Abstracts of the 20th Annual NATA Symposium on Patient Blood Management, Haemostasis and Thrombosis

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SPEAKER ABSTRACTS

Patient Blood Management – Past, Present and Future 3
Patient Blood Management in Surgery – Preoperative Preparation 6
Patient Blood Management – Does It Work in Children Too? 10
Iron Therapy in Special Indications 14
Underrated Measures in Patient Blood Management 18
Emergency Care of Patients Receiving Antithrombotics 21
Red Blood Cell Transfusion – How Low Can/Should We Go? 27
Anticoagulation 28
Stop the Bleeding! 33
Safety of Blood and Blood Products 38
Breaking News 41

POSTER ABSTRACTS

Blood Transfusion Services/Risks of Transfusion 43
Transfusion Practice 45
Blood Conservation Strategies/Autologous Transfusion 50
Anaemia Effects and Management 65
Fluid Therapy/Oxygen Carriers 94
Haemostasis and Thrombosis 95

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Speaker Abstracts

Patient Blood Management – Past, Present and Future

S1

An anniversary NATA symposium – looking back on 20 years of PBM education

Origins and foundation of NATA

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France’s infected blood scandal began in April 1991 when doctor and journalist Anne-Marie Casteret published an article in a weekly magazine proving that the Centre National de Transfusion Sanguine knowingly distributed blood products contaminated with HIV to haemophiliacs in 1984 and 1985. On January 8, 1985, the multinational health care company Abbott Laboratories sought authorization to sell equipment needed for blood testing. Response to the demand was delayed as the government was waiting for a rival French test to be ready. In 1999, the former socialist Prime Minister Laurent Fabius, former Social Affairs Minister Georgina Dufoix and former Health Minister Edmond Herve were charged with “manslaughter”. The Court of Justice of Republic found Edmond Hervé guilty and acquitted Fabius and Dufoix. Although Hervé was found guilty, he received no sentence.

France was not the only country with significant problems related to blood contamination. In this context, the international scientific community made very significant efforts to improve transfusion medicine and develop blood alternatives. In France, the haemovigilance network is defined by law and organized since 1993. Many other countries followed this initiative and haemovigilance has become a crucial part of the blood safety concept. Then, European and international haemovigilance networks were put in place. This period was also the age of glory for research in transfusion alternatives such as erythropoietin, plasma substitutes, fluorocarbons and haemoglobin solutions.

In this context, the Network for Advancement of Transfusion Alternatives (NATA) was founded in Graz, Austria in March 1998 by a group of internationally renowned experts. The objective of NATA was not to be another learned society for specific health care professionals but a real multidisciplinary network of anaesthesiologists, surgeons, blood bankers, researchers promoting international cooperation for better application of scientifically validated medical knowledge in the field of transfusion medicine and alternatives. NATA developed several high-quality multimedia tools including the website “nata-edu.org” which later became “nataonline.com”, the journal *Transfusion Alternatives in Transfusion Medicine* (TATM) and a reference book with the contribution of 60 international experts, *Transfusion Medicine and Alternatives*. The first international NATA symposium was held in Barcelona on January 31st and February 1st 2000 and gathered around 900 participants from various countries. The second symposium took place in Berlin where we are celebrating the 20th NATA symposium. NATA also organised 4 symposia in Asia (Beijing, Jakarta, etc.) and one in the USA (San Francisco).

Nowadays, the focus has significantly changed. Autologous predonation and acute normovolaemic haemodilution are now rarely performed. Research in fluorocarbons and haemoglobin solutions has been almost abandoned. Patient blood management, which includes optimization of patient red cell mass, minimization of blood loss and appropriate indications of transfusions, is certainly an evidence-based pathway to follow.

Twenty years later, the NATA multidisciplinary expertise remains the best option for postgraduate education related to patient blood management.
Patient Blood Management (PBM) is a widely used approach in quality management focusing on improving patient’s outcome by treating pre- and perioperative anaemia, implementing blood saving measures during the course of treatment and transfusion patients following evidence-based transfusion triggers.

The International Consensus Conference (ICC) on PBM was organized in order to find recommendations to the main topics in PBM: transfusion triggers for red blood cell concentrates in different perioperative and clinical situations, secondly the treatment of pre-and perioperative anaemia and thirdly if and how to implement PBM measures in an adequate way. Together with colleagues from different international scientific groups including Australia and Canada and led by the European Blood Alliance (EBA) form Association of American Blood Banks (AABB), the International Society of Blood Transfusion (ISBT) and the French (SFTS) the Italian (SIMTI) and German (DGTI) scientific societies of blood transfusion the 2018 ICC PBM was organized in Frankfurt am Main, Germany on April, 24 and 25 2018.

In the International consensus conference, the definition the definition of PBM by the World Health Organization (WHO) was used. PBM is a patient-focused, evidence-based and systematic approach to optimize the management of patients and transfusion of blood products for quality and effective patient care. To analyse all available studies, the Scientific Committee (SC) phrased specific questions within three chosen topics, first, preoperative anaemia, second, RBC transfusion triggers and third, implementation of PBM. The Centre for Evidence-Based Practice (CEBaP) carried out a systematic evidence-based review on the specific PICO (Population, Intervention, Comparison, Outcome) questions around these three topics. Based on search strategies in four different biomedical databases (Pubmed, Embase, Cochrane Library and Transfusion Evidence Library), CEBaP screened approx. 15,000 papers and included more than 160 of these within the three PBM topics. The evidence-based conclusions as well as the quality of the evidence was presented at the Frankfurt consensus conference by the SC. Based on the evidence and with the audience’s input, three multidisciplinary expert panels developed recommendations by using a transparent evidence-to-decision framework called the GRADE approach.

Basis for the consensus statements were more than 1500 publications. Consensus statements with the supporting evidence will be presented in the lecture. Independently from the outcome of the consensus conference the implementation of an evidence based patient blood management program in each hospital is rational and state of the art. It is of utmost importance to all clinicians performing haemotherapy to follow novel evidence as closely as possible in order to perform the best medical treatment possible the consensus of the first international consensus conference on the tree PBM topics mentioned above was based on using internationally accepted and evidence-based methods.

REFERENCES
S3

PBM: the standard of care!

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The pace of progress in the field of medicine has been staggering with new frontiers being reached and newer horizons being opened every day. Thanks to the advancement in technologies such as genomics and proteomics, we are gaining a far better understanding of the pathophysiological basis of diseases, with the development of many safer, more effective and targeted therapies within grasp. While transfusion medicine should be no exception to this general trend, improving the transfusion practices has been somewhat more complicated as the relationship between humans and blood has often been emotional and mixed with myths throughout the history of many cultures and civilizations. Nonetheless, there is no doubt that this discipline has gained in both knowledge and safety despite some lagging.

Patient Blood Management (PBM) is defined as “the timely application of evidence-based medical and surgical concepts designed to maintain haemoglobin concentration, optimize haemostasis and minimize blood loss in an effort to improve patient outcome [What is PBM? From the Society for the Advancement of Blood Management (SABM), available at http://www.sabm.org/]. As described in the definition, Patient Blood Management underscores a fundamental shift from a product-centred approach to a patient-centric approach. In this concept, allogeneic blood transfusion is not viewed as the treatment of default for anaemic or bleeding patients, but one among many treatment modalities that should be weighed based on its merits – potentials risks and benefits – for the individual patient in the context of other alternatives.

At the heart of the matter is the diagnosis and management of patients with anaemia. Anaemia remains a global health issue. It is estimated that one out of every three to four human beings across the world meets the WHO definition of anaemia (haemoglobin <13 g/dL in adult men and 12 g/dL in adult nonpregnant women). Anaemia is often multifactorial and various causes including nutritional deficiencies (iron, vitamin B12 and folic acid), inflammatory processes and blood loss (acute or chronic) usually play a role to some degree. The overall prevalence of anaemia in surgical patients is believed to be higher than general population. The omnipresent nature of anaemia and the assumption that a quick and easy treatment is always available (blood transfusion) might lead some to think it is a simple and even acceptable condition. This notion lacks validity because anaemia is not just a simple laboratory diagnosis and certainly not a so-called innocent bystander.

Nontreatment of preoperative anaemia is considered a substandard clinical practice. Preoperative anaemia should be considered as a contraindication for any elective major surgical procedure. Elective surgery should be rescheduled when possible until evaluation and treatment of anaemia are completed. In surgical settings, short-term treatment of preoperative anaemia with EPO and IV iron has been shown to be successful in orthopaedic and cardiac surgery and to decrease transfusion rates, postoperative infection, and length of hospital stay. PBM is built on 4 principles: anaemia management, optimization of coagulation, adoption of blood conservation strategies, and patient-centred decision, with the single goal of measurable improved patient outcomes. PBM’s approach contrasts with developing care paradigms from the perspective of transfusion medicine where the focus is on transfusion as a therapy rather than on the underlying derangement contributing to the clinical presentation and developing interventions to mitigate those conditions. Anaemia management as part of PBM can improve quality of life and improve clinical outcomes.

REFERENCES
Patient Blood Management in Surgery – Preoperative Preparation

S4

How to get started and overcome barriers to implementation?

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Patient Blood Management (PBM) is a relatively simple concept. When patients are managed optimally, i.e. when they come to the procedure (most often in the operating room) with a normal haemoglobin level, when all efforts are made to minimize bleeding during the procedure and when transfusions are avoided/kept to a minimum by optimizing the patient’s tolerance to anaemia, overall morbidity and mortality are reduced significantly.\textsuperscript{1,2}

However, implementation of PBM is much more difficult because it entails major changes to usual practices before, during and after the procedure.\textsuperscript{3} Some of these changes can be implemented at zero cost while other may be expensive. Conversely, major savings can be expected, resulting from the reduced transfusion of blood products, reduced morbidity and a decreased length of stay. As a result, implementation of PBM is extremely variable.\textsuperscript{4,5}

We describe here the steps taken to implement PBM at the Montreal University Hospital Center (CHUM). The document published by the European Union in March 2017, “Supporting Patient Blood Management (PBM) in the EU”, was used to guide our approach.

- Step #1 in getting started was to convince all those potentially involved that PBM is well worth the effort. To do so we first presented PBM to the National Transfusion Medicine Committee (CCNMT) that endorsed the concept. The CCNMT (which is part of the Ministry of Health) requested that we prepare a business plan for PBM at the CHUM as a pilot project for the Province of Quebec.
- Step #2, the business plan, described the concept, the patient’s journey prior to a procedure and put a dollar value on the resources that would be required.
- Step #3 was to present the business plan to all stakeholders involved in the paradigm change and ensure their support. The business plan was then presented to the Deputy Minister of Health who approved it and made arrangements for the necessary funding.
- Step #4 was to strike a PBM Implementation Committee at the CHUM. This was not difficult since all those potentially involved had been consulted and had supported PBM in step #3. At present (January 2019), the committee is working on establishing the Preoperative Anaemia Clinic and the patient’s journey (diagnostic tests, visit with MD, treatment plan, insertion in the operating list, etc) prior to the operation. Two surgical specialties, orthopaedics and oncological gynaecology, have been selected for the first phase of the project that is expected to begin in the Spring of 2019. For different reasons, we chose these specialties to create short-term wins on which to build the rest of the program.

An information campaign is to begin shortly, directed towards all hospital personnel, physicians and patients. Regarding patients, we will contact the media to increase public awareness of PBM and facilitate patient cooperation.

One of the major lessons learned during the process is that PBM needs a champion in order to overcome the inertia of the medical system and keep the process on track. In the case of the CHUM, an anaesthesiologist and a blood banker have taken the lead.

REFERENCES
S5

Anaemia and iron deficiency screening and evaluation: a practical approach

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Within a PBM programme, low preoperative haemoglobin and iron deficiency are some of the few modifiable risks factors for reducing red blood cell transfusion, but their correction or optimization takes planning and forethought.

Most PBM guidelines recommend surgical patients with bleeding risk should have a complete blood cell count and iron status, preferably 30 days before the scheduled procedure.

Ideally, preoperative assessment analysis should include some of these parameters to facilitate the anaesthesiologist or surgeon decide which anaemic patients may be treated straightforward (even the same day of the visit) and which ones should be referred to the haematologist or other specialist for further investigation and/or treatment. This pathway reduces health-care costs (less patient visits) and optimizes the inclusion of patients in the PBM program.

There are different laboratory parameters for the evaluation of preoperative iron status which allow a more accurate anaemia classification and treatment. Decreased iron availability is the limiting factor for the haemoglobinization of red blood cells and may be present in iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD), due to inflammation-induced iron sequestration.

Measurement of serum or plasma ferritin provides the most useful indirect estimate of body iron stores. It is universally available and well standardized, and the test of choice for detecting both iron deficiency and iron overload. In anaemic patients, ferritin levels <30 mcg/L are highly suggestive of IDA. As ferritin is a positive acute phase reactant, in patients of advanced age and those with inflammation or infection ferritin levels up to 60-100 mcg/L ferritin are also compatible with iron deficiency.

As transferrin is the only iron binding protein involved in iron transport, the transferrin saturation index (%TSAT) reflects the iron transport compartment. Its measurement is universally available and well standardized, although is influenced by daily and circadian variability of serum iron levels and transferrin (negative acute phase protein). TSAT may be reduced (<20%) in both IDA, due to absolute iron deficiency with increased transferrin concentrations, and ACD, due to iron sequestration at the reticuloendothelial system with normal or decreased transferrin levels.

The soluble transferrin receptor (sTfR) reflects the degree of iron availability by bone marrow cells. However, sTfR measurement is expensive, no universally available, and the method is non-standardised, further limiting a wider utilisation of this parameter.

Routine complete blood count yield red cell indexes, such as mean corpuscular volume (MCV), mean corpuscular Hb (MCH) or red cell distribution width (RDW), that is useful for classification of simple cases of anaemia. However, there are several important haematological indices that may also help in the diagnosis of ID in ACD, although they can only be measured by specific haematology analysers: Reticulocyte Hb content (CHr) and hypochromic red blood cells (%Hypo).

These haematological indexes are direct indicators of functional iron deficiency in contrast to the majority of biochemical markers, which measure functional iron deficiency indirectly via iron-deficient erythropoiesis. However, because of the long circulating life span of mature erythrocytes, %Hypo values are related to iron status in the last 2-3 months, whereas the CHr test provides an early (<7 days), direct measurement of iron supply to red blood cell production. These parameters are also good predictors of response to intravenous iron administration. If available, it may be the most useful and cheapest option.
S6

**Preoperative iron supplementation – when and how should it be done?**

*Patient blood management and iron therapy, a decade of advance*

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Patient Blood Management has developed from a single institutional concept in Perth Western Australia to a global program of care for all patients. Built on the three pillars the first highlights the identification and management of anaemia. Whilst anaemia is common in the preoperative setting most patients become anaemic during their hospital stay. The mainstay of correcting anaemia is ensuring the individual has the ability to recover themselves and supplementing iron stores is a fundamental factor.

In the hospitalised patient, inflammation mediated hepcidin activation prevents adequate iron absorption from the gut and intravenous iron has become an accepted and exciting therapeutic option.

In the preoperative setting, two small RCTs have produced conflicting evidence on patient effect but 2019 will see the publication of larger RCTs. In hospitalised patients there has been a reduction in blood transfusion and intravenous iron has been shown to increase haemoglobin levels in the post-operative setting.

We review the current evidence for the use of intravenous iron in the surgical pathway and potential areas for future research.
Is there a role for EPO in preoperative preparation?

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Preoperative anaemia is very frequent, accounting for around one third of the patients scheduled for major surgery. This preoperative anaemia is associated with poorer outcome and a two-fold increase in mortality. This is the rational for the implementation of “Patient Blood Management” programs, a multidisciplinary, evidence-based approach to optimize the care of patients who might need a blood transfusion. The first pillar of PBM is to improve erythropoiesis. The 2 main levers for this purpose are the use of iron and of erythropoietin (EPO). Indeed, the first cause of anaemia worldwide is iron deficiency and it concerns around half of the patients scheduled for a major surgery. Indeed iron is efficient in many cases. The second main cause of anaemia (the first for hospitalized patients) is inflammation. In these cases, iron is less or not efficient. Furthermore, inflammation impairs both the synthesis and the response to endogenous erythropoietin. This is why recombinant EPO has been proposed for the treatment of preoperative anaemia, it is a Grade 1C recommendation in the ESA guidelines. Indeed, EPO allows a reduction of transfusion by 40 to 80%, notably but not only in major orthopaedic surgery. There are very few contra-indications to EPO, but iron deficiency should be ruled out and/or treated. IV iron (i.e. a 1g injection) has been shown to increase the response to EPO (compared to oral iron). The combination of IV iron to EPO helps thus reducing the EPO doses (2 injections instead of 3 in orthopaedic surgery). There is no evidence that EPO increases the risks of complications (thrombosis, etc.). EPO together with iron are the 2 key medications for the first pillar of PBM, they allow both a reduction in transfusion rates and an improvement of surgical patient outcomes.

REFERENCES

Patient Blood Management – Does It Work in Children Too?

S8

Perioperative transfusion triggers – all the same as in adults?

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Anaemia is frequent in critically ill children and in those at risk for critical illness. Red blood cells (RBC) transfusion is the only approach to rapidly increase the haemoglobin concentration with the aim of improving tissue oxygen delivery. It has been shown to be lifesaving in severe anaemic children (haemoglobin level <5 g/dL).¹ However, RBC transfusion has been associated with morbidity and mortality, mainly related to non-infectious serious hazards such as transfusion-associated circulatory overload and transfusion-associated lung injury that have been shown to be much more prevalent in critically ill children.²

Two studies have evaluated the use of a restrictive or lower haemoglobin threshold for RBC transfusion in haemodynamically stable critically ill children.³,⁴ Both reported that a restrictive strategy does not increase morbidity-mortality in this high-risk population and reduces significantly exposure to allogeneic blood products. Despite these results, several studies reported that in practice, the haemoglobin value used as the transfusion trigger is higher than the one recommended in the literature and that paediatric intensivists and anaesthesiologists only partially adopted a restrictive transfusion strategy.⁵ This indicates that some children are exposed to RBC transfusion with an unacceptable risk to benefit ratio.

The Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) published recently consensus recommendations for RBC transfusion practice in critically ill children.⁶ The aim of these recommendation is to provide a comprehensive guide for RBC transfusion in various subpopulations of critically ill children or for those at risk for critical illness who have the highest risk to become anaemic and receiving transfusions. These recommendations emphasize that, when a transfusion is being considered, haemoglobin concentration could only be considered a surrogate marker of the body’s capacity to deliver oxygen to the different tissues. The ability of compensatory mechanisms (increased cardiac output and tissue oxygen extraction capabilities) to compensate for the decrease in blood oxygen carrying capacities (i.e. tolerance to anaemia) has to be considered into the decision-making.

As stated by the authors, the TAXI recommendations have many similarities to those published in the adult population.⁷ It is encouraging to note that the limited available paediatric data corroborate to the adult findings. However, when paediatric data were not available, TAXI used adult data to justify their recommendations. Not surprisingly, almost half of the TAXI recommendations are considered research and a major theme of these recommendations emphasizes the need for further understanding of anaemia tolerance in children and the need to determine other factors indicating the need for RBC transfusion besides haemoglobin concentration. Other physiologic parameters and/or biomarkers that could be obtained from children need to be evaluated to help clinicians in the RBC transfusion decision.

TAXI also recommend investigations that will inform primacy of RBC transfusion relative to other interventions aiming at increasing anaemia tolerance or improving oxygen delivery homeostasis by supporting physiologic compensatory mechanisms for anaemia. Finally, research is also required to define evidence that, once the decision to transfusion has been taken, will guide a titrated approach to administering RBCs, maintaining the risk of transfusion as low as possible, while monitoring the resolution of the indication for transfusion.

REFERENCES


Factor concentrates in paediatrics – top or flop?

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Management of perioperative bleeding in children is a major challenge for paediatric anaesthetists. Fibrinogen is the first coagulation factor that achieves critically low levels during massive blood loss. Clinical studies have demonstrated a beneficial role for intraoperative substitution with human fibrinogen concentrate to treat hypofibrinogenaemia with a very good safety profile. A meta-analysis of 14 randomised clinical trials in adult and paediatric cardiac surgery patients demonstrated that all-cause mortality was lower in the fibrinogen concentrate group, and bleeding and transfusion requirements were significantly lower versus a placebo or comparator group.

Data about the use of prothrombin complex concentrates (PCCs) in children is very limited. Analysis of a 5-year retrospective case series in children demonstrated favourable efficacy and safety of PCCs when used to treat elevated INR not related to Vitamin K antagonist use or for intractable bleeding post cardiopulmonary bypass surgery. Although there is little evidence on the safety and efficacy of PCCs in children, PCCs might offer a useful approach.

Factor XIII contributes to clot stability by cross-linking fibrin monomers and preventing clot lysis. However, efficacy of FXIII administration to treat acquired FXIII deficiency in paediatric surgery is currently based on clinical observation rather than on evidence-based data. For the management of intractable bleeding, administration of recombinant activated factor VII (rFVIIa) has been advocated in the past, however clinical evidence to support its use are lacking. A recent Cochrane analysis has advocated against the use of rFVIIa outside its licensed indications.

The use of coagulation factors as part of an algorithm offers great advantages for effective bleeding management as these products do not require thawing, are immediately available, have a standard dose, increase the desired coagulation factor levels reliably, and can be administered in a significantly lower volume compared to plasma transfusion. Although more clinical data in children are needed, this approach can provide a targeted and effective management and a protocol can be established within a very short time.

REFERENCES
S10

PBM in paediatric cardiac surgery: NATA guidelines

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Paediatric cardiac surgery is associated with a substantial risk of bleeding, frequently requiring the administration of allogeneic blood products. The risk of anaemia and coagulopathy observed in neonates and children is complex and multifactorial. Several risk factors have been identified and can be summarized as follows: (i) haemodilution due to CPB prime, cardioplegia, and administration of fluids in the perioperative period, (ii) activation of coagulation and fibrinolysis, (iii) a consumptive coagulopathy, (iv) anticoagulation using unfractionated heparin, as well as (v) other physiological disturbances (i.e. hypothermia, acidemia, hypocalcemia). Although all these mechanisms of injury are universal, factors specific to the paediatric population include the major differences in their haemostatic system from adults, greater haemodilution with CPB than adults, the presence of cyanotic heart disease, and the complexity of the surgical procedures performed. Efforts to optimize preoperative haemoglobin, limit blood sampling, improve haemostasis, reduce bleeding, correct coagulopathy, and incorporate blood sparing techniques are important pillars of patient blood management (PBM), and should be applied to the paediatric cardiac surgical population as it is across other disciplines. Guidelines for implementation of PBM in adults undergoing cardiac surgery were recently published, but evidence regarding the implementation of PBM in children with congenital heart disease is limited to systematic reviews and specific guidelines are missing.

The objective of the task force from the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA; www.nataonline.com) is to present the current literature regarding anaemia management and blood transfusion practices in the perioperative care of neonates and children undergoing cardiac surgery, to provide evidence-based recommendations, and to highlight potential areas where more research is urgently required.

REFERENCES

Iron Therapy in Special Indications

S11

Iron deficiency: causes, global burden and treatment options

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Iron deficiency (ID) is the most common global nutritional deficiency. Causes of ID also include but are not limited to heavy menstrual bleeding, gastrointestinal bleeding, urinary tract bleeding, malignancies or trauma. ID is the leading cause of anaemia. Of the 2.36 billion anaemic individuals (2015), 1.46 billion suffer from iron deficiency anaemia (IDA). ID and IDA are associated with weakness, fatigue, difficulty concentrating, poor work productivity, infection, heart failure, preterm labour, low birth weight, child and maternal mortality. When expressed in years lived with disability (YLD), anaemia represents 8.8% of the world’s total. In the general population of high human-development-index (HDI) countries, anaemia prevalence is approximately 12-14%. However, in the surgical settings the prevalence can reach levels of more than 70%. Moreover, many non-anaemic patients become anaemic during hospitalization, mostly due to excessive repeated phlebotomy and surgical blood loss.

