CSL Behring

Expert Comment

1. Cell salvage in cancer surgery. *Dania Fischer, Germany*

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DThere are two reasons that would make using cell saver (CS) blood salvage device in cancer a good idea:

- International guides
- Current evidence

CS is one of the strategies used in the second pillar of PBM.

In the context of cancer, salvaged blood transfusion reduces to zero the immunomodulation caused by allogeneic transfusion.

CS can contribute to mitigate the unbalance between donations and red blood cell demand caused by population aging and the resulting reduction in the number of donations.

What do guides say?

The guide on perioperative bleeding management (European Society of Anaesthesiology and Intensive Care) recommends the use of CS and autotransfusion with leukodepletion filters in liver transplant, including patients with liver cancer (evidence 2C), suggests that CS is not contraindicated in cancer surgery, because blood close to the tumor is not aspirated, and since leukodepletion filters are used (2C), CS can reduce allogeneic transfusion in the gynecological setting, including oncologic surgery (2B).

The recommendations of the Italian Society of Transfusion Medicine and Immunotherapy suggest the use of CS during oncologic surgery, provided that salvaged red blood cells are administered through leukodepletion filters and that they are irradiated (25 Gy) before being reinfused (level-2C evidence). Red blood cell irradiation is a complex procedure, not available in most hospitals.

In 2020, the German Medical Association EXCLUDED the use of CS in oncologic surgery, although this was not the case in guides published before 2014. Among scientific evidence, a meta-analysis (Transfus Med Hemother 2022 May 11;49(3):143-157) covers 34 observational studies, with 8503 subjects, 3161 of which were treated with CS during surgery. Studies compared salvages blood, filtered or not, versus not using CS, and mortality and cancer relapse were reported. The patients in the control group were treated with pre-donated autologous blood, with allogeneic blood, or did not receive any transfusion.

The meta-analysis slightly favors CS in regard to cancer relapse, and there are no differences in terms of mortality.

The big question is, are there tumor cells in the salvaged blood? The work by Zong et al in Anesthesiology 2022, using a complex methodology for chromosome marking of tumor cells, concludes that in the salvaged blood there are between 1 and 21 tumor cells in each 4 ml of blood. It is not known for the time being whether these cells have the ability or not to replicate the tumor. We do not know if it is better to assume the risk of salvaged blood reinfusion versus the immunomodulation induced by the transfusion.

IN CONCLUSION: the benefits of CS during surgery are:

- Lower need of donor blood transfusions
- Higher ability to transport O2 when compared to blood from donors
- Absence of immune adverse effects
- Absence of transfusion restrictions

IN CASES OF MALIGNANCY:

- Low level of evidence, lack of randomized clinical trials
- Data from observational studies suggests that CS, with or without filters, would seem safe.

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Expert Comment

2. TXA in patients at risk of thrombosis. *Patrick Meybohm, Germany*

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Large randomized clinical trials (CRASH2, WOMAN) have shown the efficacy of tranexamic acid (TXA) in the decrease of bleeding and mortality.

Fibrinolysis is a physiological desirable process that prevents the progression to thrombosis. TXA is included in the second pillar of PBM and, given its efficacy, we may think of a universal use of the drug in all surgical processes.

The question is to analyze whether the widespread use of TXA entails an increase in thromboembolic-ischemic events.

JAMA Surgery published a meta-analysis directed by the presenter, “Association of intravenous TXA with thromboembolic events and mortality”, using all the available evidence.

Inclusion criteria included 216 randomized controlled trials (>125,000 surgical patients), from all medical disciplines, with administration of intravenous TXA versus placebo or no treatment.

A risk difference and risk reduction statistical analysis was performed. All thromboembolic events were measured (TVE, TEP, IAM, ICTUS, Other).

Meta-analysis results favor TXa in terms of overall mortality, with no higher incidence of thromboembolic events of any kind.

Neither in the sub-analysis of patients at high risk of thrombotic events a higher incidence of thromboembolic events or overall mortality were found when using TXA.

One of the limitations of this meta-analysis is the non-performance of a screening ultrasound study in all trials, which means that the detection of thrombotic events might be underestimated. The follow-up of patients in the analyzed studies ranged from 24 hours to several months.

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Expert Comment

3. POC in bleeding patients. *Jakob Stensballe, Denmark*

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The answer to this question can be found in the 2016 Cochrane review, by Wikkelso et al., comparing the management of hemostasis using ROTEM/TEG versus conventional management in adults and children with hemorrhage. The risk of mortality is lower in the group treated according to viscoelastic tests. Furthermore, the use of blood products was significantly reduced.

The coagulation system is complex and it is finely compensated. Until a few years ago, we based our hemostatic therapy in conventional lab tests, but these take time and do not reflect the hemostatic reality, which means that using them as a guide is equals a blind therapy.

Viscoelastic tests (TVE) ROTEM or TEG provide an idea of the speed at which the clot is formed, as well as its strength, using whole blood in a short time.

ROTEM and TEG have different terminologies in their results, but they express the same reality with a very intuitive way of showing which coagulation deficits must be corrected.

In order to guide hemostatic correction, a number of action algorithms have been designed, both with ROTEM and TEG. Algorithms may lead to confusion. We must consider which ones are evidence-based and it would be desirable to agree actions common to all of them.

The Copenhagen model works like that, centralizing all VETs in the Blood Bank, with a remote vision from the OR of the evidence provided by the VET, as well as experts in interpreting VETs available 24/7. This implementation model has worked since 2004.

In spite of the invaluable support provided by VETs in hemostatic correction, there is a new concept which is not yet well known and may explain why different degrees of trauma are correlated to different coagulopathy patterns. This new concept is shock-induced endotheliopathy (SHINE). The recent publication in Frontiers in Physiology (Feb 2023) explains how the progression of endothelial damage and the release of catecholamins are represented in the different coagulopathy patterns of TEG and ROTEM. This correlation also supports the need of using VETs in goal-directed hemostasis.