recovery trajectories, and ultimately early graft performance[1-4].

Total intravenous anaesthesia (TIVA)—most commonly propofol-based with a short-acting opioid (*e.g.*, remifentanyl or alfentanil)—has gained favour as an alternative to volatile anaesthesia (isoflurane, sevoflurane, desflurane) in abdominal solid-organ transplantation. Modern TIVA typically uses target-controlled infusion (TCI), which leverages pharmacokinetic-pharmacodynamic models (often tri-compartmental) to achieve and maintain a desired effect-site concentration [5]. By smoothing plasma-concentration peaks and troughs, TCI can reduce sympathetic swings and facilitate tight control of anaesthetic depth—features that are attractive in recipients with limited cardiovascular reserve. Propofol itself exerts antioxidant and anti-inflammatory actions (free-radical scavenging, inhibition of NF- κ B signalling)[1,6], while volatile agents are associated with so-called anaesthetic preconditioning, thought to involve mitochondrial K_{ATP} channels, adenosine, and sphingosine-1-phosphate pathways[1]. Whether these mechanistic differences translate into clinically meaningful advantages in kidney transplantation remains debated.

Of particular interest is whether anaesthetic choice modulates renal blood flow (RBF), sympathetic vasomotor tone, and the susceptibility of the graft to IRI. Iguchi *et al*[7] demonstrated higher RBF and renal vascular conductance under propofol-based TIVA than under volatile anaesthesia in an ovine model, attributable to reduced sympathetic vasomotor drive. More recently, a single-centre randomised controlled study by Franzén *et al*[8] compared renal function during sevoflurane *vs* total intravenous propofol anaesthesia in surgical patients, providing additional contemporary evidence relevant to the propofol-versus-volatile renal-effects question.

The transplant operation imposes distinct physiological phases: (1) Dissection and iliac vessel preparation with relatively high surgical stimulation; (2) Graft implantation with arterial/venous clamping, lower stimulation, and evolving preload; (3) Unclamping and reperfusion, characterised by abrupt afterload reduction, transient acidosis, and pro-inflammatory mediator wash-in; and (4) Ureteroneocystostomy and closure, when emergence quality and analgesic strategy shape early extubation and postoperative recovery[4,9-12]. Concurrently, immunosuppressive induction (*e.g.*, high-dose corticosteroids, calcineurin-inhibitor exposure), diuretics/osmotic agents (mannitol, furosemide), vasopressors, and goal-directed fluid therapy interact with anaesthetic choice to affect renal microcirculation. Against this backdrop, the desirable anaesthetic profile includes a stable mean arterial pressure (MAP) with adequate cardiac output and renal perfusion pressure after reperfusion; minimal systemic vascular resistance (SVR) fluctuations; a low incidence of postop-

perative nausea and vomiting (PONV) to facilitate early enteral intake and immunosuppressant administration; rapid, smooth emergence; and neutrality with respect to alloimmune activation and graft IRI[9-12].

This narrative review synthesises data from randomised and observational studies that directly compare propofol-based TIVA with volatile anaesthesia in adult kidney transplant recipients. We foreground haemodynamic behaviour, renal injury biomarkers, early graft function [including urine output and delayed graft function (DGF)], recovery profiles (emergence times, PONV), analgesic needs, immunologic outcomes, and safety. The intent is to provide a pragmatic, clinically oriented appraisal for anaesthetists and transplant teams considering TIVA as a default or selective strategy. Throughout this review, the term “TIVA” refers specifically to propofol-based regimens (typically combined with a short-acting opioid), whereas “volatile anaesthesia” or “gas anaesthesia” refers to inhalational maintenance with sevoflurane, desflurane, or isoflurane, usually combined with intravenous opioids[1,2,12].

Directly comparable evidence in adult kidney transplant recipients is limited. Only six studies meet the strict eligibility criteria of this review: Aditjaningsih *et al*[9] in 2019, Modesti *et al*[2] in 2006, Babacan *et al*[12] in 1998, the VAPOR-1 trial (Nieuwenhuijs-Moeke *et al*[10] in 2017), Lee *et al*[3] in 2013, and Calixto-Flores *et al*[13] in 2020. Aggregate sample size across these six studies is fewer than 200 recipients. We supplement this small evidence base with four mechanistically instructive sources that do not meet the strict eligibility criteria: A randomised controlled trial (RCT) in living kidney donors (Han *et al*[11] in 2020), a contemporary single-centre RCT comparing renal function during sevoflurane *vs* propofol-based anaesthesia in surgical patients (Franzén *et al*[8] in 2022), an RCT in paediatric living-related liver transplantation (Liu *et al*[1] in 2024), and an ovine model (Iguchi *et al*[7] in 2019). Readers should weigh the conclusions of this review in the light of this limited directly-comparable evidence base.

MATERIALS AND METHODS

Review framework and reporting

This work is reported as a narrative review following the Scale for the Assessment of Narrative Review Articles framework[14]. It incorporates structured search and selection elements consistent with the PRISMA-S reporting guidance for literature searches[15]. Because the question is broad – encompassing pharmacology, haemodynamics, biomarkers, clinical outcomes, and operational considerations – a narrative synthesis was preferred to a formal systematic review with meta-analysis. The review protocol was prospectively agreed among the authors prior to database searches; no formal registration in PROSPERO was undertaken because PROSPERO does not register narrative reviews.

Databases and search strategy

Five bibliographic databases were searched: PubMed/MEDLINE, EMBASE (Elsevier), the Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science Core Collection. The search period covered database inception to 28 February, 2026. The reference lists of all included studies and of relevant prior systematic reviews and meta-analyses were hand-searched to identify additional eligible records.

The PubMed search string, adapted with appropriate syntax for each database, was as follows: (“Total intravenous anaesthesia”[tiab] OR “total intravenous anesthesia”[tiab] OR TIVA[tiab] OR propofol[MeSH] OR propofol[tiab] OR “target-controlled infusion”[tiab] OR TCI[tiab]) AND (“kidney transplantation”[MeSH] OR “renal transplantation”[tiab] OR “kidney transplant”[tiab] OR “renal transplant”[tiab] OR “graft kidney”[tiab]) AND (sevoflurane[tiab] OR isoflurane[tiab] OR desflurane[tiab] OR “volatile anaesthetic”[tiab] OR “volatile anesthetic”[tiab] OR “inhalational anaesthesia”[tiab] OR “inhalational anesthesia”[tiab] OR “balanced anaesthesia”[tiab] OR “balanced anesthesia”[tiab]).

Eligibility criteria

Inclusion criteria: (1) Adult kidney transplant recipients (≥ 18 years); (2) RCTs, prospective observational studies, or retrospective cohort studies; (3) Direct comparison of propofol-based TIVA with volatile (inhalational) anaesthesia for the maintenance phase; (4) Reporting of at least one outcome of interest (intraoperative haemodynamics, renal perfusion or urine output, renal injury biomarkers, early or late graft function, recovery, PONV, analgesia, acute rejection, or anaesthetic complications); and (5) Full text in English.

Exclusion criteria: (1) Case reports, case series of fewer than ten patients, editorials, narrative reviews, and conference abstracts without full-text peer-reviewed publication; (2) Paediatric-only cohorts (< 18 years); (3) Studies in donor nephrectomy unless they reported recipient outcomes; (4) Non-renal solid-organ transplantation (cardiac, hepatic, lung, pancreas), although mechanistically instructive findings from liver-transplant trials (*e.g.*, Liu *et al*[1]) are cited in the narrative when relevant; and (5) Purely preclinical or *in-vitro* studies, except where used to provide mechanistic context (*e.g.*, Iguchi *et al*[7] in 2019, cited as ovine-model evidence).