Retrospective observational data consistently demonstrate that anaemia is an independent risk factor for major morbidity and mortality. The adjusted odds ratio (OR) for mortality in severely anaemic compared to matched non-anaemic patients is almost threefold and patients with mild anaemia, it is 40% higher. The OR for infections is almost twofold and for red blood cell transfusion (RBC) around fivefold. Therefore, transfusion should no longer be the default treatment of anaemia. Iron-deficiency responds to iron and guidelines are now recommending administration of iron preparations whenever possible to correct IDA.

REFERENCES
Iron therapy in obstetrics – a global public health challenge

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In 2012 The World Health Organisation Assembly endorsed a policy brief to target a 50% reduction of anaemia in women of reproductive age. Despite anaemia being an avoidable and treatable condition little change has been achieved and anaemia remains a significant global health problem. It affects 38% of pregnant and 29% of non-pregnant women with even higher prevalence in developing countries. Anaemic pregnant women have a higher incidence of preterm birth, antepartum and post-partum haemorrhage and death. 600,000 deaths occur annually with 8-16% considered a direct consequence from anaemia. More than 60% of cases are caused by iron deficiency (ID). 4

A Cochrane review reported that daily iron supplementation during pregnancy resulted in a 70% reduction in anaemia at term, a 67% reduction in iron deficiency anaemia (IDA), and 19% reduction in the incidence of low birthweight. 5

Unfortunately, despite the potential negative short- and long-term consequences from ID/IDA for mother and child, disagreement among clinicians and societies continues with regard to screening and treatment. Clinicians and policy makers often fail to implement or adhere to existing guidelines. The introduction of unsel ective ferritin screening and other antenatal interventions resulted in a significant reduction in anaemia prevalence, supporting a review of current screening and treatment practice. If time permits oral iron can be prescribed but treatment effect should be monitored. Newer intravenous iron (IVI) formulations appear safe in pregnancy and, if indicated, IVI should be available to pregnant women and in the post-partum period.

REFERENCES

1. WHO. Global targets 2025. To improve maternal, infant and young child nutrition; World Health Organization; 2014.
Prevention and treatment of iron deficiency (ID) and iron-deficiency anaemia (IDA) is a major public health goal, as revealed by a systematic analysis of the Global Burden of Disease Study 2016, where IDA was the fourth leading cause of years lived with disability, especially in women.¹

The presence and severity of anaemia is usually defined according to the haemoglobin (Hb) cut-offs established by World Health Organization (WHO).² Using WHO criteria, in 2010, one third of global population was anaemic, and IDA accounted for about one-half of total anaemia burden.³ However, as remarked by the WHO, “mild” IDA is a misnomer, as ID is already advanced by the time anaemia is detected, and has health consequences even when anaemia is not clinically apparent.² The emerging evidence that non-anaemic ID is a disease in its own right that deserves attention because of the risk it poses for patients, including the surgical population.⁴

Increased iron demands, reduced absorption and/or increased losses are the main causes of ID. Accurate diagnosis, addressing the underlying cause, and selection of the appropriate iron replacement product that safely meets the patient’s needs, remain as the main challenges in ID management.⁵

ID is usually treated using a variety of oral ferrous or ferric iron supplements, which are readily available and relatively inexpensive. However, absorption of iron from oral formulations is poor, especially from ferric salts, and may be further reduced by certain medications (e.g., proton pump inhibitors) and food intake, thus making treatment time consuming (months to correct anaemia and replenish iron stores).⁵ Gastrointestinal side effects are frequent and may reduce tolerance and adherence to oral supplementation, further limiting its efficacy.⁶ Low single daily dose (<60 mg) and/or alternate day dose (<100 mg) may reduce side effects and maximize fractional absorption,⁶ due to a reduced effect of absorbed iron on hepcidin release. In elderly IDA patients, a 2-month course of daily 50 mg elemental iron was as effective as daily 150 mg at improving Hb and ferritin, but with fewer gastrointestinal side-effects.⁹

Oral supplementation with traditional iron salts has been scarcely discussed in the setting of inflammation (e.g., surgery, chronic kidney disease [CKD], inflammatory bowel disease [IBD], heart failure [HF]). As inflammation-induced hepcidin release leads to inhibition of intestinal iron absorption from oral iron, hampering efficacy and increasing gastrointestinal side effects, IV iron formulations are preferred.¹⁰ Though increasingly safer, IV iron formulations are more expensive than oral iron and still bear the need for venous access and infusion monitoring. Though the risk is very low, “IV iron products should be administered only when staff trained to evaluate and manage anaphylactic reactions, as well as resuscitation facilities are immediately available”.¹¹ In addition, except for the CKD population, data on long term safety of IV iron are scant. In contrast, available data suggest benefits of newer oral iron formulations, such as ferric maltol¹² or sucrosomial iron,¹³ that have been shown effective in this setting.

Sucrosomial iron (SI) is an innovative oral iron formulation in which ferric pyrophosphate is protected by a phospholipid bilayer plus a sucrcester matrix (sucrosome), which is absorbed through para-cellular and transcellular routes (M cells).¹⁴,¹⁵ This confers SI unique structural, physicochemical and pharmacokinetic characteristics, together with high iron bioavailability, proved efficacy and excellent gastrointestinal tolerance in variety of clinical settings, including those where IV iron is the usual treatment.¹³-¹⁵

Large, confirmatory studies are needed to ascertain whether these newer oral iron formulations for clinical use may represent a first line therapy for uncomplicated ID, and an alternative/complement to IV iron products for ambulatory treatment of ID in different patient populations.

REFERENCES


Underrated Measures in Patient Blood Management

S16

Cell salvage – still needed, or too expensive?

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The development of cell salvage and its integration into clinical practice spans the era prior to organised allogeneic blood supplies right up to the modern day where it is an integral part of patient blood management. Enthusiasts have long believed its obvious benefits of avoiding or minimising the use of allogeneic blood and maintaining the patient’s haemoglobin level as high as possible, despite surgical or traumatic blood loss. A sceptical view is held by some and there are claims that it is an expensive alternative which lacks robust economic and evidence-based support.

It is true that the literature is not abound with RCT evidence and economic assessment, but there are many reports of highly organised services that have shown significant decreases in allogeneic use, justifying the cost because of obvious clinical benefit. The vagaries of different transfusion services mean that the success of cell salvage provision depends on the type of institution and indeed the health care system’s arrangement for the provision of allogeneic blood components.

Recent NICE guidance in the UK on Blood Transfusion concurred the above view that available evidence was of low to moderate quality from both RCT and original cost effectiveness analysis. The accurate costing of cell salvage provision was hindered by the variance in both equipment used and the price of the equipment and disposables. In addition, some institutions do not have an organised approach to service delivery and therefore miss the opportunity to use the available technologies in an emergency situation. The missed opportunities for blood collection in patients who have unexpected haemorrhage can seriously undermine the cost benefit of a cell salvage service.

Examples of good and cost-effective practice show that it requires a robust service structure and strong clinical leadership to ensure optimum use of cell salvage equipment. Certainly, in the UK the provision of intraoperative cell salvage has increased dramatically in the last decade and has management, surgical and anaesthetic support as an essential adjunct to other patient blood management strategies.

REFERENCES
S17

Is haemodynamic monitoring a necessary cornerstone of PBM?

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In the perioperative setting haemodynamic monitoring is used to guide volume replacement and catecholamine treatment of patients in order to maintain an adequate stroke volume throughout surgery and postoperative intensive care treatment.1 The transfusion of red blood cells is indicated in profoundly anaemic patients to restore oxygen delivery to the organs. Patient Blood Management is a clinical and multidisciplinary concept that individualizes the treatment with blood components in order to meet the patients’ requirements (adequate oxygen delivery) and to reduce not necessary blood transfusions.2

In the literature the majority of larger clinical studies focused on assessing different transfusion triggers (usually more “restrictive” compared to more “liberal” haemoglobin values) with regard to clinical outcomes.3,4,5 The implementation of haemodynamic monitoring in a transfusion protocol to provide more physiological data, e.g. oxygen delivery and consumption or oxygen extraction rate (rather than haemoglobin only) was not part of the study protocol. Only a few studies in the setting of perioperative haemodynamic optimization included the use of red blood concentrates to achieve a certain threshold of oxygen delivery.6,7

In conclusion, haemodynamic monitoring is not yet a part of PBM and far from being a cornerstone of PBM. However, in certain patients it may be useful to apply more physiological parameters to assess the effect of red blood cell transfusion on oxygen consumption and extraction. This lecture focuses on the evidence to connect haemodynamic monitoring with the use of red blood cell concentrates and will also discuss the limitations of this approach.

REFERENCES
PBM measures in low-income countries

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Patient blood management (PBM) is a multimodal World Health Organization-endorsed concept based on three pillars aimed at reducing or eliminating the need for allogeneic blood products to improve patient outcome. The three pillars include detecting and treating preoperative anaemia, reducing perioperative blood loss, and optimizing patient-specific physiologic reserve of anaemia (including restrictive haemoglobin [Hb] transfusion thresholds).

A successful implementation of PBM programme, grounded in evidence-based medicine, optimizes patient safety and outcomes through measurable improvements. Despite PBM program can result in hospital-wide cost savings there is need for awareness about initial costs of implementing PBM, even though PBM is expected to reduce longer-term healthcare costs through lower direct expenditure, reduced complications, and shorter hospitalization times so there is a need for support from the highest levels and hospital leadership.

Implementing PBM concept in the largest hospital in Croatia was challenging, specially changing a long-standing transfusion practice and improving staff education, accepting that habits of individual practitioners can take time and re-education efforts. We have started as a part of European pilot project and built upon initial successes. Small beginner project serves as excellent education tool.

To make it comprehensive, we started with achievable goals like increasing awareness of PBM, multidisciplinary collaboration (transfusion medicine specialists, surgeons, anaesthesiologists, haematologists and critical care specialists), perioperative minimizing blood loss, improving blood utilization and most importantly continuously educating clinicians. We improved protocols for massive transfusion, implementing restrictive transfusion criteria, implementing single-unit transfusion strategies and update maximal surgical blood order schedules.

Several areas remain in need of further improvement. First is lack of PBM registries for systematic data collection and evaluation. Another major problem in Croatia is that blood is free of charge for hospital and any other intervention costs (iron therapy for example). Second obstacle in anaemia treatment was short timeframe for the preoperative assessment of anaemia in patient undergoing surgery, and pressure not to delay surgery. Outpatient clinic for early preoperative visits is, because of lack of anaesthesiologists, individual effort for now, in order to allow preoperative anaemia to be corrected before surgery. Respecting current situation, we hope to develop as ‘centre of excellence’ for PBM.

REFERENCES
Emergency Care of Patients Receiving Antithrombotics

S19

Assessing drug-induced bleeding risk and severity

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Any anticoagulant poses potential risks for bleeding, and there are multiple causes for bleeding and methods to determine the severity of bleeding. Clinical risk prediction scores were developed to determine clinical decisions about anticoagulation strategies. The HAS-BLED tool includes seven risk factors and was developed from ~4000 patients with atrial fibrillation who were or were not receiving anticoagulation. The HAS-BLED tool is recommended by the European Society of Cardiology and other societies for bleeding risk assessment.

Factors associated with increased bleeding risk from the HAS-BLED score include:

H: hypertension – uncontrolled > 160 mmHg
A: abnormal renal function, dialysis, renal transplant: Cr >2.26 mg/dL or >200 microl/L, abnormal liver function: bilirubin >2x normal, LFTsb>3x normal
S: history of prior stroke
B: bleeding history
L: labile INR
E: elderly >65 years
D: alcohol/drug use/antiplatelet agents

If three or more of these factors are present, then the risk of bleeding is increased. HAS-BLED has been well validated, and has been shown to outperform other risk scores (e.g., HEMORR(2)HAGES and ATRIA) in predicting clinically relevant bleeding. Despite limitations of prior scoring methods, the HAS-BLED score has good predictive value for intracranial bleeding compared to others. In the Swedish AF Cohort study, major bleeding and intracranial bleeding increased with higher HAS-BLED scores. The HAS-BLED score makes clinicians consider risk factors for bleeding in determining therapy. Of note is the risk of bleeding and stroke are closely related, especially balancing ischaemic stroke against intracranial bleeding. An illustrative application of the CHA2DS2-VASc and HAS-BLED scores to aid decision making has recently been published.

In this review, I will discuss how to assess drug-induced bleeding risk and review several of the scoring systems currently used including the ISTH and other scores.

REFERENCES

S20

Bleeding and emergency procedures in patients on vitamin K antagonists

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The coumarin (more accurately 4-hydroxycoumarin) derivatives are vitamin K antagonists (VKAs) and are widely used still, despite the growing use of DOACS. Warfarin is the most commonly used VKA in the world, and the coumarins have a similar action but a shorter (acenocoumarol) or longer (phenprocoumon) half-life.¹

There are three options for reversing VKAs such as warfarin: vitamin K, prothrombin complex concentrate, and fresh frozen plasma. The biochemical reversal of VKA can be achieved quickly with the use of PCC.²⁻³ All modern guidelines on warfarin use, advise rapid restoration of a normal INR, although evidence that this reduces intracranial haematoma growth in those with intracranial haemorrhage or improves clinical outcome is limited to case-series.⁴⁻⁵ one suggesting there was more improvement if PCC was given swiftly.⁷

For immediate reversal of VKAs, the missing coagulation factors Factors II, IX and X can be replaced by PCC.⁹ “Three factor” PCC has very little Factor VII. Modern PCC formulations – “four factor” PCCs contain significant amounts of Factor VII and can completely reverse the effect of VKAs as it is infused. Thus three-factor PCC, which produce poor correction of the INR, and are therefore not recommended if four-factor PCCs are available. The alternative to PCC is fresh frozen plasma (FFP) which contains the missing coagulation factors diluted among all the other constituents of plasma. However large volumes of FFP are required, reversal is not always achieved and there are risks of TACO and TRALI.⁶⁻⁷ Thromboembolic complications in published trials were observed in fewer PCC recipients (2.5%) than FFP recipients (6.4%). However, similar poor clinical outcomes were seen in both groups.² The half-life of administered Factor VII is only six hours, so it is important that phytomenadione (vitamin K₁) is given with the PCC to stimulate physiological generation of the vitamin K dependent coagulation factors after this time.⁴

Vitamin K should also be given intravenously. It is important after reversal, to check INR regularly for the next week, as a minority take over a week to clear warfarin from their blood and thus may require more vitamin K.¹¹ A rare and unpredictable but important side effect of intravenous vitamin K is an anaphylactoid reaction resulting in some cases in cardiac arrest) which has an incidence of 3 per 100 000 doses via a non-IgE mechanism, possibly due to the solubilizer.¹² “Overcorrection” of reversal with more PCC and vitamin K₁ can lead to harm. For more than 10 mg vitamin K₁ can prevent rewarfarinisation for days and overuse of PCC (giving further PCC when INR is in normal range) will provide a prothrombotic state which may lead to further thrombosis.⁹

The use of PCC is associated with an increased risk of both venous and arterial thrombosis during the recovery period, which is related to pre-existing risk and possibly the use of PCC.⁹ A higher incidence of thromboembolic events has been reported in trauma patients with the use of three-factor (3F)-PCC compared to four-factor (4F)-PCC.¹³ Therefore, in patients who have received PCC, thromboprophylaxis is prudent as early as possible after bleeding has been controlled.

Lastly there is now evidence that synthetic cannabinoids have been contaminated with long-acting VKAs in Illinois and now reaching Europe, and patient who develop a coagulopathy after their use need large amounts of vitamin K for many months until the effect has worn off.

REFERENCES


S21

Bleeding and emergency procedures in patients on direct oral anticoagulants

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Direct oral anticoagulants (DOACs) are now recognized as a major step forward for our patients. However, several issues related to DOACs deserve our attention. Reports on the pharmacokinetics and pharmacodynamics for these agents show a major intra- and inter-individual variability and a high number of drug-drug interactions. In addition, alteration of renal function interferes with most of DOACs. As a result, an unexpected high number of major bleeding events have been reported, focusing the attention on these new anticoagulant agents. As a result, there is a need for reversal agents, either non-specific and specific.

Non-specific agents:
Activated charcoal: Wang et al. reported that activated charcoal decreased the mean half-life of apixaban to 5 hours when charcoal (50 g!) was administered within 6 hours after the ingestion of the drug. Others have shown comparable data with dabigatran.

Prothrombin Complex Concentrates (PCC) and activated Prothrombin Complex Concentrates (FEIBA®) have been tested with various doses and conflicting results in different animal models and healthy volunteers, and they are now used by clinicians in bleeding patients on a non-evidence-based basis, and with a variable efficacy. However, several series, especially in neurology/neurosurgery patients show a better outcome in patients treated with PCC. The Swedish group by Majeed and Schulman has recently reported the efficacy of PCC in 84 medical bleeding patients, treated with apixaban and rivaroxaban. PCC were given at a median dose of 2000 IU. Management with PCCs was assessed as effective in 58 patients and ineffective in 26 patients. Most patients with ineffective haemostasis with PCCs had intra cranial haemorrhage (n=16). Two patients developed an ischaemic stroke, occurring 5 and 10 days after treatment with PCC. In the GIHP-NACO registry, PCC and activated PCC have been shown to partially or totally control bleeding in bleeding patients treated with DOACs.

Specific antidotes:
Three of them have already performed phase II and/or phase III studies:

- **Idarucizumab (Praxbind®)** is a fully humanized antibody fragment (Fab) which binds to the thrombin binding site of dabigatran hence inactivating the molecule. In healthy young and older volunteers, idarucizumab was associated with immediate, complete, and sustained reversal of dabigatran-induced anticoagulation (11). It was well tolerated with no unexpected or clinically relevant safety concerns. The phase III study (REVERSE-AD) has been now completed, including bleeding patients who have serious bleeding, or patients who require an urgent procedure. The results including 503 patients show a complete reversal of the anticoagulant effect of dabigatran within minutes...and 18% mortality (mainly unrelated to the antibody). Even if the European (EMA) and US (FDA) regulators have granted an approval for this compound, we need further studies and a much larger number of patients to be fully reassured. Nevertheless, this antibody may save lives.

- **Andexanet alpha** is a recombinant modified human factor Xa protein that binds factor Xa inhibitors. This specific reversal agent is designed to neutralize the anticoagulant effects of both direct and indirect factor Xa inhibitors. Its half-life is less than 90 minutes) and the bolus has to be combined with a continuous IV infusion. Up to know, no data are available after a 6hrs administration. Andexanet appears to be effective in healthy volunteers on a biological standpoint, and in a small number of patients (n=47) treated with apixaban or rivaroxaban. Additional confirming data have been released recently. Andexanet (now Andexxa®) has just been approved under the FDA's accelerated approval pathway based on effects in healthy volunteers, and continued approval may be contingent on post-marketing studies to demonstrate an improvement in haemostasis in patients. A clinical trial comparing this agent or usual care is scheduled to start in 2019 and to be reported in 2023. Andexanet was approved with a boxed warning for thromboembolic risks, ischaemic risks, cardiac arrest, and sudden death. Treatment with the agent has been associated with serious and life-threatening adverse events, including arterial and venous thromboembolic events, cardiac arrest, sudden deaths, and ischemic events, such as myocardial infarction and ischemic stroke.

- **PER977** is a small, synthetic, water-soluble, cationic molecule that is designed to bind « specifically » to unfractionated heparin, low-molecular-weight heparin, to the new oral factor Xa inhibitors, and to the oral thrombin inhibitor, dabigatran. Few data are available for the moment. Still no recent clinical data
Abstracts of the 20th Annual NATA Symposium

Speaker Abstracts

25

have been made available.

- Other more sophisticated and promising compounds are under development.16

As DOACs are very effective and increasingly popular, more and more patients are shifting from VKA treatments to DOACs. As a result, the number of DOACs treated patients undergoing an emergency procedure, a trauma or an overdose is increasing steadily and the need for long lasting, safe, user-friendly and cheap antidotes will increase.17

REFERENCES

3. Cohen D. Dabigatran: how the drug company withheld important analyses. BMJ. 2014;349:g4670. 
S22

Bleeding and emergency procedures in patients on antiplatelet agents

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Oral antiplatelet therapy is one of the pillars of treatment of atherosclerosis, particularly for the prevention of recurrence of acute atherothrombotic events. A significant proportion of patients on antiplatelet therapy will require non-elective invasive procedures or will be admitted with bleeding complications. Management of these patients requires evaluation of the level of platelet inhibition, the underlying coagulopathy, and the severity of bleeding or risk of bleeding.

In the presence of significant bleeding or when the risk of bleeding during an emergent procedure outweighs the risk of neutralizing oral antiplatelet therapy, measures should be taken to neutralize antiplatelet therapy. For non-elective invasive procedures, the possibility of postponing them for a few days or even a few hours until the elimination or sufficient reduction of the effect of the antiplatelet agent should be considered. The management of patients treated with antiplatelet agents in emergency settings is poorly codified. Due to significant variability in the response to antiplatelet therapy, platelet function testing can sometimes be used to assess the degree of platelet inhibition in bleeding patients or patients requiring non-elective invasive procedures. Platelet transfusion is often recommended to neutralize the effects of antiplatelet therapy. The rationale for transfusion in this context is to provide platelets that have not been exposed to the drug, and therefore correct the antiplatelet therapy-induced bleeding risk. Although tranexamic acid has no direct effect on platelet dysfunctions, it reduces surgical bleeding. Tranexamic acid is therefore recommended in case of periprocedural or traumatic severe haemorrhages. Although desmopressin is often mentioned among the therapeutic options for prevention or treatment of bleeding, the evidence supporting its efficacy remains poor. Recombinant activated factor VII (rFVIIa) has sometimes been proposed for ticagrelor in case of severe bleeding, but the evidence in the literature remains weak.

The aim of this lecture will be to review the evidence regarding management of bleeding and emergency procedures in patients on antiplatelet agents and offer some guidance. 1

REFERENCES

Red Blood Cell Transfusion – How Low Can/Should We Go?

Is continuous haemoglobin measurement useful?

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New technological developments in pulse oximetry have made it possible to monitor the haemoglobin concentration (Hb) continuously and non-invasively (SpHb). Although the accuracy of SpHb to reflect laboratory-measured Hb (LabHb) has been repeatedly criticized, SpHb monitoring provides continuous, real-time information of whether the Hb is stable, increasing or decreasing. The most obvious clinical benefit of SpHb monitoring is its potential to detect the development of acute anaemia due to occult or overt bleeding earlier than LabHb, which is intermittent and frequently delayed or altogether absent.

A lesser appreciated potential benefit of SpHb monitoring is its ability to make the development of acute iatrogenic haemodilution visible. One of the unintended and possibly less-appreciated consequences of liberal fluid administration is the development of acute haemodilution. Such haemodilution may lead to an actual decrease in oxygen delivery (DO2), especially in patients who do not respond to fluid loading by increasing their cardiac output (CO). In view of the fact that 70% of the fluid challenges administered during perioperative goal-directed therapy (GDT) do not produce the expected increase in CO, such a paradoxical decrease in DO2 may be more prevalent than initially thought. We may therefore need to include in the definition of ‘fluid responsiveness’ following a fluid challenge not only the change in CO but also the associated change in Hb. Excessive haemodilution may be responsible in part to the well-documented association between the administration of large amounts of fluid and increased mortality in critically ill patients. Hence, a decrease in the SpHb in the absence of bleeding in an acutely ill patient should prompt an immediate revision of the fluid administration strategy.

The real-time identification of haemodilution may have an important potential impact on the decisions to transfuse blood, especially when the Hb values decrease to a level below the acceptable transfusion threshold. Of note, the multitude of studies that have examined the possible clinical benefit of restrictive blood management strategies have all been based on specific Hb values as transfusion thresholds and have not taken the possibility of haemodilution into account. Finally, the response of the SpHb to initial blood transfusion(s) during acute bleeding may indicate that the administered blood has had a significant sustained impact on the Hb concentration, and that further transfusions are not indicated.
Coagulopathy of sepsis – time to reconsider anticoagulants?

