

LE AZIONI INTRAOPERATORIE DI CONTENIMENTO DELLE PERDITE EMATICHE

Dott.ssa Simona Celotti – V Congresso Nazionale Orthopea – 16/17 settembre 2021

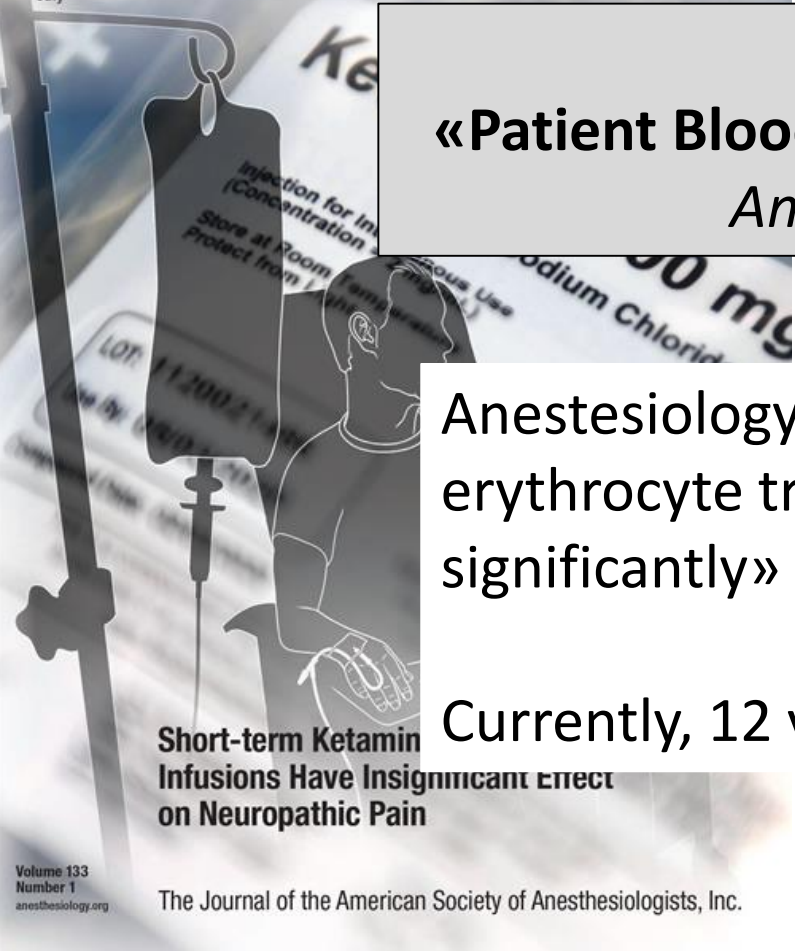
UpToDate Society guideline links: Transfusion and patient blood management

- European Society of Intensive Care Medicine (**ESICM**): A clinical practice guideline for transfusion strategies in non-bleeding critically ill adults (2020)
- European Directorate for the Quality of Medicines & HealthCare (**EDQM**): Guide to the preparation, use and quality assurance of blood components, 20th edition (2020)
- European Association for Cardio-Thoracic Surgery (EACTS)/European Association of Cardiothoracic Anaesthesiology (**EACTA**): Guidelines on patient blood management for adult cardiac surgery (2017)
- European Society of Anaesthesiology (**ESA**): Guidelines for the management of severe perioperative bleeding, first update 2016 (published 2017)

Strategie intraoperatorie chirurgiche:

- Chirurgia mininvasiva
- Emostasi meticolosa
- Gestione presidi elettrochirurgici
- Emostatici topici e colle tissutali





Spahn, Muñoz, Klein, et al.
«Patient Blood Management - Effectiveness and Future Potential»
Anesthesiology July 2020, Vol. 133, 212–222.

Anesthesiology 2008; «PBM will decrease the use of allogenic erythrocyte transfusion and its cost and adverse sequelae significantly»

Currently, 12 yr later, we can conclude this is indeed the case...

	Elective			Emergency
	Period			
	Preoperative	Intraoperative	Postoperative	
Correct anemia and iron deficiency				
Iron (IV) + EPO + vitamin B12 + folic acid (see table 2)	Dark Blue	Light Blue	Dark Blue	Light Orange
Reduce perioperative erythrocyte loss				
Improved surgical technique		Dark Blue		Dark Orange
Cell salvage and re-transfusion		Dark Blue	Light Blue	Dark Orange
Acute normovolemic hemodilution		Dark Blue		Light Orange
Avoiding coagulopathy				
Monitoring of coagulation	Light Blue	Dark Blue	Dark Blue	Dark Orange
Individualized and goal-directed coagulation algorithm		Dark Blue	Dark Blue	Dark Orange
Antifibrinolytics		Dark Blue	Dark Blue	Dark Orange
Fibrinogen		Dark Blue	Dark Blue	Dark Orange
PCC		Dark Blue	Dark Blue	Dark Orange
Factor XIII		Dark Blue	Dark Blue	Dark Orange
Low CVP, no hypertension, normothermia		Dark Blue	Dark Blue	Dark Orange
Reduced blood draws for laboratory testing		Dark Blue	Dark Blue	Light Orange
Tolerance of anemia				
Tolerate low hemoglobin values (restrictive TT)		Dark Blue	Dark Blue	Dark Orange
Optimization of hemodynamics and oxygenation		Dark Blue	Dark Blue	Dark Orange

Blue refers to elective surgery, orange to emergency surgery. Dark colors indicate application to all patients (without specific contraindications) and bright colors indicate application to some patient groups.

CVP, central venous pressure; EPO, erythropoietin; IV, intravenous; PCC, prothrombin complex concentrate; TT, transfusion trigger.

Strategie intraoperatorie NON chirurgiche:

1. Gestione dei fluidi
2. Gestione della temperatura corporea
3. Recupero ematico
4. Emodiluizione acuta normovolemica (ANH)
5. Algoritmo trasfusionale goal-directed
6. Tolleranza di valori bassi di emoglobina
7. Ipotensione controllata?
8. Anestesia locoregionale ?

