

CLINICAL PRACTICE

Chinese clinical practice guidelines for total intravenous anaesthesia: a systematic review and expert consensus-based recommendations[☆]

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Summary

Total intravenous anaesthesia (TIVA) has been widely used for general anaesthesia in clinical practice. In order to further promote the standardised application of TIVA in China, the Chinese Society of Anesthesiology of the Chinese Medical Association organised experts to formulate these clinical practice guidelines for TIVA. After collection and selection of clinical questions, the working group conducted rigorous searches of the literature, formulated recommendations, and

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reached a consensus. A total of 22 recommendations were made on 12 clinical issues, including the indications, contraindications, and advantages of TIVA, use of depth of anaesthesia monitoring during implementation, pharmacological characteristics of available i.v. anaesthetic drugs, selection and use of drugs in target- and nontarget-controlled infusion modes, and precautions for application of TIVA in special populations, thus providing guidance for anaesthetists to standardise implementation of TIVA.

Keywords: ciprofol; guideline; propofol; remimazolam; target-controlled infusion; total intravenous anaesthesia

Editor's key points

- The Chinese Society of Anaesthesiology of the Chinese Medical Association developed consensus-based guidelines to provide evidence-based recommendations for use of TIVA in clinical practice.
- Introduction of new sedative–hypnotics such as ciprofol and remimazolam provides more options for implementation of TIVA, and can reduce haemodynamic complications.
- Future studies should focus on development of ciprofol- and remimazolam-based pharmacokinetic–pharmacodynamic models and target-controlled infusion protocols, particularly for special populations.
- Large-scale, multicentre clinical studies should be conducted to verify the efficacy and safety of TIVA in different types of surgery and patient populations, with a focus on resolving controversies around post-operative delirium and neurocognitive disorders, and long-term oncologic outcomes after cancer surgery.

Total intravenous anaesthesia (TIVA) is an anaesthetic technique where induction and maintenance are accomplished solely through the administration of i.v. anaesthetic agents.¹ TIVA allows certain surgeries to be performed in spontaneously breathing patients without an airway device, thus reducing airway irritation and avoiding aerosol dispersion. TIVA not only has absolute advantages in open airway surgeries and nonoperating room anaesthesia, but also promotes early postoperative recovery,² reduces occupational exposure and air pollution caused by waste anaesthetic gases, and mitigates the impacts of inhalation anaesthetic drugs on global warming,³ aligning the principles of environmentally sustainable anaesthesia.

The 'Consensus on total intravenous anaesthesia' published by the Chinese Society of Anesthesiology, Total Intravenous Anaesthesia Expert Consensus Working Group in 2016¹ and the 'Guidelines for the safe practice of total intravenous anaesthesia (TIVA)' published by the Association of Anaesthetists and the Society for Intravenous Anaesthesia in 2018⁴ provide technical guidance for anaesthetists to implement TIVA. However, with the launch of new sedative–hypnotics (ciprofol and remimazolam), the development of target-controlled infusion (TCI) technology, and the continued emergence of new scientific evidence for i.v. anaesthetics, the existing consensus on TIVA cannot fully meet the needs of anaesthetists. Therefore, the Chinese Society of Anesthesiology of the Chinese Medical Association organised 21 experts to formulate the 'Clinical Practice Guidelines for Total Intravenous Anaesthesia in China (2024 edition)'. A total of 22 recommendations were made on 12 clinical issues, including the indications, contraindications, and advantages of TIVA, depth of anaesthesia monitoring during

implementation, pharmacological characteristics of i.v. anaesthetic drugs, selection and use of drugs in TCI and non-TCI modes, and precautions for application of TIVA in special populations, thus providing guidance for anaesthetists to standardise implementation of TIVA.

Methods

The Chinese Society of Anaesthesiology of the Chinese Medical Association took the lead in initiating and organising development of this guideline. To this end, a dedicated working group was established. All members of the working group duly filled out the Declaration of Interest form, thereby confirming that there are no direct conflicts of interest related to this guideline. This guideline has been registered on the Practice Guideline Registration for Transparency (PREPARE) as PREPARE-2024CN339.

This guideline is designed for physicians, along with other professionals in relevant disciplines, across all tiers of medical institutions. The target population of the recommendations presented in this guideline encompasses surgical patients undergoing general anaesthesia.

A systematic search was conducted on guidelines, consensus reports, and systematic reviews related to TIVA. Initially, 14 clinical issues were identified. Subsequently, based on the feedback from 21 experts surveyed via an online questionnaire, 12 issues were ultimately selected and are presented in [Supplementary Appendix 1](#).

Results

Search strategy

In line with the population, intervention, comparison, and outcome (PICO) framework, a comprehensive literature search was carried out across multiple scientific databases from their inception until March 31, 2024. These databases included PubMed, Embase, [Clinicaltrials.gov](https://clinicaltrials.gov), Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang Data, China Science and Technology Journal Database, and Chinese Biomedical Literature Database. Only studies published in either English or Chinese were included. The search keywords, used uniformly in both English and Chinese databases, were 'total intravenous anaesthesia', 'intravenous anaesthesia', 'propofol', 'ciprofol', 'remimazolam', 'etomidate', 'opioid', and 'target-controlled infusion'. The types of research encompassed systemic reviews, meta-analysis, RCTs, cohort studies, case-control studies, epidemiological investigations, bench research, and guidelines and consensus reports. Conference abstracts were excluded. Literature screening was performed by two reviewer groups; one was responsible for initial screening and the other for verification. In this process, abstracts were screened first, followed by full-

text screening. Any discrepancies were resolved through discussions between the two groups of reviewers. If necessary, a third reviewer was consulted. The search for specific clinical issues was further extended to July 31, 2024.

For simplicity of the search, screening, inclusion, and exclusion of studies, all retrieved titles and articles were allocated into eight folders: (A) i.v. anaesthesia vs inhalation anaesthesia; (B) anaesthesia monitoring during i.v. anaesthesia; (C) commonly used drugs for i.v. anaesthesia; (D) TIVA in paediatric patients; (E) TIVA in older patients; (F) TIVA in obese patients; (G) TIVA in pregnant and maternal patients; (H) TIVA for patients outside the operating room.

The article retrieval process is provided in [Supplementary Appendix 2](#). A detailed description of the search strategy and PICO are presented in [Supplementary Appendix 3](#).

Data collection and analysis

Study selection

All publications meeting inclusion criteria were included. For each PICO group, at least two authors independently screened full-text articles. Disagreements were resolved through consultation with a third reviewer not involved in the initial screening process.

Data extraction and management

Data extraction was standardised across task force groups under methodological supervision. Using structured spreadsheets, groups collected information on study design, population characteristics, interventions, and outcome measures.

Risk of bias assessment

Risk of bias was evaluated for each PICO group as follows: RCTs were assessed using the Cochrane Handbook for Systematic Reviews of Interventions, focusing on six domains including random sequence generation (selection bias), allocation concealment (selection bias), blinding of outcome assessors (performance and detection bias), incomplete outcome data, intention-to-treat (attrition bias), and selective reporting. Studies were classified as low risk of bias if all domains met adequacy criteria, medium risk with one inadequate or unclear domain, and high risk when two or more domains were inadequate or unclear. For non-RCTs, checklists from Scottish Intercollegiate Guidelines Network (SIGN) were applied.⁵ Disagreements were resolved through discussion with the methodologist (AA). Results of risk of bias assessment are shown in [Supplementary Appendix 4](#).

Rating levels of evidence

The 2009 Oxford Centre for Evidence-Based Medicine (OCEBM) was used for rating quality of evidence and strength of recommendations from level 1a (highest) to level 5 (lowest).

Development of recommendations

Drawing on evidence from China and other countries, and taking into account China's national circumstances, the working group initially formulated recommendations for each clinical issue. One round of online review and two rounds of Delphi surveys were conducted for these recommendations.

After revision according to the feedback received, a consensus was achieved. The levels of evidence were determined as follows: strong consensus (>90% agreement of the participants), consensus (75–90% agreement), majority agreement (50–75% agreement), and no consensus (<50% agreement). The details of Delphi survey are provided in [Supplementary Appendix 5](#).

Updates

The recommendations of this guideline are planned to be updated within 3–5 yr.

Clinical issues and recommendations

Clinical issue 1: What are the indications and contraindications for TIVA?

Recommendation 1: TIVA is applicable to all patients requiring general anaesthesia, except for those with difficulties in establishing venous access or hypersensitivity to i.v. anaesthetic drugs. It is particularly suitable for surgeries requiring neuroelectrophysiological monitoring (2b, B), daytime/outpatient surgeries (1a, A), patients susceptible to malignant hyperthermia (MH) (2c, B), patients with intracranial hypertension (2b, B), and patients with long QT syndrome (2b, B) (strong consensus, 100% agreement).

Evidence summary: With the introduction of novel i.v. anaesthetic drugs, evolution of pharmacokinetic (PK) and pharmacodynamic (PD) concepts, and development of advanced i.v. infusion pumps, TIVA has been increasingly applied in a wide range of fields.⁶ Contraindications for TIVA include difficulties in establishing venous access and definite hypersensitivity to i.v. anaesthetic drugs. Except for these cases, TIVA is suitable for all patients requiring general anaesthesia. Considering the surgical characteristics or patient conditions, TIVA is especially appropriate for the following surgeries or patients.