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The coagulopathy of sepsis is a complex thrombo-inflammatory response with loss of endothelial function, and a consistent pattern of haemostatic dysfunction that is also described as disseminated intravascular coagulation (DIC). As a result, coagulation and inflammation function as host responses against infection. Multiple coagulation pathways are activated by pathogens, damage-associated molecular patterns (DAMPs), neutrophil extracellular traps, extracellular vesicles, and injury to the glycocalyx damage are all responsible for the pathogenesis of sepsis-induced DIC. The hallmark of DIC is microcirculatory thrombosis, and sepsis-induced DIC is a laboratory diagnosis based on coagulation test results. In DIC, treating the underlying cause is important, and additional adjunct therapies including antithrombin, thrombomodulin, and heparins are additional potential treatments, but evidence supporting their use continues to be debated.

In this review, I will discuss the pathophysiology and role of anticoagulants in the treatment of sepsis-induced DIC, and discuss future potential therapeutic approaches regarding this complex, life-threatening complication.

REFERENCES

Hospital-acquired thrombosis: a major patient safety issue

Reducing the burden of hospital-acquired venous thromboembolism

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Hospital-acquired venous thromboembolism (VTE), also known as hospital-acquired thrombosis (HAT), is defined as a blood clot resulting from a hospitalization, surgery, or other healthcare treatment; HAT can occur during hospital stay and up to 90 days post discharge and is considered to be a consequence of the hospitalization, disease, or treatment.1–2

There are an estimated 10 million cases of HAT globally. Those who have the greatest number of HAT are not the surgical patients but the medical patients, whose numbers vastly exceed surgical patients. The estimated population of hospitalized acute medically ill patients at risk for HAT is over 5.5 million in an assessment of 6 selected countries in the European Union (EU) and close to 8 million in the United States (US).3–6 In the EU in 2007, the estimated number of VTE-related deaths per annum (543,454) was more than double the sum of deaths due to AIDS, breast cancer, prostate cancer, and transport-related fatalities.3 The risk of developing VTE persists beyond discharge for a review of multiple studies that included hospitalized medically ill patients who were not receiving thromboprophylaxis reported VTE incidence ranging from 3.65% (objectively confirmed symptomatic VTE) to as high as 17.1% (objectively confirmed symptomatic and asymptomatic events) during admission.8 These results indicated that a substantial portion of hospitalized patients are at risk for developing VTE. In addition, in a large, real-world analysis of hospital claims data, it was shown that more than 50% of VTE events experienced by patients who were hospitalized for an acute illness occurred after discharge.7 Therefore, extended duration prophylaxis for VTE in high-risk patients in both the inpatient and outpatient continuum of care remains an important clinical issue.

Those patients who do survive a VTE event may face serious and costly long-term complications, such as recurrent thromboembolism, venous insufficiency causing post-thrombotic syndrome, and chronic thromboembolic pulmonary hypertension.

In the United Kingdom, the National Institute for Health and Care Excellence (NICE) implemented VTE risk assessment guidelines in 2010, and financial sanctions were introduced by National Health Service (NHS) England at the same time for hospitals that do not adhere to the 95% threshold for VTE risk assessment for all inpatient services.8,9 Since the program’s inception, there has been a significant reduction in HAT, a 15% reduction in VTE events attributed to insufficient thromboprophylaxis, and a decrease in VTE-associated mortality.10 However, this systematic approach to HAT prevention, while much admired, has not been duplicated elsewhere. Despite thromboprophylaxis guidelines being in place, globally many patients who are at risk for VTE are still being woefully undertreated.

Currently the World Thrombosis Day team are working with the WHO to extend mandated VTE risk assessment globally. This will be discussed.

Conflict of interest
Prof. Beverley J. Hunt: Medical Director of Thrombosis UK, and chair of the World Thrombosis Day organizing committee.

REFERENCES


S28

VTE prevention: what do the guidelines say?

European guidelines on perioperative venous thromboembolism prophylaxis

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The European Society of Anaesthesiology (ESA), together with other European societies, has published original and user-friendly guidelines on the prevention of venous thromboembolism (VTE) in anaesthesia and intensive care in the European Journal of Anaesthesiology.

There are many justifications for the development of these new European Guidelines, such as:
• The steadily decreasing global post-operative VTE risk.
• The ongoing debate about the indications of VTE prophylaxis for fast track procedures and day surgery.
• The questioned efficacy of elastic compression stockings in obese and elderly patients.
• The continuous recommendation of aspirin despite availability of new agents.
• The increasing need for objective definitions for major/massive bleeding.
• The American College of Chest Physicians (ACCP) guidelines 2008 (8th edition) and 2012 (9th edition) are still considered by many to be the Holy Bible, despite conflicting statements, different scope of topics, lack of incorporation of recently published important papers and last but not least lack of coverage of several topics of interest for us anaesthesiologists. Thus, there is ample room for a challenging European perspective.

As a consequence of the above, a Task-Force was set up in 2015 with seven ESA representatives and eight representatives from invited societies: European Society of Intensive Care Medicine (ESICM), European Association of Urology (EAU), European Digestive Surgery (EDS), European Board of Colleges of Obstetrics and Gynaecology (EBCOG), European Knee Society (EKS), European Hip Society (EHS), International Society on Thrombosis and Haemostasis (ISTH) and Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA). The driving incentive was to articulate an original, clinical and helpful European guideline, and not merely to implement or to extrapolate from the North-American ones (ACCP), or the NICE guidelines. After extended discussions, the number of clinical questions (chapters) was limited to 12 taking into account the benefit/risk ratios (efficacy/safety). We chose not to start from scratch and reinvent the wheel, since one member of the leading task force members was part of the previous ACCP guidelines. ACCP was informed. However, we decided to add several clinical topics which had not been fully addressed in the 2012 ACCP guideline. The Population, Intervention, Comparator, Outcome (PICO) structured approach was used systematically. Each clinical question focused on the perioperative prophylaxis, starting with a short rationale and ending up with a graded recommendation. It was mandatory to address the clinical relevance, the population of interest, the types of prophylaxis, the impact of duration, the assessment of benefits and harms and last, but not least, if possible to provide a cost-benefit assessment. The guidelines are presented in 12 separate articles (chapters), each edited by members of the ESA VTE Task Force. Venous thromboembolism prophylaxis is discussed in nine clinical settings. The usefulness of controversial treatments is discussed in three additional chapters. The clinical settings of interest were:
1. Surgery in the obese patient
2. Surgery during pregnancy and the immediate post-partum period
3. Surgery in the elderly
4. Day surgery and Fast track surgery
5. Intensive Care
6. Cardio-vascular and thoracic surgery
7. Neurosurgery
8. Chronic treatments with antiplatelet agents
9. Patients with pre-existing coagulation disorders, and after severe perioperative bleeding

The controversial treatments were
1. Mechanical prophylaxis
2. Aspirin
3. Inferior Vena Cava Filters.
Stop the Bleeding!

S29

Fibrinogen or plasma in trauma – which way to go?

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In trauma patients, fibrinogen is the first coagulation factor which reaches critical low levels.1,2 Hypofibrinogenemia upon ER admission is an independent predictor of poor outcome and is strongly related to the severity of shock.3-4 In trauma patients fibrinogen concentration <1 g/dL upon emergency room admission is associated with an almost 4fold higher mortality compared to normal fibrinogen levels5-6 Therefore early and aggressive fibrinogen supplementation in bleeding trauma patients is mandatory.7

Fibrinogen supplementation

According to the 4th fourth edition of the European guideline on management of major bleeding and coagulopathy following trauma, fibrinogen concentration in coagulopathic patients should be maintained between 1.5-2 g/dL.8

Is plasma transfusion sufficient in order to increase low fibrinogen levels?

In current clinical practice, FFP is most frequently used to replace coagulation factors.9 FFP is usually donated by healthy volunteers, so it contains only low concentrations of fibrinogen. Many studies have revealed that plasma transfusion is insufficient to maintain or increase fibrinogen concentration in massively bleeding patients.5,10 In particular, reconstituted whole blood comprised of red blood cells, fresh frozen plasma and platelet concentrates in a 1:1:1 ratio contains only low amounts of fibrinogen.11 Thus, it remains challenging to increase fibrinogen levels using plasma-based resuscitation protocols.10 A recent study revealed that plasma fibrinogen concentration decreased in multi-transfused patients, despite a high ration of red blood cells to FFP has been administered. Only in patients who additionally received cryoprecipitate as source of fibrinogen the critical level of 1.5 g could be maintained.4

Purified Fibrinogen concentrate

In some European trauma centres fibrinogen concentrate administration is the first line therapy in severely injured patients.12,13,14 FC is easily and quickly reconstituted using water, and it can be administered without thawing or cross-matching.15 Moreover, FC contains a well-defined concentration of fibrinogen, with a much higher consistency than indicated by the labelled range. The package insert indicates a possible range of 0.9–1.3 g per vial, but actual quantities are close to the labelled quantity of 1 g.

REFERENCES

5. McQuilten ZK, Wood EM, Bailey M, Cameron PA, Cooper DJ. Fibrinogen is an independent predictor of mortality in major trauma patients: A five-year statewide cohort study. Injury. 2017 May;48(5):1074-1081


NEVER forget tranexamic acid!

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Tranexamic acid (TXA) reduces bleeding by inhibiting the enzymatic breakdown of fibrin.\textsuperscript{1,2} It is a molecular analogue of lysine that inhibits fibrinolysis by reducing the binding of plasminogen to fibrin.

It is not widely appreciated that unfortunately even in 2018 that bleeding is a not uncommon mode of premature death. The intravenous administration of TXA safely reduces death due to bleeding in patients with trauma and post-partum haemorrhage.\textsuperscript{3,4} In both situations, most deaths occur soon after bleeding onset and treatment delay reduces the benefit. It is therefore imperative that patients are treated urgently and currently trials looking at prehospital use of tranexamic acid in trauma are progressing.

The use of prophylactic tranexamic acid in surgical procedures has been studied in 100s of randomised clinical trials and its use will reduce bleeding by about one third. This has led NICE to recommend that tranexamic acid is used in all surgical procedures where blood loss of >500 mL is expected.

In orthopaedics tranexamic acid has been used topically with similar efficacy to intravenous use.

Not only is it efficacious but it is also safe. Nearly one million subjects have been studied in clinical trials and there is no evidence of increased thrombotic risk.

The above issues and future use of tranexamic acid will be discussed.

REFERENCES
Fibrinogen in high-blood-loss surgery – a must?

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Perioperatively acquired coagulation disorders include, among others, decreased fibrinogen concentration, platelet count and thrombin generation. Upon major bleeding during surgery, fibrinogen reaches critical levels first and maintaining appropriate plasma fibrinogen levels and fibrin-based clot strength may reduce bleeding. Point-of-care monitoring can successfully guide haemostatic therapy in various settings, e.g., in trauma, ROTEM-guided use of fibrinogen concentrate and prothrombin complex concentrate reduced transfusion requirements versus FFP. Findings were similar at our centre in patients undergoing cytoreductive surgery to treat peritoneal malignancy, an extensive procedure with high blood loss, changing from an FFP- to cryoprecipitate-based algorithm in response to low fibrinogen levels significantly reduced transfusions. We subsequently investigated replacing cryoprecipitate with fibrinogen concentrate, a convenient and potentially safer fibrinogen source.

FORMA-05 was a prospective, randomised phase 2 study assessing efficacy and safety of a new double virus-inactivated fibrinogen concentrate, Fibryga®, versus cryoprecipitate. The per-protocol set included 43 patients (Fibryga, n=21; cryoprecipitate, n=22). Mean total intraoperative dose was: Fibryga 6.5 g, cryoprecipitate 4.1 pools (~8.8 g fibrinogen). Overall haemostatic efficacy of Fibryga was non-inferior to cryoprecipitate (p=0.0095; Farrington–Manning test) and rated excellent/good for 100% of patients in both groups. Intraoperatively, only red blood cells (RBCs) were transfused (median [range] units: Fibryga 1.0 [0–4]; cryoprecipitate 0.5 [0–5]). No other blood products were transfused during the mean 7.9 hours of surgery. Platelet count, clot strength and thrombin generation were maintained comparably in both groups. No related adverse events were observed; no thromboembolic events occurred with Fibryga, versus seven with cryoprecipitate.

Fibryga was as efficacious as cryoprecipitate for treating bleeding in patients with acquired fibrinogen deficiency undergoing major abdominal surgery for peritoneal malignancy. Fibrinogen supplementation helped avoid FFP or platelet transfusions, while RBC transfusion was very limited, despite extensive surgery. In our practice, fibrinogen supplementation represents a must for this type of surgery.

REFERENCES

S32

Modern coagulation management – possible without POC devices?

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Standard laboratory testing (SLT), such as INR, PT and aPTT, is still widely used for perioperative detection of coagulopathy. Notably, SLTs were never designed to accurately guide coagulation therapy in complex scenarios and there is little to no evidence to support their reliable use to describe the interaction of pro- and anti-coagulant proteins during perioperative coagulopathy.\(^1,2\) In addition, turn-around-times may exceed 60 minutes\(^3\) making it almost impossible to successfully use SLTs during severe bleeding, when prompt treatment must be ensured.

There is growing evidence that viscoelastic point-of-care testing (POCT), such as TEG or ROTEM, can be used more effectively for perioperative coagulation management to reduce bleeding and blood transfusion utilization.\(^4,5\)

Pooled data from major cardiac surgery have demonstrated decreased risk of allogeneic blood product exposure following POCT-guided bleeding management.\(^6\) Furthermore, POCT-guided bleeding management has been shown to significantly lower the re-exploration rate, decrease the incidence of postoperative acute kidney injury, and lower thromboembolic events in cardiac surgery patients.\(^6\) The authors of this study concluded that POCT-guided transfusion therapy is superior to the current standard of care.\(^6\) Similar reductions in transfusion requirements following POCT-guided targeted management were also observed during liver transplantation,\(^7\) and a recently published review advocated the use of POCT as a key method for a rational approach to transfusion decision-making in liver transplantation.\(^7\) Data from other settings have demonstrated similar benefits.\(^8\)

In summary, recently published literature clearly demonstrates the usefulness of viscoelastic testing for timely and reliable detection of perioperative coagulation disorders. POCT in combination with a goal-directed approach is considered by many a beneficial and superior way forward for modern effective coagulation management.

REFERENCES

Safety of Blood and Blood Products

S33

Age of blood: do we have all the answers?

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Much has been debated about the adverse clinical effects of transfusing red blood cells (RBC) stored for prolonged time. Preclinical studies have help define the so-called “storage lesion” and its biological consequences in animal models.1 Large observational studies, both retrospective and prospective, have suggested that extended storage of RBCs may pose a significant harm to transfused patients.2,3 In contrast, controlled clinical trials published in the last 3-4 years failed to find any association between length of storage and increased morbidity and mortality.4 Based on these results, it has been claimed that further study on the length of storage question would be superfluous and that no reduction in the shelf-life of stored RBCs is necessary.5 The question arises, however, as to whether the available clinical trials actually provide a definitive answer valid to any length of storage and every clinical scenario.

In clinical trials, failure to confirm the research question (negative results or null hypothesis) is very sensitive to the trial’s statistical power, which, in turn, is critically dependent on the variability among study subjects and the actual magnitude of the investigated effect. Prior knowledge of both factors helps determine the trial’s sample size necessary to reduce the chance of false negative results below a predefined threshold (usually 20%).

With regard to the length of storage question, published clinical trials may have failed to achieve such statistical power because of several factors. First, trials assume that all RBC units are identical to one another, which is never the case. Second, the temporal dynamics of the purported clinical harm mediated by the storage lesion remains unknown, so that we actually ignore the data generating process of what we are trying to measure and its intrinsic variability.6 Third, large epidemiological studies have shown that increased mortality attributed stored blood would be relatively small (around 5%), achieves its maximum long after transfusion, and would be circumscribed to the last segment of the RBC shelf-life (30-42 days).7 In contrast, in the available clinical trials, use of blood stored for more than 35 days was rare, patients’ follow-up was too much short to detect delayed effects, and statistical potency may have been eroded by unaccounted variability.

In conclusion, the length of storage question must remain open to further research because relevant harm by blood transfused close to the end of shelf-life has not been excluded. Meanwhile, a wise application of the precautionary principle calls for a reduction of the maximum length of RBC storage to 35 days.

REFERENCES
Blood safety issues – what should be tested in 2019?

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Nowadays blood components such as red blood cell units, platelet concentrates and plasma products are safe in regard to the classical transfusion-transmitted infectious agents (HIV, HTLV, HBV, HCV). In contrast to the mid 80ties the mandatory implementation of nucleic acid amplification testing (NAT) has reduced the infectious window period and the residual risk of HIV, HBV and HCV transmission. Consequently, a near-zero risk scenario has become reality in high income countries. For the D-A-CH region (Germany, Austria and Switzerland) the national hemovigilance systems have rarely reported breakthrough infections in the last ten years. Based on this successful background experiences the awareness to further improve safeguards of national blood supply shifted to the detection of other viruses such as Cytomegalovirus, Parvo B19 virus, West Nile Virus, Hepatitis E, and Zika virus for mitigating residual risks for specific patients cohorts at risk and/or for regions where emerging viruses have become endemic. Such emerging pathogens actually challenge the national/international surveillance agencies allowing for the rapid implementation of detection assays in case of urgent clinical need (transmissibility by blood) and/or other strategies of risk minimization (e.g. donor deferral).

Besides the transmission of viruses, the contamination of blood components especially of platelet concentrates by bacteria has been brought to the foreground, regarding their growth kinetics and the causation of transfusion-associated septic reactions in recipients, partly with fatal outcome. Especially in high income countries several measures of risk reduction were discussed by a panel of experts and national authorities. However, a variety of methods for bacterial screening, such as aerobic/anaerobic culturing, oxygen consumption, pH-shift and NAT technology have major limitations.

In the last decade a paradigm shift towards the development and implementation of proactive and universal pathogen reduction technologies have been taken place in order to overcome the “add another screening test” strategy. The market acceptance of such technologies will depend upon the robustness and general applicability of the pathogen inactivation, the avoidance of additional risks/side effects, the maintenance of functional integrity of each particular “target” (e.g. platelet, red blood cell), and last but not least upon the cost effectiveness in case of controlling emerging pathogen outbreaks.
Transfusion-associated circulatory overload: increased awareness is needed

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Transfusion-associated circulatory overload (TACO) is now the leading cause of transfusion–related mortality, with an incidence reported between 0.05–8% of all transfused patients.\(^1\)\(^2\) It is defined as the onset of any four of the following symptoms occurring within six hours after transfusion: acute respiratory distress, tachycardia, increased blood pressure, acute or worsening pulmonary oedema and/or evidence of positive fluid balance. Overall mortality is 6.5% and major morbidity, which includes life-threatening situations, ICU admission, intubation and mechanical ventilation occurs in up to 40% of patients.

The pathophysiology of TACO is poorly understood. TACO is described as hydrostatic pulmonary oedema due to volume overload.\(^3\) The suggested mechanism is rapid infusion of fluids resulting in a pressure increase in the pulmonary capillaries. This is measured as an increase of pressure in the left-atrium (the most optimal source to measure transduced pressure). Specifically, those whom have underlying cardiac or renal failure seem prone to develop TACO. However, pure volume overload seems unlikely since over 20% of TACO occurs after only 1 transfused unit (approximate volume ±300 mL)\(^4\) and this effect is not expected in patients if an equivalent volume of fluid would be given. Transfusion products might be the culprit, directly damaging the endothelium, through accumulation of pro-inflammatory mediators during storage.

Results of a recent cohort study of TACO patients suggest that TACO follows a ‘two-hit’ model in which the ‘first hit’ is the underlying condition of the patient (renal or cardiac failure) and the ‘second-hit’ being the transfusion. Furthermore, the study suggests a different pathogenesis of TACO compared to cardiac overload in the absence of transfusion.\(^5\)

Currently no evidence-based prevention or treatment strategy is available for this life-threatening syndrome. Insight in the pathogenesis of TACO should pave the way for future prevention and treatment studies.

REFERENCES
4. Popovsky MA, & Taswell, H. F. Circulatory overload—an underdiagnosed consequence of transfusion. Transfusion. 1985;Vol. 25(No. 5):469-.
Breaking News

S37

Treatment of preoperative anaemia in cardiac surgery

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Anaemia is frequent in patients undergoing cardiac surgery and results in an increased rate of red blood cell (RBC) transfusions and adverse clinical outcomes including mortality \(^1^,\(^3\). Several expert groups therefore recommend treating anaemia prior to surgery \(^2^,\(^4^,\(^5\). However, a systematic assessment and treatment of anaemia prior to cardiac surgery is not yet standard of care in many health care systems today.

In an increasing number of patients cardiac surgery is being performed within a few days after an acute cardiac event \(^6\). This complicates preoperative treatment of anaemia logistically and physiologically since current treatment options, such as erythropoietin and intravenous iron increase haemoglobin concentration by 10-15 g/l per week only \(^7^,\(^9\). Therefore, every effort needs be made to start the treatment of anaemia as early as possible. This is particularly important since a high percentage of anaemic patients also suffers from iron deficiency, hence the treatment will include intravenous iron, which improves cardiac function in patients with concomitant congestive heart failure \(^10\). However, the improvement of cardiac function was first observed 4 weeks after the intravenous iron administration \(^10\).

The success of short term anaemia treatment has only been document in one study including 74 patients undergoing valve surgery \(^11\). The combination treatment of erythropoietin and intravenous iron the day before surgery resulted in a reduction of RBC transfusions and acute kidney injury \(^11\). But is this also the case in other types of cardiac surgery procedures? The prospective randomized double-blind study NCT02031289 may provide answers to this important question in the near future.

REFERENCES
Hepcidin: the new golden bullet for iron therapy?

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Our knowledge about iron metabolism has been deeply renewed 15 years ago by the discovery of its master regulator, the hepcidin. A key regulator of iron metabolism and mediator of anemia of inflammation. Blood 2003;102:783-8. Hepcidin is a peptide, synthesized by the liver, that binds to ferroportin at the cell surface (in macrophages or intestinal cells), thus preventing both the release of iron from stores (i.e. the recycling of iron from haemoglobin) and the absorption of iron from diet. Hepcidin induces hypoferremia. Hepcidin synthesis is finely regulated: iron deficiency (and erythropoiesis simulation) repress its synthesis, while inflammation and iron overload induce it. Low hepcidin levels may be indicative of iron deficiency, and high hepcidin levels of iron overload. Because hepcidin is a very small peptide (20-25 amino-acids) and very similar in different species, the development of quantification assays was difficult. Nowadays, new assays, mainly based on mass spectrometry, have been proposed and validated. It is now possible to measure hepcidin in daily clinic. Hepcidin allow to diagnose iron deficiency in complicated clinical settings, especially in presence of inflammation. For example, in critically ill patients it allows to identify a large proportion of patients with iron deficiency on discharge (around 50%), while less than 10% are identified using ferritin. However, it is not yet a “bulletproof” indicator: indeed, it may help to identify patients who respond to iron preoperatively, but we do not have the evidence that it may help in more complicated settings, such as critically ill patients.

REFERENCES
Blood Transfusion Services / Risks of Transfusion

PI

Quality of blood safety against transfusion transmissible infections in Malawi

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Introduction: Malawi Government recognizes blood as an essential component of health delivery system to save lives. Blood Transfusion Service (MBTS) has the delegated mandate since 2004 to champion the provision of quality, safe and adequate blood supplies using voluntary and non-remunerated donors. The study wanted to measure the intended quality and safety of screening Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) blood for donation nationwide; with the following objectives: to know the blood donation rate; to know the proportion of blood donations that were voluntary and non-remunerated; to ascertain the proportion of blood donations that were tested in a quality assured manner for HIV, HBV, HCV and Syphilis; and to extrapolate the prevalence of HBV and HCV infections amongst potential donors.

Methods: It was a systemic rigorous data collection methodology done quarterly to all HIV/AIDS 714 certified health facilities and MBTS centers in Malawi using the “Blood Safety” questionnaire by well-trained health workers from January to June, 2018. Data was analyzed using SPSS with p-value set at 0.01.