Study selection and data extraction

Two reviewers (Rangganata E and Castellanos De Brigard J) independently screened titles and abstracts using Rayyan [16], followed by independent full-text review of potentially eligible records. Disagreements were resolved by discussion with a third reviewer (Prionas A). For each included study, the following data were abstracted into a standardised template: Study design, country, year, sample size, donor type, recipient demographics, anaesthetic regimens (induction, maintenance, opioid co-administration, neuromuscular blockade), fluid strategy (crystalloid type, colloid use, restrictive *vs* liberal, goal-directed), use of mannitol/furosemide, vasopressor agent and threshold, monitoring (*e.g.*, bispectral index, cardiac-output monitoring), and all outcomes of interest. Authors of included studies were not contacted for clarification,

as no critical missing data were identified during extraction.

Risk-of-bias assessment

The risk of bias of each RCT in human subjects was appraised using the Cochrane Risk of Bias 2 (RoB 2) tool across five domains (randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result)[17]. Non-randomised comparative studies in human subjects were assessed using the ROBINS-I tool across seven domains (confounding, selection of participants, classification of intervention, deviations from intervention, missing data, measurement of outcomes, and selection of the reported result)[18]. The preclinical ovine model (Iguchi *et al*[7] in 2019) is not amenable to RoB 2 or ROBINS-I appraisal and is therefore not included in Table 1; its findings are discussed only for mechanistic context. Two reviewers conducted the assessment independently, with disagreements resolved by consensus. The aggregate risk-of-bias judgements are summarised in Table 1.

Synthesis

Given the marked heterogeneity in anaesthetic regimens, fluid strategies, vasopressor selection, opioid co-administration, donor type, and outcome definitions, a quantitative meta-analysis was not appropriate. Instead, findings were synthesised narratively, organised by outcome domain. We commented on the consistency of results across studies, on the era effect (older trials using routine dopamine and liberal crystalloid *vs* contemporary studies using goal-directed therapy and norepinephrine), on the opioid co-administration confounder, and on the generalisability of conclusions beyond low-risk living-donor recipients.

RESULTS

Overview of included studies

Ten studies comparing propofol-based TIVA with volatile anaesthesia in kidney transplant recipients or in mechanistically related populations were identified and included. Six studies directly meeting our eligibility criteria in adult kidney transplant recipients form the core of the synthesis: Four RCTs [Aditioningsih *et al*[9] in 2019, VAPOR-1 trial (Nieuwenhuijs-Moeke *et al*[10] in 2017), Modesti *et al*[2] in 2006, Babacan *et al*[12] in 1998], one combined retrospective and prospective comparative study (Lee *et al*[3] in 2013), and one retrospective single-arm observational analysis (Calixto-Flores *et al*[13] in 2020). Four additional studies were cited as mechanistically instructive evidence but did not meet the strict eligibility criteria: An RCT in living kidney donors referenced for recovery outcomes (Han *et al*[11] in 2020); a contemporary single-centre RCT comparing renal function during sevoflurane *vs* propofol-based anaesthesia in surgical patients (Franzén *et al*[8] in 2022); an RCT in paediatric living-related liver transplantation (Liu *et al*[1] in 2024); and an ovine model describing renal perfusion, oxygenation, and sympathetic activity under volatile or intravenous anaesthesia (Iguchi *et al*[7] in 2019). All ten studies are summarised in Table 2. Risk-of-bias appraisal of the nine human comparative studies is summarised in Table 1 (the preclinical ovine model is not amenable to RoB 2/ROBINS-I appraisal and is omitted from Table 1). Perioperative fluid and vasopressor strategies are summarised in Table 3 for the eight human comparative studies relevant to the adult kidney transplant setting (the six directly-eligible kidney-transplant studies, Han *et al*[11] donor nephrectomy, and Franzén *et al*[8] contemporary surgical cohort); the paediatric liver-transplant trial and the ovine model are omitted from Table 3 as the comparison is not directly extrapolable.

The transplant-specific implications of each anaesthetic technique are summarised in Table 4. Rather than restate the generic pharmacological differences between propofol-based TIVA, volatile anaesthesia, and balanced anaesthesia, Table 4 maps each technique to the outcome domains that matter most in kidney transplantation: Effect at reperfusion, tubular injury biomarker signal, recovery and PONV (with downstream consequences for early oral immunosuppressant absorption), acute rejection risk, hard clinical endpoints (DGF, graft survival), recipient-specific safety considerations, quality of available evidence, and practical infrastructure[1,2,12].

Haemodynamic stability (MAP, cardiac index/stroke volume index, SVR index)

Haemodynamic stability is one of the most critical considerations during kidney transplantation, especially at graft reperfusion when abrupt changes in SVR and cardiac filling pressures can jeopardise renal perfusion. Across the included studies, TIVA demonstrated comparable, and in some circumstances more favourable, haemodynamic profiles when compared with volatile anaesthetics. In the RCT by Aditioningsih *et al*[9] in 2019, reflecting contemporary goal-directed haemodynamic management with norepinephrine and balanced crystalloid, 46 kidney transplant recipients were randomised to TCI propofol or maintenance with sevoflurane. MAP, cardiac index (CI), stroke volume index (SVI), and SVR index (SVRI) were measured at defined intraoperative time points. The investigators found no differences in MAP, CI, or SVI between groups; however, SVRI was consistently lower in the propofol group during intubation and surgical incision[9]. This observation is consistent with the known vasodilatory property of propofol. Importantly, the decrease in SVR did not compromise perfusion because cardiac output was preserved and vasopressor support was easily titrated when needed. Similar results were reported by Modesti *et al*[2] in 2006 and Babacan *et al*[12] in 1998. Both trials compared propofol-based anaesthesia with isoflurane and found that haemodynamic stability could be achieved with either approach, provided that fluids and vasoactive drugs were carefully adjusted[2,12]. Both trials, however, predate modern goal-directed haemodynamic management: They used routine dopamine infusions (1-3 µg/kg/min) and a liberal crystalloid or hydroxyethyl-starch strategy that is now considered obsolete. Their findings should therefore be inter-

Table 1 Risk-of-bias appraisal of included human comparative studies

Ref.	Design	Tool	Highest-risk domain(s)	Overall judgement	Comments
Aditioningsih <i>et al</i> [9], 2019	RCT (KT)	RoB 2	Blinding of personnel	Some concerns	Adequate randomisation; small sample size
Nieuwenhuijs-Moeke <i>et al</i> [10], 2017	RCT (KT)	RoB 2	Selection of reported result	Low-some concerns	Calculation-error corrigendum acknowledged
Modesti <i>et al</i> [2], 2006	RCT (KT)	RoB 2	Era effect; concomitant interventions	Some concerns	Dopamine infusions; HES colloids - now superseded
Babacan <i>et al</i> [12], 1998	RCT (KT)	RoB 2	Reporting; randomisation detail	High	Small sample size; limited methodological detail
Lee <i>et al</i> [3], 2013 (part-I)	Retrospective (KT)	ROBINS-I	Confounding	Serious	Non-randomised treatment allocation
Lee <i>et al</i> [3], 2013 (part-II)	Prospective (KT)	ROBINS-I	Confounding	Moderate	Did not confirm part-I signal
Calixto-Flores <i>et al</i> [13], 2020	Retrospective (KT)	ROBINS-I	Confounding; single-arm	Serious	No comparator group
Han <i>et al</i> [11], 2020	RCT (donors)	RoB 2	Indirectness (donors, not recipients)	Low (for donor outcomes)	Informs recovery outcomes only
Franzén <i>et al</i> [8], 2022	RCT (surgical patients)	RoB 2	Indirectness (surgical pts, not KT)	Low (for renal function in surgical pts)	Contemporary mechanistic evidence; indirect for KT
Liu <i>et al</i> [1], 2024	RCT (paediatric LRLT)	RoB 2	Indirectness (paediatric, liver, not adult KT)	Low (for liver/kidney outcomes in infants)	Mechanistic reference only; not directly extrapolable

The preclinical ovine model (Iguchi *et al*[7] 2019) is not amenable to Risk of Bias 2 or ROBINS-I appraisal and is omitted. HES: Hydroxyethyl starch; RCT: Randomised controlled trial; KT: Kidney transplant; RoB 2: Risk of Bias 2; LRLT: Living-related liver transplantation.

puted with caution when extrapolating to contemporary practice. More recently, an observational cohort by Calixto-Flores *et al*[13] in 2020 of 30 recipients anaesthetised with TIVA demonstrated that MAP was maintained within acceptable limits throughout surgery and that spontaneous diuresis occurred in nearly 90% of cases without the need for excessive vasopressor doses. Taken together, these studies indicate that TIVA is at least non-inferior to volatile anaesthesia for haemodynamic stability. Propofol's vasodilatory effect is clinically manageable and does not compromise renal perfusion provided vigilant intraoperative management is in place.