Surgeries that are more suitable for TIVA

- (1) Surgeries requiring neuroelectrophysiological monitoring: intraoperative neuroelectrophysiological monitoring is most commonly used in neurosurgery and spine surgery, in which somatosensory-evoked potential (SEP) and motor-evoked potential (MEP) are frequently used. In comparison with inhalation anaesthetic drugs, i.v. anaesthetic drugs have a lesser impact on SEP and MEP.^{7,8} A retrospective study (142 patients undergoing supratentorial tumour resection and epilepsy surgery) explored the impact of anaesthetic drugs on MEP. The results indicated that inhalation anaesthetic drugs increased the stimulus threshold of MEP compared with i.v. anaesthetic drugs.⁹ A retrospective study (256 patients undergoing spine surgery and lower extremity MEP monitoring) demonstrated that use of inhalation anaesthetic drugs correlated with failure to acquire baseline MEP signals.¹⁰ Additionally, an RCT showed that inhalation anaesthetic drugs had a significant impact on SEP amplitude and latency, the higher the inhalation concentration, the greater the impact on SEP, whereas i.v. anaesthetic drugs had less impact on SEP.¹¹ (2) Daytime/outpatient surgeries: post-operative nausea and vomiting (PONV) is one of the primary factors prolonging the length of stay/observation

time in daytime/outpatient surgeries.¹² Compared with inhalation anaesthesia, TIVA can reduce the incidence of PONV, promote early postoperative recovery, and enhance the compliance and satisfaction of patients with same-day discharge. A systematic review and meta-analysis of 18 RCTs involving 1621 patients undergoing daytime/outpatient surgeries (including only RCTs) revealed that the incidence of PONV was significantly lower in the TIVA group than in the inhalation anaesthesia group.¹³

Patients who are better candidates for TIVA

- (1) Patients susceptible to MH: MH is a hypermetabolic syndrome affecting skeletal muscles that occurs in genetically susceptible patients during general anaesthesia. For patients at high risk of MH who need general anaesthesia, the administration of inhalation anaesthetic drugs and suxamethonium can trigger MH. Therefore, TIVA could be considered as an alternative.¹⁴ A retrospective study of 140 MH cases in mainland China showed that 91 cases (65.0%) were triggered by inhalation anaesthetic drugs and 27 cases (19.3%) were triggered by i.v. anaesthetic drugs alone, among which 23 cases (15.1%) were triggered by ketamine. The incidence of MH induced by inhalation anaesthetic drugs was significantly higher than that caused by i.v. anaesthetic drugs.¹⁵ (2) Patients with intracranial hypertension: high-concentration inhalation anaesthetic drugs (>1.0 minimum alveolar concentrations) can dilate vascular smooth muscle and increase cerebral blood flow, thus leading to an increase in intracranial pressure. Propofol-based TIVA reduces cerebral blood flow and intracranial pressure while maintaining autoregulation of cerebral blood flow.¹⁶ Therefore, it is an anaesthesia approach more suitable for patients with intracranial hypertension. A prospective RCT (90 patients) compared the effects of TIVA and inhalation anaesthesia on patients with acute traumatic brain injury. TIVA provided better brain relaxation, lower intracranial pressure, and more stable haemodynamic indicators than inhalation anaesthesia.¹⁷ (3) Patients with long QT syndrome: nearly all inhalation anaesthetic drugs can prolong the QT interval by inhibiting the potassium channel currents on the cell membrane, whereas i.v. anaesthetic drugs such as propofol, etomidate, midazolam, remifentanyl, and fentanyl have no significant impact on the QT interval. Hence, they can be safely applied in patients with long QT syndrome.¹⁸ An RCT (120 patients) explored the impact of different anaesthesia protocols on the QT interval during liver transplantation. Intraoperative QT intervals were prolonged in both groups; however, the change in QT interval in the TIVA group was significantly less than that in the inhalation anaesthesia group. Furthermore, for patients with preoperative QT interval prolongation, inhalation anaesthesia led to a further prolongation in the QT interval, whereas TIVA did not cause any additional prolongation.¹⁹

Clinical issue 2: What are the advantages of TIVA?

Recommendation 2.1: TIVA can reduce the incidence of PONV compared with inhalation anaesthesia. It is recommended for patients at high risk of PONV (1a, A) (strong consensus, 100% agreement).

Evidence summary: PONV is one of the most common complications of general anaesthesia, with an incidence of 30% in general surgical patients and up to 80% in high-risk patients.²⁰ PONV can lead to various adverse outcomes, such as gastrointestinal reactions, water–electrolyte imbalance, incision dehiscence, pulmonary aspiration, and aspiration pneumonia. It also prolongs the patient's observation time in the PACU, increases patient discomfort, and exerts an enormous economic burden.^{2,20} The risk factors of PONV are: (1) female sex; (2) young patients; (3) nonsmoking; (4) specific surgeries such as gallbladder surgery, laparoscopic surgery, gynaecological surgery, and weight loss surgery; (5) a past history of PONV or motion sickness; and (6) anaesthetic drugs including volatile anaesthetic drugs, nitrous oxide, and postoperative opioids.²⁰ Both adults and children (>1 month)²¹ included in meta-analyses, and populations susceptible to PONV,²² have a risk of PONV significantly lower with TIVA than with inhalation anaesthesia.

Recommendation 2.2: Compared with inhalation anaesthesia, TIVA might enhance the postoperative recovery quality in adult patients undergoing noncardiac surgeries, and is therefore recommended for this group of adult patients (1b, A) (strong consensus, 95% agreement).

Evidence summary: The postoperative recovery quality can reflect the quality of anaesthesia and surgery. The ultimate objective of enhanced recovery after surgery is to facilitate rapid and high-quality recovery for patients. The Quality of Recovery-40 (QoR-40) scale is used to evaluate postoperative recovery quality, providing a comprehensive health profile of patients across five dimensions.²³ Low QoR-40 scores are associated with an increased incidence of postoperative complications, a prolonged length of hospital stay, a greater economic burden, and a higher long-term disability rate and mortality.² Different anaesthesia methods can exert different effects on patient recovery. In 2021, Shui and colleagues²⁴ published a systematic review with meta-analysis and trial sequential analysis that included nine RCTs involving 922 adult patients undergoing noncardiac surgeries. The results demonstrated that TIVA might improve QoR-40 scores on the day of surgery compared with inhalation anaesthesia, but the reliability of evidence was weak. Recently, RCTs showed that TIVA was associated with an increase of QoR-40 scores in pancreatectomy ($n=132$) and laparoscopic live donor nephrectomy ($n=80$).^{25,26} However, anaesthetic methods had no effect on QoR-40 scores in endoscopic transsphenoidal pituitary surgery ($n=82$) and total laparoscopic hysterectomy ($n=102$).^{27,28} In conclusion, there is only low-reliability evidence supporting propofol-based TIVA as an option for improving recovery quality.

Clinical issue 3: What types of monitoring should be used during the implementation of TIVA?

Recommendation 3.1: It is recommended to monitor the processed electroencephalogram (pEEG) during TIVA, as it serves to maintain an appropriate depth of anaesthesia, avoid anaesthetic drug overdose, prevent intraoperative awareness, shorten early postoperative recovery, and reduce the incidence of postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) (1a, A) (strong consensus, 100% agreement).

Evidence summary: pEEG monitoring, the core of depth of anaesthesia monitoring in modern medicine, can facilitate the

maintenance of an appropriate depth of anaesthesia, avoid anaesthetic drug overdose, prevent intraoperative awareness, accelerate awakening from anaesthesia, and reduce the risk of POD and POCD.^{29,30} Additionally, a study showed that titrating propofol according to a preset pEEG value could significantly decrease propofol dosage, thus improving the postoperative quality of early recovery.³¹ pEEG monitoring should commence before anaesthesia induction and be continued until the complete restoration of neuromuscular function. Currently, the bispectral index (BIS) is the most widely used index in clinical practice, with a range from 0 to 100. The lower the index, the deeper the level of anaesthesia, and vice versa.³² It is appropriate to maintain BIS values within the range of 40–60 under general anaesthesia.³³

In 2018, Gao and colleagues³⁴ published a meta-analysis that included five RCTs involving 17 432 patients in the BIS monitoring group and 16 749 patients in the control group. The results showed that BIS monitoring could reduce the incidence of intraoperative awareness in patients undergoing i.v. anaesthesia. In 2019, Lewis and colleagues³⁵ published a meta-analysis, demonstrating that BIS monitoring not only reduced the risk of intraoperative awareness, but also shortened the early postoperative recovery period in adult patients undergoing general anaesthesia. In 2022, Chew and colleagues³⁶ published a systematic review and meta-analysis that included 10 RCTs involving 3891 older patients showing that BIS monitoring decreased the incidence of POCD by 36% compared with routine nursing care or the control group.

Recommendation 3.2: Quantitative neuromuscular function monitoring is recommended for specific populations as it can reduce the incidence of residual neuromuscular block (1b, A) (strong consensus, 100% agreement).

Evidence summary: Neuromuscular function monitoring can prevent adverse events associated with postoperative residual neuromuscular block, including upper respiratory tract obstruction, re-intubation, atelectasis, and pneumonia. Moreover, residual neuromuscular block can lead to an extended stay in the recovery room and a decline in patient satisfaction.³⁷ Specifically, neuromuscular monitoring should be performed for several groups of patients. This includes those who receive multiple high doses of nondepolarising neuromuscular blocking agents during surgery, and those with severe liver and kidney diseases, electrolyte imbalance, or myasthenia gravis. Additionally, individuals undergoing delicate surgeries (requiring no body movements) including neurosurgery or microsurgery, which demand precise control of neuromuscular function, need this monitoring. It is also indicated for laparoscopic surgeries where deep neuromuscular block is essential, and in patients where postoperative tracheal extubation is required, but the use of neuromuscular blocking agent antagonist is inappropriate or the effect cannot be accurately evaluated.³⁸ Compared with qualitative assessment or clinical evaluation, the incidence of residual neuromuscular block is lower when quantitative neuromuscular monitoring is used. When using quantitative neuromuscular monitoring, it is recommended to perform extubation when the train-of-four ratio (TOFr) is ≥ 0.9 .³⁷

In 2020, Carvalho and colleagues³⁹ published a meta-analysis with 53 clinical studies involving 12 664 surgical patients. All patients received general anaesthesia with administration of neuromuscular blocking agents. Use of quantitative neuromuscular monitoring reduced the

incidence of residual neuromuscular block (TOFr < 0.9) compared with qualitative monitoring or no monitoring. However, high-quality clinical studies are still needed to confirm the findings of this meta-analysis.

Clinical issue 4: How to prevent intraoperative awareness during the implementation of TIVA?

Recommendation 4: In addition to pEEG monitoring, it is recommended to emphasise education and training of anaesthetists on TIVA for rational use of i.v. anaesthetic drugs, thus decreasing the incidence of intraoperative awareness (5, D) (strong consensus, 100% agreement).