1. Gestione dei fluidi: La NORMOVOLEMIA

Normovolemia: ?

Ipervolemia:

- anemizzazione (perdite ematiche apparenti)
 - diluizione dei fattori della coagulazione
 - perdita di calore
- Aumenta la morbilità, la mortalità e la degenza ospedaliera

LIBERAL VS RESTRICTED Fluid Therapy

- Rahbari NN, Zimmermann JB, Schmidt T, et al. Meta-analysis of standard, restrictive and supplemental fluid administration in colorectal surgery. *Br J Surg* 2009; 96:331.
- Lobo SM, Ronchi LS, Oliveira NE, et al. Restrictive strategy of intraoperative fluid maintenance during optimization of oxygen delivery decreases major complications after high-risk surgery. *Crit Care* 2011; 15:R226.
- Corcoran T, Rhodes JE, Clarke S, et al. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesth Analg* 2012; 114:640.
- Furrer MA, Schneider MP, Löffel LM, et al. Impact of intra-operative fluid and noradrenaline administration on early postoperative renal function after cystectomy and urinary diversion: A retrospective observational cohort study. *Eur J Anaesthesiol* 2018; 35:641.
- Wuethrich PY, Burkhard FC, Thalmann GN, et al. Restrictive deferred hydration combined with preemptive norepinephrine infusion during radical cystectomy reduces postoperative complications and hospitalization time: a randomized clinical trial. *Anesthesiology* 2014; 120:365.

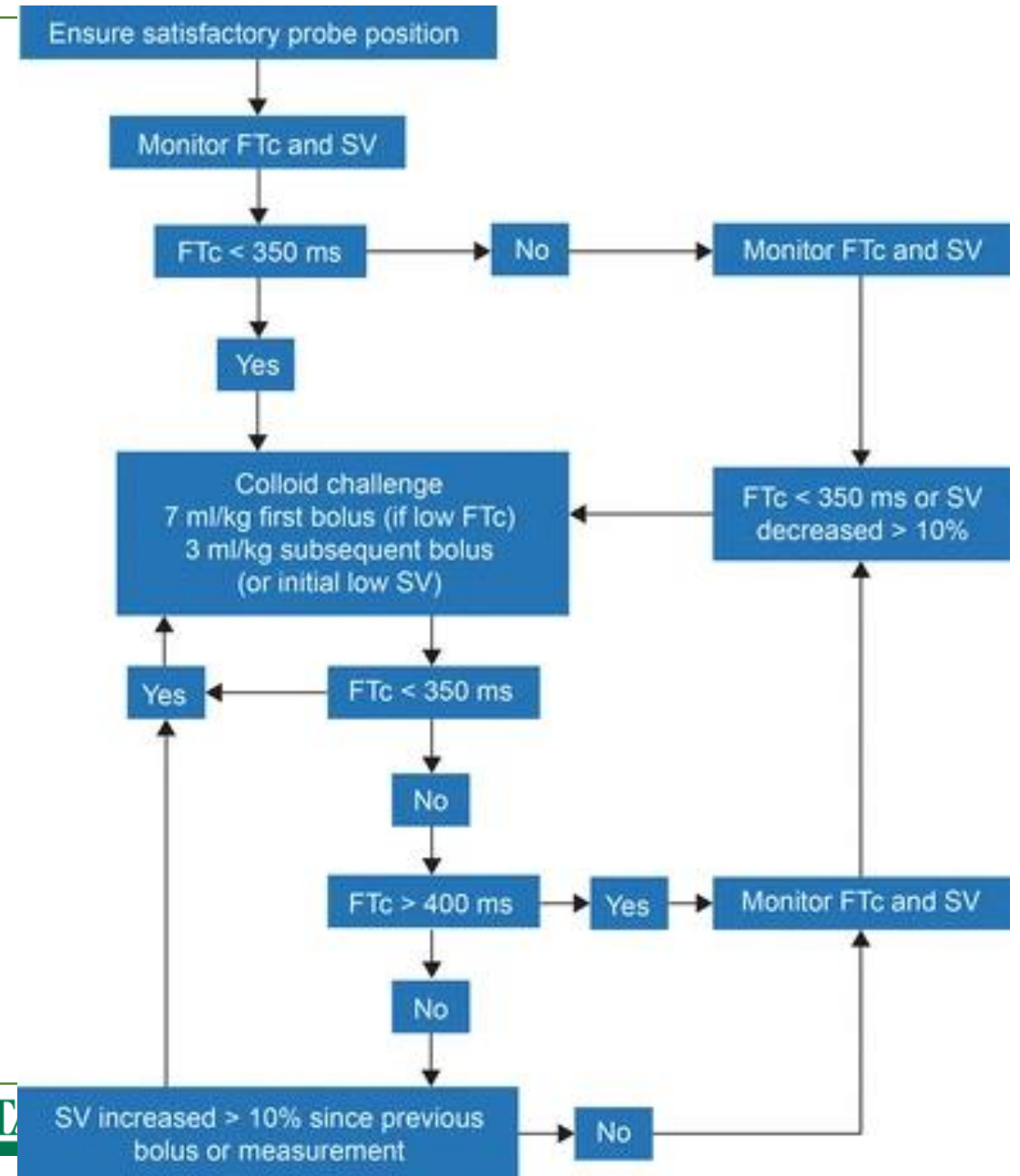
Restrictive (zero-balance) strategy:

- Intraop: cristalloidi 1-3 mL/kg/h per il mantenimento
- Se perdite ematiche, cristalloidi con proporzione 1.5:1.0, o colloidi 1:1
- Non somministrare precarichi
- Non considerare le perdite del “terzo spazio”
- Evitare la “deep anesthesia” (bispectral index values <40) che può causare ipotensione.
- Se necessario usare vasopressori

