Total Intravenous ANAESTHESIA

using target controlled infusion

A pocket reference

3RD EDITION
SPECIALTY SECTIONS
3RD EDITION

College of Anaesthesiologists,
Academy of Medicine of Malaysia

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This pocket reference serves as a practical resource guide for both first time users and experienced users of TIVA. It is mostly relevant for relatively healthy adults (American Society of Anesthesiology [ASA] physical status I or II), allowing for some degree of flexibility in different circumstances.

03 INTRODUCTION

Recent advances in our understanding of the pharmacokinetic principles and developments in infusion pump technology have enabled the development of total intravenous anaesthesia (TIVA), whereby anaesthesia is administered exclusively via the intravenous route. The primary implementation of TIVA involves administration with the use of a target-controlled infusion (TCI) pump, which allows administration of intravenous agents based on real-time pharmacokinetic simulations.

There is solid rationale for the use of TIVA in circumstances in which the delivery of inhaled anaesthetics is impossible or disadvantageous, and in scenarios where traditional anaesthetic delivery systems may be unavailable or impractical. TIVA offers several potential advantages over traditional volatile anaesthetic techniques. These include reduced incidence of post-operative nausea and vomiting, reduced atmospheric pollution, more predictable and rapid recovery, greater haemodynamic stability, ease of titration with TCI, preservation of hypoxic pulmonary vasoconstriction, reduction in intracerebral pressure and reduced risk of organ toxicity.[1]

Commonly used anaesthetic agents

The discovery of propofol in the 1970s has revolutionised the use of TIVA; currently, it is the only available intravenous hypnotic agent suitable for induction and maintenance of anaesthesia. Propofol-based TIVA techniques offer many advantages including rapid recovery of consciousness and psychomotor function, enhanced recovery speed, anti-emetic effect and a lower incidence of post-operative nausea and vomiting.[2] Propofol pharmacokinetics is well described by an open 3 compartment model. It is characterised by a large volume of distribution of about 4 L/kg, a central compartment volume that ranges from 60-228 mL/kg and a high metabolic clearance that ranges from 20-30 mL/min/kg. As its pharmacokinetics is influenced by age, a model that includes age-adjusted parameters is

necessary in elderly patients to avoid the risk of overdose.[3] Shorter acting opioids, such as remifentanil, sufentanil and alfentanil, are particularly suited for use as part of a TIVA technique.

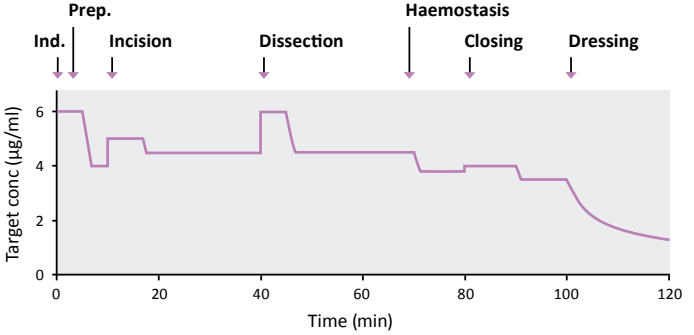
Remifentanil is an ultra short acting opioid that is about forty times more potent than alfentanil.[3] It has been established as the drug of choice for TIVA with propofol. Its pharmacokinetic profile is best described by a 3 compartment model and is characterised by a small volume of distribution at steady state (V_{ss}) of 0.3–0.4 L/kg. This explains its short-acting effect and is reflected by its very short context-sensitive half-time (3–4 min) that is independent of infusion duration. It has a rapid clearance (2.5–3.0 L/min), a short elimination half-life (50–60 min) and is easily titrable.[1,3]

Sufentanil is a potent opioid analgesic with a pharmacokinetic model that is well described by a 3 compartment model, characterised by a large volume of distribution of 6–8 L/kg and a high metabolic clearance of 1 L/min. Due to its slow redistribution from a large deep peripheral compartment, its terminal half-life is prolonged (15-20 h) although its context-sensitive half-time remains relatively short (< 60 min); thus, it has been used for long-duration sedations.[3]

