Technology Guidance

Intraoperative cell salvage

for surgeries with anticipated or possible significant blood loss

Technology Guidance from the MOH Medical Technology Advisory Committee

Guidance Recommendations

The Ministry of Health's Medical Technology Advisory Committee has recommended intraoperative cell salvage (ICS) for patients undergoing surgery, in line with the following criteria:

- ✓ Where significant blood loss is expected, as well as in emergency situations where unexpected significant blood loss occurs; and
- ✓ The decision to perform ICS shall be made by a multidisciplinary team, including the surgeon and anaesthetist (and other specialists if needed), who will ascertain patient suitability by considering various factors, such as whether the anticipated blood loss meets the minimum blood volume required to initiate blood processing using ICS.

Clinicians can consider using the Massive Transfusion Protocol (MTP) and maximum allowable blood loss (MABL) formula to guide decision on patient suitability.

ICS should be used concurrently with other patient blood management measures such as optimising pre-operative haemoglobin and minimising bleeding risks with surgical, anaesthetic or pharmacological techniques.

The use of ICS including its risks and benefits should be discussed with the patient or substitute decision maker, especially in instances where its use may be a concern, such as the presence of sepsis or malignancy.

Funding status

ICS is recommended for subsidy for patients undergoing surgeries with anticipated or possible significant blood loss, in line with the abovementioned recommendations.

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Factors considered to inform the recommendations

Technology evaluation

1.1. At the November 2024 meeting, the MOH Medical Technology Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of ICS in surgeries with significant blood loss. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions (PHIs). Published clinical and economic evidence for ICS was considered in line with its registered indication.

1.2. The evidence was used to inform the Committee's deliberations around five core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Overall benefit of the technology for the patient and/or the system;
- Cost-effectiveness (value for money), which considers the incremental benefit and cost of the technology compared to existing alternatives;
- Estimated annual technology cost and the number of patients likely to benefit from the technology; and
- Organisational feasibility, which covers the potential impact of adopting the technology, especially barriers for diffusion.

1.3. Additional factors, including social and value judgments, may also inform the Committee's deliberations.

Clinical need

2.1. The Committee acknowledged that allogeneic blood is a valuable resource that is in limited supply. Reducing reliance on donated blood transfusions is becoming increasingly important given the ageing population and expected decrease in eligible blood donors. This aligns with the World Health Organization's (WHO) endorsement of patient blood management (PBM), which is a patient-centred approach to addressing the risks of iron deficiency, anaemia, blood loss and coagulopathy. Under the PBM framework, ICS serves as a strategy to optimise blood utilisation and perioperative blood management.

2.2. The Committee noted the significance of ICS, particularly for patients unsuitable for allogeneic blood transfusions. This includes patients who decline allogeneic transfusions due to personal or religious beliefs. However, the Committee also noted some concerns about using ICS in cancer surgeries due to the potential risk for metastasis.

Overall benefit of technology

3.1. The Committee noted that most available clinical evidence compared ICS to no ICS, where no ICS typically meant using allogeneic blood transfusion. The main evidence base comprised two systematic reviews/meta-analyses (SRMAs) (including one Cochrane review), which reported the pooled effects of ICS or cell salvage (including intraoperative and postoperative) across various types of surgery. Supplementary evidence on ICS in specific surgery types was also included from one health technology assessment report and 13 SRMAs.

3.2. ICS is likely to be safe, with similar safety outcomes to allogeneic blood transfusions. Based on pooled analyses for all surgery types, cell salvage was associated with a lower infection rate than no cell salvage. However, there was no between-treatment difference in mortality rate. Similar observations were made for specific surgeries (cancer, cardiovascular, vascular, orthopaedic) when ICS was compared with no ICS.

3.3. In terms of clinical effectiveness, ICS or cell salvage demonstrated several benefits. Pooled analyses across all surgery types reported a 16%–39% reduction in the rate of exposure to allogeneic red blood cell (RBC) transfusions for ICS or cell salvage compared to no ICS or cell salvage. Each episode of cell salvage also saved an average of 0.20 units of allogeneic RBCs per patient and reduced the length of hospitalisation by 2.31 day compared to no cell salvage. Patients who received ICS or cell salvage during orthopaedic, liver or trauma surgeries needed significantly fewer allogeneic RBC units compared with patients who did not have ICS or cell salvage. Limited evidence for cancer surgeries (all types, or hepatocellular carcinoma only) showed no significant difference between ICS and no ICS for overall survival, disease-free survival and recurrence rates.

3.4. The Committee also noted that for surgeries with higher than expected blood loss, ICS could potentially augment the amount of blood saved per patient or reduce the risk of allogeneic blood transfusion. On the other hand, insufficient blood collection during surgery (which is more likely in paediatric cases) may lead to failure to initiate ICS.

3.5. With the available clinical evidence typically using allogeneic blood transfusion as the comparator, the Committee noted a gap in evidence for patients who are not suitable for allogeneic blood transfusion, such as those with rare blood types, presence of multiple alloantibodies, or objection to receiving allogeneic transfusion due to personal beliefs. For these patients, management typically involves individualised intraoperative interventions including surgery and pharmacological agents to minimise bleeding. Despite limited data, clinicians shared that ICS may be a viable treatment option for these patients.