Results: Malawi blood donation rate was 4.7 per 1000 population per year of which 74% were both tested in a quality assured manner for HIV, HBV, HCV, Syphilis and Malaria; and were voluntary and non-remunerated donors. And HBV and HCV infections amongst potential donors were 4.7% and 6.1%, respectively.

Conclusions: 26% of potential blood donors nationally were replacement or supplementary donors and were not screened comprehensively of HIV, HBV, HCV, Syphilis and Malaria. And HCV infection was more than HBV infection at the rate of 6.1% and 4.7%, respectively. Therefore, MBTS needs to be supported more by everyone to meet the blood demand nationwide. Infected clients need to be linked for confirmatory testing and eventual treatment where necessary. Further research on HCV incidence rise needs to be investigated thoroughly.
P2

Safe transfusion-awareness of TRALI and TACO in Serbia

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Background: The leading causes of blood transfusion-related morbidity and mortality are transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO). Patients with TACO cardinally manifest respiratory system-related signs and symptoms such as tachypnea, dyspnea, and decreased oxygen saturations, typically occurring during or within 12 hours of a blood transfusion and historically have been difficult to study due to under recognition. Although precautionary male-predominant plasma strategy has been implemented in the Blood Transfusion Institute of Serbia (BTIS) since 2011, it has not yet been implemented in all transfusion centres in Serbia.

Aim: To present results of reported adverse TRALI and TACO reactions submitted to the BTIS from three major blood transfusion institutes and 44 hospital blood transfusion services in 2011-2016.

Method: Retrospective analysis according to data reported in the adverse reactions and events register at the Haemovigilance Department of the BTIS.

Results: In 2011, 292 adverse reactions were reported (TACO: 7, TRALI: 0); 242 adverse reactions in 2012 (TACO: 9, TRALI: 0); 343 adverse reactions in 2013 (TACO: 7, TRALI: 0) 291 adverse reactions in 2014 (TACO: 10, TRALI: 3). 182 adverse reactions in 2015 (TACO: 3, TRALI: 1), 211 adverse reactions in 2016 (TACO: 5, TRALI: 1). In 34 cases (82.92%) TACO was reported after red cells transfusion, in 7 (17.07%) after fresh frozen plasma. One death associated to TRALI was reported.

Conclusion: TACO and TRALI are a potentially life-threatening event and clinicians should be aware of this before prescribing blood components. TACO was reported in 1.64-3.71% of all reported adverse reactions and TRALI in less than 1%. TACO prevention strategy is focused on recipient and TRALI on donor management. Implementation of modified transfusion strategies to minimize the volume and infusion rate of blood products, male-only plasma, solvent/detergent plasma, PAS platelet units are recommended to reduce adverse reactions. Transfusion medicine specialist has important role to improve transfusion safety by promoting continuous education, awareness and, significance of patient blood management and use of viscoelastic tests to guide transfusion.
**Transfusion Practice**

**P3**

**Where does the blood go in Northern Ireland?**

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**Introduction:** Red cell transfusion accounts for over 75% of all blood component use in Northern Ireland (NI) and is therefore the component that poses the greatest risk to patients and the highest financial cost for healthcare organisations. Multiple NI initiatives had already resulted in a 35% reduction in the red cell transfusion index (from 37 to 24 units issued per 1,000 of the population) in the years 2004 to 2016, making NI one of the more restrictive red cell transfusion regions in Europe. Recent pilot work has indicated that there is potential for additional improvement in red cell use and financial gains in NI. A comprehensive audit was undertaken to see where red cells are currently transfused, so that new quality improvement projects could be concentrated on the hospital specialties where there is potential to make the greatest improvement in red cell use with the limited resources available.

**Methods:** This prospective audit was designed to examine all red cell transfusions administered during a two-week period in NI in February and March 2017. Data collectors from a haemovigilance or laboratory background monitored red cell unit issues from blood bank to the bedside to determine the clinical indication and location of transfusion.

**Results:** Data was obtained for 1,462 red cell units - 95.7% of all red cell transfusions in the period. 92.1% of transfusions took place in NHS hospitals, 7.7% in a community setting and 0.2% were divided between private hospital and hospice patients. The median age for transfusion was 71 years and peaked in the 80-84 year olds. Transfusions were in medicine (28.4%), surgery and trauma (27.7%), haematology (25.3%), gastrointestinal bleeding (12.7%), obstetrics (4.5%) and neonatology (1.4%). 4.8% of transfusions occurred in patients who had a correctable haematnic deficiency. 43.9% of transfusions were as single unit, 39.7% two-unit and 16.4% 3+ unit administrations. Haemoglobin check between units was undertaken in only 9% of two-unit transfusions. 34% of transfusions were commenced out of hours.

**Conclusion:** There is scope to improve clinical practice in 4 aspects:

1. Following non-emergency transfusion, the patient should be re-assessed and haemoglobin level checked to determine whether additional red cell transfusion is required.
2. Anaemia should be investigated promptly to reduce requirement for transfusion.
3. Patient blood management should be fully implemented to minimise the requirement for red cell transfusion during undergoing elective surgery.

Non-urgent transfusions should be transfused within daytime working hours whenever possible.
P4

Allogenic blood transfusion and intensive medicine: results of the transfusion day

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Objective: Describing an approach to real transfusion practice in Spanish Intensive Medicine Service.

Methods: All patients who were admitted to the Intensive Care Unit (ICU) and who required an allogeneic blood transfusion were included in the study on the day of the study (12/11/2018); regardless of the reason for admission and/or the transfusion indication. The epidemiological variables were described using the frequency distribution if the variable was qualitative; and by means, standard deviation, median and interquartile range if they were of a quantitative type. The incidence of transfusion and its 95% confidence interval were estimated.

Results: We obtained a sample of 1,448 patients admitted to 111 ICUs in Spain. The average age was 61.77±15.66 years, being 66.16% (958) males. 50% of the patients had a SOFA ≤4 points. The most frequent reasons for admission were neurological, respiratory and infectious diseases, with the medical cause being the most frequent reason for admission (63.53%). The median hospital stay was 10.62 days (0-287). The percentage of transfusion was 9.90% (95% CI: 8.35-11.47%) and the mains rules for transfusion were the analytical - having the previous haemoglobin a median of 7.8 (6.90-8.8) g/dL and after the transfusion of 9.0 (8.40-10.00) g/dL (p <0.001) - and acute anaemia with haemodynamic repercussion. The component that was most transfused was the red blood cell concentrate with 90.21% of the total transfusions. An average of 2.58 (SD: 2.54) units were transfused, with a median of 2 units (1-20), with a pro-haemostatic drug being used 18 times (12.86%): 6 Prothrombin Complex, 5 Fibrinogen and 7 Tranexamic Acid. In 78.72% of the transfused patients, a single transfusion act was performed, without transfusion control in 15.04% of the cases and adequately performed after more than three hours in almost half of the patients.

Conclusions: The main transfusion criterion is the haemoglobin value. Pre-transfusion values of haemoglobin ≥8.8 g/dL are suggesting a component of hyper-transfusion in our units.
PS

Utilization of blood products (a five-year survey): haematology service as a major contributor in increased use of platelets and red blood cells

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Introduction: University Hospital Centre (UHC) Zagreb is a large academic hospital of maximum medical care (approximately 1799 beds). This study analysed the utilization of blood products for a five-year period (2013-2018). The aim of the study was to determine the number of transfused blood products (BP) and the number of transfused patients. Since haematology service is the most intense user of blood products, a separate analysis was performed for haematology and for all other services in UHC Zagreb.

Methods: Retrospective analyses of the utilization of red blood cell units (RBC), platelet concentrates (PLT) and fresh frozen plasma units (FFP) was performed including all services in hospital. Data of all transfused blood products between 1 January 2013 and 31 December 2017 was extracted from Hemo Tools, a comprehensive database of transfusion service.

Results: Over the study period 172,417 BP were transfused to 25,851 patients: 121,910 RBC, 43,946 PLT and 34,851 FFP. The transfusion of BP increased: RBC by 11.7% and PLT by 29.6%. In contrast, FFP decreased by 4.1%. The number of transfused patients increased; RBC by 9.5%, PLT by 15.3%, FFP by 0.6%. Between 2013 and 2017 36.8% of all transfused BP in UHC Zagreb were transfused to haematology patients: 23.6% of all transfused RBC, 73.3% of all transfused PLT and 7.4% of all transfused FFP. During that period in haematology service number of transfused RBC units increased by 21.2% and PLT by 28.6%, while FFP decreased by 0.8%. In all other services number of transfused RBC units increased by 8.7% and PLT by 32.1%, whereas FFP decreased by 4.4%.

Conclusion: The utilization of RBC and particularly PLT has steadily increased. In contrast, the utilization of FFP has slightly decreased. Over the same period, the number of patients transfused with RBC and PLT has also increased but to a lesser extent. In contrast, number of patients transfused with FFP remains almost the same. Increased use of RBC and PLT in haematology can be attributed to the development of treatment regimens and an increased number of hematopoietic stem cell transplantations (HSCT), especially unrelated allogenic HSCT. Increased utilization of RBC and particularly PLT in the group of all other services should be further analysed. Appropriate measures should be also taken to ensure rational and evidence-based use of blood products.
Anaemia and blood management practice in the setting of an emergency department within a major Australian tertiary hospital

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Introduction: Patient Blood Management (PBM) is a quality, safety and effectiveness initiative with tremendous health implications for patients. Anaemia management is the practice of evaluating and treating the underlying disease causes for anaemia, whilst managing symptoms through restrictive transfusion practices. The aim of this study was to audit and evaluate the impact of anaemia and Patient Blood Management (PBM) practices as they originate in the Emergency Department (ED) at the Royal Brisbane and Women’s Hospital (RBWH), Queensland, Australia.

Methods: A 6-month retrospective audit of patients presenting to the Emergency Department between 1st June 2018 and 30th November 2018 with anaemia was undertaken at the Royal Brisbane and Women’s Hospital. Basic patient information was recorded including: age, anaemia diagnosis, GP referral status, anaemia symptoms, Packed Red Blood Cell (PRBC) or IV iron administration and correlating pathology. Further data were collected relating to: length of stay, treatment pathway and referral, and patient outcomes.

Results: There was a total of 128 presentations to the RBWH Emergency Department with a diagnosis of anaemia between 1st June 2018 and 30th November 2018. 85 (66%) of these presentations resulted in PRBC transfusions. Of the 85 transfusion episodes, 63 (74%) were not treated accordingly to the single-unit transfusion policy in place at the RBWH. Descriptive statistics were used alongside SPSS software to further evaluate clinical applicability of transfusion and correlating patient outcome data.

Conclusion: Patient Blood Management (PBM) is an initiative which aims to enhance patient outcomes by minimising or avoiding unnecessary exposure to blood products. Pathways must be developed to minimise patient blood management practices that potentially put patients at risk of unnecessary transfusion. Such practises include: inadequate GP referral; treating a Haemoglobin number and not a patient’s condition; adhering to single unit transfusion practice when appropriate; minimizing unnecessary pathology requests; offering alternative treatment options like IV iron infusions, and ensuring appropriate referral upon discharge from the ED to guarantee the underlying cause of the anaemia, or iron deficiency anaemia is investigated.
The active role of Hospital Transfusion Committee for promoting patient blood management therapy policy in General Hospital Celje

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Introduction: There are many activities in blood transfusion practice to provide a safe, potent and correct blood component at the right time for the patient in need of blood. Hospitals in many countries constituted the Hospital Transfusion Committee (HTC) to help the blood transfusion service in developing transfusion practice, guidelines, recommendations, monitoring blood-ordering practice, collecting and evaluating data for haemovigilance.

Aims: HTC was established in GH Celje in 1999. Its main aim was to promote patient blood management policy and high standard of transfusion practice, rational use of blood and blood components, and to support all methods of autologous blood transfusion and to evaluate the data for haemovigilance, constantly, four times a year.

Methods: The use of blood components and drugs from FFP in the period 2017 and 2018 at clinical departments of General Hospital Celje (GHC) with 727 beds in 2017 and 733 beds in 2018 is presented. The data has been collected from the information system Datec and analysed in Excel.

Results: 23 departments using blood components and drugs from FFP in GHC, 9 of them diminished the use of RBC by 0.23% in total, (from 2.93% to 66.67% depending on department). 11 out of 20 departments using PLTS diminished their use by 5.07% in total (from 6.42% to 85.7% depending on department) and 9 out of 17 departments diminished the use FFP by 8.44% in total (from 10.26% to 100% depending on department). The use of HA and GGL has decreased; HA by 17% and GGL by 11% too. The use of blood components and drugs from FFP are presented in Table 1 and Table 2.

Conclusions: With the active role of Hospital Transfusion Committee (HTC) we succeeded in introducing a restrictive and safe transfusion therapy with blood components in GHC and even more rational use of drugs from FFP (HA and GGL) during the years, especially in the last year period from 2017 to 2018. The achievements of decreasing of usage of blood components and drugs from FFP in percentage are presented in green numbers in the Tables 1 and 2. More rational use of blood components and drugs from FFP is expected by respecting the Patient blood management therapy policy in all clinical departments of GHC in the future too.
Blood Conservation Strategies / Autologous Transfusion

P8

Case study of blood recycling device, Hemafuse, in urban Kenyan surgical theatres

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Introduction: Hospitals across Sub-Saharan Africa face blood banking obstacles with a 50% shortage of donor blood and reduced capacity in blood processing (WHO Global Database on Blood Safety, 2011 Schantz-Dunn and Nour). Emergency maternal and trauma cases are particularly affected by this lack of blood including ruptured ectopic pregnancy with laparotomy. The use of autologous blood transfusion has been effective in treating laparotomy cases (2001 Selo-Ojeme, 2003 Selo-Ojeme, Onwude, and Onwudiegwu). Patient’s own blood, rather than donor blood, maintains better red blood cell health, without contamination, (2007 Selo-Ojeme, and Feyi-Waboso; 2017 Sikorski, Rizkalla, Yang, Frank) and would also address concerns of disease burden and infrastructure. Sisu Global Health created the Hemafuse™ autologous transfusion system as an alternative to donor blood for cases of internal bleeding. Hemafuse™ is a handheld device that can salvage, filter, and recycle blood from hemoperitoneum or haemothorax and then provide blood to be re-transfused quickly during the same surgery. Multiple units of blood can be salvaged in each surgery. Hemafuse™ can be used in cases of abdominal bleeding, ruptured ectopic pregnancy, and trauma-related surgery.

Methods: Hemafuse™ was used at two Level 5 Hospital in Kenya for three case studies where it intervened to stabilize three women with ruptured ectopic pregnancy. Blood was salvaged from the patient using Hemafuse™ and re-transfused back to the same patient during the surgery. Hospital staff trained on the device performed the surgeries.

Results: Each patient had a pre-transfusion haemoglobin level between 6.5-9 g/dL prior to surgery with 1-1.5 L estimated blood loss. Blood salvaged by Hemafuse™ was the only source of blood used in the surgery and Hemafuse™ was able to salvage at least a unit (450 mL) of blood per case. Each patient presented with no reactions and were discharged in a few days. Hemafuse™ was able to provide blood where donor blood was delayed or not available and allowed the surgeries to begin at least one hour sooner than they might otherwise have commenced, translating to better transfusion outcomes for both patients (2018 Holcomb and Jenkins; 2014 Strandenes-Spinella).

Conclusion: These cases suggest the safety of a manual autologous blood salvage device in cases of first trimester haemorrhage.
Do coagulation profiles change in vitro and in vivo post re-infusion of autologous blood collected during caesarean section?

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Introduction: Cell salvage and autologous blood is a safe alternative to allogeneic red blood cell transfusion and routine use of cell salvage for caesarean sections (C/S) in the maternity theatre has reduced demand for allogeneic blood¹-². We have observed re-infusion of autologous blood has little effect clinically on coagulation, whereas transfusing a similar volume of allogeneic blood frequently results in a coagulopathy and need for further blood product support. This observation has been reported in abdominal aneurysm surgery following autologous blood re-infusions as part of a PBM strategy³. Our study aim is to identify if there is a measurable effect on the coagulation profile in vivo after return of autologous blood collected following C/S. A secondary aim was to identify and compare the differences of in vitro coagulation profiles of autologous and allogeneic red cells when mixed with allogeneic plasma and platelets. This study was ethically approved under REC reference: 17/NW/0586.

Methods: Women were recruited to the study and consented prior to their planned C/S. If at the time of C/S sufficient blood was collected for processing and re-infusion they were included in the study. Samples were taken from the woman pre re-infusion of autologous blood. Two further samples were taken from the bag of autologous blood before it was re-infused and a final coagulation sample was taken from the woman approximately 45 mins after the re-infusion was completed.

Coagulation samples were processed on a coagulation analyser for PT, APTT, thrombin time, fibrinogen, and D-Dimer, as well as on a Haemonetics® TEG6s analyser (Braintree, Massachusetts, USA). A sample of autologous blood taken from the re-infusion pack before re-infusion was processed in the same way.

Autologous and allogeneic blood was also mixed with allogeneic plasma and platelets in a 4:4:1 ratio and tested in the same way on the coagulation analyser and TEG6s.

Results: Data shows there was no clinically significant change in the woman’s coagulation profile in vivo pre and post autologous blood re-infusion (n=42). However, mixing of autologous and allogeneic red blood cells with plasma and platelets showed a reduced fibrinogen and prolonged clotting time with allogeneic red blood cells compared to autologous blood.

Conclusion: The routine use of intra-operative cell salvage in obstetrics is a safe alternative to allogeneic blood. Using autologous blood not only reduces the demand for allogeneic blood but also reduces requirement for additional blood products. Whilst autologous blood in vitro has no clotting properties, when given in vivo it behaves like whole blood and does not affect coagulation in the same way as allogeneic blood does. The in vitro results support this observation.

REFERENCES
2. Sullivan IJ, Ralph CJ. Obstetric intra-operative cell salvage: a review of an established cell salvage service with greater than 1000 re-infused cases. Anaesthesia 2019, accepted for publication.
Cell salvage blood re-infusion following caesarean section: introducing a sticker for recovery notes to improve documentation

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Introduction: Obstetric haemorrhage is still a leading cause of mortality and morbidity. The most recent MBRRACE-UK report (published 15th June 2018) on maternal health, ‘Saving Lives, Improving Mothers’ Care’ showed deaths from haemorrhage have not reduced. Delivery by caesarean section (CS) presents a risk of haemorrhage. Allogeneic blood transfusion (ABT) in the United Kingdom is a scarce resource and still carries some risk, such as transfusion reactions and transmission of yet-unknown pathogens. Cell salvage blood (CSB) provides a physiologically-preferable alternative with minimised potential for adverse reactions. Unlike ABTs, the documentation of CSB re-infusion has not previously been audited. We aimed to improve documentation of CSB re-infusion following CS by introducing a notes sticker.

Methods: The sticker, which includes space for recording date, time, estimated blood loss, CSB volume and observations before and after re-infusion, was introduced at the Royal Cornwall Hospital Trust (RCHT) obstetrics department in July 2018. Midwives were instructed to complete the stickers and apply them to patients’ recovery notes. Sticker use was audited between July - September 2018 using patients’ notes and compared with documentation from the same period in 2017. Data was analysed using Microsoft Excel.

Results: 35 patients’ notes which documented receipt of CSB re-infusion following CS in the 2018 audit period were reviewed. The sticker was used in 62.9% of cases (n=22). When the sticker was not used, it was difficult to identify whether CSB had been re-infused. The poor documentation seen with no sticker was similar to that found on review of notes (n=43) in 2017, where CSB was recorded in varying locations in the patients’ notes, if at all, and there was no documentation of patients’ observations in many cases.

Conclusion: Implementation of the sticker has improved the documentation of CSB re-infusions, improving the record of patient observations and allowing appropriate follow-up. However, usage of the sticker could increase, so recovery teams will be re-briefed to achieve this. The sticker will be implemented in other specialties where CSB is used to improve documentation and traceability of all CSB re-infusions across the RCHT.
P11

Cell salvage use in major orthopaedic surgery: a retrospective analysis

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Introduction: Patient Blood Management (PBM) is an international multidisciplinary, evidence-based initiative in best practice for transfusion medicine (1). Blood conservation techniques such as cell salvage (CS), form a key part of this strategy. Allogenic blood transfusion (AT) is associated with rare but life-threatening complications; reducing its use is important due to cost and scarcity. Patients with hip dysplasia (HD) often require corrective therapy as adults either as total hip replacement (THR) or peri-acetabular osteotomy (POA). Both procedures carry a risk of significant blood loss and need for transfusion. CS is a safe and effective means of reducing AT and maintaining post-operative haemoglobin concentration. The use of CS has the potential to improve patient outcome by reducing associated complications and reducing the cost burden of AT (2). We investigated the use of CS in hip dysplasia (HD) patients in a 4-year period and the potential cost saving to our trust.

Methods: A 4-year retrospective analysis of elective major orthopaedic surgery for HD was conducted. Demographic data, operation type (THR, PAO, bilateral and complex/revision hip) and volume of CS blood was collected between 2015 and 2018. The Unpaired Student’s t-test was used to detect significant differences. Cost of CS (collection, and re-transfusion excluding CS machine and washing) is £65 per use, and per unit cost of AT by packed red cells ranges between £125-£140.

Results: A total of 248 elective procedures were carried out with 28.91% males and 71.08% females undergoing surgery. The overall mean age was 35.38 (SD+/-13.91; males mean age 36.51 (SD+/-14.24) and females 35.11 (SD+/-13.80), p=0.477). The commonest procedure was THR (52%, males 42, female 86). The 4-year total cell salvage volume (CSV) collected, was 56,391 mL, 61.0% (34,399 mL) during elective POA, with females requiring significantly less CSV during POA than men, p=0.0004). The average annual CSV was 14,097 mL, with males receiving a mean CSV of 296.69mL (SD338.32 mL), females 195.96 mL (SD 144.14 mL), (p=0.001) and 225.06 mL/patient CS blood. Total 4-year calculated costs for CS in THR and POA are £8385 and £7215 respectively. This compares to an estimated cost range of £16125-£18060 if minimal AT were used for THR and £13320-15540 in PAO. A saving range of £7740-9675 (THR) and £6105-8325 (PAO).

Conclusion: PBM through CS is known to be effective in reducing requirement and amount of AT (1,2). We observed a statistically significant difference in CSV between males and females and a large cost benefit in surgical HD patients. Limitations include costings excluding price of purchasing CS machine saline washing and data on AT use. We hope to further this study by prospectively comparing actual AT use with CS use for the same population group and total costs in each group.

REFERENCES
1. https://doi.org/10.1016/S0741-5214(96)70096-4
**P12**

**Evaluation of patient blood management measures in obstetrics – Intraoperative cell salvage (IOCS) and tranexamic acid (TXA)**

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**Introduction:** Patient blood management includes IOCS at caesarean section (CS) (NICE CS) and use of TXA (WOMAN trial). The SaLVO trial of IOCS demonstrated a non-significant reduction in transfusion rates (2.5% vs 3.5%); routine use of cell salvage in caesarean section was not cost effective. TXA reduces death due to bleeding. Our aims were to establish adherence to local guidance for cell salvage at CS and TXA use.

**Methods:** Data was collected retrospectively from 1/8/17 to 31/1/18. All women with an estimated blood loss (EBL) of over 1000 mLs, those with risk factors for haemorrhage at CS, or who required a blood transfusion were included. The maternity (Euroking), blood transfusion and IOCS databases and scanned notes were cross referenced.

**Results:** There were 3033 deliveries in 6 months: 909 CS (30% all deliveries), EBL over 1000 mLs occurred in 14% vaginal delivery (VD) and 7% CS (12.5% of Category 1 and 2 CS, 55% antepartum haemorrhage, 50% placenta praevia, 17% failed instrumental, 27% multiple pregnancy and 22% unstable lie). IOCS was used in 37% of all CS: collection only was set up in 73%. 30.4 litres of blood were returned to patients in 6 months, with an average of 324 mLs (range 108-1656 mLs) per patient. TXA was administered to 32% of all women with EBL >1000 mLs (34% in VD, 21% in CS). For EBL >2000 mL, administration was 89% for VD, 45% for Emergency (Em) CS and 25% for elective (El) CS. Transfusion rates were 1.9% for all deliveries (2.3% for VD, 1.5% for Em CS, and 0.5% for El CS). Only 1 patient received allogenic blood when appropriate IOCS was omitted.