Renal perfusion and urine output at reperfusion

Early graft perfusion and urine output following reperfusion are among the most immediate indicators of graft viability. The anaesthetic technique itself does not appear to critically influence these outcomes. Calixto-Flores *et al*[13] in 2020 demonstrated robust spontaneous diuresis in the majority of recipients following reperfusion under TIVA, with no signal of impaired graft perfusion. Aditioningsih *et al*[9] in 2019 and Modesti *et al*[2] in 2006 likewise reported no significant differences between TIVA and volatile groups in urine output either intraoperatively or in the early postoperative period. These findings suggest that anaesthetic choice may affect certain physiological parameters but that immediate graft diuresis is determined more by systemic perfusion goals, fluid management, and adjunctive agents such as mannitol or furosemide than by whether the recipient receives propofol or a volatile agent.

Biomarkers of renal injury (tubular stress)

Beyond clinical endpoints such as urine output and creatinine, biochemical markers of tubular injury provide a more sensitive window on the degree of IRI[10]. The VAPOR-1 trial conducted by Nieuwenhuijs-Moeke *et al*[10] in 2017 is the most detailed study in this regard. This randomised trial compared propofol with sevoflurane in living-donor kidney transplantation ($n = 57$ donor-recipient pairs) and measured urinary concentrations of kidney injury molecule-1 (KIM-1), N-acetyl- β -D-glucosaminidase (NAG), and heart-type fatty-acid-binding protein[10]. On postoperative day two, biomarker levels were significantly higher in the sevoflurane group, indicating more pronounced tubular stress compared with propofol. A subsequent corrigendum corrected calculation errors but preserved the overall direction of effect[10]. Importantly, however, the biomarker differences did not translate into measurable disparities in serum creatinine, dialysis requirement, or one-year graft survival. Lee *et al*[3] in 2013 compared volatile anaesthetics with propofol and initially observed that desflurane was associated with a higher early estimated glomerular filtration rate, although a subsequent prospective analysis failed to confirm a durable clinical advantage. The discordance between molecular signal and clinical endpoint is explored in detail in the Discussion.

Early graft function and DGF

In terms of early graft function, as assessed by creatinine decline, urine output, and the need for dialysis, no consistent differences have been demonstrated between TIVA and volatile anaesthesia. In the VAPOR-1 trial, despite higher biomarker elevations with sevoflurane, serum creatinine trajectories and dialysis requirement were equivalent across

Table 2 Summary of all ten studies included in this review (six directly eligible kidney-transplant studies plus four mechanistically instructive supplementary studies)

Study	Title	Design	Population	Intervention	Key outcomes
Aditjaningsih <i>et al</i> [9], 2019	TCI PROP <i>vs</i> SEVO haemodynamics in KT	Prospective RCT	46 adult KT recipients	TCI PROP <i>vs</i> SEVO	Similar MAP, CI, SVI; lower SVRI with PROP
Nieuwenhuijs-Moeke <i>et al</i> [10], 2017	PROP <i>vs</i> SEVO in LDKT	RCT	57 donor-recipient pairs	PROP, SEVO, PROSE	Higher urinary KIM-1, NAG with SEVO; non-significant numerical trend to higher acute rejection in PROP arm (did not reach statistical significance)
Modesti <i>et al</i> [2], 2006	Balanced <i>vs</i> TIVA for KT—older-era regimen	RCT	40 adult KT recipients	TIVA (PROP + remifentanyl) <i>vs</i> balanced (isoflurane + fentanyl)	TIVA: Faster recovery; balanced: Marginally better early pain control (likely opioid-driven)
Babacan <i>et al</i> [12], 1998	Assessment of TIVA in renal transplantation—older-era regimen	RCT	18 adult KT recipients	TIVA (PROP + alfentanil) <i>vs</i> balanced (isoflurane + fentanyl)	Faster recovery with TIVA; better early analgesia with balanced (likely opioid-driven)
Lee <i>et al</i> [3], 2013	Preconditioning effects of donor anaesthetic on grafted kidney function	Retrospective + prospective	LDKT recipients (adult)	SEVO, iso, desflurane <i>vs</i> PROP	Desflurane: Better early estimated glomerular filtration rate (part I); no significant difference in part II
Calixto-Flores <i>et al</i> [13], 2020	Effect of intravenous total anaesthesia on haemodynamic changes in renal transplant	Retrospective observational (single-arm)	30 adult KT recipients	TIVA (single arm)	Stable haemodynamics; spontaneous diuresis in approximately 90%
Han <i>et al</i> [11], 2020	PROP <i>vs</i> SEVO in laparoscopic donor nephrectomy	RCT	80 healthy kidney donors	PROP <i>vs</i> SEVO	Higher QoR-40, better ambulation, lower PONV, shorter LOS with PROP
Franzén <i>et al</i> [8], 2022	Renal function during SEVO or TIVA PROP—single-centre RCT	RCT	Surgical patients (not transplant)	SEVO <i>vs</i> PROP-based TIVA	Contemporary mechanistic evidence on renal function under SEVO <i>vs</i> PROP
Liu <i>et al</i> [1], 2024	PROP <i>vs</i> desflurane in infant LRLT	RCT	76 infants with LRLT	PROP <i>vs</i> desflurane	Lower ALT, AST, SCr, AKI in PROP group; mechanistic relevance only
Iguchi <i>et al</i> [7], 2019	Renal perfusion, oxygenation, and sympathetic nerve activity during volatile or intravenous general anaesthesia in sheep	Preclinical (ovine)	Sheep	PROP-based TIVA <i>vs</i> volatile anaesthesia	Higher RBF and renal vascular conductance under TIVA; reduced sympathetic vasomotor drive; mechanistic background only

TIVA: Total intravenous anaesthesia; TCI: Target-controlled infusion; KT: Kidney transplant; RCT: Randomised controlled trial; MAP: Mean arterial pressure; CI: Cardiac index; SVI: Stroke volume index; SVRI: Systemic vascular resistance index; LDKT: Living-donor kidney transplant; PROP: Propofol; SEVO: Sevoflurane; PROSE: Propofol induction and sevoflurane maintenance; KIM-1: Kidney injury molecule-1; NAG: N-acetyl- β -D-glucosaminidase; PONV: Postoperative nausea and vomiting; LOS: Length of stay; LRLT: Living-related liver transplantation; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SCr: Serum creatinine; AKI: Acute kidney injury; RBF: Renal blood flow.

both groups [10]. Aditjaningsih *et al* [9] in 2019 reported no difference in creatinine clearance or DGF between TIVA and sevoflurane arms. The observational findings of Calixto-Flores *et al* [13] in 2020 also documented significant postoperative reductions in serum creatinine with TIVA and a low incidence of DGF. Most of these studies enrolled living-donor recipients, who inherently carry a low baseline risk of DGF due to short ischaemia times and favourable graft quality [19]. Equivalence in these populations may therefore not generalise to higher-risk settings such as deceased-donor or donation-after-circulatory-death (DCD) transplantation, where DGF is a strong predictor of long-term graft and patient survival [19].