Evidence summary: The incidence of intraoperative awareness during general anaesthesia is 0.1–0.2%, but approaches 1% in high-risk procedures such as cardiac surgery, Caesarean delivery, and trauma surgery.^{40,41} Intraoperative awareness can cause severe harm, including repeated intraoperative memory retrieval, nightmares, panic disorder, and post-traumatic stress disorder in severe cases.⁴⁰ Although clinicians often avoid TIVA on the basis of high risk of intraoperative awareness, evidence supporting this is limited. This limitation arises from substantial heterogeneity in the drug combinations and techniques of TIVA used in large-scale studies.^{42,43} Conversely, tightly controlled clinical studies have not demonstrated an increased incidence of intraoperative awareness with the use of TIVA.^{44–46} The Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland conducted the Fifth National Audit Project (NAP5) with the aim of prospectively assessing the incidence of intraoperative awareness during general anaesthesia and its associated risk factors. This study encompassed approximately 2 800 000 patients undergoing general anaesthesia, out of which 300 patients experienced accidental awareness. During the induction period, predisposing factors were identified as thiopental administration, rapid-sequence induction, obesity, difficulty in airway management, neuromuscular blocking agent administration, and disruptions in anaesthetic drug delivery from the anaesthesia room to the operating room. During the recovery period, patients perceived residual neuromuscular block as accidental awareness and this was associated with incomplete recovery of motor function. Notably, 43.3% of the accidental awareness occurred during the maintenance period, primarily attributed to insufficient anaesthesia depth during induction or at the end of anaesthesia.⁴⁷

During TIVA, several high-risk periods for intraoperative awareness are notable^{4,48}: (1) anaesthesia induction when neuromuscular blocking agents are administered before the onset of sedative–hypnotics or when surgery commences with inadequate sedation and analgesia; (2) anaesthesia recovery when neuromuscular block has not subsided; and (3) conversion from inhalation anaesthesia to TIVA when the concentration of inhalation anaesthetic drug decreases while insufficient i.v. anaesthetic drugs are administered for maintenance. It is essential to check for issues such as malfunction of infusion access, block of infusion access, or drug leakage, as these can all lead to intraoperative awareness. Therefore, anaesthetists must be trained to master the principles and precautions related to implementation of TIVA.

Education and training regarding TIVA should include the following: (1) TIVA devices: before implementation of TIVA,

anaesthetists must inspect the drugs to be used, the settings of the infusion pump, the infusion devices, and the venous access. The syringe should be labelled with the drug name, date, and concentration. During the course of TIVA, the infusion pump must be maintained in an optimal state, and the venous access should remain unobstructed without any drug leakage. The infusion tubing should be monitored throughout the anaesthesia procedure, specifically every 15 min. In cases of concurrent infusions, anti-siphon and anti-reflux valves should be used to prevent siphoning and reflux. The infusion connector should be positioned as close to the patient as feasible to minimise dead space. At the end of the surgery, all venous access devices used during TIVA should be flushed with a volume at least twice the dead space to avoid inadvertent administration of residual anaesthetic drugs.⁴ (2) Intravenous anaesthetic drugs: anaesthetists need to have a comprehensive understanding of the pharmacological characteristics of i.v. anaesthetic drugs, and the appropriate plasma or effect-site concentrations tailored to patient characteristics, compatible drugs, and clinical conditions. This is of utmost importance for the rational use of sedatives, analgesics, and neuromuscular blocking agents, maintaining appropriate depth of anaesthesia, and preventing the incidence of intraoperative awareness. (3) Specific prevention and treatment for intraoperative awareness: reference can be made to the 'Consensus on the prevention of intraoperative awareness and electroencephalogram monitoring (2020 edition)'.⁴⁹

The forms of TIVA education and training should be individualised in accordance with the requirements of anaesthetists. Currently, popular approaches include flipped classroom, problem- and capacity-oriented learning, and simulation training.⁵⁰ A study of virtual simulation in clinical anaesthesia revealed that the combination of simulation with traditional teaching significantly improved the excellent rates in clinical anaesthesia theory, practical skills, and internships, compared with traditional teaching alone.⁵¹ Further research should focus on determining which methods are most effective in enhancing both theoretical knowledge and practical application of TIVA among anaesthetists.

Clinical issue 5: What types of anaesthetic drugs are indicated for implementation of TIVA, and what are their pharmacological characteristics?

Recommendation 5: It is recommended to administer i.v. anaesthetic drugs that exhibit rapid onset of action, short action time, short context-sensitive half-time, quick recovery, and minimal side-effects for TIVA (1a, A) (strong consensus, 100% agreement).

Evidence summary: With the implementation of TIVA, three essential elements to achieve general anaesthesia are loss of consciousness (LOC), adequate analgesia, and satisfactory neuromuscular block, which are realised through the use of sedative-hypnotics, opioid analgesics, and neuromuscular blocking agents. The combination of these drugs helps to achieve a complete and balanced anaesthetic effect while minimising the dosage of each drug, thereby reducing the related side-effects.^{6,52} Although these three types of drugs are not interchangeable, sedative-hypnotics and opioid analgesics have a significant synergistic effect, enabling a lower dose of each. For example, remifentanyl can

reduce the dose of propofol by 50%, and propofol can also decrease the dose of remifentanyl owing to its analgesic properties, thus mitigating the incidence of hyperalgesia from remifentanyl.^{6,53}

The drugs used in TIVA should have rapid onset, short action time, high clearance rate, low accumulation, minimal side-effects, and inactive metabolites.⁵⁴ Anaesthetists should have a comprehensive understanding of the pharmacological characteristics of i.v. anaesthetic drugs and select appropriate agents for TIVA according to the patient's condition and the type of surgery.

1. Sedative-hypnotics

Propofol, one of the most widely used intravenous sedative-hypnotics in clinical practice, is frequently used during the induction and maintenance of general anaesthesia. Its PK characteristics facilitate a rapid induction of anaesthesia and a quick recovery of consciousness (ROC), with minimal residual effects. However, in clinical practice, the administration of propofol is constrained by some limitations during the administration process.

Etomidate is another widely used sedative-hypnotic. It presents advantages such as rapid induction and stable haemodynamics. Hannam and colleagues⁵⁵ compared the impacts of etomidate and propofol on haemodynamics in patients undergoing cardiac surgery ($n=156$) and showed that after anaesthesia induction, propofol resulted in a 34% decrease in the area under the baseline of MAP compared with etomidate, indicating that etomidate is more stable than propofol in terms of haemodynamics. In 2021, Dai and colleagues⁵⁶ published a study on patients with coronary heart disease who underwent major noncardiac surgery ($n=80$), showing that there were fewer cardiovascular events and reduced haemodynamic changes with etomidate compared with propofol. Lu and colleagues⁵⁷ published a multicentre, parallel-group, noninferiority RCT in 2022. This study included 1944 older patients undergoing abdominal surgery, which found that anaesthesia maintenance with etomidate was associated with a lower risk of intraoperative hypotension compared with propofol. Although etomidate induced transient adrenal suppression, it did not increase the overall incidence of major complications after abdominal surgery in older patients.

The introduction of new sedative-hypnotics, such as ciprofol and remimazolam, has provided more favourable options for older and critically ill patients. These drugs can ensure stable sedation and anaesthesia effects while improving the comfort and safety during anaesthesia. Akhtar and colleagues⁵⁸ published a systematic review and meta-analysis in 2024 to assess the safety and efficacy of ciprofol in comparison with propofol during the induction of general anaesthesia. This analysis included 13 RCTs involving 1998 patients and showed that, in contrast to propofol, ciprofol was associated with a lower incidence of injection pain while attaining an anaesthesia success rate comparable with that of propofol. In terms of safety, the incidence of hypotension was significantly lower in the ciprofol group. Among the RCTs included in this meta-analysis, only two compared the efficacy and safety of ciprofol-based and propofol-based TIVA. In a single-blind, parallel-group, phase 3 RCT (involving 129 patients undergoing elective surgeries, excluding emergency, cardiothoracic,

Table 1 Sedative–hypnotics commonly used in clinical practice.

Drug name	Drug type	Advantages	Disadvantages
Propofol ⁶²	Alkylphenol	(1) Rapid onset of action, high controllability, quick and complete recovery (2) Decreases intracranial pressure, cerebral blood flow, and cerebral metabolic rate	(1) Injection pain (2) Significant inhibition of circulatory function, characterised by the main symptoms of decreased blood pressure, particularly in the frail older patients or those with insufficient effective circulating blood volume (3) Significant respiratory depression, with the extent of this inhibition being dose-dependent
Etomidate ⁶³	Carboxylated imidazole derivative	(1) Rapid induction and recovery of anaesthesia with minor impacts on haemodynamics, rendering it particularly suitable for anaesthesia induction in older patients, those at high risk of cardiovascular events, and critically ill patients (2) No significant accumulation in the body after continuous infusion	(1) Inhibition of adrenocortical function, thus limiting its application in the anaesthesia maintenance period
Esketamine ⁶⁴	Phencyclidine derivative; ketamine dextrorotatory isomer	(1) Both anaesthetic and analgesic effects (2) Mild respiratory repression (3) Decreases dose of other sedative or analgesic drugs when used in drug combinations for general anaesthesia, thus minimising the fluctuation of haemodynamics and lowering the incidence of respiratory depression	(1) Can cause an increase in blood pressure, an acceleration of heart rate, excessive dreaming, nightmares, headache, hallucination, restlessness, most of which are transient (2) Can cause an elevated pulmonary vascular resistance and increased respiratory secretion. The possibility of respiratory depression cannot be ruled out during rapid high-dose i.v. injection (3) As it has not been available on the market for a long time, clinical experience remains limited.
Midazolam ⁶⁵	Short-acting benzodiazepine	(1) Water solubility and rapid onset of action (2) Short half-life and less accumulation in the body (3) Induction of antegrade amnesia	(1) It may increase the risk of postoperative delirium in older patients
Ciprofol ^{66–68}	Novel alkylphenol	(1) Rapid onset of action and quick recovery (2) Wider safety window, less severe respiration repression, fewer adverse cardiovascular events, more stable circulation, and less injection pain compared with propofol	(1) As it has not been on the market for a long time, clinical experience remains limited.
Remimazolam ^{69,70}	Novel short-acting benzodiazepine	(1) Rapid onset of action and elimination (2) Anterograde amnesia, minor inhibition of respiratory system and circulatory system, less dependence on liver and kidney function, with specific antagonist, but almost no injection pain	(1) As it has not been on the market for a long time, clinical experience remains limited (2) Clinical observation found that long-term high-dose administration of remimazolam for anaesthesia may result in delayed recovery