**Conclusion:** Although our results demonstrate that IOCS was not used in all indications according to local guidance, increasing targeted use, particularly in Category 1 and 2 CS may be appropriate for cost effectiveness. TXA use, particularly in women with more significant haemorrhage requires improvement. Transfusion rates for CS are low, which may reflect the increased use of IOCS in our unit. Modifying local guidelines to target IOCS further and educational intervention to improve the administration of TXA is needed.
P13

Orthopaedic patient blood management

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Introduction: Recommendations from NICE Guidance 2015 (NG 24) emphasise pre-optimisation with iron, including intravenous iron and the use of tranexamic acid (TXA). NICE guidance (QS 138) highlighted the need for iron supplementation pre and post-surgery for those with iron deficiency anaemia and haemoglobin checks following each unit of transfused blood. We sought to establish our compliance with these guidelines at our trust.

Methods: We audited 60 patients from January to December 2017, who received major orthopaedic surgery against NICE guidelines for patient blood management. Case notes were reviewed and cross referenced against electronic databases.

Results: 25% patients presenting to the Pre-Operative Assessment Clinic (POAC) had a Haemoglobin (Hb) <130 g/L amendable to optimisation. Patients who were pre-optimised with intravenous iron demonstrated, on average, a gain in Hb perioperatively (Hb POAC – Hb post op) of 7 g/L, vs a drop in 25 g/L for the rest of the cohort. 50% of those eligible for IV Iron had to have their surgery delayed by 4-6 weeks post IV Iron treatment. The average length of stay was lower in patients with a pre-operative Hb >130 g/L. Compliance with intra-operative tranexamic acid administration was excellent (93% eligible cases). Average blood returned through ICS was 329 mLs per patient which prevented a Hb drop of >10 g/L. Only 38% eligible cases received ICS. 66% of patients transfused with allogenic blood had interim Hb checks. 74% of orthopaedic patients were discharged anaemic without iron prescription. 23% had a discharge Hb of <100 g/L.

Conclusions: We found preoperative optimisation of anaemia with IV Iron reduces the risk of post-operative Hb drop. Earlier identification through haemacue screening at surgical booking clinic is necessary to prevent postponing surgery at the time of POAC. Raising the intervention threshold from 120 g/L to 130 g/L may be worthwhile. Compliance with intra-operative TXA administration was excellent. Increased use of ICS needs to be encouraged through clinical teams. Oral iron on discharge and/or intravenous iron administration pre-discharge should be considered to improve postoperative recovery, especially in patients with co-morbidities.
Applying a patient blood management program in patients undergoing urologic surgery with potential bleeding risk

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Introduction: Anaemia has a high prevalence in urologic cancer patients, its cause is multifactorial, highlighting iron deficiency due to the haematuria that often occurs in these patients. Haemoglobin values <12 g/dL in oncologic patients have been linked to worse oncological results, constituting an independent risk factor for mortality. Furthermore, preoperative anaemia is the main risk factor for receiving a preoperative blood transfusion, which is related with greater morbi-mortality and hospital stay length. The PBM (Patient Blood Management) is a multimodal strategy focused on the patient whose objective is to reduce anaemia, as well as the transfusion rate through the application of three pillars, highlighting the optimization of the pre-surgical erythrocyte mass. For all this, a PBM circuit has been implemented in potentially bleeding urologic surgery. This circuit was already implanted in our hospital for colon, esophago-gastric and traumatic orthopaedic surgery, obtaining favourable results (transfusion rates for these surgeries inferior to the national media). To carry it out, a preoperative anaemia study with iron metabolism is performed on all patients and those with anaemia are treated according haematology department protocols, which indicates the treatment, mainly the intravenous administration of carboxymaltose iron.

Methods: We performed a retrospective analysis of the patients who underwent urological surgery in our hospital before (n=476) and after (n=368) the implementation of the PBM program (years 2017 and 2018 respectively). Collecting the number of transfusions, haemoglobin levels, parameters of iron metabolism and the optimization of the anaemia that was performed and compared the results in both groups.

Results: After the implementation of the PBM program over patients undergoing potentially bleeding urological surgery, we have objectified a tendency of the reduction of anaemic patients, as well as blood transfusions, although the differences are not statistically significant probably due to some failures detected in the circuit.

Conclusion: The implementation of PBM in the scenario of urological surgery is a promising strategy that can reduce the percentage of patients who arrive anaemic at surgery, as well as the transfusion rate.
Continuous improvement of patient blood management (PBM) in programmed orthopaedic surgery

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Introduction: Several techniques of auto-donation are integrated in a second step of the PBM and try to avoid or diminish allogenic blood transfusion. The cost-effectiveness-safety ratios are controversial, so they are indicated in a selected group of patients.

Objective: To analyse the auto-donation program and transfusion in an orthopaedic hospital of 180 beds, with the aim of reaching a progressive reduction of auto in programmed arthroplasties ("do not do").

Material and methods: Retrospective analysis of the types of programmed surgery performed between 2013-2017 and the number of units of auto extracted in the Regional Blood Bank, rejected patients and expired (Ex) units (U).

Results: Of the 301 patients, only 53 received allotransfusion (17%). The number of surgeries has been stable since 2014. In 2017 the use of tranexamic acid is stablished in the pre-surgical protocol and more effective surgical techniques were implemented in the orthopaedic department.

<table>
<thead>
<tr>
<th>Surgery/patients</th>
<th>2013</th>
<th>Ex</th>
<th>2014</th>
<th>Ex</th>
<th>2015</th>
<th>Ex</th>
<th>2016</th>
<th>Ex</th>
<th>2017</th>
<th>Ex</th>
</tr>
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<tbody>
<tr>
<td>Spine (auto/total)</td>
<td>35/117</td>
<td>44</td>
<td>25/144</td>
<td>30</td>
<td>14/138</td>
<td>18</td>
<td>21/157</td>
<td>17</td>
<td>17/192</td>
<td>26</td>
</tr>
<tr>
<td>Hip</td>
<td>39/679</td>
<td>70</td>
<td>29/738</td>
<td>36</td>
<td>18/689</td>
<td>22</td>
<td>15/680</td>
<td>42</td>
<td>17/731</td>
<td>30</td>
</tr>
<tr>
<td>Knee</td>
<td>16/427</td>
<td>27</td>
<td>24/649</td>
<td>23</td>
<td>18/717</td>
<td>22</td>
<td>10/606</td>
<td>1</td>
<td>11/564</td>
<td>21</td>
</tr>
<tr>
<td>Extract U/expired U/rejected</td>
<td>283/141/9</td>
<td>202/89/6</td>
<td>132/62/7</td>
<td>157/60/9</td>
<td>158/77/6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Transfused Patients/Auto/allo</td>
<td>90/114/17</td>
<td>80/96/16</td>
<td>50/56/11</td>
<td>46/52/6</td>
<td>45/46/3</td>
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The percentage of patients received in the Blood Bank that could not reach auto was very low (4.5%), selection criteria were appropriated. A total of 830 U of auto were extracted: 43.8% of them were transfused, 51.7% expired. The largest percentage of units expired has been detected the last year with an expiration higher than the 65%. If we analyse the auto U depending on the surgical procedure, we find that the percentage of units expired is very similar, being the lowest percentage in spine procedures and the highest expiration in hip and knee prosthesis surgery. Patients, Auto U and Allogenic blood transfusion has been progressive decreasing up to 82%.

Conclusions: The results of our study show that the implantation of a multidisciplinary PBM program in our institution is suitable. The program allows to know the presurgical haemoglobin levels in patients to improve them and detect anaemia. Our results demonstrate that auto-donations must only indicated in patients that will undergo hip prosthesis replacement or bleeding spine surgeries (scoliosis).
P16

Continuous improvement of patient blood management (PBM) in hip replacement (THR) and knee arthroplasty (TKA)

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Introduction: Progressive implementation of PBM programs has demonstrated its value in “continuous improvement” due to multidisciplinary work and review of medical results. Our objective is to demonstrate the efficacy of a PBM program in our county hospital of 123 beds.

Methods: Pre-surgical self-donation and a high transfusion rate of over 60% was observed during 2011-2012. After that period, a PBM program was developed. The results were recorded prospectively and periodically evaluated in Hospital Transfusion Committee.

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<tbody>
<tr>
<td>THR</td>
<td>65,4%</td>
<td>32,8%</td>
<td>61</td>
<td>17,5%</td>
</tr>
<tr>
<td>TKA</td>
<td>59,4%</td>
<td>8,5%</td>
<td>114</td>
<td>7,6%</td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>12,5%</td>
<td>16</td>
<td>25%</td>
</tr>
<tr>
<td>Total</td>
<td>61%</td>
<td>21%</td>
<td>191</td>
<td>11,6%</td>
</tr>
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</table>

Results: After the withdrawal of self-donation and the beginning of the presurgical haemoglobin optimization program during 2013-2014, transfusion rate dropped more than 50%. With the withdrawal of the blood recovery systems, the transfusion continued to decrease and has decreased even more significantly with the use of tranexamic acid.

Conclusions: PBM programs are effective, reducing transfusion needs; currently transfusion is an anecdotic medical practice in programmed simple arthroplasties. Due to these results it has been proposed to eliminate the systematic request for pre-transfusion tests in the preoperative period and to perform them only in selected cases. The economic study as a result of the implementation of PBM programs is still pending.
Effect of PBM measures and Enhanced Recovery After Surgery (ERAS) protocols in post-operative outcomes of elective colorectal surgery (POWER Study sub-analysis)*


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Introduction: Postoperative complications after elective major surgery and preoperative anaemia have been shown to increase the length of stay, cost, and mortality. Enhanced recovery after surgery (ERAS) protocols combine utilization of a multidisciplinary team and protocolization of perioperative management. ERAS have become prevalent in colorectal surgery. Patient Blood Management (PBM) programs, based on an optimal use of red blood cell transfusion (RBCT) centred on the patient, include measures for evaluation and treatment of preoperative anaemia, which have been effective in multiple setting.

Methods: Sub-analysis of POWER Study*, a multicentre prospective cohort study to evaluate ERAS protocols on postoperative complications, that recruited consecutive adults scheduled for elective colorectal surgery from 80 Spanish centres, during a single period of two months between September and December 2017. Sub-analysis was performed to determine the effect of anaemia, RCBT and PBM management. Evaluation of haemoglobin (Hb), use of iron therapy and/or RBCT, were assessed in all included patients, whether being part of an established PBM program or not. The primary outcome was moderate to severe postoperative complications within 30 d after surgery.

Results: 2,084 patients (61.7% males) with a mean age 68 years were included. 566 patients (27.1%) presented moderate-severe complications, being lower in ERAS centres (25.2% vs 30.3%, p=0.011). Hb mean level was 13.1+/-1.96 g/dL. 1,100 (52.8%) patients had at diagnosis Hb level >13 g/dL; 837 (40.2%), Hb between 10-13 g/dL; 124 (5.9%), Hb 8-10 g/dL; 9 (0.4%), Hb <8 g/dL. RBCT rate: 108 (5.18%) pre-operative, 0.11 (0.57) U; 124 (5.95%) intra-operative, 0.09 (0.42) U; and 178 (8.55%) post-operative, 0.19 (0.80) U.

1,137 (54.8%) patients from centres with PBM program, but only 351 (16.8%) were treated pre-operative with iron: 128 (6.1%) oral, 43 (2.1%) sucrose and 168 (8.1%) carboxymaltose. 676 (73.3%) anaemic were not treated, 57 non-anaemic were treated (2.74%), only 294 (26.7%) anaemic received iron. Hb medium pre-treatment was 10.1 (1.64) g/dL and 11.6 (1.81) post-treatment. Moderate-severe complications risk factors in the univariate study: previous RCBT, OR 2.15 (95% IC 1.44-3.17; p <0.001); pre-operative Hb level OR 0.92 (95% IC 0.85-0.97; p<0.001); anaemia OR 1.31 (95% IC 1.08-1.59; p=0.006); Hb 8-10 g/dL OR 2.32 (95% IC 1.58-3.39; p <0.001); Hb post iron treatment OR 0.82 (p <0.001). After the regression multivariate analysis, only RBCT post-operative OR 4.47 (95% CI 3.10-6.51; <0.0001) was observed.

Conclusions. Hb level, anaemia and RBCT are risk factor of moderate-severe post-operative complications in colorectal surgery. However, in the real world, PBM is poorly applied. We need include anaemia study and treatment in the ERAS protocols to improve Hb level without post-operative RBCT.
P18

Expansion of a patient blood management (PBM) service at a tertiary referral centre with the introduction of a dedicated blood conservation practitioner

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Introduction: In 2015, North Bristol NHS Trust’s tertiary referral centre appointed a blood conservation practitioner. The initial objectives were to develop PBM pathways, education, training, clinical support and establish a steering group to provide governance. Integral to ongoing quality improvement is robust data collection. This allows us to evaluate the service development and its resource impact as outlined in the 2015 NICE costing statement¹.

Methods: Utilising our comprehensive PBM database, we examined all non-obstetric patients receiving 2 interventions: preoperative intravenous iron for pre-optimisation of anaemia and/or intraoperative cell salvage (2015-18). We evaluated the resource impact on these 2 interventions for 2018: administration/staffing/disposable costs vs the NHS tariff for treatment of iron deficiency anaemia (SA04) & savings of allogeneic blood (£ 170/unit). Business analyst data for 5 months of the preoperative iv iron service was evaluated.

Results: IOCS (2015 vs 2018): No. of cases for non-obstetric patients: 237 to 551. Collection only: 8% to 32%, 12 L to 16.3 L per annum reinfused. In 2018 the average IOCS volume was 436 mLs for 372 patients, preventing a drop of Hb between 10-15 g/L. Allogeneic saving in 2018 (equivalent to 1/3rd of autologous reinfused, as lower transfusion trigger threshold): £ 33,500. IOCS disposables: £ 38,000.

Patients receiving preoperative iv iron (2015 vs 2018): 93 to 237. Average pre iron Hb 104 g/L, ferritin 37 mcg/L, and postoperative Hb 99 g/L. 11/237 in 2018 required a transfusion.

Income minus costs over a 5-month period for the iv iron service was £ 16,900.

Conclusions: The blood conservation practitioner has been a vital role in ensuring the success of our PBM service. Improvements were reflected in a £132,000 saving of surgical blood usage in 2016/17. Indirect savings may also arise from reduced length of stay (LOS); in a cohort of 900 orthopaedic patients at our hospital in 2017 average LOS in patients not requiring an allogeneic blood transfusion was 6 days compared to 15 days in those that did. Initial set up of IOCS collection only is increasingly employed to reduce disposable costs. We continue to work with wider services to improve early identification of preoperative anaemia to prevent delay to surgery and optimise postoperative PBM measures.

REFERENCE
Patient blood management (PBM) in England – 4 years on

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Introduction: Patient blood management (PBM) is a multidisciplinary, evidence-based approach to optimising the care of patients who might need a blood transfusion. PBM was launched in England in 2014. In November 2018 NHS Trusts were asked to complete a third survey to demonstrate success with implementation of PBM and to identify gaps that may require further support.

Methods: The survey was implemented using online methodology (SnapSurveys©). The data was analysed in the same system.

Results: A total of 111/147 (76%) eligible NHS Trusts responded. A lower response rate from the 2013 (97%) and 2015 (91%) surveys. 98% of responders have at least one transfusion practitioner (TP) in post with education being their top priority, followed by incident investigations and competency assessments. Implementing PBM initiatives were a low priority for TPs with a lack of TP time expressed as one of the barriers (23%). Further barriers include; lack of funding (24%) and lack of engagement from clinical colleagues (26%). 79% of Trusts had policies linked to the National Institute of Health and Care Excellence (NICE) quality standards (QS) in blood transfusion. Greatest compliance demonstrated with QS 2, use of tranexamic acid (64.7%) with least compliance with QS1, post-operative use of iron supplementation, (27%). Significant success demonstrated with patient involvement in the decision to transfuse, 60% from 20% in 2015 and identification and correction of underlying anaemia prior to transfusion, 45.5% from 32% in 2015. Providing PBM education has fallen 5% from 2015.

Conclusion: There continues to be success with implementing specific areas of PBM in England since the 2015 survey. However, further support is required to overcome the main barriers for implementation, compliance with NICE QS and strengthening PBM education for clinical staff.
Implementation of “Choosing Wisely” campaign in Norway: Transfusion medicine recommendations from the Norwegian Patient Blood Management (PBM) working group

National Patient Blood Management (PBM) working group, Norway

Introduction: “Choosing Wisely” is an international medical campaign that aims to reduce inappropriate use of diagnostic tests, treatments and procedures. The campaign started in the United States in 2012, and it has now been implemented in at least twelve countries worldwide. The Norwegian Medical Association launched “Choosing Wisely” in Norway in 2018, and more than ten medical specialties have elaborated national recommendations. The patients are encouraged to actively participate in the decision-making, including discussing with the medical staff regarding potential treatment alternatives, benefits and risks related to the therapy. The main principles for the “Choosing Wisely” campaign are in great accordance to the general PBM principles in transfusion medicine.

Methods: The national PBM group elaborated recommendations on transfusion medicine and submitted them for revision and comments to colleagues in transfusion medicine and other relevant medical specialties such as Haematology, Surgery, Oncology, Obstetrics, Anaesthesiology and Internal Medicine. Each recommendation included a short explanatory text and a reference list. The PBM group produced teaching material to facilitate the implementation of the recommendations in transfusion medicine. Posters with suggestions in vignette form were provided by the campaign organizers to be displayed at the local hospitals. The recommendations were presented at local “Choosing Wisely” meetings at Norwegian hospitals arranged to promote the campaign.

Results: The following six recommendations were defined: 1. Single blood unit policy should be adopted in haemodynamically stable, non-bleeding patients. 2. The adequate treatment for iron deficiency anaemia in haemodynamically stable patients is iron therapy, and not blood transfusion. 3. Avoid blood sampling for cross-match if blood transfusion is probably not needed. 4. In non-emergency situations, the appropriate treatment for reversal of Vit. K-antagonists is Vit. K supplementation rather than plasma or prothrombin complex. 5. Avoid prophylactic platelet transfusion in haemodynamically stable, non-bleeding patients with platelet count >10x10e9/L. 6. A balanced transfusion protocol should be initiated as soon as possible in patients with life-threatening bleeding.

Conclusion: A collaborative effort to establish recommendations for best transfusion practice as in the “Choosing Wisely” campaign is beneficial. Hospitals should promote the implementations of the national guidelines. Monitoring the effect of the recommendations in the next years is necessary to measuring the impact of the campaign.
P21

Severely anaemic patient refusing blood transfusion from religious reasons – the role of PBM

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Introduction: Even with the numerous studies underlining the transfusion-related risks, transfusion of allogenic red blood cells (RBC’s) still remains standard treatment for acutely severely anaemic patients. Those who refuse the treatment despite their life-threatening condition are often challenging. These patients have legal agency, while their physicians have moral and legal duty to treat them according to the best of their knowledge and abilities. Recombinant human erythropoietin (EPO) enhances endogenous erythropoiesis in the bone marrow. EPO and intravenous iron provide an alternative treatment to RBC transfusion.

Methods: We present a case of 59-year old female patient transferred to our centre from a regional hospital with subacute cholecystitis, with concurrent MSCT finding of hepatosplenomegaly, ascites and post-ischaemic spleen lesions, and laboratory finding of pancytopenia. The patient is Jehovah’s Witness and refuses blood transfusion, and potentially surgical patient.

Results: Patient’s medical history includes T- prolymphocytic leukaemia, now in remission, and her current pancytopenia is thought to be either the consequence of infection, or a side-effect of her past chemotherapy. During hospitalization, fully aware that it presents a serious threat to her life, she continually refused RBC transfusion. During that time, we monitored her red blood count, with lowest values of Hb 3.3 g/dL. As only alternative treatment, we treated her with EPO injections. Even though her cholecystitis resolved with conservative treatment, she still needed surgery for splenomegaly. Multidisciplinary team of haematologist, surgeon and anaesthesiologist decided to postpone the surgery until her anaemia was resolved. She was discharged from the hospital but continued to receive EPO by patronage nurse, as well as iron and vitamin B12 infusions through outpatient clinic, where her blood count was regularly checked. By her surgery 6 months later, her RBC profile was optimised and the splenectomy went through uneventfully, without the need for transfusion.

Conclusion: This case shows that, even in the case of severe acute anaemia, with continuous monitoring, interdisciplinary cooperation, strong health care system on all levels and well-developed patient blood management (PBM) program it is possible to safely avoid blood transfusion and respect the patient’s religious beliefs.
Bloodless obstetric surgery in University of Calabar Teaching Hospital

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Introduction: Bloodless care is often thought to be impossible in a low-resource setting, especially in obstetrics. Cases done in the past one year in our centre proves otherwise.

Methods: Data was collected prospectively from all obstetric patients referred to the Bloodless Surgery Programme in University of Calabar Teaching Hospital from January 2018 to December 2018 in a purpose-designed proforma. Demographic data, diagnosis and indication for surgery, pre-op haemoglobin, type of surgery done, category of surgeon, blood conservation techniques employed, SaO2 at end of surgery, post-op haemoglobin, haematological intervention, length of hospital stay, wound complications and any other complications, were entered in Excel spreadsheet and analysed.

Results: Eight obstetric patients were referred to the Bloodless Surgery Programme with 7 different diagnoses and indications for surgery including placenta praevia type 3 with ante-partum haemorrhage, cephalopelvic disproportion, prolonged labour with multiple uterine fibroids, post-date macrosomia, foetal congenital renal cyst, twin gestation and previous caesarean section. Pre-op haemoglobin ranged from 9.7-12.7 g/dL (mean 11.3 g/dL). All 8 had caesarean section, 2 as emergency and 6 as elective, and one elective case also had bilateral tubal ligation. Two surgeries were done by consultants, 6 by residents. All 8 patients received tranexamic acid and vitamin K at surgery and 1 patient also received intravenous colloid infusion. SaO2 at end of surgery ranged from 96-99%. Post-op haemoglobin at day 3 ranged from 6.3-13.5 g/dL (mean 10.05 g/dL). One patient received intravenous iron and erythropoietin. Length of hospital stay was 3-8 days (median 4 days). Haemoglobin at discharge ranged from 8.3-13.5 g/dL (mean 10.3 g/dL). There was no wound complication and no other complications noted 30 days after surgery.

Conclusion: Bloodless surgery is safer surgery even in a resource-poor setting. Infectious hazards of blood transfusion are completely avoided. Adverse outcomes of blood transfusion such as immunomodulation and hypoxia from storage lesions are also avoided. A multidisciplinary approach following a protocol and blood conservation techniques tailored to the individual patient make for best results.
Anaemia Effects and Management

P23

Iron deficiency alters synaptic integrity in the substantia nigra in the mouse brain

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Introduction: Non-haematological effects of iron deficiency (ID) include neural manifestations of fatigue, ‘brain fog’ and restless leg syndrome. Specific areas of the brain, such as the substantia nigra which is important for movement, contain high concentrations of iron and may therefore be implicated in the pathogenesis of neurological complications of ID. Our aim was to assess the effects of ID on synaptic integrity in the substantia nigra and motor fatigue.

Methods: In a validated animal model, C57/Bl6 mice were trained to run on a treadmill to exhaustion (starting speed 13 m/min, increasing 2 m/min every 5 min). 3 groups were compared:

- Control (normal diet: n=10; 50-58 ppm total iron)
- Iron Deficient (ID: n=20; 2-6 ppm total iron)
- ID treated with intravenous (IV) iron (IR: n=10; IV iron carboxymaltose 15 mg/kg)

At six weeks the ID groups became anaemic (Hb <136 g/L) and 10 received a single tail vein iron carboxymaltose (15 mg/kg) infusion (IR group). The final exercise comparison was performed 72 hours later and cryostat sections immunolabelled for pre- (Synaptophysin) and post- (PSD95) synaptic markers were assessed.