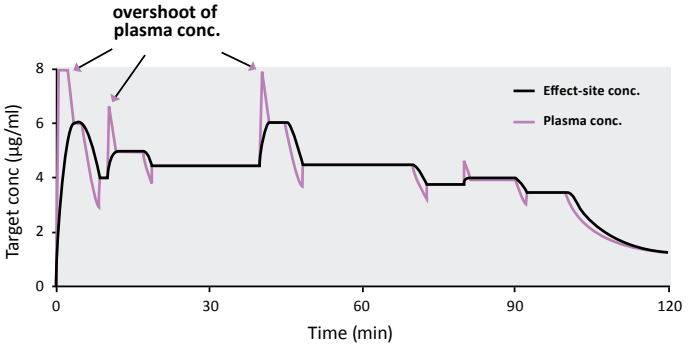
Alfentanil is a structural analogue of fentanyl, but is seven to ten times less potent. Its low ionisation constant at physiological pH allows for rapid penetration in the brain; thus, its onset of action is reached in 45 seconds after intravenous injection. Its context-sensitive half-time is longer than that of remifentanil and close to that of sufentanil, reaching 50 min after 3 hours and remaining at this level for longer infusions (> 10 h). The total clearance of alfentanil is essentially a metabolic clearance; the variability of its pharmacokinetics appears large; therefore, special attention is required in certain populations of patients. Due to its chemical properties and small V_{ss}, alfentanil effect-site concentrations may vary rapidly and widely – the choice of pharmacokinetic model is particularly important.[3]

03 INTRODUCTION

A target controlled infusion allows the anaesthesiologist to match the concentration of drug to the degree of stimulation.



Targeting the effect-site has the advantage of a more rapid onset of action, but may result in greater side effects due to the overshoot of the plasma concentration.



04 APPROPRIATE INDICATIONS FOR TOTAL INTRAVENOUS ANAESTHESIA

TIVA is appropriate for all surgical procedures unless contraindicated. TIVA is especially useful in:

1. Neurosurgical procedures
2. Surgical procedures requiring neurophysiological monitoring, such as spine surgery
3. Oocyte retrieval
4. Ambulatory surgery
5. Malignant hyperthermia susceptible patients
6. Patients at risk of post-operative nausea and vomiting
7. Bronchoscopy/ENT-Laser surgery
8. Lobectomy via thoracotomy/pneumonectomy/video-assisted thoracoscopic surgery
9. Procedural sedation and monitored anaesthesia care

05 PRINCIPLES OF TOTAL INTRAVENOUS ANAESTHESIA

1. **Ensure adequate hypnosis.**
   a. Application of pharmacokinetic and pharmacodynamic knowledge will ensure correct dosage that leads to smooth anaesthesia and quick recovery
   b. Depth of anaesthesia monitoring (e.g. BIS) helps to ensure adequate hypnosis without overdepressing the cardiovascular system; however, it is not essential for all patients

2. **Ensure adequate analgesia/suppression of reflex.**
   a. Titrate remifentanil or alfentanil infusion to intensity of surgical stimulus
   b. Higher doses of remifentanil or alfentanil can prevent movement. This cannot be achieved with the longer acting opioids such as morphine and fentanyl, without delayed recovery
   c. Ensure adequate post-operative analgesia as remifentanil and alfentanil have short durations of action

3. **Ensure haemodynamic stability.**
   a. Haemodynamic instability may occur despite adequate hypnosis and analgesia
   b. Consider hypotensive agents if blood pressure is persistently elevated
   c. Consider fluids, vasoactive agents or inotropic agents if blood pressure is persistently low
   d. Consider atropine if brachycardia develops

4. **Ensure muscle relaxation.**
   a. Propofol has weaker muscle relaxant properties than inhalation agents. Thus, more frequent doses of neuromuscular blockers may be required when using propofol for maintenance of anaesthesia without remifentanil/alfentanil

06 GENERAL CONSIDERATIONS

1. **Ensure that the necessary information is available for calculation of the infusion rate.**
   - This includes weight, age, height and gender

2. **Select the appropriate pharmacokinetic model.**

Table 1. Pharmacokinetic model selection for total intravenous anaesthesia using target controlled infusions

Drug	Target	Pharmacokinetic model
Propofol	Plasma concentration	Marsh model
	Effect-site concentration	Schnider model
Remifentanil	Plasma/effect-site concentration	Minto model

3. **Start TCI at a low concentration and titrate upwards.**

4. **Depth of anaesthesia monitoring such as BIS, Entropy and AEP, can reduce the incidence of intraoperative awareness, but is not mandatory for all patients.**

5. **Drug dosage should always be adjusted according to the response of the patient.**

6. **Post-operative rescue analgesia is required once a remifentanil infusion has been switched off.**

06 GENERAL CONSIDERATIONS

7. **Consider lowering the dose and target concentration in patients who are graded as American Society of Anesthesiologists Physical Status 3 (ASA III) and above.**

8. **A lower concentration may also be required in the elderly.**

9. **Actual body weight may be inappropriate for calculation of the infusion rate in obese patients. The weight entered may need to be adjusted (see section on TIVA in the obese patient).**

10. **A fully functional anaesthetic machine together with inhalation anaesthetic agents, vaporisers and gas monitors are mandatory.**