and neurosurgical surgery), ciprofol-based TIVA was non-inferior compared with propofol-based TIVA (both groups achieving a 100% success rate in maintaining general anaesthesia), and exhibited good tolerability.⁵⁹ In another prospective, randomised, single-blind, controlled study (involving 120 patients undergoing renal transplantation under general anaesthesia), both the propofol and ciprofol groups achieved a 100% success rate. However, the ciprofol group exhibited a shorter time for loss of eyelash reflex and for BIS to reach 60. Additionally, it required a lower dose maintaining more stable MAP throughout the transplantation process. These findings indicate that ciprofol is safe for patients undergoing renal transplantation.⁶⁰ Wu and colleagues⁶¹ published a systematic review and meta-analysis in 2023, which included eight RCTs involving 998 patients. The results showed that, compared with propofol, remimazolam was associated with a lower incidence of hypotension, more stable MAP before and after tracheal intubation, and better haemodynamic stability. Nevertheless, given that ciprofol and remimazolam have not been available on the market for an extended period, the clinical experience regarding these drugs remains limited. Further clinical studies need to be conducted to amass additional clinical evidence, which can better guide their clinical application. The commonly used sedative–hypnotics in clinical practice are presented in Table 1.

2. Opioid analgesics

In clinical practice, commonly used opioid analgesics include fentanyl, sufentanil, alfentanil, and remifentanyl. Remifentanyl is characterised by its rapid onset and elimination, rendering it the most widely used opioid analgesic intraoperatively. The commonly used opioid analgesics in clinical practice are listed in Supplementary Appendix 6.

3. Neuromuscular blocking agents

During TIVA, medium- and short-acting nondepolarising neuromuscular blocking agents are frequently used, such as vecuronium, rocuronium, and cisatracurium. These drugs facilitate timely titration of the level of neuromuscular block and promote rapid recovery of neuromuscular function. Unlike inhalation anaesthetics, i.v. anaesthetic drugs do not augment the effects of neuromuscular blocking agents.

4. Intravenous adjuvants

Various i.v. adjuvants can be used during TIVA to reduce intraoperative and postoperative complications. The i.v. adjuvants used during TIVA and their associated benefits are showed in Table 2.

Clinical issue 6: Selection and use of drugs in TCI mode

Recommendation 6: Drugs with shorter context-sensitive half-times are indicated for TCI. Propofol- or remifentanyl-based TCI is recommended (2b, B) (strong consensus, 100% agreement).

Evidence summary: TCI is an i.v. method that applies PK-PD principles to adjust the concentration of anaesthetic drugs at the target site (plasma or effect-site), thus controlling or maintaining an appropriate depth of anaesthesia to meet clinical requirements.⁶² From the perspective of biomedical

Table 2 Benefits of i.v. anaesthetic drugs combined with i.v. adjuvants during TIVA.

Drug name	Clinical benefits of i.v. anaesthetic drugs combined with i.v. adjuvants
Dexmedetomidine ⁷¹	When dexmedetomidine is i.v. infused at a dose of 0.5–1.0 $\mu\text{g kg}^{-1}$ over 10–15 min during anaesthesia induction, the dosage of etomidate can be reduced by one-third to half, and that of fentanyl or sufentanil can be reduced by 20–30%.
Dexamethasone ^{72–74}	When performing propofol-based TIVA, a single administration of 8 mg of dexamethasone could reduce the incidence of postoperative nausea and vomiting and concomitantly achieve higher postoperative quality of recovery.
Lidocaine ⁷⁵	A single i.v. injection of lidocaine at a dose of 1.0–1.5 mg kg^{-1} , followed by continuous i.v. infusion at a rate of 1.5 $\text{mg kg}^{-1} \text{h}^{-1}$, is capable of reducing the dosage during the maintenance period of TIVA. In addition, lidocaine administered at a dose of 1.0–1.5 mg kg^{-1} can alleviate the injection pain associated with propofol.
Magnesium sulphate ⁷⁶	A single i.v. injection of magnesium sulphate at a dose of 30–50 mg kg^{-1} , followed by continuous i.v. infusion at a rate of 10 $\text{mg kg}^{-1} \text{h}^{-1}$, can improve postoperative analgesic effect.
Esmolol ^{77,78}	I.V. injection of esmolol at a dose of 1 mg kg^{-1} (over 60 s) before preoxygenation can lead to an 18.5% reduction in the dose of propofol during the induction period. Perioperative i.v. infusion of esmolol can reduce overall requirements for anaesthetic and analgesic drugs and simultaneously alleviate postoperative pain.

engineering, TCI systems can be categorised as open-loop and closed-loop modes; additionally, they can be classified as plasma or effect-site TCI according to the target concentration. TCI, the core technology of TIVA, provides a more accurate, simple, and controllable approach for i.v. anaesthesia, significantly improving both the controllability and the safety of clinical anaesthesia.

Not all drugs are appropriate for use in TCI mode for TIVA, except for those with shorter context-sensitive half-times. Currently, propofol and remifentanyl are the most frequently used drugs for TCI in clinical practice. Niewiadomski and colleagues⁷⁹ published a single-centre pilot study ($n=50$) that compared the effects of propofol combined with remifentanyl in the TCI mode with the constant infusion mode on cardiovascular parameters in patients with intracranial lesions undergoing craniotomy. The results showed that MAP was more stable in the TCI group at each time point. Yildirim and colleagues⁸⁰ published a single-centre, prospective, unblinded

Table 3 Plasma or effect-site target concentrations of different i.v. anaesthetic drugs for TCI during induction, maintenance, and recovery of anaesthesia. Note: The doses of the drugs should be in accordance with published literature, package inserts, and guidelines for their clinical application. Clinicians should adjust the drug dose based on the patient's condition during surgery. LOC, loss of consciousness; ROC, recovery of consciousness; TCI, target-controlled infusion.

Drug name	Induction	Maintenance	Recovery
Propofol ^{1,4,83}	The plasma target concentration ranges 4–6 $\mu\text{g ml}^{-1}$ when propofol is administered alone and 3.0–3.5 $\mu\text{g ml}^{-1}$ when propofol is administered in combination with other drugs. Observe and record the effect-site concentration corresponding to an individual's loss of consciousness.	The plasma concentration should be maintained at slightly above the effect-site concentration, which can be set at 3–6 $\mu\text{g ml}^{-1}$ (without opioids) or 2–4 $\mu\text{g ml}^{-1}$ (with opioids).	The effect-site concentrations of LOC are equal to or higher than those for ROC.
Etomidate ⁸⁴	The plasma target concentration ranges from 0.2 to 0.4 mg L^{-1} .	The plasma target concentration ranges from 0.3 to 0.5 mg L^{-1} .	Discontinue the infusion 10 min before the expected awakening time.
Remifentanyl ^{4,83,85}	The plasma target concentration of remifentanyl ranges 2–6 ng ml^{-1} when administered in combination with propofol in TCI mode (a plasma target concentration exceeding 4 ng ml^{-1} can effectively inhibit the tracheal intubation response).	The plasma target concentration ranges 2–4 ng ml^{-1} .	The effect disappears quickly after drug discontinuation (3–10 min).
Alfentanil ⁸²	The plasma target concentration ranges 100–150 ng ml^{-1} .	The plasma target concentration ranges 50–150 ng ml^{-1} .	Discontinue the infusion 20–40 min before the end of the surgery, depending on the duration of the continuous infusion.
Sufentanil ^{1,82}	The plasma target concentration is 0.6 ng ml^{-1} .	The plasma target concentration is 0.3 ng ml^{-1} .	Discontinue the infusion 30–40 min before the end of the surgery in general.

RCT ($n=200$) that compared the incidence of hypotension after anaesthesia induction with propofol in the TCI mode or the constant infusion mode. The results showed that the incidence of hypotension after anaesthesia induction was significantly lower in the TCI group than in the constant infusion group. TCI can also be achieved with etomidate, sufentanil, and alfentanil,^{81,82} but use of these drugs is less common. The plasma or effect-site target concentrations for different i.v. anaesthetic drugs are shown in Table 3. Furthermore, the use of ciprofol and remimazolam in TCI is beneficial owing to their rapid onset of action and quick recovery, and a TCI model for ciprofol is currently under development. Nondepolarising neuromuscular blocking agents are not suitable for TCI.

Anaesthetists should determine the individualised target concentration based on patient characteristics, including age, sex, and body weight, along with the expected extent of surgical stimulus. During the anaesthesia induction period, i.v. anaesthetic drugs should be administered slowly until the patient loses consciousness. Simultaneously, the effect-site concentration of i.v. anaesthetic drugs at that moment is documented. Anaesthesia should be maintained at a level slightly higher than the effect-site concentration that corresponds to an individual's LOC. In case of inadequate analgesia or neuromuscular block, appropriate drugs can be administered to address the issue. The relationship between effect-site concentrations at LOC and ROC remains controversial. Some studies report that during TCI, the calculated effect-site concentration at LOC is typically higher than that at ROC, a phenomenon attributable to neural inertia, a resistance to transitions between arousal states.⁸⁶ Conversely, some studies

propose that concentrations at LOC and ROC are essentially equivalent.^{87,88} This perspective suggests that the time required for awakening can be estimated by referring to the effect-site concentration at the point of LOC after drug discontinuation.