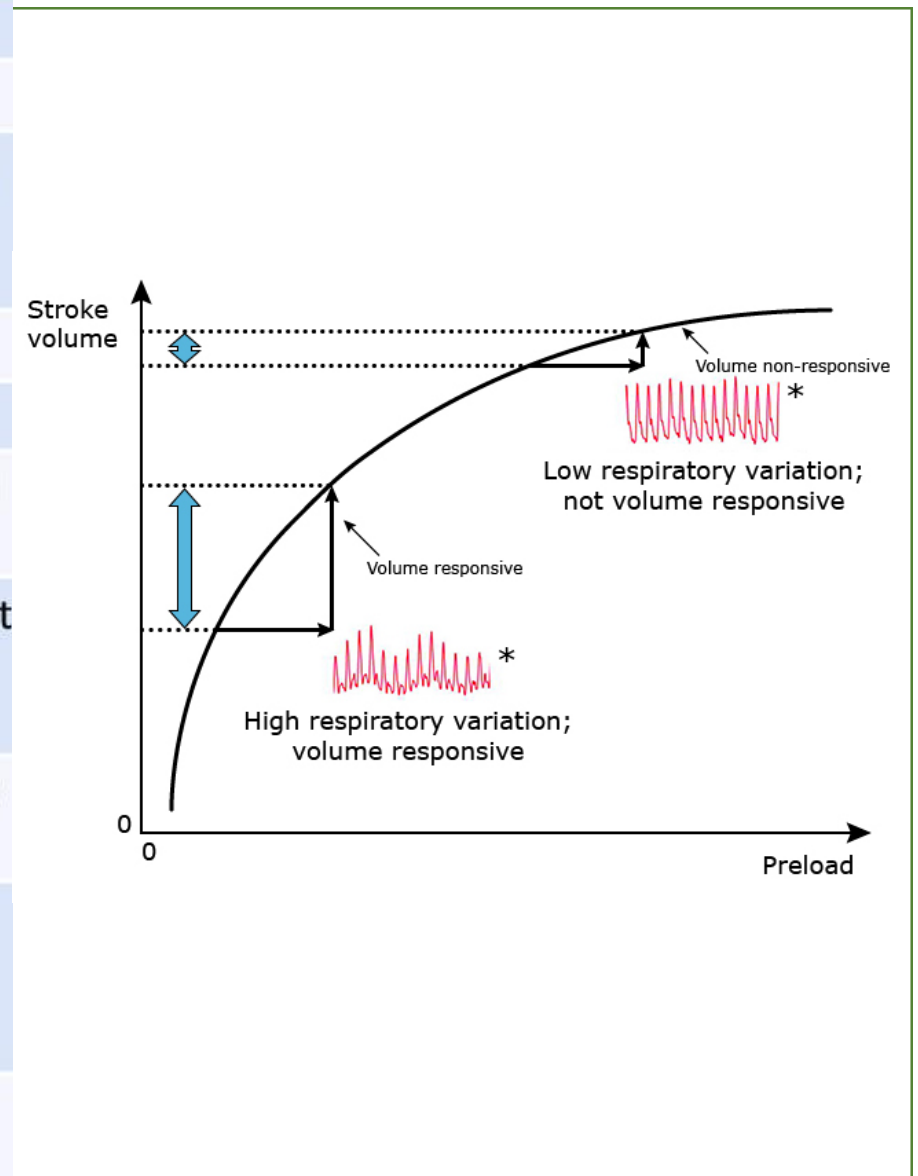
Goal-directed fluid therapy (ERAS)

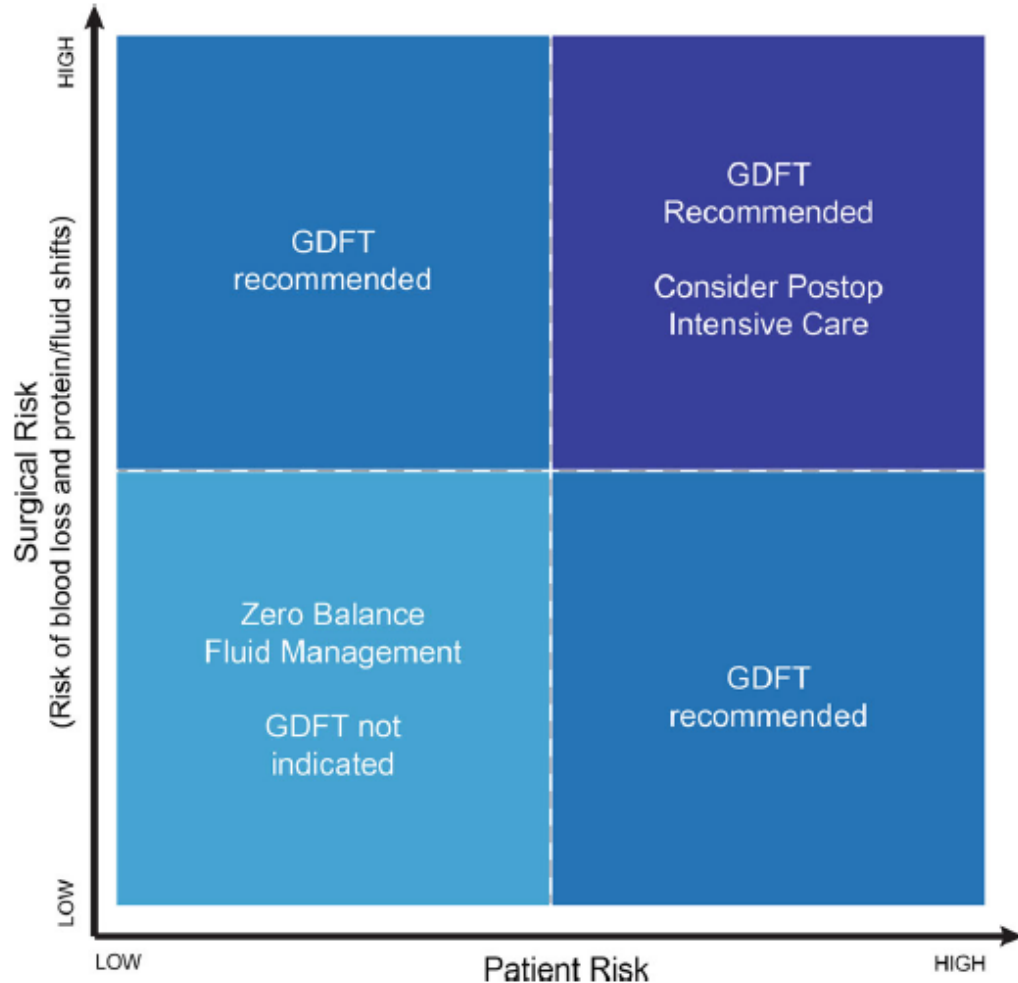
Miller, Roche, et al. “**Fluid management and goal-directed therapy as an adjunct to Enhanced Recovery After Surgery (ERAS)**” *Can J Anesth/J Can Anesth* (2015) 62:158–168