07 GENERAL PRINCIPLES OF OPERATION

1. A checklist minimises errors during TIVA pre-anaesthetic setup (see Appendix 1).
2. Conduct an apparatus checkout before administration of anaesthesia. Ensure that the batteries of the pumps are charged.
3. Backup equipment is useful, but not mandatory.
4. Ensure the occlusion alarm has been set.
5. Select a syringe of an equivalent diameter from the pump library.
6. Use non-return/one-way valves on any intravenous line.
7. If a one way valve is not available, use a dedicated intravenous cannula G20 and above for TCI.
8. It is advisable to use Luer Lock systems.
9. Clearly label intravenous connectors and valves.
10. Minimise dead space.

11. Avoid non-invasive blood pressure (NIBP) monitoring on the same arm as the intravenous infusion.
12. It is advisable to choose a large peripheral vein.
13. Sites of intravenous infusions should be visible and intermittently monitored for dislodgement or extravasation.
14. Check for leakage at all points intermittently.
15. Check for kinks in the infusion tubing intermittently.
16. Remove air bubbles from syringe.
17. Do not run vasoactive drugs and TCI through the same intravenous line.
18. Avoid high concentrations of drugs running at low speeds.

Table 2. Dosage schemes for induction of total intravenous anaesthesia

Drug	Target controlled infusion	Constant rate infusion	Single bolus dose	Comments
Propofol	Set initial target concentration at 4 µg/ml and titrate upwards to LOC	Not recommended	1–2 mg/kg*	Administer at "Flash" rate
Remifentanil	Set initial target concentration at 2 ng/ml. Titrate up to 4 ng/ml for placement of ETT if BP > 120/80§	0.5 µg / kg / min x 5 min	Not recommended	Administered over 60 s
Alfentanil	Not recommended	Not recommended	10–20 µg/kg†	
Fentanyl	Not recommended	Not recommended	1–2 µg/kg†	

In addition to the above, other agents (e.g. etomidate, midazolam) may be given as a bolus for induction of anaesthesia. This is followed by a target controlled infusion of propofol.

LOC – Loss of consciousness

* Single bolus dose at induction is followed by propofol TCI.

† Single bolus dose at induction is followed by remifentanil TCI, remifentanil constant rate infusion or alfentanil constant rate infusion.

§ Hypotension seen when targeting the effect-site may be greater than when targeting the plasma concentration.

If a no-relaxant technique is used, the remifentanil concentration will need to be 8-12 ng/ml for endotracheal intubation. However, such a technique should only be used if there is a clear clinical indication.

Table 3. Dosage schemes for maintenance of total intravenous anaesthesia

Drug	Target controlled infusion	Constant rate infusion#	Intermittent bolus dose
Propofol	Range: 2.5–6 µg/ml*	Not recommended	Not recommended
Remifentanil	Range: 1–8 ng/ml†	0.25 µg/kg/min titrate within a range of 0.1 - 1 µg/kg/min	Not recommended
Alfentanil	Not recommended	0.2–2.0 µg/kg/min	Not recommended

* The lower limit of the target concentration is 2 µg/ml when BIS monitoring is used.

† The recommended range for spontaneously ventilating patients is 2–3 ng/ml. At higher concentrations, assisted ventilation may be necessary.

Patients may require a remifentanil concentration of at least 4 ng/ml to tolerate the endotracheal tube.

10 ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA

Suggested total intravenous anaesthesia regimen

1. Administer oral midazolam (3.75–7.5 mg) or intravenous midazolam 1–2 mg as pre-medication prior to induction of anaesthesia.
2. Start remifentanil TCI at a target concentration of 2 ng/ml.
3. After the target concentration of remifentanil has been reached, start propofol TCI at a target concentration of 4 µg/ml.
   a. If loss of consciousness is not achieved within 1 minute, step up the target concentration by 0.5 µg/ml every 30 sec until LOC is achieved.
   b. Note the estimated effect-site concentration at LOC. It is advisable to maintain the target concentration above this value.
4. Administer muscle relaxant to facilitate endotracheal tube (ETT) placement.
5. If intubation is planned, titrate remifentanil upwards to 4 ng/ml if BP > 120/80.
6. Manage hypotension with intravenous fluids or a vasopressor.
7. Consider atropine if brachycardia develops.
8. Insert ETT/LMA when patient is relaxed.

10 ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA

9. Ensure remifentanil TCI is at a target concentration of at least 3 ng/ml at the start of surgery if BP > 100/60, otherwise maintain remifentanil at 2 ng/ml. Consider giving IV fluids or vasopressors if BP is low.
   Note: It may be necessary to assist ventilation when a target concentration above 3 ng/ml is used.