Intraoperative wake-up test is used in brain tumour resections and scoliosis surgeries, where patients are required to participate in intraoperative neurological function assessments at a specific level of sedation and analgesia while maintaining stable haemodynamics and respiration.⁸⁹ Propofol, remifentanyl, and dexmedetomidine are frequently used drugs during intraoperative wake-up tests. Under monitored anaesthesia care in TCI mode, the target effect-site concentrations should be in the range of 0.25–0.50 $\mu\text{g ml}^{-1}$ for propofol and 1–3 ng ml^{-1} for remifentanyl. At 15 min before the wake-up test, the propofol infusion should be halted and the remifentanyl infusion rate should be decreased to 0.010–0.025 $\mu\text{g kg}^{-1} \text{min}^{-1}$ to effectively alleviate pain and other discomforts. This process ensures the smooth implementation of neurological assessment and tumour resection without significant impact on respiration or haemodynamics. Propofol infusion can be resumed once the dura has been closed. Further details are discussed in the 'Consensus on intraoperative wake-up test during neurosurgeries (2020 edition)'.⁹⁰

Clinical issue 7: Selection and use of drugs in non-TCI mode

Recommendation 7.1: Propofol is the most commonly used drug during anaesthesia induction. Etomidate (2b, B), ciprofol

Table 4 Context-sensitive half-times of i.v. anaesthetic drugs commonly used in clinical practice.

Drug name	Context-sensitive half-time
Propofol ⁹²	The context-sensitive half-time is less than 40 min after continuous i.v. infusion for 8 h. Patients can awaken soon even after prolonged infusion, as the plasma concentration required for awakening is generally reduced to less than 50% of the peak concentration during propofol anaesthesia.
Ciprrolol ⁶⁶	The context-sensitive half-time is 3.0 min after continuous i.v. infusion at a rate of 0.3 mg kg ⁻¹ h ⁻¹ for 4 h.
Remimazolam ⁶⁹	The mean context-sensitive half-time ranges 7–8 min after continuous i.v. infusion at a rate of 50 mg h ⁻¹ for 2–8 h.
Etomidate ⁸⁴	The context-sensitive half-time is not significantly prolonged by long-term i.v. infusion (~10 min after continuous infusion for 4 h), allowing patients to awaken within 10–15 min after drug discontinuation.
Remifentanyl ⁶²	The context-sensitive half-time ranges 3–5 min after long-term i.v. infusion, allowing patients to awaken within a few minutes after drug discontinuation.
Other opioids ¹⁰⁰	The context-sensitive half-time after continuous i.v. infusion for 4 h was 262.5 min for fentanyl, 58.2 min for alfentanil, and 33.9 min for sufentanil.

(1a, A), and remimazolam (1a, A) can be used in haemodynamically unstable patients (strong consensus, 100% agreement).

Evidence summary: Patients are susceptible to haemodynamic changes during induction of general anaesthesia, mainly including hypotension after induction and sympathetic response after tracheal intubation.⁹¹ Propofol, one of the most commonly used anaesthetic drugs during induction of general anaesthesia, should be administered at doses of 1.0–2.5 mg kg⁻¹ in adults.⁹² However, propofol exhibits significant inhibition of cardiovascular function. Etomidate, ciprofol, and remimazolam are more suitable for haemodynamically unstable patients owing to their relatively reduced impacts on cardiovascular function. The RCTs conducted by Hannam and colleagues⁵⁵ and Dai and colleagues⁵⁶ demonstrated that etomidate had superior haemodynamic stability compared with propofol. Akhtar and colleagues⁵⁸ conducted a systematic review and meta-analysis, revealing that the incidence of hypotension was significantly lower in the ciprofol group than in the propofol group. Another systematic review and meta-analysis⁶¹ showed a significantly lower incidence of hypotension and more stable MAP before and after tracheal intubation in the remimazolam group compared with the propofol group.

When etomidate is used for anaesthesia induction, the recommended dose ranges from 0.2 to 0.6 mg kg⁻¹.⁸⁴ For ciprofol, the initial dose should not exceed 0.4 mg kg⁻¹, and the infusion rate should be relatively low; subsequent doses can be administered if necessary, each not exceeding 0.2 mg kg⁻¹ with an interval of ~1 min.⁶⁶ Remimazolam can be administered by i.v. injection at a dose of 0.2–0.3 mg kg⁻¹ in adults for anaesthesia induction, or by continuous i.v. infusion at a rate

Table 5 Dose ranges of i.v. anaesthetic drugs and neuromuscular blocking agents commonly used during anaesthesia maintenance. Note: The doses of the drugs should be in accordance with the published literature, package inserts, and guidelines for their clinical application. Clinicians should adjust the drug dose based on the patient's condition during surgery.

Drug name	Anaesthesia maintenance
Propofol ^{1,59}	The dose is 3–12 mg kg ⁻¹ h ⁻¹ for adults, which should be adjusted according to the response to surgical stimulus.
Ciprrolol ⁶⁶	The recommended initial dose for continuous i.v. infusion is 0.8 mg kg ⁻¹ h ⁻¹ , which should be adjusted according to the patients' response. Doses of 0.4–2.4 mg kg ⁻¹ h ⁻¹ can reach the ideal depth of anaesthesia. When ciprofol is used for anaesthesia maintenance in general elective surgeries that can be completed within 2 h, the mean awakening time is <10 min after drug discontinuation.
Remimazolam ⁶⁹	The i.v. infusion rate is 0.2–1.0 mg kg ⁻¹ h ⁻¹ . However, long-term high-dose administration may cause delayed awakening. For prolonged surgeries, drugs can be discontinued early or the infusion rate can be reduced before the end of surgery to facilitate rapid awakening and tracheal extubation.
Etomidate ⁸⁴	After induction with a single i.v. injection at a dose ranging 0.2–0.6 mg kg ⁻¹ , etomidate can be i.v. infused at a rate of 5–20 µg kg ⁻¹ min ⁻¹ for anaesthesia maintenance. Etomidate is now considered safe for anaesthesia maintenance in surgeries lasting <4 h.
Remifentanyl ^{1,59}	The i.v. infusion rate is 0.1–0.4 µg kg ⁻¹ min ⁻¹ .
Sufentanil ¹	The i.v. infusion rate is 0.25–1.00 µg kg ⁻¹ h ⁻¹ . It should be noted that the infusion rate of sufentanil should not exceed the upper limit, and the infusion duration should not exceed 3–4 h when the tracheal extubation is required immediately after surgery.
Alfentanil ⁸²	During continuous i.v. infusion, the rate should be within the range of 50–75 µg kg ⁻¹ h ⁻¹ for the first 30 min, followed by a maintenance dose of 30.0–42.5 µg kg ⁻¹ h ⁻¹ .
Fentanyl ¹	It is not suitable for continuous i.v. infusion in anaesthesia maintenance. It is recommended for intermittent administration.
Vecuronium ⁹⁶	The continuous i.v. infusion rate is 0.8–1.0 µg kg ⁻¹ min ⁻¹ .
Rocuronium	The continuous i.v. infusion rate is 9–12 µg kg ⁻¹ min ⁻¹ .
Cisatracurium ⁹⁶	The continuous i.v. infusion rate is 1–2 µg kg ⁻¹ min ⁻¹ .

of 6 mg kg⁻¹ h⁻¹ for ≤3 min; if the depth of anaesthesia is insufficient, subsequent doses can be administered at a rate of 12 mg kg⁻¹ h⁻¹ for 1 min.⁶⁹ The doses of these drugs should be in accordance with published literature, package inserts, and guidelines for their clinical application. Clinicians should

adjust the drug dose based on the patient's condition during surgery.

Recommendation 7.2: Different opioids at equivalent doses exhibit similar effects on preventing cardiovascular responses to tracheal intubation. It is recommended to optimise the sequence of anaesthetic induction drugs, with the combination of lidocaine (1b, A), esmolol (2b, B), or dexmedetomidine (1b, A) effectively preventing the haemodynamic responses to tracheal intubation and reducing the dose of opioids (strong consensus, 100% agreement).

Evidence summary: During anaesthesia induction, sedative–hypnotics should be administered in combination with opioids and neuromuscular blocking agents. Opioids are mainly used to decrease the stress response associated with tracheal intubation during anaesthesia induction, and exert a synergistic effect when combined with sedative–hypnotics. The common doses of opioids for anaesthesia induction are: 1–2 $\mu\text{g kg}^{-1}$ for fentanyl, 0.15–0.25 $\mu\text{g kg}^{-1}$ for sufentanil, 25–35 $\mu\text{g kg}^{-1}$ for alfentanil,⁸² and 1–5 $\mu\text{g kg}^{-1}$ for remifentanyl.⁹³ Different opioids at equivalent doses exhibit similar effects on preventing cardiovascular responses to tracheal intubation. The common doses of nondepolarising neuromuscular blocking agents are: 0.1–0.2 mg kg^{-1} for vecuronium, 0.6–1.0 mg kg^{-1} for rocuronium, and 0.15–0.20 mg kg^{-1} for cisatracurium.^{94–96} The doses of these drugs should be in accordance with the published literature, package inserts, and guidelines for their clinical application. Clinicians should adjust the drug dose based on the patient's condition during surgery.

During anaesthesia induction, the conventional sequential induction approach (sedation, analgesia, and neuromuscular block) can result in excessive cardiovascular depression before tracheal intubation. This is because the peak effects of various drugs do not coincide. Tracheal intubation should be performed when the general anaesthesia induction drugs reach their peak efficacy, thus minimising cardiovascular responses. Therefore, optimising the administration sequence of anaesthesia induction drugs is essential to ensure that each drug attains its maximum effect simultaneously during tracheal intubation, effectively preventing excessive haemodynamic responses during the induction period.⁹¹ In addition, lidocaine, esmolol, and dexmedetomidine can reduce haemodynamic responses associated with tracheal intubation.^{97–99}

Recommendation 7.3: It is recommended to maintain anaesthesia with drugs characterised by shorter context-sensitive half-times, such as propofol, ciprofol, remimazolam, and remifentanyl, to facilitate rapid recovery after long-term continuous i.v. infusion (1b, A) (consensus, 95% agreement).