GDFT= serve per ottimizzare il reintegro delle perdite e il mantenimento dello stroke volume. Riduce la degenza e le complicanze in chirurgia Maggiore.



Dynamic indices	Static indices
Heart rate	Serum lactate
Mean arterial blood pressure (>65)	Serum base excess
Urine output (>0.5 mL/kg/h)	Haematocrit (i.e., when elevated, may indicate hypovolemia and haemoconcentration)
Pulse pressure variation (<10%)	Serum blood urea nitrogen
Stroke volume variation (<13%)	Serum creatinine
Stroke volume index (>35)	Urine electrolytes (including fractional excretion of sodium: FENa)
Inferior vena cava diameter (ultrasound; <3 cm but >1 cm)	Vascular pedicle width on a P-A upright chest radiograph (rarely available in trauma patients)
Respiratory variability of the inferior vena cava (ultrasound)	Central venous pressure (8–12 mmHg)
Response to passive leg raising (decreased pulse pressure variation or increased central venous pressure)	Pulmonary artery occlusion pressure (<12 mmHg)
End-expiratory occlusion pressure (when mechanically ventilated; decreased pulse pressure variation at end-expiratory occlusion)	





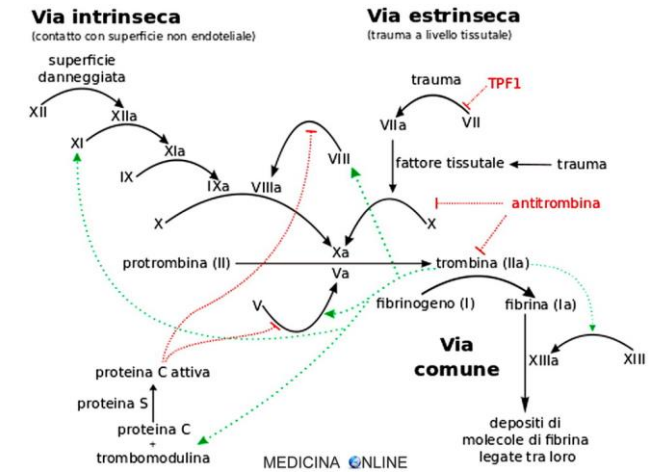
Key points

- evitare sia ipo- che iper-volemia
- evitare il digiuno prolungato preop
- I fluidi devono essere somministrati mantenendo il peso corporeo (=zero-balance fluid therapy).
- Postop: reintegrare presto NE e fluidi per os.
- tollerare l'oliguria se non ci sono altri problemi concomitanti

2. Gestione della Temperatura corporea: La NORMOTERMIA

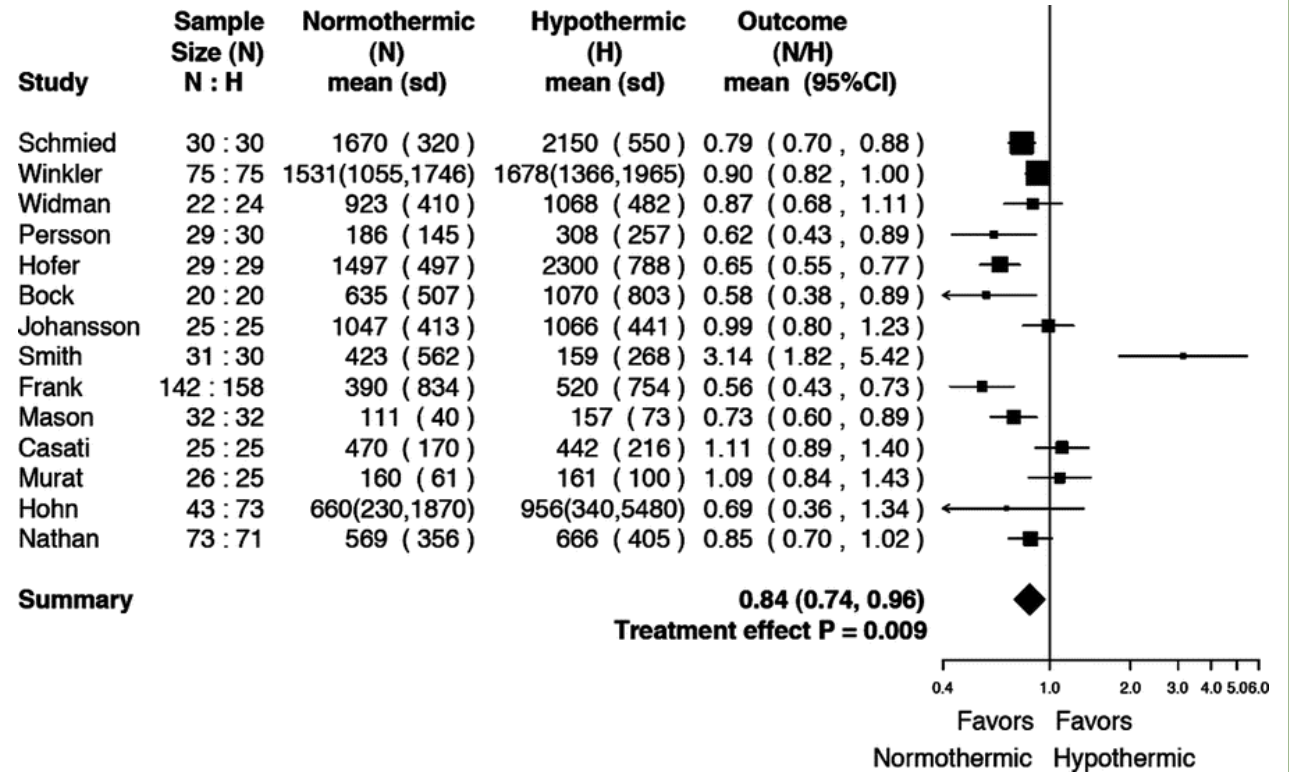
Effetti dell'ipotermia sull'emostasi:

- Disturbi funzionalità piastrinica
- Riduzione attività enzimatiche dei fattori della cascata coagulatoria



Anesthesiology 2008; 108:71–7 *The Effects of Mild Perioperative Hypothermia on Blood Loss and Transfusion Requirement*
Rajagopalan, Mascha, et al. (Cleveland)

- Metanalisi (14 studi)
- **Mild Hypotermia (<1°C)**
 - aumenta significativamente le perdite ematiche (circa 16%)
 - e aumenta il rischio relativo di emotrasfusione del 22%.



Di Marco P, Canneti A
SIAARTI Clinical Best Practice:
Perioperative Normothermia,
Published March 2017

NORMOTERMIA PERIOPERATORIA



OBIETTIVO: CORE $\geq 36^{\circ}\text{C}$

Per Interventi superiori a 30 Min**



1. MANTENERE / RIPRISTINARE LA NORMOTERMIA PRIMA DEL TRASFERIMENTO DEL PAZIENTE NEL BLOCCO OPERATORIO
2. INCORAGGIARE IL PAZIENTE A CAMMINARE PER RAGGIUNGERE IL BO (QUANDO OPPORTUNO E SE POSSIBILE)
3. RISCALDARE PAZIENTE E FLUIDI, APPENA POSSIBILE, DOPO L'INGRESSO NEL BLOCCO OPERATORIO *
4. CONSIDERARE IL PRERISCALDAMENTO (MIN. 10-30 MINUTI) PER EVITARE IPOTERMIA DA RIDISTRIBUZIONE
5. MONITORARE LA TC DURANTE L'INTERVENTO (OGNI 30 MINUTI) E PER TUTTA LA DURATA DELL'ANESTESIA E REGISTRARE SEMPRE IL DATO IN CARTELLA
6. REGISTRARE SEMPRE LA TC IN RR/PACU (OGNI 15 MIN) E ALLA DIMISSIONE DAL BLOCCO OPERATORIO, FORNENDO INDICAZIONI/ALERT AL PERSONALE IN CONSEGNA.

*CONSIDERARE SEMPRE:

- TEMPERATURA AMBIENTALE BLOCCO OPERATORIO (NEI LIMITI PREVISTI)
- RISCALDAMENTO ATTIVO DEL PAZIENTE
- RISCALDAMENTO DEI FLUIDI DA INFONDERE E DI QUELLI DI IRRIGAZIONE



**PAZIENTE PEDIATRICO:

1. RISCALDARE SEMPRE ANCHE PER INTERVENTI <30 MIN.
2. NON SVESTIRE IL PAZIENTE ALL'INGRESSO NEL BO
3. RISCALDARE IMMEDIATAMENTE, CON MEZZI DEDICATI

T° CORE IN ANESTESIA GENERALE

- Esofagea
- Sensore servo controllato riscaldato
- Timpanica a contatto
- Vesicale*
- PAC/Catetere art. PICCO o EV1000 o analoghi*
- *se indicati

T° CORE IN ANESTESIA LOCO-REGIONALE

- Timpanica a contatto
- Sensore servo controllato riscaldato
- Vesicale*
- *se indicati

SE T°C < 36:

1. VALUTARE IMPLEMENTAZIONE DEI MEZZI DI RISCALDAMENTO (AD ARIA CALDA FORZATA SE POSSIBILE, MATERASSINI E COPERTE TERMICHE IN BASE A VALUTAZIONE RISCHI/BENEFICI)
2. **NON DIMETTERE IL PAZIENTE DAL BLOCCO OPERATORIO FINO AL RAGGIUNGIMENTO DEI 36°C** (ESCLUSI I PAZIENTI DA TRASFERIRE IN TERAPIA INTENSIVA)

NECESSARIO

AUSPICABILE

WARNING

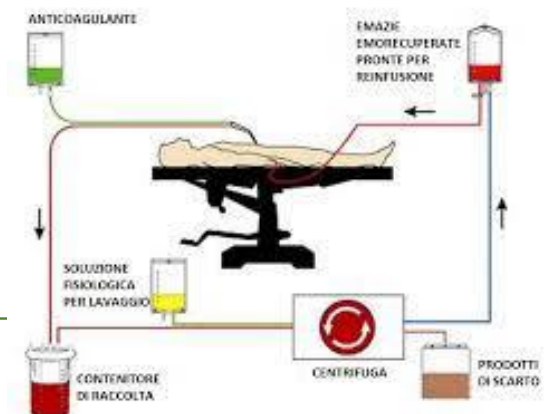
Strategie:

- Coperta ad aria calda
- Materassino riscaldato
- Infusore termostato per liquidi e emoderivati
- Temperatura della sala operatoria
- Monitoraggio della temperatura (quale?)