10. During surgery, adjust target concentrations of propofol TCI within a range of 2.5–6 µg/ml and remifentanil TCI within a range of 1–8 ng/ml, according to the clinical responses of the patient and the co-administration of other agents. Refer to Figure 1.
    Note: If BIS is not used, the propofol target concentration should be gradually decreased to and then maintained at 2.5 µg/ml.

11. Increase remifentanil TCI target concentration when surgical stimulation is expected.

12. Administer morphine or any other appropriate analgesic towards the end of the surgery.

13. Maintain propofol TCI target concentration during skin closure. The propofol infusion can be stopped once the final sutures or dressings are applied, upon return of muscle power.

14. Aim for a remifentanil concentration of 1 ng/ml at the end of dressing.

15. Reverse paralysis if neuromuscular blockers were used.

10 ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA

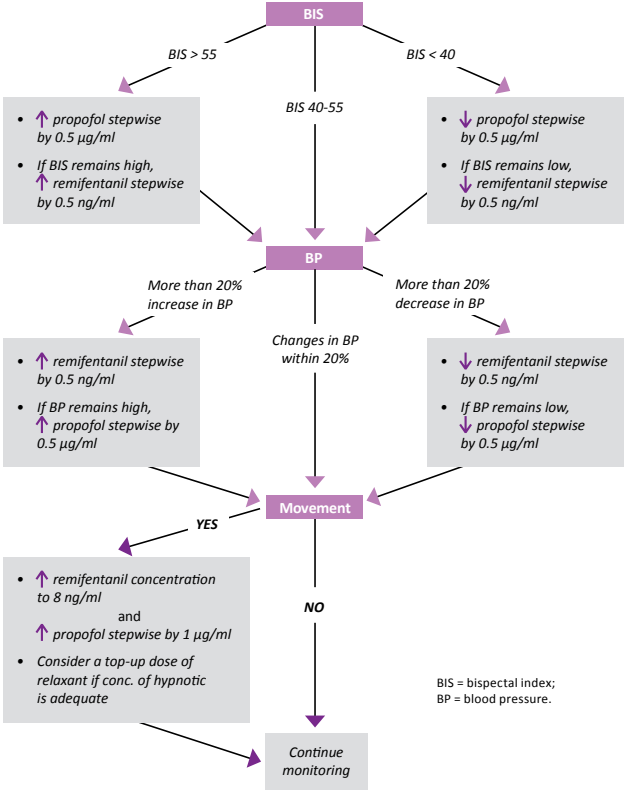


Figure 1. Dosage adjustment during maintenance of total intravenous anaesthesia

11 ALTERNATIVE TOTAL INTRAVENOUS ANAESTHESIA REGIMEN

1. If a constant rate infusion of remifentanil is used:
   a. Administer a bolus dose of opioid (fentanyl or alfentanil) before starting
   b. After the bolus dose, start remifentanil infusion at 0.1 µg/kg/min and titrate according to Figure 2.
   c. Alternatively, remifentanil can be started at 0.5 µg/kg/min x 5 min. It is important to keep this infusion rate for 5 minutes unless there is a need to decrease the rate because of the patient's response. The remifentanil infusion can then be continued at 0.25 µg/kg/min and titrated within a range of 0.1 - 1 µg/kg/min.

2. If alfentanil is used, refer to the corresponding dosage and infusion rates as detailed in Table 2 & Table 3:
   a. Administer a bolus dose of opioid (fentanyl or alfentanil) before starting
   b. After intubation, start alfentanil infusion at 0.2 µg/kg/min and titrate according to Figure 2

3. If long acting opioids are used during maintenance instead of remifentanil or alfentanil:
   a. The opioids should be given according to the practice of the attending anaesthesiologist
   b. More muscle relaxants will be required

4. If it is planned to induce anaesthesia using a bolus dose of a hypnotic:
   a. Administer a titrated dose of the hypnotic agent e.g. etomidate, midazolam, thiopental or propofol
   b. After successful induction of anaesthesia, start TCI propofol at 1 µg/ml and titrate upwards