Evidence summary: After long-term i.v. infusion of anaesthetic drugs, the rate at which the drug concentration decreases mainly hinges on the context-sensitive half-time. The context-sensitive half-times of i.v. anaesthetic drugs commonly used in clinical practice, along with precautions during anaesthesia maintenance, are given in Table 4. Their dose adjustments are detailed in Table 5.

Based on the clinical protocols for monitored anaesthesia care during surgeries requiring an intraoperative wake-up test, the following dose adjustment strategy should be implemented. Firstly, the dose of propofol and remifentanyl should be adjusted to 0.8–1.0 $\text{mg kg}^{-1} \text{h}^{-1}$ and 0.05–0.10 $\mu\text{g kg}^{-1} \text{min}^{-1}$, respectively. At 15 min before the wake-up test, propofol infusion should be discontinued and remifentanyl infusion should be decreased to 0.010–0.025 $\mu\text{g kg}^{-1} \text{min}^{-1}$. Propofol infusion can be resumed once the dura has been closed. Further details

are provided in the 'Consensus on intraoperative wake-up test during neurosurgeries (2020 edition)'.⁹⁰

The systematic review and meta-analysis by Akhtar and colleagues⁵⁸ showed no significant difference in the time to complete awakening between the ciprofol group and the propofol group across different surgery types and dose subgroups. Ko and colleagues¹⁰¹ published a systematic review and meta-analysis that included eight randomised controlled studies involving 738 patients. They found no significant difference in the time to tracheal extubation and eye opening between the propofol group and the remimazolam group. Wang and colleagues¹⁰² published a systematic review and meta-analysis that included 14 randomised controlled studies involving a total of 927 patients. The results demonstrated that both the time to awakening and tracheal extubation were significantly shortened in the remifentanyl group compared with the sufentanil group.

Recommendation 7.4: For patients with hepatic or renal dysfunction, it is recommended to use propofol in combination with remifentanyl for TIVA while carefully monitoring the dose of the anaesthetic drug (2b, B) (strong consensus, 100% agreement).

Evidence summary: Propofol is not solely dependent on the liver and kidney for elimination; it can also be excreted through extrahepatic routes, making it suitable for patients with hepatic and renal dysfunction.¹ There was no significant difference in the serum protein binding rate of propofol among healthy subjects, non-dialysed chronic renal failure patients, dialysed patients, and cirrhosis patients. It is unlikely that patients with renal and hepatic disorders would experience exaggerated pharmacological responses after receiving standard doses of propofol; however, attention should be paid to drug dose owing to individual differences.¹⁰³ Some PD factors can influence dosing requirements. Wu and colleagues¹⁰⁴ proposed that propofol requirements to maintain similar depths of hypnosis depend on the severity of chronic virus-related liver dysfunction. Patients with the most severe liver dysfunction required the lowest propofol doses. This might be related to the increased volume of distribution. Goyal and colleagues¹⁰⁵ suggested that a larger volume of distribution could influence propofol dosing requirements in end-stage renal disease.

For ciprofol, no dose adjustment is required for patients with mild to moderate hepatic dysfunction (Child–Pugh A or B) or mild to moderate renal dysfunction (eGFR 30–89 $\text{ml min}^{-1} 1.73 \text{ m}^{-2}$). However, it should be administered with caution in patients with severe hepatic or renal dysfunction because of the lack of clinical data.⁶⁶ It is generally accepted that no dose adjustment is required for remimazolam in patients with mild to moderate hepatic impairment; however, a lower dose is recommended for those with severe hepatic impairment. Considering that the PK of remimazolam are not affected by renal dysfunction, no dose adjustment is required for patients with renal dysfunction.⁶⁹ Patients with hepatic and renal dysfunction are at an increased risk of drug accumulation when higher doses of fentanyl, sufentanil, or alfentanil are administered. Remifentanyl's elimination is independent of liver and kidney function; therefore, its PK are not affected by hepatic and renal failure.¹ It has been demonstrated that the PK of remifentanyl in patients with hepatic and renal failure were not significantly different compared with healthy subjects.^{106,107} For patients with end-stage hepatic and renal failure, it is recommended to reduce the doses of propofol and remifentanyl during TIVA.¹ One

Table 6 Recommended plasma target concentrations of propofol and remifentanyl in TCI mode during anaesthesia maintenance.¹²⁷
 Note: *The lower limit of plasma target concentration is $2 \mu\text{g} \cdot \text{ml}^{-1}$ when monitoring depth of anaesthesia. The doses of above drugs should be in accordance with the published literature, package inserts, and guidelines for their clinical application. Clinicians should adjust the drug dose based on the patient's condition during surgery.

Drug	Minor surgeries (spontaneous breath)	Minor surgeries (positive pressure ventilation)	Major surgeries (positive pressure ventilation)
Propofol	$2.5\text{--}4.0 \mu\text{g} \cdot \text{ml}^{-1*}$	$2.5\text{--}4.0 \mu\text{g} \cdot \text{ml}^{-1*}$	$3\text{--}5 \mu\text{g} \cdot \text{ml}^{-1}$
Remifentanyl	$1\text{--}2 \text{ ng} \cdot \text{ml}^{-1}$	$2\text{--}4 \text{ ng} \cdot \text{ml}^{-1}$	$3\text{--}6 \text{ ng} \cdot \text{ml}^{-1}$

study compared the recovery parameters of propofol vs remifentanyl during TIVA in patients with end-stage renal failure and normal renal function ($n=44$). End-stage renal failure, along with its related biochemical and physiological changes, did not prolong the recovery time for either propofol or remifentanyl during TIVA.¹⁰⁸

Clinical issue 8: Implementing TIVA in paediatric patients

Recommendation 8.1: Propofol-based TIVA in paediatric patients can reduce the incidence of emergence agitation and postoperative pain; however, the induction and maintenance doses of propofol are generally higher than those in adult patients (1a, A) (strong consensus, 100% agreement).

Evidence summary: Propofol-based TIVA can be safely performed in paediatric patients; however, it is not recommended for those under 1 month of age. Propofol should be used with caution in paediatric patients with low body weight, congenital heart disease, or severe systemic diseases.¹ There are significant PK-PD differences between paediatric and adult patients, and among paediatric patients of different ages. Paediatric patients (excluding neonates) exhibit higher clearance rates of propofol and remifentanyl compared with adults, and higher infusion rates for anaesthesia induction and maintenance to achieve the target effect-site concentration.¹⁰⁹ In neonates with hepatic and renal immaturity, the clearance rates of drugs that rely on the liver and kidney for elimination are at their lowest; conversely, drugs that do not rely on these organs for elimination (e.g. remifentanyl) are mainly eliminated through hydrolysis by nonspecific esterase in the plasma or tissues, which peaks during the neonatal period and then declines with age.¹¹⁰ Therefore, the implementation of TIVA in paediatric patients should strictly adhere to the principles of individualisation and use pEEG monitoring for TIVA management.¹¹¹

The dose of propofol in paediatric patients is higher than that in adult patients, with induction dose range of $2.5\text{--}4.0 \text{ mg} \cdot \text{kg}^{-1}$ and maintenance doses of $9\text{--}15 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Attention should be paid to possible transient respiratory depression.¹¹² The combination of propofol and dexmedetomidine can reduce the incidence of respiratory depression associated with propofol. Etomidate is rarely used in paediatric patients because of the challenges in controlling the depth of anaesthesia and its high infusion volume.¹¹³ Remifentanyl should be injected i.v. at a loading dose of $0.5\text{--}2.0 \mu\text{g} \cdot \text{kg}^{-1}$,^{114,115} followed by a maintenance infusion rate of $0.05\text{--}1.0 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.^{116,117} Fentanyl and alfentanil can also be used during TIVA in paediatric patients; however, they can result in delayed recovery. Midazolam can be administered alone for sedation or as an adjuvant for i.v.

general anaesthesia in paediatric patients. I.V. midazolam offers the benefit of antegrade amnesia; however, adverse reactions such as prolonged awakening time and respiratory depression can occur when combined with other anaesthetic drugs. The doses of these drugs should be in accordance with the published literature, package inserts, and guidelines for the clinical application of drugs. Clinicians should adjust the drug dose based on the patient's condition during surgery.

Cipfol can serve as an alternative to propofol in paediatric patients owing to its noninferiority.¹¹⁸ The incidence of injection pain in paediatric patients is significantly lower with cipfol compared with propofol. This effectively reduces crying, enhances comfort, and improves family satisfaction.¹¹⁹ However, the current clinical experience with cipfol in paediatric patients remains limited.

Abdallah and colleagues¹²⁰ published a systematic review and meta-analysis that included 13 RCTs involving 1174 paediatric patients. The results showed that the overall rate of postoperative pain in the sevoflurane group was nearly two-fold that in the propofol group. Zhao and colleagues¹²¹ published a meta-analysis with 20 RCTs involving 1550 paediatric patients under general anaesthesia with either propofol or sevoflurane. They found that propofol-based anaesthesia could significantly reduce the incidence of agitation, PONV, and postoperative pain compared with sevoflurane-based anaesthesia; however, it was associated with a slightly prolonged recovery.

Recommendation 8.2: Propofol-based TCI can be performed in paediatric patients with a paediatric TCI model (2b, B) (consensus, 95% agreement).