Recovery profile and emergence

Recovery is a domain where TIVA has demonstrated consistent advantages. Several trials observed that patients anaesthetised with propofol experienced shorter times to extubation and higher early recovery scores compared with isoflurane. These include the studies by Modesti *et al* [2] in 2006 and Babacan *et al* [12] in 1998. Both used opioid regimens (alfentanil and fentanyl) that are now uncommon and predate the widespread adoption of remifentanyl and goal-directed perioperative management. Propofol has a favourable context-sensitive half-time that permits rapid emergence, especially when combined with ultra-short-acting opioids such as remifentanyl [5]. Volatile anaesthetics, by contrast, depend on pulmonary elimination and may accumulate in tissue compartments, slowing recovery after long procedures. These differences have important operational implications: Faster emergence can facilitate earlier intensive care unit (ICU) transfer and streamlined perioperative pathways. However, the magnitude of TIVA's recovery advantage in the

Table 3 Perioperative fluid and vasoactive regimens in the eight human comparative studies

Ref.	Fluid type	Fluid strategy	Vasopressor	Mannitol/furosemide	Era effect
Aditioningsih <i>et al</i> [9], 2019	Balanced crystalloid	Goal-directed; SVV-guided	Norepinephrine	Mannitol 0.5 g/kg	Contemporary
Nieuwenhuijs-Moeke <i>et al</i> [10], 2017	Balanced crystalloid; albumin if needed	Goal-directed	Norepinephrine, ephedrine	Both, at reperfusion	Contemporary
Modesti <i>et al</i> [2], 2006	Crystalloid + HES colloid	Liberal; CVP-guided	Dopamine infusion	Mannitol routinely	Older era
Babacan <i>et al</i> [12], 1998	Crystalloid (Ringer)	Liberal	Dopamine infusion	Mannitol + furosemide	Older era
Han <i>et al</i> [11], 2020	Balanced crystalloid	Restrictive	Ephedrine, phenylephrine	Not reported	Contemporary
Lee <i>et al</i> [3], 2013	Balanced crystalloid	Goal-directed	Mixed	Mannitol; furosemide	Contemporary
Calixto-Flores <i>et al</i> [13], 2020	Balanced crystalloid	Goal-directed; conservative	Norepinephrine	Mannitol	Contemporary
Franzén <i>et al</i> [8], 2022	Balanced crystalloid	Goal-directed (per institutional protocol)	Norepinephrine	N/A (non-transplant surgery)	Contemporary

The preclinical ovine model (Iguchi *et al*[7] in 2019) and the paediatric living-related liver transplant trial (Liu *et al*[1] in 2024) are omitted because the comparison of perioperative fluid and vasopressor protocols is not directly relevant to the adult kidney transplant setting. SVV: Stroke volume variation; CVP: Central venous pressure; HES: Hydroxyethyl starch; N/A: Not available.

published trials is confounded by the choice of opioid in each arm, as discussed in the Discussion section on opioid co-administration.

PONV

PONV is a recognised cause of patient discomfort and can delay oral intake and timely administration of immunosuppressive medications. Propofol possesses intrinsic antiemetic properties[6], and its use in TIVA protocols has consistently been associated with lower rates of PONV than volatile anaesthetics. Han *et al*[11] in 2020, while focusing on living kidney donors, demonstrated significantly reduced PONV with TIVA, and transplant-recipient studies have reported similar trends, underscoring a reproducible benefit. This reduction in PONV not only improves patient comfort but also has direct clinical relevance in transplant medicine, where early and reliable absorption of calcineurin inhibitors and corticosteroids is crucial for graft protection. Erratic enteral intake during the first 48 hours can produce tacrolimus trough variability and sub-therapeutic immunosuppression at precisely the most immunologically vulnerable phase of recovery.

Analgesic consumption and early pain control

Analgesic requirements in the immediate postoperative period vary depending on anaesthetic regimens and intraoperative opioid use. Modesti *et al*[2] in 2006 found that recipients maintained with volatile anaesthesia reported slightly better pain control in the first postoperative hour, largely due to longer-acting opioids in the balanced anaesthesia regimen. This difference was short-lived, as standardised multimodal analgesia in the recovery room equalised pain scores within hours[2]. In contemporary practice, where multimodal and opioid-sparing strategies are increasingly standard, the influence of anaesthetic maintenance on pain outcomes is likely minimal. Both the Modesti finding and the broader recovery and analgesia signal in the literature are, however, confounded by opioid choice—a point discussed in detail below.

Immunologic outcomes (acute rejection)

Immunologic outcomes such as acute rejection are, in theory, susceptible to modulation by anaesthetic technique, given that both propofol[6] and volatile agents exert immunomodulatory effects. Evidence in humans is sparse and inconsistent. In the VAPOR-1 trial a numerically higher incidence of early biopsy-proven acute rejection was reported in the propofol arm, although this did not reach statistical significance and was likely confounded by variability in immunosuppressive regimens and donor-recipient characteristics[10]. No other study has corroborated this finding, and at present no compelling evidence indicates that anaesthetic maintenance influences rejection risk in a clinically meaningful way.

Complications and length of stay

With respect to complications and length of hospital stay, no significant differences were observed between TIVA and volatile anaesthesia. None of the trials reported serious anaesthesia-related adverse events, and postoperative length of stay appeared more dependent on institutional protocols, patient comorbidities, and surgical factors than on anaesthetic choice. While faster emergence and reduced PONV with TIVA may theoretically shorten recovery-room or ICU stays, this has not consistently translated into shorter hospitalisation in published series.

Table 4 Transplant-specific implications of propofol-based total intravenous anaesthesia vs volatile anaesthesia in kidney transplantation

Aspect	TIVA (propofol-based)	Volatile (sevoflurane/isoflurane/desflurane)	Clinical implication in kidney transplantation
Effect at reperfusion	Modest vasodilatation; SVR drops; manageable with norepinephrine and balanced crystalloid	Stable SVR; theoretical preconditioning <i>via</i> mitochondrial K _{ATP} channels	Both techniques are safe at unclamping when fluid and vasopressor support are titrated; no signal of reperfusion-related haemodynamic collapse with either
Tubular injury biomarkers (KIM-1, NAG)	Lower urinary concentrations in VAPOR-1 (<i>n</i> = 57 LDKT pairs)	Higher urinary concentrations in VAPOR-1	Biomarker signal favouring TIVA at the molecular level in a single small LDKT trial; not yet translated into hard clinical endpoints
Time to extubation and recovery quality	Faster (favourable context-sensitive half-time); often combined with remifentanyl	Slower (pulmonary elimination, tissue accumulation); often combined with fentanyl in published comparisons	Earlier ICU step-down with TIVA, but recovery comparisons are confounded by opioid choice (see Discussion)
PONV incidence	Significantly lower (intrinsic anti-dopaminergic and 5-HT ₃ antiemetic effect)	Higher	Reliable early oral tacrolimus and MMF absorption – clinically important for stable trough levels in the most immunologically vulnerable post-operative phase
Acute rejection risk	Non-significant numerical trend to higher rejection in propofol arm of VAPOR-1 only; not replicated	No significant signal	No compelling evidence that anaesthetic maintenance meaningfully alters rejection risk
DGF/1-year graft survival	No demonstrated difference	No demonstrated difference	Hard clinical endpoints comparable; LDKT-dominant evidence limits generalisability to ECD/DCD recipients
Recipient-specific safety	Injection pain; hypertriglyceridaemia (lipid emulsion); rare PRIS with prolonged infusion; bacterial-contamination risk; awareness risk (no end-tidal monitoring)	Historical concern re compound A (sevoflurane in low-flow systems) now considered low-risk; end-tidal MAC monitoring straightforward	Both safe in modern practice; TIVA requires vigilance in dyslipidaemic, diabetic, or pancreatitis-prone recipients
Quality of direct KT evidence	Six small studies (< 200 recipients total); LDKT-dominant; era-heterogeneous	Same evidence pool	Conclusions for both techniques are constrained by the same small, low-risk evidence base
Practical infrastructure	TCI pump, pharmacokinetic-pharmacodynamic models, processed-EEG monitoring (<i>e.g.</i> , BIS) for awareness mitigation	Vaporiser, end-tidal MAC monitoring	Volatile may be the practical default in resource-limited transplant programmes; TIVA preferred where TCI and processed-EEG are available

TIVA: Total intravenous anaesthesia; SVR: Systemic vascular resistance; KIM-1: Kidney injury molecule-1; NAG: N-acetyl- β -D-glucosaminidase; LDKT: Living-donor kidney transplant; ICU: Intensive care unit; PONV: Postoperative nausea and vomiting; MMF: Mycophenolate mofetil; DGF: Delayed graft function; PRIS: Propofol infusion syndrome; MAC: Minimum alveolar concentration; ECD: Extended-criteria donor; DCD: Donation-after-circulatory-death; KT: Kidney transplant; TCI: Target-controlled infusion; EEG: Electroencephalographic; BIS: Bispectral index.