Results: Exercise capacity was reduced by 30-40% with ID (p<0.05) however this returned to normal following the iron infusion in the IR group (p<0.05).

Synaptophysin (pre-synaptic marker) in the substantia nigra was significantly lower in ID mice compared with control mice (p<0.001). PSD95 (post-synaptic marker) was also significantly lower in ID mice compared with control mice (p<0.001). Both markers were significantly and positively correlated with the time to exhaustion (p=0.001 for Synaptophysin, p=0.005 for PSD95). However, neither Synaptophysin nor PSD95 correlated with haemoglobin levels (p=0.132).

Following iron infusion, both markers were partially restored to normal levels (p=0.03 for Synaptophysin, p=0.006 for PSD95).

Conclusion: ID negatively impacts exercise capacity and this was associated with reduced synaptic markers in the substantia nigra, indicating a relationship between ID, synaptic density in the substantia nigra and fatigue.
P24

Tired of brain fog? Symptoms of patients self-referred for an iron infusion

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Introduction: Iron deficiency is common and for patients where oral iron has failed or is not tolerated intravenous iron infusions is standard of care. Data on patient symptoms are derived from clinical patients and clinical trials. These may not reflect ‘real world’ problems and symptoms from ‘normal’ individuals (without concurrent illness). We wished to assess causality and symptoms of iron deficiency from a self-referred patient population.

Methods: Data was audited from patients undergoing treatment at one central London outpatient clinic. Data included simple demographics, risk factors, presenting symptoms, blood results before and after intravenous iron infusion. All patients were treated with a dosage of 20 mg/kg of intravenous iron preparations.

Results:
DEMOGRAPHICS: 232 Patients were given an iron infusion. 218 were female. The median age was 38 (IQR 12.5). All patients self-referred. Common risk factors were; vegetarian diet (39%), heavy menstrual bleeding (38%) recent pregnancy (26%), the remainder were IBD, recent surgery etc.,
SYMPTOMS: The five most common symptoms after fatigue (98%) were; brain fog (55%), shortness of breath (51%), hair loss (43%), restless legs (40%) and heart palpitations (38%). Pica was present in 16% and associated with a significantly lower baseline ferritin (average 8 mcg/L). Average duration of symptoms was 10 months and most (83%) had been taking oral iron.
LAB VALUES: Average baseline Hb was 121 g/L and average baseline Ferritin 15 mcg/L. Median treatment dose was 1200 mg (range 500-2000 mg). There were no cases of anaphylaxis, three mild cases of urticaria which resolved with hydrocortisone IV and 14 patients had a flu-like response in the following week. At follow up (6-8 weeks) average Hb was 134 g/L and average ferritin was 223 mcg/L.

Conclusions: Vegetarians, those with heavy menstrual bleeding and recent pregnancy should be considered high risk for iron deficiency and questioned for the top 5 symptoms of; brain fog, breathlessness, hair loss, restless legs or palpitations. Intravenous iron is an effective treatment.
First trimester haemoglobin and maternal morbidity: a prospective cohort study with multivariable analysis

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Introduction: Maternal screening for anaemia in the first trimester using haemoglobin testing lacks a prognostic basis for improving maternal outcomes. The objective of this work was to explore the relationship between first trimester haemoglobin and maternal morbidity at birth in a prospective cohort study.

Methods: We used first trimester haemoglobin values collected as baseline data from women participating in a randomised trial to conduct multilevel and linear regression analyses to analyse the relationship between haemoglobin and maternal morbidity. Maternal morbidity was defined in three ways: post-delivery haemoglobin, blood loss at delivery and length of hospital stay, with separate models developed for each outcome. Causal pathway diagrams developed with an expert multidisciplinary panel were used to identify clinically relevant confounders, all of which were included in the final models. The regression analyses made adjustments for the following confounding variables: age, ethnicity, parity, BMI, placentation, pre-eclampsia, and aspirin intake. All analyses were undertaken using a complete case record; sensitivity analyses using multiple imputation strategies for missing data were conducted.

Results: If first trimester haemoglobin increased by 1g/L the post-delivery haemoglobin increased by 0.38 g/L (95% CI 0.28 to 0.48, p value: <0.000), after adjustment for well recognised confounders among women treated in accordance with national guidelines for anaemia prevention. Length of hospital stay and blood loss at delivery were not associated with first trimester haemoglobin.

Conclusion: Prevention and prompt treatment of maternal anaemia if diagnosed in the first trimester remains an antenatal priority.
Iatrogenic anaemia in major cancer surgery

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Introduction: Patients undergoing major cancer surgery are susceptible to perioperative anaemia due to their disease, surgical blood loss and iatrogenic anaemia by the volume of blood taken for investigations and diagnostic testing. Consequently, they often require blood transfusion, with its consequent physiological and cost implications. We aim to investigate the volume of blood sampled from patients undergoing major surgery for cancer, at a tertiary cancer centre in the UK.

Methods: Patients who underwent major cancer surgery, with planned ICU admission, between April 2017 and September 2018 were identified. The number of blood samples taken from the decision to operate until discharge, in addition to surgical blood loss and blood product usage was recorded. Blood bottles were assumed to be filled in accordance with laboratory standards.

Results: 493 patients were identified and analysed, 200 males and 293 females, with a mean age of 61 years. Blood sampling accounted for 26.4% of all blood lost during the perioperative journey.

Conclusion: This is the first large scale study investigating perioperative blood sampling in the cancer population, following on from a small pilot study of 86 patients undertaken at the same institution in 2016. We continue to take a substantial volume of blood during the perioperative journey. Comparison of our data with the 2016 data allows interesting conclusions to be drawn. Whilst the daily volume of blood sampled from each patient has remained stable (a 2.23% increase compared to 2016), with similar contributions of each blood testing modality, patient length of stay has fallen by 47.82%, with a 46.47% reduction in mean total blood sampled from each patient. Additionally, blood product usage has significantly fallen since 2016, with a 77.31% reduction in packed red blood cell usage.

We can attribute these positive changes to improvements in multiple elements of the perioperative care pathway at our centre, including enhanced recovery programmes, minimally invasive surgical techniques, iron infusion services and more restrictive blood product usage policies.

Importantly, there is still room for improvement, with the potential to implement more advanced patient blood management strategies, including closed loop blood gas sampling systems, real time non-invasive multi-wavelength pulse co-oximetry haemoglobin measurement, and the adoption of paediatric blood bottles in the adult population.
Anaemia and blood transfusion in 2 stage spinal surgery

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Introduction: Pre-operative anaemia is a recognised risk factor for adverse outcomes in major surgery. Elective surgery is postponed when anaemia is detected pre-operatively to allow treatment. For patients undergoing multi-stage surgery, anaemia often arises following the first stage due to blood loss. However, the prevalence and consequences (particularly blood transfusion) are not known, and surgery is rarely cancelled due to this anaemia.

Methods: A retrospective audit of patients (adult and paediatric) undergoing 2-stage spinal surgery during the same hospital admission between January 2016 to May 2018 was performed. Anaemia was defined as Hb <120 g/L for females and <130 g/L for males of all ages.

Results: 180 patients had 2-stage surgery during the time period analysed, of which 115 were less than 18 years of age (range 11-17 years), and 65 were adult.

Paediatrics
7.8% of patients were anaemic on pre-operative testing, rising to 67.3% pre-second stage surgery. 85.6% of patients were anaemic after the second stage and all patients were anaemic at discharge. 36.5% of patients received a blood transfusion. Of these transfusions, 97% were administered during or after stage 2.

Adults
11.3% of patients were anaemic pre-operatively, rising to 70% pre-second stage surgery. On day 1 post second stage, all patients were anaemic. 30.8% of adult patients received a blood transfusion – 90% of patients transfused received this blood during or after stage 2.

Conclusion: Improvements have been made in the detection and treatment of pre-operative anaemia. Anaemia treatment prior to the second stage (usually 1 week after the first stage) remains an unmet need and is associated with increased transfusion rates. The use of intravenous iron between stages in these patients may be of benefit. This data also shows that anaemia at discharge is prevalent and could easily be addressed with the prescription of post-operative oral iron when discharged from hospital.
P28

The first study of pre-operative anaemia in patients presenting for major surgery to a tertiary hospital in the West of Ireland

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Introduction: Preoperative anaemia increases the risk of adverse outcomes postoperatively. The international consensus statement released by Munoz et al in 2016 made recommendations with regard to the investigation and treatment of preoperative anaemia. The aim of this study was to identify the prevalence of anaemia in patients presenting to our centre for elective major surgery and to examine the association of anaemia with increased morbidity and mortality. This is the first study examining preoperative anaemia in a tertiary centre in the West of Ireland.

Methods: A retrospective review of theatre and electronic records was performed on 377 patients, 18 years and older, who underwent major elective surgery between January and June 2018. The outcome measures were number of red cell transfusions, length of post-operative stay and in hospital mortality.

Results: Age of patients ranged from 28 to 92 years with a mean age of 64 years. Surgical categories included were cardiothoracic surgery (30%), gynaecology (20%), general surgery (19%), urology (15%), orthopaedics (10%), plastics (3%) and ENT (3%). 43% of the cohort were anaemic with a pre-operative haemoglobin of <13 g/dL. The prevalence of anaemia was higher in women (52%) than men (36%). Of the patients with preoperative anaemia (n=161) who underwent elective major surgery, 39% were transfused. Of the patients who did not have anaemia (n=216), 16% were transfused. General surgery had the highest prevalence of patients with anaemia (56%). The overall mean length of postoperative stay was 8.6 days. Mean length of stay was higher in the anaemic group (10.3 vs 7.5 days). A total of 9 patients died during their hospital stay (2.3%). 44% of the group who died were anaemic preoperatively.

Conclusion: A large proportion of patients presenting for elective major surgery have preoperative anaemia. Preoperative anaemia is related to the increased need for blood transfusion and increased length of postoperative stay. This supports the need for increased optimisation of haemoglobin concentration prior to elective surgery.
P29

Calculation of risks associated with preoperative anaemia and the health-economic footprint of patient blood management (PBM)

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Introduction: Erythrocyte concentrate (EC) transfusions during surgeries have been shown to lead to increased risks, including increased mortality, morbidity and prolonged length of hospital stay. Compared to other EU countries, Germany has a high rate of EC blood donations and usage. Final goal of PBM programs is to optimize use of blood products, among others by management of preoperative anaemia. The aim of this assessment was to quantify the risks associated with preoperative anaemia due to iron deficiency and the potential health economic benefits of PBM for elective surgeries.

Methods: A 10% random sample of the complete survey from the German DRG statistics was used (approx. 1.8 mill. patients; Source: RDC of the Federal Statistical Office and Statistical Offices of the Länder. DRG-Statistik 2015). Calculations focused on elective operations and iron deficiency anaemia (defined as ICD-10-GM codes D50.8 and D50.9). Footprint calculations were performed under the assumption that 50% of the patients could be effectively treated by preoperative anaemia management prior to elective surgery. The value of statistical life (VSL, €2.996 mill.) and statistical day (VSD, €101.74 day) was used.

Results:
We show that preoperative iron deficiency anaemia prior to elective surgeries leads to:
- Increased transfusion rates (relative risk (RR): 5.031; 95% CI (4.929; 5.137)),
- increased length of stay and hospital costs,
- increased mortality (RR: 3.633; 95% CI (3.404; 3.878));

The effects of PBM implementation were calculated:

<table>
<thead>
<tr>
<th>Category</th>
<th>Result</th>
<th>Multiplication factor</th>
<th>Value for footprint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidable direct hospital costs</td>
<td>€479 mill.</td>
<td></td>
<td>€0.479 x 10^2 mill.</td>
</tr>
<tr>
<td>Avoidable hospital days</td>
<td>528,531</td>
<td>€101.74 (=VSD)</td>
<td>€0.054 x 10^2 mill.</td>
</tr>
<tr>
<td>Avoidable deaths</td>
<td>2,752</td>
<td>€2.996 mill. (=VSL)</td>
<td>€8.246 x 10^2 mill.</td>
</tr>
<tr>
<td>Therapy and treatment costs</td>
<td>€176.68</td>
<td>58,884 (patients)</td>
<td>€0.010 x 10^2 mill.</td>
</tr>
</tbody>
</table>

The benefit for society (health economic footprint) of implementing PBM would amount to:
Avoidable cost – treatment cost = (€0.479 + €0.054 + €8.246 – €0.010) x 10^2 mill. = €8.769 x 10^2 mill.

Conclusion: The dataset shows that implementing preoperative anaemia management in the sense of PBM would lead to prevention of unnecessary deaths, expenditures, overuse of hospital structure, and to better outcomes for patients, resulting in a health-economic benefit of €8.769 billion.
P30

The UK cardiac and vascular surgery interventional anaemia response (CAVIAR) study

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Introduction: Anaemia is associated with worse outcomes after cardiac surgery, including increased mortality and hospital stay. However, the impact of identification and treatment of anaemia with intravenous iron as part of routine health service management is unknown.

Methods: We performed a feasibility observational trial in 11 UK hospitals. This trial took place during the introduction of active anaemia management into routine NHS practice. We included consecutive subjects with and without anaemia undergoing cardiac surgery and compared them with subjects with iron deficiency anaemia treated pre-operatively with intravenous iron isomaltoside as part of their routine care. The primary outcome was the change in Hb in treated patients; secondary outcomes included blood transfusion and hospital stay.

Results: We recruited 228 subjects over 2 years; 92 patients were not anaemic, 72 were anaemic but not treated & 64 received intravenous iron pre-operatively; 7/11 hospitals successfully set up anaemia clinics over the study period. Blood transfusion rates in the study centres varied from 30 to 65%. Patients in the treated anaemia group were at higher risk, were more likely to have chronic kidney disease and were more severely anaemic than the non-treated group. The mean (95% CI) change in Hb was +8.4 (5.0 to 11.8) g/L between treatment and surgery, p=0.0005. More patients and more units of blood were transfused in the treated anaemia group than the other groups (Table 1).

Table 1: CAVIAR study outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Non-anaemic (n=92)</th>
<th>Anaemic not treated (n=72)</th>
<th>Anaemic treated (n=64)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfused</td>
<td>31 (34%)</td>
<td>35 (47%)</td>
<td>40 (63%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Units transfused</td>
<td>0 (0-1)</td>
<td>0 (0-2)</td>
<td>1 (0-2)</td>
<td>0.009</td>
</tr>
<tr>
<td>Died</td>
<td>4 (4%)</td>
<td>3 (4%)</td>
<td>2 (3%)</td>
<td>0.922</td>
</tr>
<tr>
<td>ITU stay, d</td>
<td>2 (1-4)</td>
<td>2 (1-4)</td>
<td>3 (1-5)</td>
<td>0.304</td>
</tr>
<tr>
<td>Hospital stay, d</td>
<td>9 (7-14)</td>
<td>9 (7-16)</td>
<td>10 (7-15)</td>
<td>0.477</td>
</tr>
</tbody>
</table>

Conclusion: Pre-operative anaemia clinics were feasible and selected higher risk patients to receive pre-operative intravenous iron. Intravenous iron increased Hb concentration in cardiac surgical patients pre-operatively. However, due to selection bias, adequate effect comparison was not possible, emphasizing the need for a properly powered randomised controlled trial, which is now underway (https://www.itacs.org.au).
P31

Tearing your hair out about screening for anaemia

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Introduction: Anaemia is common in women, but validated screening tools have not been incorporated into clinical practice. We have previously validated a risk questionnaire for anaemia. Separately a large survey identified the top symptoms reported for iron deficiency. We wished to assess whether a combined anaemia prediction tool could be used to screen for anaemia in the general population.

Methods: 400 healthy female volunteers were asked to participate and gave consent (UCL Ethics Approval ID 12477/001). The anaemia prediction tool, comprised 11 questions about risks factors and symptoms of anaemia. Haemoglobin was estimated using the Masimo RAD-67 (SpHb). Prevalence of anaemia was compared between groups of; no risk factors or symptoms, risk factors alone, symptoms alone and both risk factors and symptoms.

Results: Median age was 36 yrs (IQR 28yrs-46yrs). Prevalence SpHb <120 g/dL was 10% and SpHb <130 g/dL 33%. In those with no risk factors or symptoms average SpHb was 132.3 g/dL and 13% were anaemic. Risk factors: 88% had risk factors for anaemia; 41% history of iron deficiency, 30% heavy menstrual bleeding, 20% past obstetric bleeding, 17% blood donors, 15% vegetarian or vegan. Average SpHb was 132.7 g/dL (SD+/−11.7) and 11% were anaemic (compared to those with no risk factors or anaemia p=0.12) The prevalence of anaemia did not increase with more than one risk factor.

Symptoms: 73% had symptoms of anaemia of whom 37% hairloss, 33% Brainfog, 28% Restless legs, 27% shortness of breath, 27% palpitations and 5% pica. Average SpHb was 132 g/dL (SD+/−10.8) and 10.6% were anaemic (compared to those with no symptoms or anaemia p=0.02)

55% had both risk factors and symptoms Sphb was 132 g/dL (SD+/−12.2) and 12.6% were anaemic (compared to those with no risk factors or anaemia p=0.06)

Analysis of anaemic (<120 g/dL) and non-anaemic groups (>120 g/dL) showed that combination of heavy menstrual bleeding risk factor and hairloss symptom was the only combination associated with anaemia (chi squared p-value 0.02) (14% of people average SpHb 136 g/dL (SD+/−11.4)). ‘Pica’ also had the highest specificity with 96.1% having anaemia.

Conclusions: Following preliminary work, the combined anaemia prediction tool, was unable to detect anaemia in the general population.
Preoperative screening and treatment of iron-deficiency anaemia - Implementing at a large tertiary referral hospital

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Introduction: Anaemia due to iron deficiency (IDA) contributes to peri-operative morbidity. A pilot study at a tertiary referral hospital has indicated that pre-operative screening and treatment of IDA reduced hospital length-of-stay, transfusion rate and volume.

Methods: The blood bank implemented a preoperative IDA screening and treatment program in two surgical departments to evaluate the feasibility of such a program. A simple algorithm using haemoglobin concentration (hgb) and transferrin saturation (tSat) for diagnosis was applied:

- Hgb. and tSat at presurgical consult.
- Evaluation by blood bank doctor or nurse specialist.
- I.v. iron treatment in outpatient clinic by nurse specialists.

Based on data from the pilot study we expected to screen 1100 patients and treat 300 IDA patients with iv. iron over a period of one year.

Results (preliminary): Over a 3-months period we screened 305 patients, 88 (29%) lacked relevant samples. Of the remaining 217 patients, 75 (35%) were anaemic and of these 51 (68%) had IDA - 39 (76%) of IDA patients received an iron-infusion. 7 of 12 IDA patients not receiving an iron infusion were scheduled for surgery within four days from the presurgical consult.

Conclusion: Based on preliminary data it is feasible to perform preoperative anaemia screening and treatment on a larger scale. The major challenges are the logistics of blood sampling and the narrow time window from presurgical consult to surgery in time-critical disease.
The earlier, the better: a real-world experience of peri-operative anaemia management from Royal United Hospital, Bath, UK

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Introduction: The 2015 NG24 NICE Guidance recommends IV iron as an alternative to blood for peri-operative anaemia management. Oncology/haematology or surgical patients attend the patient blood management (PBM) service at Royal United Hospital, Bath, UK. Monofer (iron isomaltoside 1000, 10%), an IV iron allowing high single doses of ≤20 mg/kg, is used in this service. This study evaluated our PBM service.

Methods: Notes of 70 randomly selected patients from all specialities that attended the service between Apr’17 – Apr’18 were reviewed, and data on haematinics, length of hospital stay (LOS) and blood transfusions was analysed. The impact of IV iron clinic was evaluated by comparing the above parameters in patients undergoing colorectal or orthopaedic surgery, pre- (Feb’11–Feb’12) and post- (Apr’17–Apr’18) the anaemia clinic introduction. In this sub-analysis, patients were divided into three groups; Group I: non-anaemic patients (n=243), Group II: anaemic patients not receiving IV iron (n=44) and Group III: anaemic patients receiving IV iron (n=40).

Results: Mean patient age was 71 years and weight 75 kg. All patients received their prescribed dose (mean 1400 mg, range 500-2000 mg) in one appointment, and no patients experienced adverse drug reactions. Mean pre-infusion Hb was 99 g/L and increased to 118 g/L post-infusion. Among surgical patients with available data, IV iron was administered on average 49 days before surgery; 27 patients received iron <30 and 27 ≥30 days before surgery. In the <30 vs. ≥30-day groups, mean pre-infusion Hb was 95 g/L vs. 101 g/L, post-infusion Hb 106 g/L vs. 125 g/L (increase from baseline 12 g/L vs. 25 g/L), post-surgery Hb 94 g/L vs. 101 g/L, discharge Hb 101 g/L vs. 105 g/L, proportion of transfused patients 19% vs. 7%, blood units/patient 0.3 vs. 0.07 and LOS 6.2 vs. 7.2 days. In the sub-analysis, which evaluated the impact of IV iron clinic, mean pre-operative Hb was 135 g/L (range 116-166 g/L) in Group I, 106 g/L (82-115 g/L) in Group II and 103 g/L (76-113 g/L) in Group III. All patients in Group III received their prescribed iron dose in one appointment, resulting in an increase of mean Hb by 17 g/L pre-operatively. Mean Hb dropped post-surgery in Group I to 109 g/L (82-161 g/L), Group II 93 g/L (70-116 g/L) and Group III 98 g/L (72-142 g/L). 12% of patients in Group I, 57% in Group II and 18% in Group III were transfused. Mean LOS stay was 6.6, 8.7 and 7.1 days in Groups I, II and III, respectively.

Conclusion: Pre-operative administration of IV iron resulted in substantial Hb increases. The introduction of the anaemia management clinic has reduced the proportion of patients being transfused and this coincided with a shorter LOS. Early diagnosis of anaemia and administration of IV iron could result in better outcomes.
Assessing iron deficiency anaemia before surgery: Can we do better?

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**Introduction:** Iron deficiency anaemia (IDA) is one of the most common causes of chronic anaemia globally (1). To confirm iron deficiency anaemia in patients with low haemoglobin (Hb) levels, it is also recommended that ferritin, Vit B12, folate and CRP levels are tested (2). Very little data exist to confirm the prevalence of iron deficiency in orthopaedic surgical patients in Australia (3).

**Methods:** This retrospective audit aimed to assess the prevalence of different laboratory tests. All orthopaedic surgical patients during 2016 (n=1714) were assessed. Data collected from an electronic patient record system was manually imported into a password protected Microsoft Excel spreadsheet. Relevant ethics approvals were received.

**Results:** In 2016, 1714 patients underwent orthopaedic procedures (760 emergency, 954 elective). In the elective group (n=954) 685 patients had an Hb test conducted within 12 months before their surgery. By using the WHO (World Health Organisation) definition for anaemia (females ≤120 g/L, male ≤130 g/L), we identified 56/14.93% female (n=375) and 39/12.58% male (n=310) patients as anaemic, in total 95/13.87% (1). 8 patients had valid ferritin tests done, of whom 3 were >100 ug/L, 4 were 30-100 ug/L, 1 was <30 ug/L and of whom only 1 patient received Vit B12, folate and CRP tests.

**Conclusions:** Of the 954 elective orthopaedic procedures at the RBWH in 2016, 685 patients had valid Hb tests. At least 95 (13.87%) of these patients were anaemic before surgery and only one of these anaemic patients received the recommended ferritin, Vit B12, folate and CRP tests. We hope to use this valuable information to advocate for the full panel of appropriate tests for all anaemic surgical patients at the RBWH in future.

**REFERENCES**
P35

Abstract withdrawn
P36

Optimising anaemia with intravenous iron before major surgery

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On behalf of Preoperative Assessment Clinic, Department of Anaesthesia, Royal Victoria Infirmary, Newcastle-upon-Tyne, UK

Introduction: In the UK, NICE Quality Standard ‘Diagnosis and Treatment of Anaemia’, 2017, states that patients with iron deficiency anaemia that are having surgery should be offered iron before and after surgery’. Intravenous (IV) iron can be used to increase iron stores and haemoglobin concentration in patients with hepcidin mediated anaemia and where oral iron does not have time or ability to be absorbed and replenish stores. With this in mind, this quality improvement project aimed to improve patient blood management.