11 ALTERNATIVE TOTAL INTRAVENOUS ANAESTHESIA REGIMEN

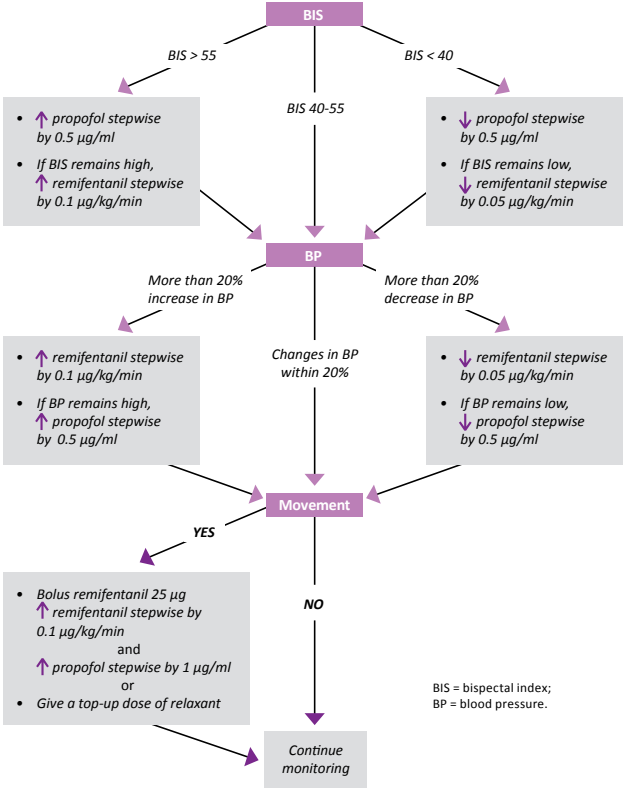


Figure 2. Dosage adjustment during maintenance of anaesthesia with constant rate infusion of remifentanil

12 TREATING POST-OPERATIVE PAIN AFTER REMIFENTANIL/ ALFENTANIL

1. Consider regional anaesthetic techniques/local infiltration.

2. Analgesia appropriate to the surgery should be administered. Morphine 0.05 - 0.1 mg/kg should be given early or at least one hour before the end of surgery. Alternatively, fentanyl 0.5 - 1.0 µg/kg can be given 20 minutes before the end of the operation.

3. Consider intravenous parecoxib 40 mg or ketorolac 30 mg or paracetamol 1 gm, 30 minutes before end of surgery, unless contraindicated.

4. If the patient reports severe pain in the Recovery Room, consider intravenous fentanyl 25 µg or intravenous morphine 1–2 mg boluses.

5. Intravenous pethidine or tramadol can be used as an alternative to morphine.

6. Consider anti-emetics when opioids are used.

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Disclaimer: The contents of these guidelines are based solely on currently available scientific evidence or best clinical practice. Healthcare professionals are expected to utilise the information contained within these guidelines when exercising their clinical judgement. However, these guidelines should not replace the individual responsibility of the user to make decisions appropriate to the circumstances of the individual patient and informed by the current indications and accuracy of the drug they are considering. Doses should be titrated according to individual patient characteristics, anaesthetic needs and clinical effect.

This pocket reference serves as a practical resource guide for both first time users and experienced users of TIVA. It is mostly relevant for relatively healthy adults, obese patients, elderly patients and ASA III patients, allowing for some degree of flexibility in different circumstances.

14 TIVA IN THE OBESE PATIENT

1. Is TIVA appropriate for the obese patient?

a. In 2007, the overall national prevalence of obesity among adult Malaysians was reported to be at 11.7%.[4]

b. TIVA is an appropriate method of administering general anaesthesia to obese patients.

c. However, the use of TIVA in obese patients is limited by the factory set defaults in the TCI pump:

- Maximum weight of 150 kg when using the Marsh model.
- Maximum Body Mass Index (BMI) of 42–43 for males, 35–36 for females when using the Schnider and Minto models.

d. Pharmacokinetic models are usually derived using data from non-obese subjects. As such, these models do not accurately describe the disposition of drugs in obese patients.

e. Actual pharmacokinetics for TCI are mostly guess-work in obese patients.[5]

f. **Propofol** kinetics is best described by a model with volumes normalised using TBW, as it is a very lipid-soluble drug, and the peripheral compartment is expected to increase with an increase in body weight.[6]

g. **Remifentanil** is less lipid soluble and LBW may be a better coefficient for calculating its pharmacokinetic parameters because of the relatively smaller increase in peripheral volume in the obese.[6]

h. Constant rate infusion for remifentanil may be used, but TCI is preferable in obese patients.