Intraoperative fluid and vasopressor strategies across studies

A central limitation of all current comparisons of TIVA *vs* volatile anaesthesia in kidney transplantation is the marked heterogeneity in fluid and vasoactive co-management. Because intraoperative fluid type, volume, timing, vasopressor selection, and the use of osmotic and loop diuretics independently influence renal perfusion, urine output, and biomarker concentrations, this heterogeneity is a critical confounder when attributing differences to the anaesthetic technique alone [7,8]. The principal regimens used in the included studies are summarised in Table 3.

Several patterns emerge. Older trials (Babacan *et al* [12] in 1998; Modesti *et al* [2] in 2006) employed routine dopamine infusions (1–3 μ g/kg/minute) and a liberal crystalloid strategy targeting central venous pressure rather than dynamic indices, in keeping with the standards of the time. By contrast, contemporary studies [Aditjaningsih *et al* [9] in 2019; VAPOR-1 (Nieuwenhuijs-Moeke *et al* [10] in 2017); Calixto-Flores *et al* [13] in 2020] used goal-directed haemodynamics, predominantly balanced crystalloid (Ringer's lactate or plasma-Lyte) with restrictive total volumes, and norepinephrine titrated to a MAP threshold of 80–95 mmHg before reperfusion. Modesti *et al* [2] in 2006 used hydroxyethyl-starch colloids – a practice now generally avoided in kidney transplantation because of the recognised risk of osmotic nephrosis and the EMA/FDA restrictions on starch use in patients with renal compromise. Mannitol (0.5–1 g/kg) and furosemide (20–40 mg) at reperfusion were used inconsistently. These differences profoundly affect renal microcirculation, glomerular filtration pressure, and post-reperfusion biomarker concentrations, and they may account for at least part of the observed inter-study variability in biomarker and clinical outcomes [4,7,8]. Future comparative trials must standardise fluid type, fluid strategy, vasopressor selection, and use of adjunctive agents if anaesthetic technique is to be the mea-

ningful experimental variable.

DISCUSSION

The collective evidence from randomised trials, cohort studies, and observational reports suggests that propofol-based TIVA is a safe and effective option for kidney transplantation. Across multiple domains – haemodynamic stability, early graft function, biochemical markers of IRI, postoperative recovery, and complication rates – TIVA performs at least equivalently to volatile anaesthesia, with signals of superiority in recovery time, PONV, and renal tubular biomarkers. The heterogeneity of study designs, sample sizes, fluid and vasopressor regimens, opioid co-administration, and clinical endpoints, however, warrants cautious interpretation and highlights the need for further research.

Haemodynamic stability

The consistent finding across studies is haemodynamic comparability between TIVA and volatile anaesthesia. Aditiansih *et al*[9] in 2019, reflecting contemporary goal-directed management with norepinephrine and balanced crystalloid, and Modesti *et al*[2] in 2006, reflecting an older era of dopamine infusion and hydroxyethyl starch colloid use, both demonstrated that propofol-based regimens do not destabilise blood pressure or cardiac output relative to sevoflurane or isoflurane. The marginally lower SVR under propofol is well recognised and readily managed with fluid optimisation and vasopressor support. None of the available studies reported increased rates of reperfusion-related haemodynamic collapse with TIVA, supporting its safety in this critical phase. The ability to titrate effect-site concentration with TCI may even be an advantage during the rapid afterload changes of unclamping[5].

Opioid choice as a confounder of recovery and analgesia comparisons

When interpreting recovery and pain outcomes across the included trials, the choice of opioid co-administration is at least as important as the anaesthetic maintenance technique itself, and it has been inconsistently addressed in the literature. Modesti *et al*[2] in 2006 compared propofol + remifentanyl against isoflurane + fentanyl; Babacan *et al*[12] in 1998 compared propofol + alfentanil against isoflurane + fentanyl. In both designs, the TIVA arm received an ultra-short-acting opioid while the volatile arm received a longer-acting one. The faster emergence reported in the TIVA arm is therefore plausibly driven, at least in part, by the predictable rapid offset of remifentanyl or alfentanil, rather than by propofol's favourable context-sensitive half-time alone[2,5,12]. Likewise, the marginally better first-hour analgesia reported in the volatile arm of Modesti *et al*[2] reflects the residual analgesic effect of intraoperative fentanyl, not a property of isoflurane *per se*. The VAPOR-1 trial also used differential opioid regimens (remifentanyl in the propofol arm; sufentanil in the sevoflurane arm), though this is less commonly highlighted in interpretation[10]. The practical consequence is that none of the existing trials cleanly isolate the anaesthetic maintenance agent: They compare two whole regimens, each of which differs in both the maintenance technique and the opioid. Any future trial that genuinely tests TIVA *vs* volatile anaesthesia should standardise the opioid (*e.g.*, remifentanyl in both arms) or stratify by opioid choice. Until that is done, recovery and analgesia comparisons across the available literature should be interpreted accordingly.

Biomarker-clinical discordance: Alternative explanations

A central question raised by VAPOR-1 is why higher urinary KIM-1 and NAG concentrations under sevoflurane did not translate into differences in serum creatinine, DGF, or graft survival. The original interpretation – that propofol exerts a renoprotective effect blunted by ceiling effects in low-risk grafts – is one plausible reading, but several alternative explanations must be considered before a definitive renoprotective claim can be made[4,10].

A substantial part of the discordance is likely attributable to the population in which VAPOR-1 was conducted. In living-donor recipients with cold-ischaemia times of 1-3 hours, optimal donor selection, and pre-emptive transplantation, the baseline injury burden is so low that sensitive tubular biomarkers can readily detect transient stress without crossing the threshold for clinically apparent dysfunction[19]. The biomarker elevations observed in the sevoflurane arm may therefore reflect reversible epithelial stress rather than ischaemic injury sufficient to alter creatinine kinetics or dialysis requirement, and the corresponding biomarker kinetics are themselves short-lived: KIM-1 and NAG concentrations typically peak between 24 hours and 72 hours after injury and return to baseline within days, so the long-term prognostic significance of an acute day-two difference remains uncertain in the absence of prolonged follow-up[4].

Statistical power is a related concern. With 57 donor-recipient pairs, VAPOR-1 was designed to compare biomarkers but was not adequately powered to detect plausible differences in DGF (event rates of less than 5% in living donation) or biopsy-proven acute rejection[10,19]. The numerically higher rejection signal in the propofol arm did not reach statistical significance and is therefore vulnerable both to chance and to inter-group differences in immunosuppression timing; a modest reversible biochemical signal, taken on its own, does not necessarily predict structural or functional graft impairment.

Residual confounding by perioperative co-management is also plausible. As detailed in the results and Table 3, the included trials used markedly different fluid types, volume strategies, and vasopressor protocols[7,8], each of which independently influences glomerular filtration pressure, tubular oxygenation, and biomarker excretion. Immunosuppression timing and dosing were similarly heterogeneous: Calcineurin-inhibitor initiation, induction agent choice (basiliximab *vs* anti-thymocyte globulin), and corticosteroid dosing all affect early tubular biomarker concentrations, and none of these elements were standardised across the included trials.