Evidence summary: Currently, two paediatric TCI models are in use in clinical practice: the Kataria model and the Paedfusor model. The Kataria model is applicable to paediatric patients aged >3 yr or with a body weight of $>15 \text{ kg}$, whereas the Paedfusor model is indicated for those aged >1 yr or with a body weight of $<15 \text{ kg}$.^{122,123} Although the Paedfusor model has been extensively investigated, attention should be paid to the injection dose, as it can be overestimated, particularly in paediatric patients with haemodynamic instability. Paediatric TCI models do not predict the concentration at the effect site. Therefore, before airway intervention, it is essential to reconfirm whether the patient has lost consciousness. For obese paediatric patients, because the dose calibration does not strictly follow a linear increase, the dose should be increased by 20% based on calculations using the ideal body weight (IBW). In order to reduce the risk of neonatal propofol infusion syndrome, it is recommended to maintain an infusion rate $<10 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ when the i.v. infusion exceeds 8 h.¹²⁴

During anaesthesia induction with propofol-based TCI in paediatric patients, the initial target plasma concentration

typically is 4–6 $\mu\text{g ml}^{-1}$, which is adequate to achieve anaesthesia while minimising adverse reactions (e.g. hypotension). Kang and colleagues¹²⁵ published a retrospective observational study that investigated the efficacy and safety of propofol-based TCI in paediatric patients aged <3 yr. After propensity score matching, there were 109 patients in the propofol anaesthesia group and 109 patients in the inhalation anaesthesia group. The results showed that propofol-based TCI was effective for general anaesthesia, without serious perioperative adverse events related to propofol. Mu and colleagues¹²⁶ published an RCT that compared the recovery time of propofol-based TCI and constant infusion in 74 paediatric patients aged 1–12 yr. TCI could increase the propofol dose without prolonging awakening time compared with constant infusion. To address the injection pain associated with propofol-based TCI in paediatric patients, remifentanyl-based TCI can be implemented at a target plasma concentration of 4 ng ml^{-1} for 2 min for anaesthesia induction, followed by propofol-based TCI. This strategy can not only reduce injection pain but also prevent and reduce agitation. During anaesthesia maintenance, the target plasma concentrations of propofol and remifentanyl are shown in Table 6.¹²⁷

Recommendation 8.3: Administration of an appropriate dose of lidocaine to paediatric patients before implementation of propofol-based TIVA can reduce the injection pain associated with propofol (1b, A) (strong consensus, 100% agreement).

Evidence summary: Injection pain is one of the major disadvantages of propofol, particularly in paediatric patients. The incidence of injection pain related to propofol varies from 28% to 85%. Injection pain affects haemodynamics during the induction period; more importantly, it affects the physical and mental health of paediatric patients.¹²⁸ Pre-injection of lidocaine,¹²⁹ esketamine,⁶⁴ or dexmedetomidine¹³⁰ before the intravenous infusion of propofol or infusion via the vena cava can reduce injection pain associated with propofol while preventing or reducing agitation.

Clinical issue 9: Implementing TIVA in older patients

Recommendation 9: In older patients undergoing TIVA, the doses of anaesthetic drugs should be decreased. Etomidate and ciprofol can be considered for anaesthesia induction because of their minor impacts on haemodynamics (2b, B) (consensus, 95% agreement).

Evidence summary: The pathophysiological alterations associated with ageing frequently lead to changes in the PK-PD of anaesthetic drugs, and increased sensitivity. Therefore, during the induction period, the doses of i.v. anaesthetic drugs should be reduced, the time interval between administrations should be extended, and the administration rate should be reduced. Similarly, drug doses should be lowered during the maintenance period. Given the vulnerability of the circulatory system in older patients, sedatives with less cardiovascular depression should be selected for anaesthesia induction,¹³¹ such as etomidate and ciprofol.^{66,84} The recommended dose of etomidate is 50–75% of the adult dose, and that of ciprofol is 75% of the adult dose. An RCT evaluated the efficacy and safety of ciprofol-based vs propofol-based anaesthesia in older patients undergoing endoscopic retrograde cholangiopancreatography ($n=284$). Compared with the propofol group, patients in the ciprofol group experienced a shorter emergence duration, a shorter length of hospital stay, and a lower incidence of injection

pain.¹³² Hannam and colleagues⁵⁵ found that etomidate was superior to propofol in terms of haemodynamic stability during anaesthesia induction. Drug doses should be adjusted according to the patient condition. Vital signs should be closely monitored throughout drug administration. Although remimazolam has a relatively small inhibitory effect on the circulation, its potential to increase the incidence of POD in older patients remains unclear. Therefore, remimazolam should be used with caution in older patients.

For older and critically ill patients receiving propofol, vasoconstrictors (e.g. norepinephrine at a dose of 0.05–0.10 $\mu\text{g kg}^{-1} \text{ min}^{-1}$) should be administered before anaesthesia induction.¹³³ In older patients, the volume of the central compartment can decrease by 25%, and drug clearance can decline by 20%. Consequently, the loading dose for older patients should be reduced accordingly. It is recommended to initiate propofol-based TCI using a step-by-step method. For instance, an initial plasma target concentration of 1 $\mu\text{g ml}^{-1}$ can be gradually increased in increments of 0.5–1.0 $\mu\text{g ml}^{-1}$,⁴ and the optimal dose is achieved when the eyelash reflex is lost or when monitoring indicates a sufficient depth of anaesthesia for tracheal intubation. In the event of hypotension, administration of propofol should be suspended until haemodynamic stability is restored. Opioids should be initiated at a low dose, along with close monitoring of respiratory depression.

Clinical issue 10: Implementing TIVA in obese patients

Recommendation 10: For obese patients, propofol combined with remifentanyl in the TCI mode is indicated (5, D). In non-TCI mode, doses of i.v. anaesthetic drugs should be calculated based on lean body weight (LBW) or adjusted body weight (ABW), depending on the drug characteristics (5, D). Remimazolam and ciprofol exhibit a reduced incidence of respiratory depression during TIVA in outpatient surgeries for obese patients (2b, B) (strong consensus, 100% agreement).

Evidence summary: Obesity is associated with an increase in adipose tissue mass, LBW, blood volume, and cardiac output, and changes in drug PK parameters (such as an increase in volume of distribution and clearance rate), resulting in a requirement for higher drug doses.¹³⁴ In addition to calculating the drug dose based on the total body weight (TBW), IBW, LBW, and ABW can also be used for obese patients.¹³⁵ TIVA in morbidly obese patients must be implemented with caution because they have a higher risk of intraoperative accidental awareness, particularly when neuromuscular blocking agents are administered. Therefore, continuous clinical evaluation is especially critical for obese patients. It is recommended to perform pEEG monitoring for morbidly obese patients.

For obese patients, propofol combined with remifentanyl in the TCI mode is recommended. The Eleveld PK model is considered appropriate for obese patients, even those weighing up to 152 kg. Thus, the Eleveld model of propofol is suitable for TCI.¹³⁶ The effect-site concentration predicted by the Marsh PK model with TBW as the body weight input is significantly higher than that in non-obese patients. Therefore, it is recommended to use ABW as the input for propofol-based TCI to prevent overdose during anaesthesia maintenance.¹³⁵ For remifentanyl, it is recommended to use LBW as the input for TCI, with a target plasma concentration of ~4 ng ml^{-1} .¹³⁵ The combination of propofol and remifentanyl in the

TCI mode should be performed with monitoring of BIS and haemodynamics.

For non-TCI anaesthesia in obese patients, the initial dose of propofol is recommended to be calculated based on LBW, with an increase to prevent insufficient anaesthesia induction.¹³⁷ The continuous infusion dose should be calculated based on ABW. Given that the PK characteristics of etomidate and propofol are similar, the etomidate dose should be calculated based on ABW and readministered as needed. The doses of fentanyl and remifentanyl are recommended to be calculated based on LBW, whereas the doses of alfentanil and remimazolam should be calculated based on ABW.^{1,138} Studies on the ciprofol administration protocol based on different body weights in obese patients are in progress. Considering the high risk of hypoxemia in obese patients, ciprofol and remimazolam exhibit the advantage of contributing to less severe respiratory depression.^{66,69} Studies have shown that the incidence of hypoxaemia was lower in the remimazolam¹³⁹ and ciprofol¹⁴⁰ groups than in the propofol group in obese patients undergoing gastroscopy; however, further exploration is required to determine whether these findings can be extended to inpatient obese patients.

Clinical issue 11: Implementing TIVA in pregnant women

Recommendation 11.1: No definite evidence of teratogenesis (5, D) or adverse effects on fetal neurodevelopment (2b, B) have been identified in non-obstetric surgeries with conventional i. v. anaesthetic drugs during pregnancy. Midazolam (5, D) should be avoided during the first trimester of pregnancy (strong consensus, 100% agreement).

Evidence summary: Animal studies have shown that nearly all anaesthetic drugs can produce teratogenesis; however, clinical studies have not reported teratogenesis, nor is there evidence that exposure to the usual administration doses of anaesthetic drugs in clinic practice can result in abnormalities in fetal neurodevelopment and subsequent intelligence.¹⁴¹ The American College of Obstetricians and Gynecologists asserts that currently used i.v. anaesthetic drugs exhibit no teratogenesis at the usual dose for pregnant women across various gestational ages.¹⁴² Ing and colleagues¹⁴³ reported an observational cohort study on prenatal anaesthesia exposure and behavioural deficits in children ($n=2024$). This study revealed that children who were exposed to general anaesthesia during fetal period exhibited higher externalising behaviour scores. However, a correlation cannot be concluded owing to the nature of the observational study and confounding factors. Bleaser and colleagues¹⁴⁴ published a bidirectional cohort study ($n=582$) that prospectively compared the neurodevelopment between children exposed to prenatal anaesthesia and those not exposed to anaesthetic drugs while retrospectively evaluating exposure status. There was no evidence supporting a correlation between prenatal anaesthesia and impaired neurodevelopmental outcomes in the general population. However, animal studies have shown that early exposure to midazolam can alter chromatin accessibility and resting gene expression in neural stem cells within the hippocampus of mice. This alteration limits their proliferative ability, thus resulting in reduced neurogenesis associated with hippocampal-dependent memory impairment.¹⁴⁵ Therefore, midazolam should be avoided during the first

trimester of pregnancy.¹⁴⁶ In non-obstetric surgeries performed during pregnancy, it is essential to monitor fetal heart rate, uterine tone, and the depth of anaesthesia. Anaesthetic drugs can reduce baseline fetal heart rate; therefore, specific monitoring values must be established taking into account the factors such as anaesthetic drugs.¹⁴¹

Recommendation 11.2: Propofol-based TIVA can be applicable in Caesarean delivery. In pregnant women with hypertension, after a comprehensive preoperative assessment, remifentanyl can be used for anaesthesia induction, accompanied by preparations for neonatal resuscitation (1b, A) (strong consensus, 100% agreement).