14 TIVA IN THE OBESE PATIENT

2. Principles of performing TIVA in the obese patient

a. The algorithm for obese patients in this reference guide is appropriate for patients weighing 90 kg and above.

b. **Always key in the Total Body Weight** (TBW) to the TCI pump and allow the selected model to calculate the infusion rates for the desired target concentration.

c. The recommended target concentration in obese patients may be lower than in non-obese patients as in obese patients, the actual blood concentration may be higher than the calculated target concentration.

d. **Cerebral function/awareness monitoring** during TIVA in obese patients is highly advisable as the plasma and effect site concentrations cannot be determined with a high degree of confidence.

e. Choice of model for propofol
   - Marsh model, which inputs TBW

f. Choice of model for remifentanil
   - Minto model (which automatically calculates LBW from TBW and height)
     → target effect site

g. Target concentrations similar to non-obese patients except for starting propofol at a lower concentration (i.e. 3 µg/ml). See Appendix 3.

h. The "no-relaxant" technique (for intubation) is not advisable for obese patients.

i. Suxamethonium for intubation after induction using a TCI is acceptable.

j. TIVA/TCI can safely be used in patients with obstructive sleep apnoea (OSA)[7]

15 TIVA IN THE ELDERLY PATIENT

1. Is TIVA appropriate for the elderly patient?

a. There are advantages when administering TIVA to elderly patients (see **Table 4**).

b. Pharmacokinetics and pharmacodynamics of drugs change with age.

c. Elderly patients tend to have more co-morbid conditions, e.g. ischaemic heart disease, diabetes mellitus.

d. As such, elderly patients are more sensitive to changes in drug concentrations, and large changes in plasma concentrations should be avoided.

e. **Propofol:** plasma rather than effect site concentration should be targeted, as the overshoot in plasma concentration may lead to hypotension.

f. **Remifentanil:** effect site concentration can be targeted, as the overshoot in plasma concentration is relatively small and remifentanil is relatively cardio-stable.

g. **Cerebral function/awareness** monitoring during TIVA in elderly patients is highly advisable as the actual plasma concentrations may be very different from the predicted concentration; and the effect of propofol may be more marked when compared to the young patient.

h. Constant rate infusion for remifentanil may be used, but TCI is preferable in elderly patients.

15 TIVA IN THE ELDERLY PATIENT

2. Is TIVA advantageous for the elderly patient?

Table 4. Advantages of TIVA in the elderly patients

Cognitive function	Compared with inhalation anaesthesia, TIVA is more suitable as it has **less observable effects on cognitive function** in elderly patients after surgery, especially those carrying the ApoE4 allele.[8,9]
Circulatory complications	Inhalational anaesthetics may augment complications related with reduced lung blood flow and circulatory depression. **Inhalational anaesthetic agents may further reduce cardiac output** and cause potentially lethal increase in alveolar concentration.[10,11]
Psychomotor performance	**There is only a minor deficit in psychomotor performance** in elderly patients 2 hours after the end of anaesthesia with TIVA.[12]

15 TIVA IN THE ELDERLY PATIENT

3. Principles of performing TIVA in the elderly patient

a. The algorithm for elderly patients in this reference guide is appropriate for patients aged 65 years and above.

b. **Always key in the Total Body Weight** to the TCI pump and allow the selected model to calculate the infusion rates for the desired target concentration.

c. Always start with a low concentration/infusion rate and slowly work upwards. However, the rapid infusion rate for propofol can still be set at “flash”.

d. It is important to avoid hypotension. Consider intravenous fluids and vasopressors when appropriate.

e. A lower minimum target propofol concentration (1.5 µg/ml) is acceptable. See Appendix 3.

f. There are potential benefits of intra-operative monitoring of anaesthetic depth as a pragmatic intervention to reduce POCD (post-operative cognitive dysfunction).[13]

g. Avoid low BIS values.
   - Elderly patients lose consciousness at a higher BIS.[14]
   - BIS-guided anaesthesia reduces anaesthetic exposure and decreases the risk of POCD.[15]
   - Hospital stay and mortality are increased in patients having a “Triple Low” of Low BP, Low BIS and Low MAC of volatile anaesthetics.[16]

h. Choice of model for propofol
   - Marsh model, which inputs TBW

15 TIVA IN THE ELDERLY PATIENT

i. Choice of model for remifentanil
   - Minto model (which automatically calculates LBW from TBW and height)
     → target effect site

j. The most appropriate target concentrations may change according to the patient's physical condition:-
   i. Fit elderly patients behave more like young patients
   ii. Sick elderly patients will need a lower target concentration

k. Keep BIS at 50–65 (i.e. higher than in young patients)

16 TIVA IN THE ASA III PATIENT

1. Is TIVA appropriate for the ASA III patient?

a. TIVA can be given to seriously ill patients in whom their systemic disease is not a constant threat to their life (ASA III).

b. Pharmacokinetics and pharmacodynamics of drugs will be affected and as such, ill patients are more sensitive to the anaesthetic medication.

c. There are no specific protocols for TIVA in ASA III patients, but the algorithm for TIVA in elderly patients can be adopted as in both situations, the protocol describes a reduction in drug concentration and dosage. See Appendix 3.