- Sessler DI. Current concepts: Mild Perioperative Hypothermia. *New Engl J Med*. 1997; 336(24):1730-1737.
- Sessler, DI. Perioperative Heat Balance. *Anesth*. 2000;92:578-596.
- Sessler DI, Kurz A. Mild Perioperative Hypothermia. *Anesthesiology News*. October 2008: 17-28
- Hypothermia: prevention and management in adults having surgery (CG65). NICE 2008
- Brauer A, et al. Comparison of forced-air warming systems with upper body blankets using a copper manikin of the human body. *Acta Anaesthesiol Scand*. 2002;46:965-972.
- Brauer A, et al. Construction and evaluation of a manikin for perioperative heat exchange. *Acta Anaesthesiol Scand*. 2002;46:43-50
- Brauer A, et al. Comparison of forced-air warming systems with upper body blankets using a copper manikin of the human body. *Acta Anaesthesiol Scand*. 2003;47:58-64.
- Engelen S, et al. An evaluation of underbody forced-air and resistive heating during hypothermic, on-pump cardiac surgery. *Anesthesia* 2011; 66: 104-110 (comparison of 3M Bair Hugger forced-air warming system and Inditherm resistive electric mattress)
- Roeder G, et al. Comparison of a Forced-Air and a Resistive Warming Device for Intraoperative Rewarming. *ASA Abstracts* 2010;A076. (comparison of 3M Bair Hugger forced-air warming system and Hot Dog resistive electric mattress)
- NICE (2016) Hypothermia prevention and management in adults having surgery, Clinical guideline [CG65]. Data di pubblicazione: Aprile 2008, Ultimo aggiornamento: Dicembre 2016
- Torossian A. Brauer A. et al, (2014) S3 German and Austrian Guideline: Preventing Inadvertent Perioperative Hypothermia, Published May 2014
- Di Marco P, Canneti A(2017) SIAARTI Clinical Best Practice: Perioperative Normothermia, Published March 2017

3. Recupero intraoperatorio del sangue:

- Aspirazione sangue intero dal campo operatorio → Centrifugazione e lavaggio → Reinfusione come emazie concentrate
- Controindicazione assoluta: Aspirazione di sostanze tossiche per infusione endovenosa (acqua ossigenata, iodio-povidone, emostatici topici, cemento metile metacrilato)
- Controindicazioni relative: Patologia neoplastica, Infezioni localizzate o sistemiche
- Limite: Volume minimo processabile 400-700 ml, costi



Meybohm, Choorapoikayil, et al.

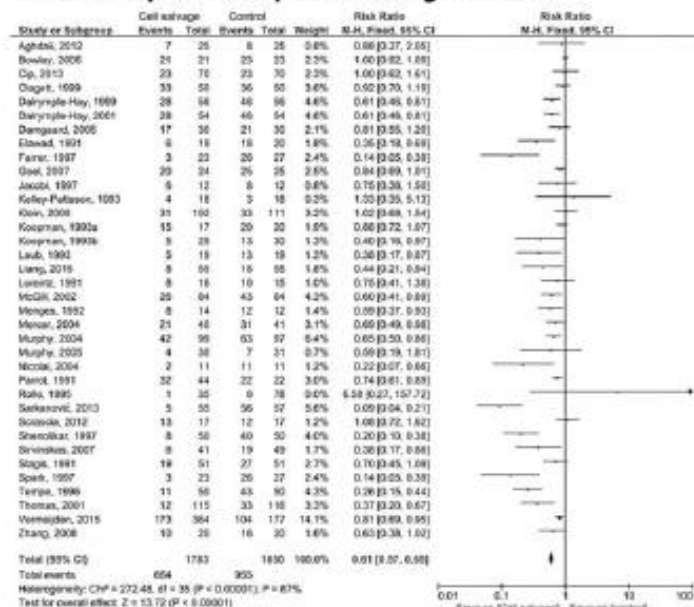
Washed cell salvage in surgical patients. A review and meta-analysis of prospective randomized trials under PRISMA

Medicine (Baltimore). 2016 Aug; 95(31): e4490.

- Metanalisi su 47 trials (1140 esaminati)
- Suddivisi per chirurgia (CCH, Ortopedia, Vascolare)
- Conclusioni: *l'emorecupero riduce il numero di trasfusioni e il rischio infettivo*