Method: We used 3 cycles of audit of matched oesophagogastric cancer surgery patients to determine the effect of introduction and modification of a preoperative anaemia pathway in high risk patients presenting with a high incidence of anaemia.

Cycle 1: 2014: baseline data collected and initial anaemia management pathway introduced utilising ferric carboxymaltose IV iron treatment.
Cycle 2: 2017: data collection and production of comprehensive perioperative guideline and optimisation of IV dosing with change to Iron Isomaltoside prescription.
Cycle 3: 2018: data confirms sustained improvement. Point of care Hb testing started.

Results: Increased Hb and decreased range: median (range) 125 (77-131) 2014 to 131 (95-174) 2018.
Severe anaemia (Hb <100 g/L) decreased from 10.2% (2014) to 1.6% and 1.8% (2017, 18)

<table>
<thead>
<tr>
<th>Haemoglobin measured before surgery (g/L)</th>
<th>2014</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50-59</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>60-69</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>70-79</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>80-89</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>90-99</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100-109</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>110-119</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>120-129</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>130-139</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>140-149</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>150-159</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>160-169</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: Implementation of this pathway has improved preoperative haemoglobin and reduced the number of post-operative blood transfusions in this high risk surgical group.
Scottish consensus on the management of preoperative anaemia

S. McKinlay¹ & C. Beecroft²
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On behalf of the Scottish Perioperative Medicine Leads Anaemia Workstream

Introduction: Preoperative anaemia is associated with increased perioperative morbidity and mortality, both as a result of the anaemia itself and the resultant blood transfusion (1). It should be seen as a modifiable preoperative risk factor. The Royal College of Anaesthetists has developed a collaborative programme for the delivery of perioperative care across the UK, which aims to deliver more efficient healthcare and better outcomes for patients from contemplation of surgery until full recovery (2). Detection and management of preoperative anaemia is one of the programme’s priorities.

Methods: To support Scottish hospitals in developing preoperative anaemia pathways to reduce the number of patients presenting for elective and urgent surgery with untreated anaemia, an evidence-based guideline for the management of preoperative anaemia was developed.

Results: A consensus guideline was agreed for both the diagnosis and management of preoperative anaemia. The consensus was launched to all Scottish hospitals in October 2018 at an event with the support of the Scottish Government Access Collaborative. A national audit tool and database has been developed, again supported by the Scottish Government. Scotland will become the first country in the UK to provide national data on the effectiveness of local pathways for the management of preoperative anaemia.

Conclusion: We hope that Scotland will become the leading region in the UK for the detection and management of preoperative anaemia, with an associated reduction in anaemia-related complications and blood transfusion in the perioperative period.

REFERENCES
P38

The impact of the international consensus on pre-operative management of anaemia and iron deficiency in an urban colorectal surgical population in the United Kingdom

C. Lees, R. West, J. Williams & C. Pritchard
Buckinghamshire NHS Trust, Buckinghamshire, UK

Introduction: Pre-operative anaemia defined as Haemoglobin (Hb) <130 g/L is associated with adverse outcomes. (1) Methods to avoid unnecessary blood transfusions has been highlighted in the recent expert consensus. (2) We studied the impact of the international consensus statement on the pre-operative management of anaemia and iron deficiency in a colorectal surgical population of a hospital outside London.

Methods: This is a retrospective study of 207 patients who underwent major colorectal surgery for malignancy between January-December 2017. Each patient was seen in pre-operative clinic around 2 weeks before surgery. Pre-operative anaemia was identified and treated as per the updated local guidelines. Data collected includes patient demographics, date of pre-operative assessment and surgery, blood results including Hb and iron studies, IV iron administration, RBC transfusion and the trend in Hb.

Results: 100% of patients had their Hb tested in the pre-operative clinic. Anaemia was identified in 87 patients (42%). The mean pre-operative Hb was 115 g/L. Iron studies were appropriately investigated in 84% of the patients and 82% were identified as being absolute iron deficient. 42% of these patients were treated with IV iron infusion, 23% received oral iron and 10.3% (mean Hb 90) received RBC transfusion. Patients who were classified as mildly anaemic did not receive any treatment. Mean Hb in the anaemic patients increased by 2 g/L pre-surgery and 15.6% of patients achieved a Hb of ≥120 g/L. The average time between the administration of IV iron prior to surgery was 12 days.

Conclusions: Our study highlighted that the majority of patients classified as anaemic from the current guidelines were treated with IV iron infusion. Due to limited time we were only able to witness a small increment in Hb prior to surgery. However, the benefit of increasing iron stores pre-operatively continues into the post-operative period. (2) By using IV iron infusion we were able to minimise the use of blood transfusions in the pre-operative period. In conclusion the international consensus has had a positive impact on the way pre-operative anaemia is managed in our institution.

REFERENCES
P39

Intravenous iron infusion services in a tertiary cancer centre: a year in review

M. Evans, A. Hegarty, E. Black & R. Raobaikady
The Royal Marsden Hospital NHS Foundation Trust, London, UK

Introduction: The Royal Marsden NHS Trust is a world renowned tertiary cancer hospital. Over the last 10 years we have adapted our intravenous iron infusion service to treat iron deficiency anaemia in a complex cancer population. Over the years, advancements in research have changed guidelines in the transfusion world. Following the 2017 International consensus statement on the perioperative management of anaemia and iron deficiency, greater efforts were made to analyse our practice with a view toward quality improvement and staff education.

Method: All patients receiving intravenous iron infusions (Monofer 20 mg.kg$^{-1}$) during 2017 were analysed. Baseline iron studies, haemoglobin trends, operative data and blood transfusion requirements were recorded. This enabled characterisation of our study population and analysis of their response to iron infusion. Patients were divided into surgical and non-surgical cohorts. The surgical cohort was subdivided into those who received their iron pre-operatively and post-operatively.

Results: 198 iron infusions were administered in 2017. The mean iron study values and resultant haemoglobin trends can be seen in Table 1. Notably 82% of recorded transferrin saturations were below 16%, in line with the WHO definition of iron deficiency anaemia. Importantly there were no significant adverse effects attributed to iron infusion throughout 2017.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Number</th>
<th>Mean Ferritin (ng/mL)</th>
<th>Mean TSAT (%)</th>
<th>Mean Baseline Hb (g/L)</th>
<th>Mean 2 week Hb (g/L)</th>
<th>Mean 6 week Hb (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op infusion</td>
<td>26</td>
<td>207.58</td>
<td>11.68</td>
<td>110.35</td>
<td>96.62</td>
<td>115.60</td>
</tr>
<tr>
<td>Surgical:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-op infusion</td>
<td>42</td>
<td>111.05</td>
<td>11.63</td>
<td>103.50</td>
<td>101.45</td>
<td>116.48</td>
</tr>
<tr>
<td>Non-Surgical</td>
<td>130</td>
<td>359.32</td>
<td>10.61</td>
<td>95.16</td>
<td>101.52</td>
<td>110.48</td>
</tr>
<tr>
<td>Total</td>
<td>198</td>
<td>255.05</td>
<td>11.00</td>
<td>99.87</td>
<td>100.97</td>
<td>112.19</td>
</tr>
</tbody>
</table>

Table 1

Conclusion: Our data suggests more could be done to target the pre-operative surgical cohort. Delayed iron study reporting may hinder administration of iron in this group. We propose that to further develop our already established service, we should strive towards same day reporting of iron studies, in addition to taking baseline iron studies in non-anaemic patients, to allow an increased rate of post-operative infusion. Currently there is an ongoing business case to further expand our service with a dedicated Anaemia Clinic and Anaemia Nursing Staff. We foresee that this would not only help streamline the service, but also play a crucial role in staff education, which we believe is key for ongoing service quality improvement.
**P40**

**Peri-operative anaemia management: a real-world experience of the Intravenous (IV) Iron Service at the Surgical Day Unit, University Hospital Southampton, UK**

L. Sheppard, J. Plumb & M. Wakatsuki  
*University Hospital Southampton NHS Foundation Trust, Southampton, UK*

**Introduction:** Pre-operative anaemia is common that may result in unnecessary blood transfusion and worsen clinical outcome. The 2017 International consensus statement on the peri-operative management of anaemia and iron deficiency recommended pre-operative treatment of all surgical patients with iron deficiency anaemia (IDA), with emphasis on those patients undergoing major surgery. At University Hospital Southampton, a pre-operative anaemia clinic that accepts referrals from different surgical specialties was introduced in 2016. Monofer (iron isomaltoside 1000, 10%), an IV iron allowing high single doses of up to 20 mg of iron per kg of patient body weight, is used in this clinic. This study evaluated our IV iron service and assessed the efficacy and safety of Monofer.

**Methods:** We reviewed medical notes of 50 patients undergoing colorectal, urology, hepatopancreaticobiliary, upper gastrointestinal, orthopaedics and other subspecialties that attended the IV iron service between Jul’18-Dec’18. Data on haematinics, blood transfusion and length of hospital stay (LOS) was analysed.

**Results:** Half of our patient group (50%) administered with IV iron were scheduled to undergo colorectal surgery. Mean patient age was 66 years and mean weight was 74.7 kg. 60% of patients were female. Most patients (86%) received their prescribed dose (mean 1330 mg, range 500-2800 mg) in one appointment, and 58% of patients required >1000 mg of iron. No ADRs of hypersensitivity reported. The average time interval between IV iron infusion and the surgery was 26 days. Among surgical patients with available data, mean pre-infusion Hb was 105 g/L and rose to 117 g/L post-infusion prior to surgery, dropped to 94 g/L post-surgery, then rose to 102 g/L at hospital discharge, and reached 119 g/L post discharge at outpatient clinic. Proportion of patients with a Hb of ≥120 g/L was 4% (pre-infusion) vs. 57% (post-infusion prior to surgery) vs. 3% (post-surgery) vs. 6% (at discharge) vs. 64% (post-discharge). Among patients receiving pre-op IV iron infusion, only 2% (1/50) of them needed a blood transfusion intra/post-surgery. Average LOS was 6 days.

**Conclusion:** Treatment of anaemic patients with iron isomaltoside resulted in a substantial increase in haemoglobin, with a higher proportion of patients reached a Hb level of ≥120 g/L. Some patients remained anaemic even after IV iron treatment indicating that patients have high iron needs, and possibly required to be treated earlier in order to reach a satisfactory Hb level at the time of surgery. Only one patient required blood transfusion in this dataset highlighting effectiveness of this treatment.
The management of preoperative anaemia in cardiac surgery patients: A retrospective data analysis

C. Quarterman¹ & S. Agarwal²

¹Liverpool Heart and Chest Hospital; ²Manchester University Hospital, UK

Introduction: Cardiac surgery patients frequently require transfusion in the peri operative period, many have multiple comorbidities with existing anaemia. The treatment of preoperative anaemia is one of the tenets of Patient Blood Management however little is known about the response to iron therapy. We present the results of our clinic.

Method: The preoperative anaemia treatment clinic was set up in January 2017; patients are given one dose of iv iron (20 mg/kg) approximately 2 weeks prior to surgery if they are found to have an Hb <130 g/L in conjunction with iron deficiency (ferritin <100). Comprehensive data is collected, this data was analysed with regard to rise in Hb achieved; we aim to achieve a preoperative Hb of 130g/L or above in all patients.

Results: The data of 200 consecutive patients who were treated in the clinic was analysed. The results are shown in the table below.

<table>
<thead>
<tr>
<th>Haemoglobin after iv iron, prior to surgery,</th>
<th>ALL</th>
<th>&gt;130 g/L</th>
<th>120-130 g/L</th>
<th>&lt;120g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>n=200</td>
<td>39.5</td>
<td>35.5</td>
<td>25</td>
</tr>
<tr>
<td>Baseline Hb (mean)</td>
<td>118.4</td>
<td>123</td>
<td>118.5</td>
<td>110.2</td>
</tr>
<tr>
<td>Baseline ferritin (mean)</td>
<td>68.5</td>
<td>74</td>
<td>69</td>
<td>57.9</td>
</tr>
<tr>
<td>Rise in Hb (mean)</td>
<td>7.7</td>
<td>11</td>
<td>6.7</td>
<td>3.9</td>
</tr>
<tr>
<td>Time from Fe to Sx (days)</td>
<td>26.65</td>
<td>29.3</td>
<td>24.6</td>
<td>22.5</td>
</tr>
<tr>
<td>Transfusion (mean)</td>
<td>1.27</td>
<td>0.93</td>
<td>1.12</td>
<td>2.04</td>
</tr>
<tr>
<td>CVVH (%)</td>
<td>9.5</td>
<td>5</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>ITU LOS (days)</td>
<td>4.95</td>
<td>4.22</td>
<td>4.19</td>
<td>7.33</td>
</tr>
<tr>
<td>Discharge Hb</td>
<td>95.7</td>
<td>97.6</td>
<td>94.9</td>
<td>93.9</td>
</tr>
</tbody>
</table>

As can be seen only 39.5% of patients achieved the aim of an Hb >130 g/L. These patients had a higher baseline Hb but also had a better response to iv iron with a higher rise in the given time. These patients had a lower transfusion requirement.

Conclusion: Not all patients with iron deficiency anaemia respond adequately to iv iron, further work is required to elucidate the cause and enable practitioners to target patients appropriately.
Abstracts of the 20th Annual NATA Symposium

Poster Abstracts

P42

Optimising outpatient intravenous iron therapy and efficiency in a Day Clinical Centre. Audit of iron isomaltoside therapy in a district general hospital in Northern Ireland

A. Cullen
Craigavon Area Hospital, Portadown, Northern Ireland, UK

Introduction: Craigavon Area Hospital is part of the Southern Health and Social Care Trust that provides health and social care to over 350,000 people. Patients with iron deficiency anaemia requiring intravenous iron supplementation can be treated on an outpatient basis in the Day Clinical Centre (DCC). In July 2017 following the international consensus statement on the perioperative management of anaemia and iron deficiency, the Trust introduced iron isomaltoside (Monofer®) as its main intravenous iron. This preparation enables larger doses of iron to be prescribed. With the potential to improve treatment of iron deficiency anaemia, reduce outpatient attendances, improve convenience for patients and increase efficiency for the Trust, this audit aimed to assess the impact of the introduction of iron isomaltoside over an 18-month period (July 2017- December 2018).

Methods: Patients prescribed iron isomaltoside in the DCC were entered into a database. Prescription was based on the simplified dosing table recommended by the manufacturer. Information was gathered including age, weight, gender, haemoglobin (Hb) concentration, ferritin, transferrin saturation index (TSAT), dose of iron prescribed, requirement for a second appointment to achieve full iron repletion, post-infusion Hb and adverse drug reactions.

Results: 138 patients received intravenous iron supplementation during the 18-month period. 94 patients were female and 44 male. Pre-treatment, mean Hb was 99 g/L, mean ferritin was 50 mcg/L and mean TSAT was 14%. Mean time between intravenous iron infusion and post-infusion Hb was 49 days (2-190). Following treatment, mean Hb level increased to 117 g/L, mean ferritin to 433 mcg/L and TSAT to 30%. 110/138 (80%) of patients received their prescribed iron in one visit and of these, 61 patients received greater than 1 g. Two minor hypersensitivity drug reactions (numbness around cannula site, flushing of face, neck and arms) were noted in 154 (1.3%) administrations.

Conclusion: The ability to give higher doses of intravenous iron improved efficiency and convenience for this population of patients. 61 patient appointment slots were saved resulting in significant financial gains and allowed access to the Day Clinical Centre resource for other patients. Iron isomaltoside therapy allows optimal and convenient intravenous iron treatment for patients.
P43

Optimising iron therapy and efficiency for surgical patients in a Day Clinical Centre. Audit of iron isomaltoside therapy in preoperative patients in a district general hospital in Northern Ireland

A. Cullen
Craigavon Area Hospital, Portadown, Northern Ireland, UK

Introduction: Craigavon Area Hospital is part of the Southern Health and Social Care Trust that provides health and social care to over 350,000 people. Patients with iron deficiency anaemia requiring intravenous iron supplementation before surgery can be treated on an outpatient basis in the Day Clinical Centre (DCC). In July 2017 following the international consensus statement on the perioperative management of anaemia and iron deficiency, the Trust introduced iron isomaltoside (Monofer®). This preparation allows larger doses of iron to be delivered. With the potential to improve treatment of iron deficiency anaemia, reduce outpatient attendances, improve convenience for patients and increase efficiency for the Trust, this audit aimed to assess the impact of the introduction of iron isomaltoside over an 18-month period (July 2017-December 2018).

Methods: Preoperative patients prescribed iron isomaltoside in the DCC were entered into a database. Prescription was based on the simplified dosing table recommended by the manufacturer. Information was gathered including age, weight, gender, haemoglobin (Hb) concentration, ferritin, transferrin saturation index (TSAT), dose of iron prescribed, requirement for a second appointment to achieve full iron repletion, post-infusion Hb and adverse drug reactions.

Results: 87 patients received intravenous iron supplementation in preparation for a surgical procedure. 62 patients were female and 25 male. Pre-treatment, mean Hb was 101 g/L, mean ferritin was 60 mcg/L and mean TSAT was 12%. Mean time between intravenous iron infusion and post-infusion Hb was 45 days (2-190). Following treatment, mean Hb level increased to 118 g/L, mean ferritin to 506 mcg/L and mean TSAT to 27%. 39 patients received greater than 1 g in a single appointment. One case of extravasation occurred in 97 administrations.

Conclusion: The ability to give higher doses of intravenous iron improved efficiency and convenience for this population of patients. 39 patient appointment slots were saved resulting in significant financial gains. This allowed access to DCC resource for other patients. Iron isomaltoside therapy allowed optimal and timely intravenous iron treatment for patients being prepared for surgery.
P44

Treatment of preoperative anaemia with high IV iron dose

Hospital Universitario Central de Asturias, Asturias, Spain

Introduction: One of the pillars of a Patient Blood Management (PBM) program is the detection and treatment of preoperative anaemia. On the other hand it is well known that the figure of pre-surgical haemoglobin is a predictive factor of transfusion, so its correction is related to a decrease in the transfusion rate.

Objective: We present the results of a circuit in Central University Hospital of Asturias, from July 2016 to May 2017, designed for the correction of anaemia in patients who are on the surgical waiting list in our centre that allows the detection and treatment of the same in a single visit to hospital.

Material and Methods: Patients sent from the pre-anaesthesia clinic with a haemoglobin (Hb) <12 or 13 g/dL (male or female) are referred to the Transfusion Service for evaluation and treatment with intravenous iron (IV) (isomaltoside iron). In all cases the determination of serum iron (normal >30 mg/dL), ferritin (normal: 13 ng/mL), IST (normal >20%), vitamin B12 (normal >211 pg/mL) and folic acid (normal >3.89 ng/mL). The iron dosage I.V. was performed based on the Hb and weight. The maximum dose administered in a session is 1,500 mg. Allergic reactions or active infection were exclusion criteria for the administration of the treatment.

Results: 81 patients were analysed (29.6% of cardiac surgery, 24.6% of general surgery, 18.5% of traumatology, and another 27.16%). 51.9% were women, the median age was 72 years (31-85). The average Hb level was 10.5 g/dL (7.70-12.8). The greatest increase in Hb was observed in patients with Hb <10 with an Hb increase of 1 g. In all patients, the IST was <20%. It was also found 3 cases of vitamin B12 deficiency and 18 (22%) with folic acid deficit. 65 patients (80.25%) were treated with Iron I.V (isomaltoside iron), of which 3 received a total dose of 2,000 mg (in 2 days) and 3 in two weeks, 24 received 1,500 mg (21 in 1 day only). The rest received 1,000 mg in a single day. In all cases, the treatment was well tolerated. Of the 65 patients, 43 were operated on. The average number of days between treatment and surgery was 25 days (1-129). In all cases, at 4 weeks the IST was >20%. Of the patients who underwent surgery, 22 (51%) required transfusion during surgery.

Conclusions: Patients with haemoglobin levels <12 g/dL present in a very high percentage of cases iron deficiency and up to a third of the same associated vitamin deficits. Treatment with iron IV (isomaltoside iron) is effective in the repletion of iron deposits and reduction of transfusion requirements and allows to safely administer up to 1,500 mg in a single day which allows to reduce the number of visits to the hospital.
Pre-operative IV iron infusion clinic – a patient experience survey

R. Horner, J. Trattles & L. Roberts
Sunderland Royal Hospital, Sunderland, UK

Introduction: Iron deficiency anaemia is the most common cause of anaemia in the surgical population, and is associated with increased morbidity, mortality and length of stay. In December 2017, a pre-operative iron infusion service was set up within the Perioperative Risk Evaluation and Preparation (PREP) clinic. The advantages of a PREP delivered service include: rapid access in cases where surgery is urgent. The ability to provide greater continuity of care, improved co-ordination of care and close monitoring of patient, with no additional workload pressure on day-case areas currently delivering parenteral iron. In July 2017, an assessment of the patient experience was undertaken by the Clinical Governance department to help shape the future direction of the clinic

Method: Fifty patients were asked to complete a survey following a total dose iron infusion given in our PREP clinic. The survey consisted of thirteen questions and there was an opportunity for free text.

Results: 60% of the patients responded to the survey. 83% of patients felt that their health had improved following the infusion, 97% of patients were happy with their appointment time, 86% of patients rated their care as ‘very good’ or ‘good’. Free text comments included: ‘I was fast tracked and had my pre-op on Friday morning and asked to come back later on the same day for an Iron infusion.’ And ‘the environment was relaxing, staff very informative, and the whole experience professionally executed.’

Conclusion: Embedding an IV iron service within our PREP clinic has provided a unique opportunity for patients to be given an iron infusion at a time that suits them and has provided an opportunity to diagnose and treat iron deficiency anaemia on the same day. Infusions are given by a blood transfusion practitioner or PREP nurse who has built up a relationship with the patient and can use the time during the infusion to reinforce lifestyle modifications and health promotion as part of the optimisation and work-up prior to undergoing major surgery. Feedback from patients has been very positive and encouraging as we continue to expand the service.

REFERENCE
P46

Pre-operative anaemia management for total joint arthroplasty (TJA) reduces post-operative blood transfusions and length of stay (LOS)

R. Horner, L. Roberts & J. Trattles
Sunderland Royal Hospital, Sunderland, UK

Introduction: Anaemia is common in surgical patients and associated with increased use of blood products in the intra and post-operative periods, which in turn is associated with poorer surgical and patient outcomes. In 2014 an anaemia pathway was introduced with the aim to identify and treat anaemic patients prior to surgery. We have evaluated the effect of this initiative on blood transfusion rates and LOS in patients undergoing TJA.

Methods: We conducted a retrospective analysis of primary TJA over six months for incidence of preoperative anaemia, blood transfusion and length of stay (LOS). This demonstrated that anaemic patients had a 27% chance of receiving a blood transfusion compared to 3% of non-anaemic patients. LOS was increased in anaemic patients compared to non-anaemic patients.

An anaemia pathway was introduced using the local definition of anaemia, Hb 130 for males and 115 for females. Following introduction of the pathway we re-audited patients undergoing TJA over a 6-month period in 2017.

Results: Following implementation of the anaemia pathway, transfusion rates have fallen from 7.4% overall to 1.7% for all patients undergoing TKR/THR in our trust. We can also demonstrate a decrease in hospital length of stay from 4.2 days to 3.5 days for THR and 4.6 days to 3.6 days for TKR. 9 patients were transfused in 2017, 5 of whom were women with a Hb between 115-130.

Conclusion: Pre-operative anaemia management has resulted in a reduction in perioperative blood transfusion and LOS in our hospital. This confers benefits to both the patient and the trust, in terms of experience and patient flow through the hospital.

We are able to demonstrate that women are at higher risk of blood transfusion when using a lower threshold for anaemia definition compared to males. As a result we have modified our anaemia pathway trigger to include all men and women with a Hb less than 130, in line with the international consensus statement on the perioperative management of anaemia and iron deficiency. We aim to re-audit again to assess the impact of this change in practice.