2. Principles of performing TIVA in the ASA III patient

a. Choice of model for propofol
   - Marsh model, which inputs TBW

b. Choice of model for remifentanil
   - Minto model (which automatically calculates LBW from TBW and height)
     → target effect site

c. Choose the most appropriate target concentration according to the patient's physical condition:-
   - Whether the patient is elderly or young.
   - Whether the patient is obese or non-obese.

d. Keep BIS at a level suitable for the age of the patient (i.e. a higher BIS is acceptable in elderly patients).

e. Pre-induction
   - Midazolam 1–2 mg (if no premedication) is useful to provide amnesia in suitable patients.

f. Induction of anaesthesia
   - Narcotic: Remifentanil TCI preferable.
   - Hypnotic: Propofol TCI preferable.

   Alternative: Etomidate 0.2–0.3 mg/kg for induction, followed by TCI propofol at 1 µg/ml.

g. BIS may decrease during hypotensive episodes because of hypo-perfusion of the brain.
   - Adjust the hypnotic drug concentration during such episodes.
   - Balance the need to reduce CVS depression with that of maintaining unconsciousness.
   - In general, always keep BIS < 65 and propofol concentration > 1.2 µg/ml.

17 TCI IN MAC

1. Is TCI advantageous for Monitored Anaesthesia Care (MAC)?

a. **Rapid response** to titration, rapid and predictable recovery profile[17,18]

b. **Tight correlation** between drug dose/plasma concentration and pharmacological effects, including adverse effects[19,20]

c. **Simple**: Target controlled infusion systems – simplification of the IVI for anaesthesia[19]

d. **Better pain control**;[21] more applicable as most of patients' distress is due to pain[22]

2. Principles of performing TCI for MAC

a. The algorithm for performing MAC in this reference guide covers TCI for conscious sedation to deep sedation (unresponsive).

b. All standard precautions when performing a TIVA should be undertaken.

c. All standard monitoring for a patient under general anaesthesia should be applied.

d. Cerebral monitoring is highly advisable for patients who require deep sedation. For patients under conscious sedation, there should be constant communication between the anaesthetist and the patient.

e. Continuous respiratory rate monitoring (capnography is an excellent choice) is required in patients who require deep sedation and/or require remifentanil at the higher end of the dose range.

f. Choice of model for propofol
   - Marsh and Schnider models are both equally as effective.

g. Choice of model for remifentanil
   - Minto model targeting the effect site.

h. Patients will start to lose responsiveness to call at a propofol concentration of about 1.2 µg/ml, and almost all will be unresponsive by 2 µg/ml.

i. Remifentanil causes some sedative effects but is a poor sedative when used alone.

j. However, propofol and remifentanil are synergistic in their sedative effects.

k. Target a BIS of 60–80 for deep sedation.

l. Supplemental oxygen should always be given.

3. Recommended target concentration and drug dosage for hypnotics & analgesics during MAC

a. Propofol
   - 0.5–2 µg/ml; titrated to desired level of sedation.
   - Only propofol is required if the patient already has a regional block.

b. Remifentanil
   - 0.5–2 ng/ml; titrated in steps of 0.2 ng/ml.

c. Fentanyl
   - May be given in 25–50 µg boluses, if remifentanil is not available.

d. Dexmedetomidine
   - May be used as a sole agent in the following dosage:
     - 0.05–1.0 µg/mg x 10 minutes (loading dose), then
     - 0.2–1.0 µg/kg/hr

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APPENDIX 1: TIVA CHECKLIST

PLEASE ENSURE THAT THIS CHECKLIST HAS BEEN COMPLETED BEFORE STARTING TOTAL INTRAVENOUS ANAESTHESIA FOR YOUR PATIENTS

1. Target Controlled Infusion pumps with power cables. ☐

2. Drug filled syringes with perfusor tubings. ☐

3. Dedicated IV line or non-return valves with 2 three way taps connected to patient's IV cannula. Ensure secured tightly. ☐

4. Propofol 1% (10 mg/ml) & remifentanil (50 µg/ml). ☐

5. TCI programme for **propofol**
   - Schnider or Marsh Model (Age, Weight, Height and Sex must be entered). ☐
   - Choose plasma or effect-site concentration. ☐
   - Set target concentration (i.e. 4–6 µg/ml for Target Concentration) (*ensure correct units). ☐
   - Connect to 3 way connector attached to patient's IV cannula. ☐

6. TCI Programme for **remifentanil**
   - Ensure correct dilution for remifentanil (Add 4 mls NaCl to a 5 mg vial of remifentanil, take 2 mls & dilute to 50 mls with NaCl i.e 50 µg/ml). ☐
   - Minto model, plasma or effect-site concentration. ☐
   - If effect-site concentration, aim for 3-8 ng/ml (ensure correct units). ☐
   - Adjust according to surgical stimulus. ☐
   - Connect to 3 way connector attached to patient's IV cannula. ☐