Finally, two more specific caveats deserve mention. The VAPOR-1 corrigendum, while preserving the direction of effect, narrowed the magnitude of the inter-group difference and should be borne in mind when extrapolating to higher-risk grafts[10]. In addition, propofol's lipid-emulsion vehicle and its urinary metabolites may themselves modulate measured biomarker concentrations; although direct evidence for this remains limited, it represents a non-renoprotective explanation for the lower urinary KIM-1 and NAG observed under propofol-based maintenance[6].

Taken together, the VAPOR-1 findings provide intriguing mechanistic evidence that anaesthetic technique may differentially modulate tubular stress, but they fall short of demonstrating a clinically meaningful renoprotective effect. A robust test of the renoprotection hypothesis requires adequately powered trials in higher-risk cohorts [extended-criteria donor (ECD) and DCD grafts] with standardised perioperative protocols and patient-relevant endpoints.

Recovery and PONV

Recovery characteristics and PONV represent the most reproducible advantages of propofol-based TIVA. The pharmacokinetic basis is well understood: Propofol's favourable context-sensitive half-time and the predictable offset of remifentanyl enable rapid emergence and early extubation, even after prolonged infusion[5]. Operationally, these features are valuable in transplant centres where ICU and recovery-room throughput are critical[2]. The intrinsic antiemetic property of propofol—partly mediated by central anti-dopaminergic and 5-HT₃ receptor effects—consistently reduces PONV rates, as confirmed by Han *et al*[11] in 2020 in living kidney donors and replicated in recipient cohorts[6]. The downstream effect on early oral tacrolimus and mycophenolate absorption is clinically meaningful: Erratic enteral intake produces trough variability and sub-therapeutic immunosuppression at a phase when graft acceptance is being established. As noted above, the magnitude of TIVA's recovery advantage is partly confounded by opioid choice in the published trials.

Immunologic implications

The potential immunologic implications of anaesthetic technique remain an open question. Volatile anaesthetics have been proposed to modulate the inflammatory response, while propofol has antioxidant and anti-inflammatory effects[6]. The VAPOR-1 trial reported a non-significant numerical trend toward higher acute rejection rates in the propofol group, though the study was not powered for this endpoint and confounders such as immunosuppressive regimen and donor characteristics were not fully controlled[10]. No other study has corroborated this finding, and at present no compelling evidence exists that anaesthetic technique exerts a clinically meaningful influence on rejection risk. Nevertheless, the immunologic milieu of transplantation justifies further mechanistic exploration of anaesthetic effects on T-cell activation, regulatory T-cell function, and cytokine release at reperfusion[4].

Length of stay and complications

Length of hospital stay and postoperative complications were broadly similar between groups across all included studies. Serious anaesthesia-related complications were not reported, underscoring the safety of both techniques. Although faster recovery and lower PONV with TIVA might theoretically shorten recovery-room or ICU stays, the overall hospital length of stay appears to be driven primarily by institutional practices, surgical complications, and recipient comorbidities.

Pharmacological strengths of propofol-based TIVA

Beyond reproducible recovery and PONV advantages, propofol-based TIVA offers several pharmacological strengths relevant to kidney transplantation: A favourable context-sensitive half-time enabling rapid emergence after long procedures[5]; intrinsic antiemetic activity through central anti-dopaminergic and 5-HT₃ receptor mechanisms; antioxidant and anti-inflammatory actions through free-radical scavenging and NF-κB inhibition[1,6]; and the ability to titrate effect-site concentration with TCI in haemodynamically fragile recipients. Whether these mechanistic advantages translate to long-term graft survival benefits in higher-risk grafts is the outstanding clinical question, addressed in the future directions section below.

Safety considerations and disadvantages of propofol-based TIVA

A balanced appraisal of TIVA in kidney transplantation must address the recognised disadvantages and safety considerations of propofol, particularly in recipients with metabolic dysregulation, dyslipidaemia, and impaired renal clearance. Although the favourable profile described above generally outweighs these concerns for the duration of a typical kidney transplant procedure, vigilance is essential.

Injection pain

Pain on intravenous injection is the most common immediate adverse effect of propofol, reported in 28%-90% of patients depending on injection site, infusion rate, and concomitant pre-treatment[20]. The pain results from venous endothelial irritation by the aqueous propofol phase and the activation of the kininogen-kallikrein system. In transplant induction, where smooth induction and avoidance of sympathetic surge are desirable, this is not trivial. Effective mitigation strategies include lidocaine 20-40 mg pre-treatment or co-administration in the propofol solution, large-vein cannulation (antecubital fossa rather than dorsal hand), and slower induction rates[20]. Alternative formulations [e.g., propofol-long-chain triglyceride (LCT)/medium-chain triglyceride (MCT)] have a lower incidence of injection pain than the original LCT-based emulsion.

Propofol infusion syndrome

Propofol infusion syndrome (PRIS) is a rare but potentially fatal complication characterised by metabolic acidosis, rhabdomyolysis, hyperkalaemia, hepatomegaly, cardiac arrhythmias, and acute kidney injury[21]. The pathophysiology involves impaired mitochondrial fatty-acid oxidation and uncoupling of oxidative phosphorylation. Recognised risk factors include propofol infusion rates greater than 4 mg/kg/hour sustained beyond 48 hours, concomitant catecholamines, corticosteroids, sepsis, traumatic brain injury, and pre-existing metabolic acidosis[21]. Although kidney transplant recipients typically receive corticosteroids and may receive catecholamines, the duration of propofol infusion during transplantation (typically 3-5 hours) is well below the threshold associated with PRIS in critical-care populations. Nonetheless, anaesthetists should remain alert to early metabolic signs (unexplained acidosis, lactate rise, electrocardiography changes) and limit the cumulative dose. PRIS has not been reported in transplant maintenance series, but the possibility justifies ongoing surveillance, particularly if TIVA is continued into the postoperative ICU phase.

Hypertriglyceridaemia and lipid load

Propofol is formulated as a 1% or 2% oil-in-water emulsion containing 10% soya-bean oil (LCTs) and glycerol, delivering a lipid load of approximately 0.1 g per millilitre of 1% solution. In recipients with pre-existing dyslipidaemia, diabetes, or pancreatitis susceptibility – common comorbidities in the ESRD population – this lipid load is clinically relevant. Documented complications of propofol-induced hypertriglyceridaemia include acute pancreatitis and pseudo-Pickwickian syndrome[22]. Routine triglyceride monitoring is recommended for prolonged (> 48 hour) infusions, although in single-procedure transplantation the risk is small. Newer microemulsion and MCT/LCT formulations reduce lipid load and may be preferred in metabolically vulnerable recipients.

Bacterial contamination of lipid emulsion

The lipid-based vehicle of propofol supports rapid microbial growth, and propofol-related bacteraemia has been documented historically, prompting incorporation of ethylenediaminetetraacetic acid or sodium metabisulfite as antimicrobial preservatives[23]. In immunosuppressed transplant recipients, strict aseptic handling is therefore non-negotiable: Dedicated infusion sets, sterile drawing technique, single-use vials whenever possible, and disposal of open vials within six hours after opening[23]. Failure to observe these precautions has resulted in outbreaks of gram-negative and gram-positive bacteraemia in published case series.

Pharmacokinetic considerations in ESRD

Propofol is highly lipophilic (97%-99% protein-bound, predominantly to albumin), hepatically conjugated, and renally excreted as glucuronide and sulphate metabolites[5]. In ESRD, reduced albumin concentration and competitive binding by uraemic toxins increase the free fraction, potentially augmenting the clinical effect at any given plasma concentration. Conversely, accumulation of inactive renally excreted metabolites does not appear to produce clinically significant prolongation of effect. Practical implications are: Cautious titration of effect-site concentration, particularly at induction; awareness of the slightly higher likelihood of vasodilator-related hypotension; and consideration of TCI models that have been validated in patients with renal impairment (the Schnider model is generally preferred over the Marsh model in this population, although neither was specifically derived in ESRD)[5].