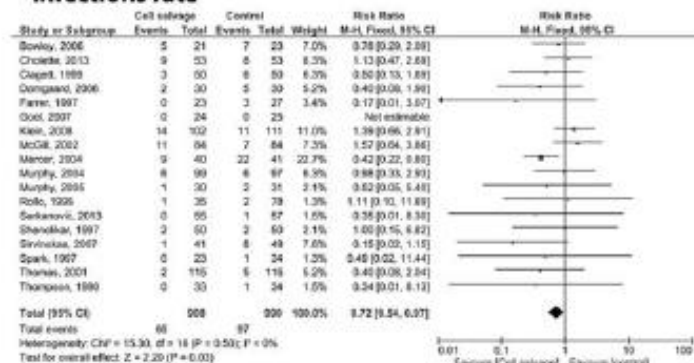
All types of surgery

Number of patients exposed to allogeneic RBC



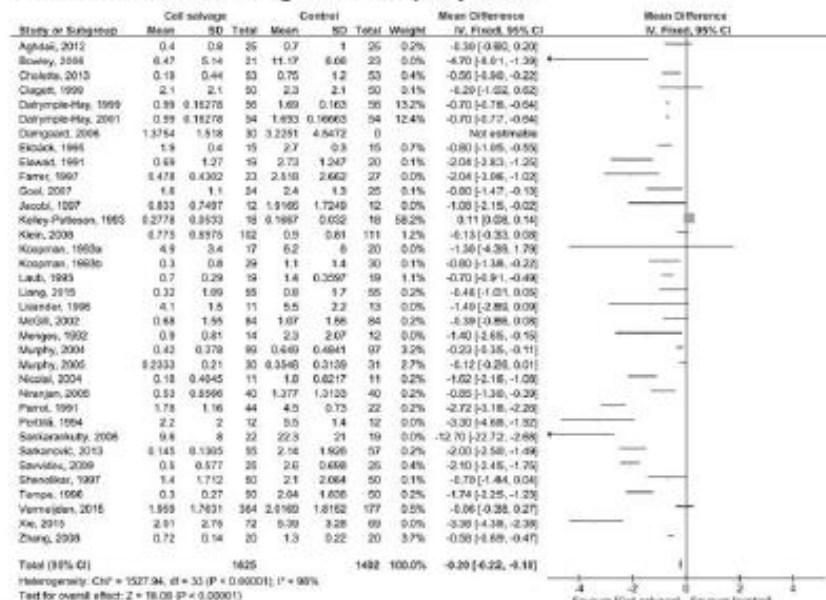
A

Infections rate



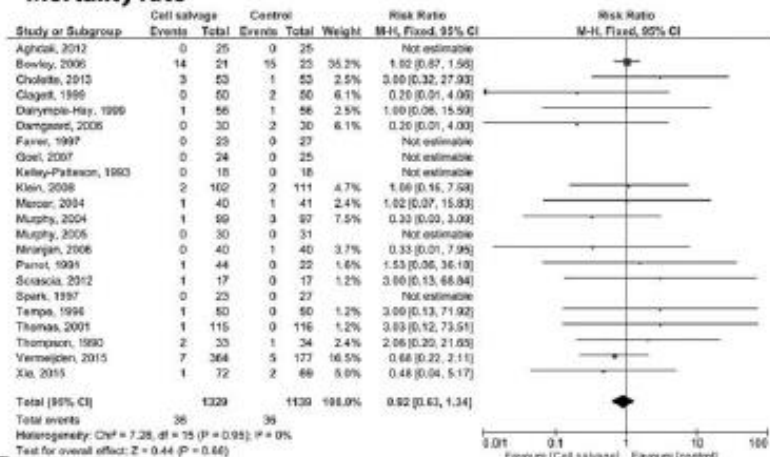
C

Number of units of allogeneic RBC per patient



B

Mortality rate



D

Figure 2. Forest plot of cell salvage compared with control intervention in all types of surgery. (A) Number of patients exposed to allogeneic RBC, (B) number of units of allogeneic RBC per patients, (C) infections, (D) mortality rate. RBC = red blood cell.

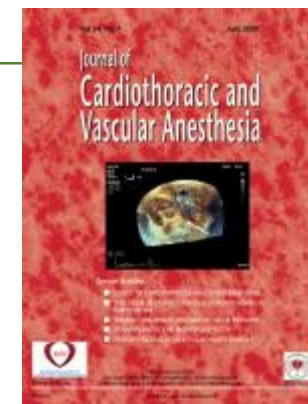
4. Emodiluizione acuta normovolemica (ANH):

- **WHAT:** Prelievo di sangue intero da paziente intraoperatorio, dopo l'induzione dell'anestesia, con ripristino delle perdite con cristalloidi per mantenere la normovolemia
- **WHY:** diminuire la concentrazione dell'Hb nel momento in cui avvengono le perdite ematiche; reinfondere il sangue intero (quindi anche con i fattori della coagulazione) quando servono a fine intervento
- **WHO:** ?

Shander, Brown, Licker et al.

Standards and Best Practice for Acute Normovolemic Hemodilution: Evidence-based Consensus Recommendations

Journal of Cardiothoracic and Vascular Anesthesia 34 (2020) 1755-60



SABM standards and best practice for acute normovolemic hemodilution

ANH acceptable with these conditions

- Pre-autologous donation
- Left main stenosis in a stable compensated cardiac surgery patient
- Previous cardiac surgery
- Anticipated prolonged cardiopulmonary bypass (e.g., >2.5 hours)

Use clinical judgment

- Unstable angina
- Symptomatic LV dysfunction
- Presence of symptomatic CV disease
- Severe AS
- Combination of CAD and severe AS
- Emergency surgery
- Severe COPD
- Hypoxemia (e.g., O₂sat <90% on room air)
- Severe pulmonary HTN
- History of CVA
- Presence of carotid stenosis (>70% stenosis)
- Presence of renal insufficiency (GFR <60)
- Presence of hemoglobinopathy
- Presence of significant coagulopathy (history of spontaneous or challenged bleeding and/or high risk of bleeding)

No ANH

- Hemodynamically significant arrhythmia
- Presence of acute infection (i.e., bacteremia or sepsis)



SOCIETY FOR THE ADVANCEMENT
OF BLOOD MANAGEMENT®

Fig 1. Standards and best practice for acute normovolemic hemodilution. ANH, acute normovolemic hemodilution; AS, aortic stenosis; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; CVA, cerebrovascular accident; GFR, glomerular filtration rate; HTN, hypertension; LV, left ventricle; SABM, Society for the Advancement of Blood Management.

- Limiti:
 - Presidi ad hoc
 - Fattore tempo
- Indicazioni diverse per chirurgie diverse
 - Chirurgia generale (epatica, renale, npl)
 - Ortopedia
 - CCH

5. Algoritmo trasfusionale goal-directed

1. Monitoraggio della coagulazione con esami «standard» + TEG/ROTEM
2. Algoritmo trasfusionale individualizzato e goal-directed (Evidence-based in *ostetricia, CCH e trauma*, non solo per la *riduzione delle trasfusioni*, ma anche per la riduzione della *degenza ICU* e della *mortalità*)
 - Antifibrinolitici
 - Fibrinogeno
 - PCC
 - ...
 - PFC (?)