Evidence summary: During implementation of TIVA in Caesarean delivery, attention must be paid to the health and safety of both pregnant women and their fetuses. A significant challenge lies in the selection of anaesthetic drugs for induction (before the fetus is delivered). Propofol and etomidate, when combined with nondepolarising neuromuscular blocking agents, can be used for anaesthesia induction in Caesarean delivery. Currently, there is no TCI model specifically designed for pregnant women; therefore, a non-TCI approach is generally adopted. For healthy pregnant women, i.v. injection of propofol at a dose ranging $1.5\text{--}2.5\text{ mg kg}^{-1}$ combined with rocuronium at $0.6\text{--}1.0\text{ mg kg}^{-1}$ can be used for rapid-sequence induction. The dose of propofol typically should not exceed 2.5 mg kg^{-1} and the continuous i.v. infusion dose should not exceed $9.0\text{ mg kg}^{-1}\cdot\text{h}^{-1}$. Otherwise, neonatal depression can occur.^{147,148} However, for pregnant women with haemodynamic instability or poor tolerance to haemodynamic fluctuations, an i.v. injection of etomidate at a dose ranging $0.2\text{--}0.3\text{ mg kg}^{-1}$ is recommended.^{148–150} During anaesthesia induction for Caesarean delivery, an i.v. injection of esketamine at a dose of 0.5 mg kg^{-1} can achieve sufficient analgesia. It can protect the safety of pregnant women and fetuses when combined with other general anaesthetic drugs.⁶⁴ Midazolam is contraindicated for anaesthesia induction during Caesarean delivery because of its inhibitory effect on neonatal respiration.¹ The doses of those drugs should be in accordance with the published literature, package inserts, and guidelines for the clinical application of drugs. Clinicians should adjust the drug dose based on the patient's condition during surgery.

The use of opioids for induction of anaesthesia for Caesarean delivery remains a topic of ongoing debate. Traditionally, opioids are not recommended owing to the potential risk of respiratory depression in neonates. However, current consensus suggests that, after comprehensive preoperative assessment, low doses of opioids can be used in pregnant women with hypertension, preeclampsia, and cardiovascular or cerebrovascular diseases who have poor tolerance to haemodynamic fluctuations, such as i.v. injection of remifentanyl at $0.5\text{ }\mu\text{g kg}^{-1}$. White and colleagues¹⁵¹ published a systematic review and meta-analysis to investigate the use of opioids for general anaesthesia induction during Caesarean delivery, including their adverse effects on neonates. It included 17 RCTs involving 987 patients. The results showed that opioids were effective for general anaesthesia induction. It also demonstrated the safety of remifentanyl, showing no significant effect on Apgar scores. When remifentanyl is used, it is essential to prepare for neonatal resuscitation.^{150,152} Anaesthesia can be maintained following a routine TIVA protocol after the fetus is taken out. Caesarean delivery is one of the most common surgeries during which intraoperative

awakening can occur,^{47,153} so benzodiazepines can be given after the fetus is delivered. Intraoperative monitoring of the depth of anaesthesia should be considered.¹⁵⁴

Clinical issue 12: Implementing TIVA in patients undergoing anaesthesia or painless diagnostic and therapeutic procedures outside the operating room

Recommendation 12: TIVA is indicated for patients undergoing anaesthesia or painless diagnostic and therapeutic procedures outside the operating room. It should be performed in accordance with the same standards of procedures and monitoring as those in the operating room. Propofol-based TIVA is recommended. Ciprofol- or remimazolam-based TIVA can also be considered owing to their characteristics of lower cardiovascular and respiratory depression, higher patient comfort, and shorter recovery time (1a, A) (strong consensus, 100% agreement).

Evidence summary: Anaesthesia requirements for painless diagnostic and therapeutic procedures outside the operating room refers to patients undergoing surgeries, diagnostic examinations, or therapeutic procedures, which include high patient comfort, rapid onset of action and recovery, and high quality of awakening under the premise of ensuring patient safety. When TIVA is performed outside the operating room, it should be in accordance with the same standards of procedures and monitoring as those in the operating room, and performed by a qualified anaesthetist. Different anaesthesia protocols can be used based on the purpose of diagnosis and treatment and the depth of sedation and anaesthesia requirements. Commonly used drugs include propofol, midazolam, etomidate, and opioids (e.g. fentanyl, sufentanil, alfentanil, remifentanyl), whereas new sedative–hypnotics (e.g. ciprofol, remimazolam) exhibit promise in sedation and anaesthesia outside the operating room. Gao and colleagues¹⁵⁵ published a double-blind RCT ($n=164$) that compared the efficacy and safety of ciprofol and propofol in colonoscopy. The results showed that during colonoscopy, the sedation or anaesthesia effect of ciprofol at a dose of 0.4 mg kg^{-1} was equivalent to that of propofol at a dose of 2.0 mg kg^{-1} . Ciprofol did not cause injection pain and had a lower risk of respiratory depression and hypotension. Xu and colleagues¹⁵⁶ reported a meta-analysis to compare the safety and efficacy of ciprofol and propofol for general anaesthesia in gynaecological surgeries that included six RCTs involving 741 patients. The results showed that compared with the propofol group, the changes in MAP, SAP, and DAP before and after anaesthesia induction in the ciprofol group were lower, as were the incidences of injection pain, respiratory depression, body movements, and hypotension. Barbosa and colleagues¹⁵⁷ published a systematic review and meta-analysis with 15 studies, involving 4516 patients undergoing gastrointestinal endoscopy. This study compared the sedative efficacy and safety of remimazolam and propofol in adult patients undergoing gastrointestinal endoscopic surgeries, revealing that the efficacy of remimazolam was similar to that of propofol; however, the incidence of respiratory depression, hypotension, hypotension requiring treatment, and bradycardia was significantly lower than that for propofol. Detailed anaesthesia protocols are described in ‘Guidance on sedation and anaesthesia protocols for diagnostic and therapeutic procedures’.^{158–162}

Discussion

These practice guidelines were developed by the Chinese Society of Anaesthesiology of the Chinese Medical Association with the aim of providing evidence-based recommendations. In recent years, the introduction of new sedative–hypnotics, such as ciprofol and remimazolam, has provided more options for the implementation of TIVA, particularly by offering broad prospects for reducing haemodynamic complications. The working group updated this section by systematically reviewing the literature and evaluating the available evidence. Future studies should focus on development of ciprofol- and remimazolam-based TCI, improving the accuracy and safety of anaesthesia. In addition to anaesthetic drugs, more attention should be paid to the implementation details of TIVA. The PK-PD models of i.v. anaesthetic drugs should be optimised to make them more suitable for special populations. The monitoring techniques for depth of anaesthesia should be improved to realise more accurate anaesthesia management. Moreover, large-scale, multicentre clinical studies should be conducted to verify the efficacy and safety of TIVA in different types of surgery and patient populations, thus ensuring patient safety and improving the quality of medical services.

Several controversies persist in the field of TIVA, with the most prominent debates centred on the following two issues: (1) impact of TIVA on POD and POCD; and (2) influence of TIVA on long-term oncologic outcomes.

Impact of TIVA on POD and POCD: large-scale retrospective studies (including 30 075 and 738 600 older patients, respectively),^{163,164} have demonstrated that TIVA can reduce the risk of POD in older patients undergoing noncardiac surgeries, especially tumour surgeries. Additionally, meta-analyses have shown that TIVA can reduce the risk of POCD by 54%.¹⁶⁵ Nevertheless, opponents argue that RCTs have failed to show any improvement in POD in laparoscopic¹⁶⁶ and cardiac surgeries.¹⁶⁷ Moreover, studies on POCD are of insufficient reliability owing to significant heterogeneity and small sample sizes.¹⁶⁸ Therefore, future research should focus on designing RCTs with stratified approaches, grouping patients according to surgical types and cognitive status while controlling confounding factors. It is also essential to identify biomarkers of perioperative inflammation and nerve injury to establish a prediction model for TIVA efficacy, and to unify the diagnostic criteria for POCD and develop objective monitoring tools for POD.

Influence of TIVA on long-term oncologic outcomes: pre-clinical research has indicated that inhalation anaesthetic drugs might promote cancer cell migration, invasion, and proliferation, induce immunosuppression, and suppress natural killer cell function. All these factors are associated with unfavourable oncologic outcomes.² In contrast, propofol-based TIVA might have potential benefits in enhancing tumour prognosis compared with inhalation anaesthesia.¹⁶⁹ Nevertheless, evidence from clinical studies is scarce. Li and colleagues¹⁷⁰ presented a systematic review and meta-analysis that encompassed three prospective RCTs and 17 retrospective studies. The results from the retrospective studies indicated a significant reduction in the risk of cancer metastasis or recurrence within the TIVA cohort. However, significant heterogeneity was observed among these studies. Conversely, in the three prospective RCTs, this potential benefit of TIVA was not statistically significant. Yoon and

colleagues¹⁷¹ reported a nationwide cohort study involving 312 985 patients demonstrating no discernible correlation between the type of general anaesthetic drugs used in cancer surgeries and the postoperative overall survival rate, and 1-yr and 5-yr survival rates. Mincer and Buggy¹⁷² conducted a long-term follow-up study based on a multicentre randomised trial that involved 1195 older patients undergoing major cancer surgeries. Their results showed no significant difference in the long-term survival rate after major cancer surgeries when comparing i.v. and inhalation anaesthetic drugs. Overall, the current clinical evidence is not sufficient to advocate for propofol-based TIVA as a clearly superior alternative to inhalation anaesthesia in the context of cancer surgeries. However, this is a field of active exploration.

As anaesthetists increasingly take on the diverse responsibilities of perioperative physicians, the significant influence of various anaesthetic strategies on long-term patient outcomes has attracted considerable attention from both the medical community and researchers alike. Surgery continues to stand as the cornerstone of treatment for solid tumours, and as such, optimising anaesthetic protocols to enhance oncologic prognosis has emerged as a crucial interdisciplinary research priority, situated at the dynamic intersection of anaesthesiology and oncology, where collaboration and innovation are essential for enhancing patient care and improving survival rates.

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Declaration of interest

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Appendix A. Supplementary data

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