Operational and infrastructure considerations

TCI requires dedicated pump infrastructure, pharmacokinetic modelling, and trained personnel[5]. Cost and availability of TCI pumps may limit the routine use of TIVA in low- and middle-income transplant programmes. The risk of intraoperative awareness, although small, is also higher with TIVA than with volatile anaesthesia because end-tidal monitoring is not available and reliance must instead be placed on processed electroencephalographic (e.g., bispectral index or entropy) and on infusion-line integrity[24]. In settings where TCI is unavailable, manual infusion based on weight-based dosing can be used, but with reduced precision. These operational considerations should be weighed against the clinical benefits when planning anaesthetic protocols for individual transplant programmes.

Net safety assessment

In aggregate, the recognised disadvantages of propofol-based TIVA are manageable within the typical duration of a kidney transplant procedure. Injection pain is preventable[20]; PRIS is rare[21]; hypertriglyceridaemia[22] and bacterial contamination[23] are negligible risks with appropriate vigilance; pharmacokinetic adjustments are intuitive[5]; and operational requirements are achievable in most modern transplant centres. The risk-benefit profile remains favourable, but the safety considerations summarised here should inform clinical practice and form part of the consent and protocol discussion for recipients with pre-existing dyslipidaemia, pancreatitis, or metabolic dysregulation.

Limitations of the available evidence

The current evidence base for TIVA in kidney transplantation is constrained by several interrelated methodological issues. Sample sizes are universally small, ranging from 18 to 80 patients across the directly-comparable kidney-transplant cohort, which restricts the statistical power available to detect modest but clinically meaningful differences in DGF, biopsy-proven rejection, and one-year graft survival[17,18]. Most studies have enrolled living-donor recipients with short cold-ischaemia times and excellent baseline graft quality, in whom any anaesthetic-attributable effect on IRI is likely to be attenuated, and the predominance of single-centre designs further limits the external validity of the available findings[4, 19].

A further source of bias arises from the heterogeneity of the anaesthetic regimens themselves. The available trials have compared whole regimens rather than isolated maintenance agents: Opioid co-administration varied considerably (remifentanyl, alfentanil, fentanyl, sufentanil), as did induction agents, neuromuscular blocking agents, and reversal strategies, all of which confound the inter-group comparison[2,10,12]. Fluid type, fluid strategy, vasopressor choice, and the use of mannitol or furosemide also differed markedly between studies (Table 3), introducing a further layer of confounding that cannot be adequately resolved by narrative synthesis.

The interpretation of biomarker findings is complicated by methodological variability between studies. Biomarker definitions, sampling time points, and normalisation strategies (such as creatinine-indexed *vs* absolute concentrations) differ across the included studies, limiting direct cross-study comparability. Immunosuppression and surgical-technique heterogeneity – including induction agent choice, calcineurin-inhibitor timing, vascular anastomosis duration, and graft preservation method – is also inconsistently reported, leaving several potentially relevant confounders unaccounted for.

A particular era effect must also be acknowledged. Several of the included trials predate the widespread adoption of goal-directed haemodynamic management and the contemporary restriction of synthetic colloids in patients with renal compromise, and their findings cannot be straightforwardly generalised to current practice[2,12]. Finally, this review itself, as a narrative synthesis[14], does not provide quantitative pooled estimates; the directly-comparable evidence base in adult kidney transplant recipients comprises only six small studies, three of which were conducted at single centres.

Future directions

Building on the limitations summarised above, the field requires a well-designed, adequately powered, multicentre RCT that directly compares propofol-based TIVA with contemporary volatile anaesthesia in kidney transplantation. The most informative trial would deliberately recruit higher-risk cohorts – particularly recipients of ECD and DCD grafts – in whom IRI is more pronounced and any renoprotective effect of TIVA is most likely to manifest as a clinically meaningful difference[4,19].

Equally important is the standardisation of the perioperative environment, so that the anaesthetic technique itself becomes the true independent variable. This entails a defined fluid protocol (balanced crystalloid as the default), goal-directed haemodynamics with norepinephrine as the preferred vasopressor, explicit MAP targets before unclamping, and harmonised use of mannitol and furosemide at reperfusion[7,8]. The opioid regimen should likewise be standardised across arms – for example, remifentanyl in both groups – since the existing literature has demonstrated that the choice of opioid is itself a substantial confounder of recovery and analgesia outcomes[2,10].

The choice of endpoints must shift from biomarker surrogates toward clinically meaningful and patient-centred outcomes. Primary endpoints should include the incidence and duration of DGF, one-year death-censored graft survival, and a composite of patient-relevant outcomes capturing quality of recovery and cost-effectiveness[19]. Sensitive biomarkers (KIM-1, NGAL, urinary L-FABP, plasma cystatin C) retain value as secondary mechanistic endpoints provided that sampling times are prospectively defined[10], and mechanistic sub-studies examining cytokine release, T-cell activation, and regulatory T-cell function during the hyperacute reperfusion phase would clarify the immunomodulatory consequences of anaesthetic choice[4,6].

Pre-specified subgroup analyses by donor type and by ischaemia time would allow the heterogeneity of the transplant population to inform the interpretation of any anaesthetic-attributable effect, and longer-term outcomes – quality of recovery scores, return to baseline activity, and one-year graft and patient survival – would provide a more complete picture of clinical benefit. In the interim, a network meta-analysis incorporating individual-patient data from the existing trials may offer a quantitative synthesis while such a trial is being designed and conducted.

CONCLUSION

Propofol-based TIVA provides haemodynamic control comparable to volatile anaesthesia[2,9,12,13] and does not impair immediate graft diuresis[2,9,13]. In one small trial of living-donor recipients, it may attenuate biochemical markers of tubular injury at the cellular level[10]. However, this signal has not translated into measurable clinical benefit in DGF, dialysis requirement, serum creatinine, or one-year graft survival. TIVA also offers smoother recovery profiles and lower PONV rates[2,11,12], with downstream operational and immunosuppression-absorption benefits. It shows no evidence of inferiority in graft function, rejection, or anaesthesia-related complications[3,9,10]. The available evidence is limited by small sample sizes, low-risk living-donor cohorts, era effects, opioid co-administration heterogeneity, and variability in fluid and vasopressor protocols[7,8,19]. Within these limits, the evidence supports propofol-based TIVA as a safe and potentially advantageous anaesthetic technique for kidney transplantation. Recognised disadvantages – injection pain [20], the rare but serious risk of PRIS[21], hypertriglyceridaemia[22], and lipid-emulsion contamination[23] – are manageable with appropriate vigilance. Whether the biomarker advantages of TIVA translate into long-term graft survival benefits in higher-risk grafts must be tested in adequately powered, protocol-standardised multicentre trials in extended-criteria-donor and DCD recipients with standardised opioid regimens. Until such evidence is available, the choice between TIVA and volatile anaesthesia should be individualised. The decision should take into account patient characteristics, institutional resources, and team expertise, while acknowledging that both techniques are compatible with excellent perioperative outcomes.