APPENDIX 1: TIVA CHECKLIST

7. Ensure no leakages and that patient's IV cannula is always visible during the surgery. ☐

8. No other drugs should be administered via the TCI infusion line (unless absolutely necessary e.g. during induction). A separate IV line should be used for infusion of IV fluids. ☐

9. Infusion lines should be checked every 15 minutes during surgery (akin to checking for disconnection of the breathing circuit). ☐

10. If BIS is used check placement before and after surgical draping. Be careful of surgical antiseptic solution getting between the skin and the BIS electrode. ☐

At conclusion of case, ensure all tubings/IV cannulae which had remifentanil are flushed to prevent inadvertent boluses in the ward.

20 APPENDIX 2: REMIFENTANIL

Remifentanil is an opioid agonist with rapid onset and an ultra-short duration of action. It rapidly equilibrates with the brain and has a constant context-sensitive half time of 3 to 6 minutes. The time taken to reach a steady-state conc. = 5–10 minutes.

However, severe adverse may occur if remifentanil is used incorrectly.

1. Haemodynamic effects
   (a) Dose-dependent hypotension and bradycardia
   (b) Bradycardia can be reversed with glycopyrrolate, atropine or ephedrine
   (c) Hypotension - reduce rate of infusion or administer fluids or vasopressors

2. Respiratory effects
   (a) Depression of respiration in a dose-related fashion
   (b) Spontaneous respiration occurs at 4 to 5 ng/ml

3. Muscle rigidity
   (a) related to the dose and speed of administration
   (b) occurs when > 1 µg/kg is administered in less than 60 seconds
   (c) decreased by decreasing infusion or administering a neuromuscular blocker

4. In view of the above an IV bolus should only be given
   (a) to intubated patients during the maintenance of general anaesthesia
   (b) for induction of anaesthesia in non-intubated patients
   (c) < 1 µg/kg over 60 seconds

5. Stopping remifentanil
   (a) there is rapid dissipation of respiratory depressant effect
   (b) analgesic effects fade off very fast after terminating an infusion - need to ensure rescue analgesics are given before or soon after end of surgery

21 APPENDIX 3: TARGET CONCENTRATIONS AND DRUG DOSAGES

1. Recommended target concentration and drug dosage for induction of anaesthesia with TIVA

Drug	Patients < 90 kg, < 65 years, ASA I - II	Patients 90 kg and above	Patients 65 years and above	ASA III Patients
Propofol	Start at 4 µg/ml Titrate up till LOC	Start at 3 µg/ml Titrate up till LOC	Start at 2 µg/ml x 1 min, ↑ to 3 µg/ml x 1 min, ↑ to 4 µg/ml if no LOC	Same as patients 65 years and above
Remifentanil	Start at 2 ng/ml, ↑ up to 4 ng/ml before intub. if BP not low	Same as non-obese patients	Start at 2 ng/ml, ↓ to 1 ng/ml after intubation	Same as patients 65 years and above
Alfentanil	Bolus of 10–20 µg/kg TCI not recommended	Same as non-obese patients	Bolus of 5–10 µg/kg TCI not recommended	Same as patients 65 years and above
Fentanyl	Bolus of 1–2 µg/kg TCI not recommended	Same as non-obese patients	Bolus of 0.5–1 µg/kg TCI not recommended	Same as patients 65 years and above

LOC = loss of consciousness

21 APPENDIX 3: TARGET CONCENTRATIONS AND DRUG DOSAGES

2. Recommended target concentration and drug dosage for maintenance of anaesthesia with TIVA

Drug	Patients < 90 kg, < 65 years, ASA I - II	Patients 90 kg and above	Patients 65 years and above	ASA III Patients
Propofol	TCI : 2–6 µg/ml Constant infusion: not recommended	Same as non-obese patients	TCI : 1.5–4 µg/ml Constant infusion: not recommended	Same as patients 65 years and above
Remifentanil	TCI : 1–8 ng/ml Constant infusion: 0.1-1.0 µg/kg/min	Same as non-obese patients	TCI : 1–4 ng/ml Constant infusion: 0.05–0.1 µg/kg/min	Same as patients 65 years and above
Alfentanil	TCI : not recommended Constant infusion: 0.2-2.0 µg/kg/min	Same as non-obese patients	–	–
Fentanyl	Bolus of 25–50 µg prn	Same as non-obese patients	Bolus of 25–50 µg prn	Same as patients 65 years and above

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