Cost effectiveness

4.1. The Committee noted that there was no local cost-effectiveness analysis (CEA) comparing ICS versus no ICS across all surgery types. There were however two CEAs from the United Kingdom (UK): one by the National Institute for Health and Care Excellence (NICE) in 2015 which evaluated various surgery types and another by the National Institute for Health Research (NIHR) in 2018 which focused on obstetric surgeries. Additionally, there was one cost analysis from Turkey which focused on orthopaedic surgeries. ICS was more costly than no ICS in all three studies as it is often used as an adjunct to usual care, which is usually allogeneic blood transfusion.

4.2. The CEA from NICE conducted in 2015 found that for high bleeding risk surgeries in the UK, tranexamic acid (TXA) alone was the most cost-effective option to minimise blood loss compared to standard treatment, ICS, post-operative cell salvage or ICS+TXA. Nevertheless, NICE noted that adding ICS to TXA may still be cost-effective if the transfusion volume is expected to be very high, as ICS+TXA showed greater relative treatment benefit than TXA alone, assuming similar mortality benefits. The 2015 NICE guideline on blood transfusion recommended to consider ICS with TXA for patients who are expected to lose a very high volume of blood. In Singapore, TXA is also used for surgeries with expected substantial blood loss, barring contraindications.

4.3. In 2018, NIHR prepared a CEA as part of the multicentred SALVO (cell SALVage in Obstetrics) trial in obstetrics surgeries (n=3,028). The CEA reported an incremental cost-effectiveness ratio (ICER) of £8,110 per donor blood transfusion avoided for ICS compared with no ICS for obstetric surgery in the UK. Although a willingness-to-pay threshold for a blood transfusion avoided was not specified, the study concluded that routine ICS in obstetric surgery was not cost-effective in the UK. Despite these findings from the NIHR study, NICE's 2019 surveillance review upheld their 2015 recommendation which supported the use of ICS + TXA, citing uncertainty around the cost-effectiveness of ICS for obstetrics surgeries in the NIHR trial. While the trial showed that routine ICS slightly reduced the need for allogeneic blood transfusion, it was unclear whether it was more or less costly than standard care. This uncertainty arose from limited long-term health outcomes, lack of standardised benefit measures (e.g. quality-adjusted life years), and unclear long-term cost implications of adapting routine ICS use.

4.4. As the published studies from the UK and Turkey focused on specific surgery types, the Committee noted that it was difficult to generalise their findings to local clinical practice and to all surgery types.

4.5. To supplement the evidence base, a cost analysis was conducted to evaluate the net expenditure of using ICS in surgeries with significant blood loss. The Committee

noted that the incremental cost of using ICS, compared to no ICS, was estimated to be <SG$2K per surgical case, with the total cost being approximately four times higher for a surgery with ICS than without. The cost difference between ICS and no ICS diminishes in surgeries with higher blood loss or transfusion requirements (e.g. trauma surgeries). Additionally, given that ICS is associated with shorter hospital stays, the overall cost difference is further reduced. Ideally, a comprehensive estimate for the cost of the entire blood processing and blood transfusion process (e.g. blood donation stage encompassing testing and storage, and supply chain logistics) should be accounted for, but this data was not readily available for Singapore.

4.6. ICS is reimbursed in the UK when used with TXA for patients who are expected to lose a significant amount of blood. No specific reimbursement information was found for Australia, Canada, Japan, New Zealand, South Korea and Taiwan.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system was estimated to be between SG$1 million to less than SG$3 million. This is based on the projection of approximately 1,165 eligible patients in Singapore who would benefit from Government subsidy for the use of ICS in surgeries with anticipated or possible significant blood loss.

Organisational feasibility

6.1. The Committee noted that most PHIs are using ICS in surgeries. No major organisational feasibility issues are anticipated with the use of ICS in surgeries with anticipated or possible significant blood loss. Some organisational issues identified include potential capacity or workflow issues arising from lack of manpower to operate the ICS machines and the need for regular training and clinical protocols. Nevertheless, job redesign programmes are available for existing nursing staff, along with vendor-provided training on the use of ICS.

Additional considerations

7.1. A total of eight published clinical practice guidelines from the WHO, Singapore, Australia, South Korea, the UK, and the US recommended the use of ICS in elective and emergency procedures, and for paediatrics and adults in procedures with significant blood loss, provided clinical governance is in place with properly trained staff and appropriate ICS devices and consumables used.

Recommendations

8.1. Based on the evidence presented, the Committee considered that ICS was safe, clinically effective and likely to represent an acceptable use of healthcare resources. It provided a viable way to reduce allogeneic blood transfusions and offered an alternative method for patients unsuitable for allogeneic blood transfusions. Given the available evidence, the Committee recommended subsidy for ICS for patients undergoing surgery, in line with the following criteria:

- Where significant blood loss is expected, as well as in emergency situations where unexpected significant blood loss occurs; and
- The decision to perform ICS shall be made by a multidisciplinary team, including the surgeon and anaesthetist (and other specialists if needed), who will ascertain patient suitability by considering various factors, such as whether the anticipated blood loss meets the minimum blood volume required to initiate blood processing using ICS.

✓ Clinicians can consider using the Massive Transfusion Protocol (MTP) and maximum allowable blood loss (MABL) formula to guide decision on patient suitability.

✓ ICS should be used concurrently with other patient blood management measures such as optimising pre-operative haemoglobin and minimising bleeding risks with surgical, anaesthetic or pharmacological techniques.

✓ The use of ICS including its risks and benefits should be discussed with the patient or substitute decision maker, especially in instances where its use may be a concern, such as the presence of sepsis or malignancy.

Agency for Care Effectiveness - ACE Agency for Care Effectiveness (ACE)

About the Agency

The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government funding decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

The guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at www.ace-hta.gov.sg/about

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