REFERENCES

- 1 Liu W, Du M, Zhang M, Dai X, Wang H, Le Y, Zhi S, Bo L, Quan J. Impact of propofol versus desflurane anesthesia on postoperative hepatic and renal functions in infants with living-related liver transplantation: a randomized controlled trial. *BMC Med* 2024; **22**: 397 [RCA] [PMID: 39285414 DOI: 10.1186/s12916-024-03622-6] [FullText]
- 2 Modesti C, Sacco T, Morelli G, Bocci MG, Ciocchetti P, Vitale F, Perilli V, Sollazzi L. Balanced anesthesia versus total intravenous anesthesia for kidney transplantation. *Minerva Anesthesiol* 2006; **72**: 627-635 [RCA] [PMID: 16865081] [FullText]
- 3 Lee JH, Joo DJ, Kim JM, Park JH, Kim YS, Koo BN. Preconditioning effects of the anesthetic administered to the donor on grafted kidney function in living donor kidney transplantation recipients. *Minerva Anesthesiol* 2013; **79**: 504-514 [RCA] [PMID: 23419340] [FullText]
- 4 Nieuwenhuijs-Moeke GJ, Pischke SE, Berger SP, Sanders JSF, Pol RA, Struys MMRF, Ploeg RJ, Leuvenink HGD. Ischemia and Reperfusion Injury in Kidney Transplantation: Relevant Mechanisms in Injury and Repair. *J Clin Med* 2020; **9**: 253 [RCA] [PMID: 31963521 DOI: 10.3390/jcm9010253] [FullText] [Full Text(PDF)]
- 5 Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, Shafer SL, Youngs EJ. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. *Anesthesiology* 1998; **88**: 1170-1182 [RCA] [PMID: 9605675 DOI: 10.1097/0000542-199805000-00006] [FullText]
- 6 Vasileiou I, Xanthos T, Koudouna E, Perrea D, Klonaris C, Katsargyris A, Papadimitriou L. Propofol: a review of its non-anaesthetic effects. *Eur J Pharmacol* 2009; **605**: 1-8 [RCA] [PMID: 19248246 DOI: 10.1016/j.ejphar.2009.01.007] [FullText]
- 7 Iguchi N, Kosaka J, Booth LC, Iguchi Y, Evans RG, Bellomo R, May CN, Lankadeva YR. Renal perfusion, oxygenation, and sympathetic nerve activity during volatile or intravenous general anaesthesia in sheep. *Br J Anaesth* 2019; **122**: 342-349 [RCA] [PMID: 30770052 DOI: 10.1016/j.bja.2018.11.018] [FullText]
- 8 Franzén S, Semenas E, Taavo M, Mårtensson J, Larsson A, Frithiof R. Renal function during sevoflurane or total intravenous propofol anaesthesia: a single-centre parallel randomised controlled study. *Br J Anaesth* 2022; **128**: 838-848 [RCA] [PMID: 35279277 DOI: 10.1016/j.bja.2022.02.030] [FullText]
- 9 Aditjaningsih D, Sukmono B, Agung TA, Kartolo WY, Adiwongso ES, Mochtar CA. Comparison of the Effects of Target-Controlled Infusion of Propofol and Sevoflurane as Maintenance of Anesthesia on Hemodynamic Profile in Kidney Transplantation. *Anesthesiol Res Pract* 2019; **2019**: 5629371 [RCA] [PMID: 31885551 DOI: 10.1155/2019/5629371] [FullText] [Full Text(PDF)]
- 10 Nieuwenhuijs-Moeke GJ, Nieuwenhuijs VB, Seelen MAJ, Berger SP, van den Heuvel MC, Burgerhof JGM, Ottens PJ, Ploeg RJ, Leuvenink HGD, Struys MMRF. Propofol-based anaesthesia versus sevoflurane-based anaesthesia for living donor kidney transplantation: results of the VAPOR-1 randomized controlled trial. *Br J Anaesth* 2017; **118**: 720-732 [RCA] [PMID: 28510740 DOI: 10.1093/bja/aex057] [FullText]
- 11 Han S, Park J, Hong SH, Lim S, Park YH, Chae MS. Comparison of the impact of propofol versus sevoflurane on early postoperative recovery in living donors after laparoscopic donor nephrectomy: a prospective randomized controlled study. *BMC Anesthesiol* 2020; **20**: 273 [RCA] [PMID: 33115408 DOI: 10.1186/s12871-020-01190-9] [FullText] [Full Text(PDF)]
- 12 Babacan A, Ayhan G, Akçabay M, Olgay G, Öztürk E. Assessment of total intravenous anesthesia in renal transplantation. *Transplant Proc* 1998; **30**: 750-753 [RCA] [PMID: 9595083 DOI: 10.1016/s0041-1345(98)00033-5] [FullText]
- 13 Calixto-Flores A, Moreno-Arias JA. Effect of Intravenous Total Anesthesia on Hemodynamic Changes in Renal Transplant. *Transplant Proc* 2020; **52**: 1106-1109 [RCA] [PMID: 32192744 DOI: 10.1016/j.transproceed.2020.02.012] [FullText]
- 14 Baethge C, Goldbeck-Wood S, Mertens S. SANRA-a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev* 2019; **4**: 5 [RCA] [PMID: 30962953 DOI: 10.1186/s41073-019-0064-8] [FullText] [Full Text(PDF)]
- 15 Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB, PRISMA-S Group. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. *Syst Rev* 2021; **10**: 39 [RCA] [PMID: 33499930 DOI: 10.1186/s13643-020-01542-z] [FullText] [Full Text(PDF)]
- 16 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016; **5**: 210 [RCA] [PMID: 27919275 DOI: 10.1186/s13643-016-0384-4] [FullText] [Full Text(PDF)]
- 17 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366**: 14898 [RCA] [PMID: 31462531 DOI: 10.1136/bmj.14898] [FullText]
- 18 Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; **355**: i4919 [RCA] [PMID: 27733354 DOI: 10.1136/bmj.i4919] [FullText] [Full Text(PDF)]
- 19 Yarlagadda SG, Coca SG, Formica RN Jr, Poggio ED, Parikh CR. Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis. *Nephrol Dial Transplant* 2009; **24**: 1039-1047 [RCA] [PMID: 19103734 DOI: 10.1093/ndt/gfn667] [FullText]
- 20 Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg* 2000; **90**: 963-969 [RCA] [PMID: 10735808 DOI: 10.1097/0000542-200004000-00035] [FullText]
- 21 Krajčová A, Waldauf P, Anděl M, Duška F. Propofol infusion syndrome: a structured review of experimental studies and 153 published case reports. *Crit Care* 2015; **19**: 398 [RCA] [PMID: 26558513 DOI: 10.1186/s13054-015-1112-5] [FullText] [Full Text(PDF)]
- 22 Devlin JW, Lau AK, Tanios MA. Propofol-associated hypertriglyceridemia and pancreatitis in the intensive care unit: an analysis of frequency and risk factors. *Pharmacotherapy* 2005; **25**: 1348-1352 [RCA] [PMID: 16185179 DOI: 10.1592/phco.2005.25.10.1348] [FullText]
- 23 Sklar GE. Propofol and postoperative infections. *Ann Pharmacother* 1997; **31**: 1521-1523 [RCA] [PMID: 9416392] [FullText]
- 24 Pandit JJ, Andrade J, Bogod DG, Hitchman JM, Jonker WR, Lucas N, Mackay JH, Nimmo AF, O'Connor K, O'Sullivan EP, Paul RG, Palmer JH, Plaat F, Radcliffe JJ, Sury MR, Torevell HE, Wang M, Hainsworth J, Cook TM; Royal College of Anaesthetists; Association of Anaesthetists of Great Britain and Ireland. 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. *Br J Anaesth* 2014; **113**: 549-559 [RCA] [PMID: 25204697 DOI: 10.1093/bja/aeu313] [FullText]

FOOTNOTES

Specialty type: Transplantation

Country of origin: United Kingdom

Author contributions: Rangganata E conceived the review, performed the literature search, drafted the manuscript, and led the response to peer review; Castellanos De Brigard J performed the second independent screening and quality appraisal and contributed to the discussion of immunologic implications; Prionas A provided third-reviewer adjudication on study selection and critically reviewed the manuscript; Habib N contributed to the interpretation of mechanistic and surgical-technique aspects; Papalois VE supervised the project, contributed to the framing of clinical priorities, and approved the final manuscript; and all authors approved the submitted and revised versions.

AI contribution statement: The authors take full responsibility and accountability for all content of this manuscript, including any portions for which AI tools were used as assistive technologies. All AI-assisted outputs were carefully reviewed, validated, and approved by the authors. AI tools were not used to generate original scientific data, perform independent scientific analyses, or draw scientific conclusions.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest, financial or otherwise, relevant to the content of this manuscript. No author has any financial relationship with manufacturers of propofol, volatile anaesthetic agents, target-controlled infusion equipment, or any other product or service discussed in this review. This work received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Corresponding Author's Membership in Professional Societies: The European Society for Organ Transplantation, No. MN_000658.

S-Editor: Lin C

L-Editor: A

P-Editor: Zhao YQ



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