ACIDO TRANEXAMICO:

- Riduce perdite ematiche e trasfusioni in:
 - Cardiochirurgia
 - Chir. ortopedica protesica
 - Gineco/ostetricia
 - Trauma
- close to 200 meta-analyses describe its effectiveness in reducing blood loss and erythrocyte transfusions, and in improving postoperative hemoglobin concentration without evidence of increased thromboembolic complications

FIBRINOGENO:

- in bleeding patients the level should be maintained at greater than or equal to 1.5 g/l*
- Fresh frozen plasma is not a good source of fibrinogen (Emodiluizione, perchè ne contiene <2g/l)
- Another source of fibrinogen is cryoprecipitate

*Spahn et al. **The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition** *Critical Care* (2019) 23:98

*Callum et al. **Effect of fibrinogen concentrate vs cryoprecipitate on blood component transfusion after cardiac surgery: the FIBRES randomized clinical trial** *Jama* 2019: 1-11

6. Tolleranza di valori bassi di emoglobina

For the majority of patients a transfusion threshold of less than 70 g/l is adequate, and for high-risk cardiac surgical patients, a threshold of less than 75 g/l has been shown to be safe. (Spahn, Muñoz, Klein, et al. «**Patient Blood Management - Effectiveness and Future Potential**» *Anesthesiology July 2020, Vol. 133, 212–222*)

- Hébert PC, Carson JL. **Transfusion threshold of 7 g per deciliter—the new normal.** *N Engl J Med.* 2014; 371:1459–61)
- Mazer CD, Whitlock RP, Fergusson DA, et al. **Six-month outcomes after restrictive or liberal transfusion for cardiac surgery.** *N Engl J Med.* 2018
- Mazer CD, Whitlock RP, Fergusson DA, et al. **TRICS Investigators and Perioperative Anesthesia Clinical Trials Group. Restrictive or liberal red-cell transfusion for cardiac surgery.** *N Engl J Med.* 2017; 377:2133–44

Vlaar, Oczkowski, Sanne de Bruin, Wijnberge, Cecconi, et al.

Transfusion strategies in *non-bleeding* critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine (ESICM)

Intensive Care Med. 2020; 46(4): 673–696.

Objective: To develop evidence-based clinical practice recommendations regarding transfusion practices in non-bleeding, critically ill adults.

Design: A task force involving 13 international experts

Methods: The task force identified four main topics: red blood cell transfusion thresholds, red blood cell transfusion avoidance strategies, platelet transfusion, and plasma transfusion. The panel developed structured guideline questions using population, intervention, comparison, and outcomes (PICO) format.

Results: The task force generated 16 clinical practice recommendations (3 strong recommendations, 13 conditional recommendations), and identified five PICOs with insufficient evidence to make any recommendation.

Red blood cell (RBC) transfusion thresholds in non-bleeding, critically ill adults:

- We recommend a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in a general ICU population, with or without ARDS
- We suggest a liberal transfusion threshold (9–10 g/dL) vs. a restrictive transfusion threshold (7 g/dL) in critically ill adults with acute coronary syndromes (conditional recommendation, low certainty).
- We suggest a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in critically ill adults with sepsis and septic shock ...and in critically ill adults with prolonged weaning from mechanical ventilation (conditional recommendation, low certainty).
- We recommend a restrictive transfusion threshold (7.5 g/dL) vs. a liberal transfusion threshold (8.5–9.0 g/dL) in critically ill adults undergoing cardiac surgery (strong recommendation, moderate certainty).
- We do not make a recommendation for a restrictive (7 g/dL) vs. a liberal (9–11.5 g/dL) transfusion threshold in critically ill adults with acute neurologic injury,
- ...ECMO.
- ...in critically ill adults with malignancy (haematologic or solid tumour).
- ...in critically ill elderly patients.

RBC transfusion *prevention* in non-bleeding, critically ill adults:

- We suggest not using iron therapy (oral or intravenous) to prevent RBC transfusion
- We suggest not using erythropoietin to prevent RBC transfusion (conditional recommendation, low certainty).
- We suggest using small-volume blood collection tubes to prevent RBC transfusion
- We suggest using blood conservation devices versus conventional blood sampling systems

7. Ipotensione controllata?

- Definizione poco chiara
 - PA < 100 mmHg
 - MAP 50-60 mmHg
 - Riduzione della MAP del 30% rispetto al basale
- Efficace in
 - chir. ORL e maxillo
 - NCH spinale
 - ortopedia



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CVP, central venous pressure; EPO, erythropoietin; IV, intravenous; PCC, prothrombin complex concentrate; TT, transfusion trigger.

Basi fisiopatologiche:

$$\text{Flusso } D = P/R$$

→ scopo: ridurre la pressione senza alterare il flusso!

→ Strumenti*:

- anestesia e anestetici
- Vasodilatatori (SNP, TNG, adenosina, diltiazem, fenoldopam)
- Inibitori SNA (clonidina, urapidil, labetalolo)
- ACEI

* Degoute **Controlled hypotension: a guide to drug choice (Review)** *Drugs* **2007**;67(7):1053-76.

8. Anestesia locoregionale ?

- Blocchi neuroassiali (spinale/peridurale) vs. anestesia generale
- Riduzione perdite ematiche intraoperatorie 25-30%
- Evidenza di bassa qualità, limitata a chirurgia della pelvi
- Effetto di ALR non discernibile da quello dell'ipotensione
«controllata»

***Take Home message:* come contenere le perdite ematiche intraoperatorie?**

1. Individuare il rischio di perdite
 - Chirurgia
 - Paziente fragile
2. Monitorare correttamente il paziente ed evitare la coagulopatia «iatrogena»
 - Normotermia
 - Normovolemia (Gestione fluidica GDT o zero-balance)
 - Normotensione (stop ipotensione controllata)
3. Considerare sempre (TIME OUT!):
 - Recupero intraoperatorio
 - ANH
4. Se perdite importanti:
 - Coagulazione e test viscoelastici
 - Strategia trasfusionale Goal-directed e individualizzata