REFERENCES
P47

Incidence and management of perioperative anaemia and iron deficiency in orthopaedic surgery

S. Zalba1, A. Aranguren1, E. Martin2, E. Ongay2, B. Apesteguia2, M. L. Antelo1 & J. A. García Erce3
 xHematology Service Complejo Hospitalario de Navarra; 2Clinical Analysis Service Hospital García Orcoyen; 3Bank of Blood and Tissue of Navarra, Spain

Introduction: The prevalence of anaemia in orthopaedic surgery varies between 10-75%. Descriptive analysis of preoperative anaemia and iron deficiency in programmed arthroplasty and effectiveness of a PBM program in a region of northern Spain.

Methods: During the 2013-2018, 580 patients included in the arthroplasty program were analysed. Between 2-3 months before surgery, patients were managed according to the following guidelines: If haemoglobin (Hb) level >14 g/dL: No treatment; If Hb 12-14 g/dL and ferritin <100 µg/L and/or IST <20%: oral iron; If: Hb 12-14 g/dL with high ferritin and IST >20% or Hb <12 g/dL: study and individual assessment.

Results: 17% of patients presented Hb <13 g/dL (higher prevalence in women); in 26% we detected “iron deficiency” (IST <20%), 57% presented also with Ferritin <100 µg/L.

<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>Mean Age</th>
<th>Hb &lt;14</th>
<th>Hb &lt;13</th>
<th>Hb &lt;12</th>
<th>Hb &lt;10</th>
<th>IST &lt;20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men ♂</td>
<td>307</td>
<td>69</td>
<td>16.6%</td>
<td>5.6%</td>
<td>2.5%</td>
<td>0</td>
<td>15.2%</td>
</tr>
<tr>
<td>women ♀</td>
<td>273</td>
<td>71</td>
<td>56.1%</td>
<td>22.9%</td>
<td>6.1%</td>
<td>0.8%</td>
<td>31.7%</td>
</tr>
</tbody>
</table>

Re-surgery treatment: (THR: Total Hip Replacement; TKR: Total Knee R.) 24 other surgeries.

<table>
<thead>
<tr>
<th>Surgery</th>
<th>No. pat</th>
<th>Mean Age</th>
<th>Oral iron</th>
<th>IV. iron</th>
<th>SC. Epo</th>
</tr>
</thead>
<tbody>
<tr>
<td>THR</td>
<td>214</td>
<td>67.6</td>
<td>38 (17.75%)</td>
<td>3 (1.4%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>TKR</td>
<td>342</td>
<td>70.8</td>
<td>83 (24.3%)</td>
<td>8 (2.3%)</td>
<td>2 (0.6%)</td>
</tr>
</tbody>
</table>

Post-surgery data: Women were more transfused (x3).

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Transfused patients (%)</th>
<th>IV. iron treatment</th>
<th>Discharge Hb levels g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>THR</td>
<td>(36) 17%</td>
<td></td>
<td>&lt;9</td>
</tr>
<tr>
<td>♂ 146</td>
<td>10.7%</td>
<td>7.4%</td>
<td>0 %</td>
</tr>
<tr>
<td>♀ 73</td>
<td>29.6%</td>
<td>2.1%</td>
<td>5%</td>
</tr>
<tr>
<td>TKR</td>
<td>(27) 8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>♂ 151</td>
<td>4.6%</td>
<td>11%</td>
<td>0%</td>
</tr>
<tr>
<td>♀ 191</td>
<td>11.6%</td>
<td>5.4%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Conclusions: Oral iron administration well in advance was effective in most patients avoiding other more expensive treatments. Anaemia and suboptimal iron deposits are more prevalent in women even in post-menopausal age (ratio 4/1 vs men). Given that women present more frequently anaemia, iron deficit and/or suboptimal deposits, it would be advisable to use at least the same Hb threshold of 13 g/dL for women and men. This PBM strategy has achieved lower transfusion rates and optimal Hb levels at discharge.
P48

‘Iron’ing out the creases: A service evaluation of the real-world efficacy of a pre-operative oral and intravenous iron pathway in a UK District General Hospital for patients undergoing elective primary and revision hip and knee arthroplasty

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Introduction: In June 2016 a preoperative anaemia management pathway was instigated in our District General Hospital. This included provision of oral or IV iron depending on clinical need. Prior to 2016 no formal pathway existed. In 2018 and 2017 service evaluations were undertaken of perioperative anaemia management in patients undergoing primary and revision hip and knee arthroplasty.

Methods: Perioperative anaemia was defined locally as a haemoglobin of less than 120 g/L. Individual electronic and paper patient records were manually reviewed. Quantitative data such as test dates, haemoglobin values and treatments used were analysed. Qualitative process analysis was also undertaken.

Results:

<table>
<thead>
<tr>
<th>Audit Period (Months)</th>
<th>Number of patients (No.)</th>
<th>Prevalence Anaemia Hb &lt;120 g/L (%/(No.))</th>
<th>Identified as anaemic preoperatively (% / (No.))</th>
<th>Having oral iron therapy (% / (No.))</th>
<th>Having IV iron therapy (% / (No.))</th>
<th>Last bloods to op mean (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>1</td>
<td>44</td>
<td>15.9% (7)</td>
<td>85.7% (6)</td>
<td>4.5% (2)</td>
<td>6.8% (3)</td>
</tr>
<tr>
<td>2017</td>
<td>3</td>
<td>132</td>
<td>16.7% (22)</td>
<td>81.8% (18)</td>
<td>5.3% (7)</td>
<td>3.0% (4)</td>
</tr>
</tbody>
</table>

Comparing 2017 and 2018 data, the prevalence of preoperative anaemia at booking remained static (15.9% in 2018 vs 16.7% in 2017). The number of patients identified as anaemic preoperatively however improved (85.7% in 2018 vs 81.8% in 2017). Patients receiving oral iron remained static (4.5% in 2018 vs 5.3% in 2017) whilst numbers of patients having IV iron therapy increased (6.8% in 2018 vs 3.0% in 2017). Improvements in days between last haemoglobin test and operative date (58.8 days in 2018 vs 82.3 days in 2013) continued to improve despite booking to operative times increasing from a mean of 206.9 days in 2018 to 102.2 days in 2017. Low blood transfusion rates have continued (6.8% in 2018 vs 14.3% in 2013).

Mean haemoglobin drop (last pre-op test to first post op) was across the whole cohort 21.25 g/L in 2018 and 21.4 g/L in 2017. This compared to patients identified and treated for iron deficiency anaemia having drops of 11.6 g/L in 2018 and 8.7 g/L in 2017. This indicates ‘real world improvement’ since pathway implementation. In January 2019 the local anaemia threshold has been changed to less than 130 g/L, in line with international standards. This is expected to increase service use by approximately 25-30% of patients.

Conclusion
Significant improvements in perioperative anaemia management can be achieved with a simple pre-operative pathway to identify and treat patients with iron, including provision of an IV iron service. However, a rigorous process of service evaluation and constant quality improvement is needed to maximise this potential benefit.
P49

Postoperative outcome following hip and in knee arthroplasty in non-anaemic iron replete patients treated with intravenous iron carboxymaltose supplementation vs control

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Introduction: Iron deficiency anaemia is strongly associated with poor outcomes after surgery. However, preoperative non anaemic iron deficiency (anaemia precursor status) could have a negative impact on the outcomes of the patients.

Our goal is to identify before hip and knee arthroplasty non anaemic patient with iron deficiency in pre-admission assessment and to treat them with intravenous iron at least 4 weeks before hospital admission.

Materials and methods: Observational-monocentric-cohort-retrospective study. Two groups of patients: one group treated with iron carboxymaltose (74 patients, 89%) and control group (61 patients, 89% female).

Inclusion criteria: patients with haemoglobin levels between 12-14 g/dL and ferritin levels lower than 100 mcg/L. Patients with iron allergy, treated with anticoagulant therapy and septic patients were not included. Patients that received other type of iron during the perioperative period were excluded. Selected patients were treated with intravenous iron carboxymaltose 1 g in pre-admission assessment, 4 weeks before surgery. Control group same criteria, but not treated with iron.

Primary end point is the outcome in the first 4 weeks after surgery in term of alive day and with the comparison between haemoglobin delta (= Hb at hospital pre admission-Hb at 4 weeks after surgery) of treated patient’s group and of not treated patient’s group.

Secondary end points are: haemoglobin levels, white b-cell, red cell at pre-admission assessment, at first and fourth day after surgery, allergic reaction, number of blood transfusion.

Results: In treated patients group the average of haemoglobin levels at the hospital admission was 13.1± 0.7 g/dL. No difference between haemoglobin levels at pre-admission assessment and at hospital admission. The average haemoglobin levels at 4 weeks after surgery was 11.9±1.2 g/dL with delta 1.2± 1.3 g/dL. Urticarial reaction and nausea after administration in 2 patients. In no treated group the average of haemoglobin level at the hospital admission was 13.5± 0.6 g/dL (p <0.001). The average haemoglobin level at 4 weeks after surgery was 11.8±1.4 g/dL (p=0.799) with delta 1.8±1.6 g/dL (p=0.027).

No difference in the bleeding during surgery and in the drop of haemoglobin. No evidence of significant differences in allogenic red cell transfusion.

The increase of haemoglobin after surgery was greater and faster than in not treated group and it is time dependent. In non-treated group the increase between admission and 1 day after surgery in wbc (0.2±0.5 vs 0.7±0.6, p <0.0001) was greater than in treated group.

Discussion: Intravenous iron carboxymaltose infusion showed safety because not inducing important allergic reaction. The iron replacement has a positive impact in the outcome not immediately but after 4 weeks post-surgery. In iron deplete non-anaemic patients the infusion of iron doesn’t affect the number of blood transfusion but improve the outcome of the patient and make faster the recover to a good quality of life.
P50

Efficacy and safety of intravenous iron as an alternative to blood transfusion in chronic very severe anaemias without hospitalization. When the practice overcomes the guidelines

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Introduction: Current international guidelines, mostly focused on hospitalized haemodynamically stable patients (pts), suggest red blood cell transfusion (RBCT) when haemoglobin (Hb) is ≤7–8 g/dL. At Anaemia clinic is common to treat with intravenous iron (IVI) very severe anaemias on an outpatient basis without RBCT.

Methods: We collected already published and unpublished data of sideropenic and severely anaemic (Hb ≤7 g/dL) pts treated with IVI and without RBCT at 4 Spanish and 3 Italian Anaemia clinics.

Results: We evaluated a total of 202 pts, (86.0% females), mean age 50 years (range 14–93). The mean Hb at first visit was 6.3 g/dL (±SD 0.6 – range 3.7–7.0). Eight pts had Hb ≤5 g/dL. The pts were mostly referred to Anaemia clinic by Primary Care Doctors (45.0%) and by Emergency Department (35.0%). Anaemia was caused by gynaecological bleeding in 108 cases (53.4%), gastroenteric bleeding in 26 cases (12.9), malabsorption in 12 cases (5.9%), other causes (comprising occult gastrointestinal bleeding) in 28 cases (13.8%) and anaemia of unknown origin or a still pending diagnosis in 28 cases (13.8). Ferric Carboxymaltose was administered to all pts at a median dose of 1500 mg. Median Hb recovery was 6.5 g/dL (Interquartile Range 6.1-6.8). The Figure shows a box plot graph of Hb recovery categorized by diagnosis. In all pts Hb increased more than 2 g/dL. A rise in Hb ≥5.0 g/dL was obtained in 143 pts (70.8%) and in 55.9% of cases the post-therapy Hb was more than 12.0 g/dL with a median interval from the first IVI and the last control of 35 days. Only seven pts (3.5%) experienced side effects, all of them not serious (mild allergic reaction 4, diarrhea 2, extravasation 1).

Conclusion: In chronic sideropenic very severe anaemias, third generation intravenous iron is effective and safe to quickly correct anaemia and avoid RBCT. We feel that in this clinical setting more specific guidelines are warranted.
Pooled analysis of the PHOSPHARE-ID 04/05 studies: findings relevant to respiratory muscle function

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Introduction: Hypophosphatemia is associated with respiratory muscle weakness, which is particularly relevant in the surgical setting. Ferric carboxymaltose (FCM) is associated with high rates of hypophosphatemia that are not observed with iron isomaltoside (IIM). This analysis assessed the efficacy of IIM and FCM in correcting iron deficiency anaemia (IDA), and ascertained the occurrence of hypophosphatemia and the short-term effects of treatment on respiratory muscle strength/function.

Methods: In two identically designed, open-label, controlled trials, adults with IDA were randomised 1:1 to receive IIM (single infusion of 1,000 mg) or FCM (FDA-approved dosing schedule: two infusions of 750 mg administered 1 week apart). Data were pooled to compare the effect of IIM and FCM on blood parameters (haemoglobin [Hb], ferritin, and transferrin saturation [TSAT]), incidence of hypophosphatemia (phosphate <2.0 mg/dL), and effects on skeletal and respiratory muscle function. Blood samples were collected at baseline (Day 0) and on Days 1, 7, 8, 14, 21, and 35. Grip strength, large proximal muscle strength (arm lift, and chair stand tests) and respiratory muscle strength were tested on Days 0, 14 and 35.

Results: A total of 245 patients with IDA were randomised to IIM (n=123; mean dose 1,008 mg) and FCM (n=122; mean dose 1,468 mg). During the 35-day assessment period, Hb and ferritin rapidly normalised in both groups; TSAT initially peaked but was relatively unchanged by Day 35. The incidence of hypophosphatemia was significantly higher in the FCM versus the IIM group (74.4% versus 8.0%, p<0.0001). Coincident with improvement in IDA, grip strength and large proximal muscle function improved in both groups. Maximal expiratory pressure was significantly improved with IIM versus FCM (Day 14, p=0.013; Day 35, p=0.021). Maximal inspiratory pressure was improved in the IIM group at Day 14 (p=0.06 vs FCM), with the improvement maintained at Day 35 (p=0.68 vs FCM). There were three serious or severe hypersensitivity reactions (HSRs): one (swollen eyelid) in the IIM group (0.8%), and two (swelling, and dyspnoea) in the FCM group (1.7%).

Conclusion: Treatment with IIM and FCM rapidly corrected IDA. FCM caused hypophosphatemia in the majority of patients. Two weeks after treatment, when serum phosphate reached its nadir in the FCM group, patients’ respiratory muscle strength was improved in the IIM group, but not in the FCM group. Rates of HSRs were low in both groups. Blood managers administering iron preoperatively should be aware of hypophosphatemia as a complication of FCM that occurs within 1 to 4 weeks after iron administration and can influence muscle function.
P52

Blood transfusion in cardiac surgery children receiving hydroxyethyl starch: the influence of the ABO group

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Introduction: Hydroxyethyl starches (HES) affect haemostasis through different mechanisms including a decrease of the VIII-von Willebrand factor complex. This effect can result in higher blood loss and blood transfusion, especially in patients of the O blood group, who have genetically a lower plasmatic level of VIII-von Willebrand complex.

This retrospective study assessed the effects of O blood group on blood components transfusion in children undergoing elective cardiac surgery under cardiopulmonary bypass (CPB) where 6% HES 130/0.4 was used as the priming fluid.

Materials and methods: Following IEC approval, all children undergoing cardiac operation with CPB between 2005 and 2016 were included. Jehovah Witnesses, newborns and ASA V patients were excluded. Anaesthetic, surgical and CPB techniques were standardized. Patients with blood group O were compared to patients with non-O blood group using Wilcoxon rank test or Chi square. Univariate and multivariate analyses were used to define the independent predictive factors for blood components transfusion.

Results: Among the 1381 patients included, 579 (42%) had O blood group and 802 (58%) had non-O blood group. Demographic and surgical data were not different between groups except for the RACHS-1 (Risk adjustment for congenital heart surgery-1) score, which was higher in the non-O blood group patients. Blood losses and blood transfusion were not different between groups (Table: data presented as median [interquartiles] or %).

<table>
<thead>
<tr>
<th></th>
<th>O blood group</th>
<th>Non-O blood group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative blood loss (ml/kg)</td>
<td>25 [14 to 44]</td>
<td>26 [14 to 47]</td>
<td>0.25</td>
</tr>
<tr>
<td>Total calculated blood loss (ml/kg)</td>
<td>21 [11 to 31]</td>
<td>20 [11 to 30]</td>
<td>0.70</td>
</tr>
<tr>
<td>Blood components exposure (%)</td>
<td>384 (66)</td>
<td>503 (63)</td>
<td>0.17</td>
</tr>
<tr>
<td>Red blood cells transfusion (%)</td>
<td>370 (64)</td>
<td>476 (59)</td>
<td>0.10</td>
</tr>
<tr>
<td>Red blood cell transfusion (ml/kg)</td>
<td>23 [15 to 36]</td>
<td>26 [17 to 39]</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Independent predictive factors for blood components transfusion included preoperative weight, haemoglobin, ASA score, priming volume, surgery duration, intraoperative blood loss, and 24h postop blood loss.

Conclusion: In the conditions of our study, O blood group was not a predictive factor for blood components transfusion in children undergoing cardiac surgery with CPB where 6% HES 130/0.4 was used as the priming fluid.
P53

Introduction of a formal bleeding assessment into use in pre-admission surgical clinic

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**Introduction:** Appropriate pre-operative bleeding risk assessment is crucial to identify surgical patients with potential bleeding disorders, as supported by relevant guidelines. Inappropriate screening coagulation testing is wasteful, can provide false reassurance or delay surgery with unnecessary further testing. In 2016 a bleeding risk questionnaire was introduced into pre-admission clinic in our institution with the aim of reducing indiscriminate coagulation testing and to facilitate diagnosis and management of patients with bleeding disorders. In 2017, this was replaced with the HEMSTOP questionnaire, a validated bleeding risk assessment tool. Prior to 2016, bleeding risk was not formally assessed/documented.

**Methods:** The records of all patients attending pre-admission clinic from start November 2017 to start February 2018 were reviewed (n=360). The percentage of patients attending pre-admission clinic in the month of November who had coagulation tests ordered, was compared for years 2015 to 2018.

**Results:**
- The baseline rate of coagulation test ordering in November 2015 was 67% (n=81). Following introduction of a bleeding risk assessment, there has been a substantial and sustained reduction in test ordering, to 50% (n=83) in November 2016, 41% (n=59) in November 2017 and 45% (n=61) in November 2018.
- During the 2017-2018 audit period, 62% (n=185) of patients completed the HEMSTOP questionnaire. The rate of coagulation test ordering was comparable in those who did not complete the HEMSTOP: 50% (n=75); those who completed the HEMSTOP: 41% (n=75); and those with a HEMSTOP score of ≥2 (predicted to be at higher risk of bleeding): 46% (n=6). The HEMSTOP had been completed in only 50% (n=75) of patients in whom coagulation tests were ordered. 17% (n=26) of requested coagulation tests were abnormal, attributable to anti-coagulants in 69% (n=18).
- 13 patients (7%) scored ≥2. Ultimately a potential bleeding disorder was identified in 5 patients (1%) following anaesthetic review and exclusion of bleeding due to focal pathology or anticoagulants, consistent with population estimates.

**Conclusion:** Coagulation test ordering in pre-admission clinic has reduced by 22% and has stabilised at 40-45%. This appears to be due to a general change in requesting patterns and is not directly attributable to the use of the bleeding risk questionnaire or the derived score.
Advantages of automatic detection of platelet dysfunction

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Introduction: Disorders of platelet function can be inherited or acquired, manifesting either as haemorrhage or thrombosis. Diagnosis and treating of such disorders may largely benefit from automatic platelet function analysers.

Aim: We are showing our two-year experience of automatic platelet function analyser use in patients with platelet dysfunctions.

Methods: Time period observed was from 13/JAN/2017 to 12/JAN/2019. Machine used was Multiplate® analyser. Patient data were acquired from Hospital Information System and transfusion protocols.

Results: Testing of platelet function was done in 78 patients, with a total of 314 tests. These patients can be roughly divided in one of three groups.
- The first group was 30 (38.4%) patients in which the efficacy of anti-aggregation therapy was monitored. A total of 91 tests were done (28.8%). Lack of efficacy was found in 9 patients (7 using clopidogrel, 2 using aspirin).
- The second group was comprised of 40 (51.3%) patients who were taking anti-aggregation therapy and being prepared for surgery. They were monitored for the risk of perioperative bleeding. A total of 198 (63%) tests were done in this group. Prolonged anti-aggregation effect (more than 2 days) was found in 15 patients.
- The third group of 8 (10.3%) patients was screened for haematological disorders - Von Willebrand’s disease (VWD) and heparin-induced thrombocytopenia (HIT). Nineteen (6.4%) tests were done. In 2 patients VWD was confirmed. In 5 patients HIT was confirmed.

Conclusion: Monitoring of anti-aggregation therapy effect on thrombocyte function has pivotal importance in surgery and internal medicine, directly leading to decrease in morbidity and mortality rates. Use of automatic analysers is simple and yields results quickly. This makes them ideal for personalization of anti-aggregation therapy, haemorrhage risk stratification, and improvement of healthcare.
Should we implement platelet function assessment as a strategy of patient blood management in cardiac surgery?

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Introduction: Cardiovascular diseases are the main cause of death in the world. To reduce new cardiac events and death antiplatelet therapy (AT) is the mainstay. However, when patients need to undergo coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) that can lead to severe bleeding, coagulopathy or even death. ROTEM PLATELET is a point-of-care platelet function test used before cardiac surgery, at Hospital de Santa Cruz, to measure platelet aggregation and assess quantitatively the effect of AT in platelet function.

Methods: A prospective, observational, single-centre study of 50 patients undergoing CABG of three vessel disease with platelet dysfunction assessed with ROTEM PLATELET were enrolled. The primary outcomes examined were blood loss at 1h, 2h, 6h, 18h and 24h after surgery and blood transfusions. We excluded patients with anaemia or haematologic diseases, diabetes, peripheral artery disease, chronic liver disease and patients with bleeding of surgical causes. To understand the influence of assessing platelet function in cardiac surgery we analysed the same outcomes of a group control of 50 patients submitted to the same surgery and exclusion criteria to whom the platelet function was not assessed.

Results: From the 50 patients undergoing CABG of three vessels all received blood transfusions. However, when compared with the group control, the patients assessed with ROTEM PLATELET received less than a half of red blood cells, all intraoperatively. Concerning platelet transfusion, we observed an increase, comparing with group control, mainly in the beginning of surgery or immediately after. The median postoperative blood losses were significantly reduced comparing with the group control in all times after surgery. The most remarkably difference between the groups is observed 6h after the surgery with a mean difference bigger than 40% and always bigger than 20% in the remaining times analysed.

Conclusion: The PBM in cardiac surgery is still a great challenge. The blood losses are an independent risk factor for morbidity and mortality that can be modified assessing the platelet function in patients under antiplatelet therapies. The usage of the technique allowed a substantial reducing of blood losses and blood transfusions, reason why we propose to include as a strategy of patient blood management to implement in cardiac surgery.
Improved patient outcomes and blood product management in surgical settings with thromboelastography-guided haemostatic therapy: systematic review and analysis

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Introduction: TEG® is a viscoelastic monitoring system capable of providing rapid results evaluating the coagulation process holistically. Guidelines recommend using thromboelastography to guide haemostatic therapy in perioperative settings. This systematic review and meta-analysis compared transfusion requirements and patient outcomes for TEG®-guided haemostatic therapy in patients undergoing surgery versus therapy guided by clinical judgement or conventional coagulation tests only (control).

Methods: A systematic search for relevant randomised clinical trials (RCTs) was conducted using predefined search strings on MEDLINE (PubMed) and EMBASE for articles published up to January 2018. Predefined inclusion/exclusion criteria were used to identify eligible RCTs. Relevant data was extracted from these articles, and a meta-analysis was conducted following the DerSimonian-Laird random effects method.

Results: Nine eligible RCTs in elective surgery settings were identified and included in the meta-analysis. The meta-analysis of elective surgery studies identified reduced levels of transfusion for plasma (p <0.001), platelets (p=0.004) and red blood cells (p=0.14) for TEG®-guided transfusion versus control. Furthermore, significant reductions were also observed in bleeding rate (p=0.002), as well as operating room (p=0.005) and intensive care unit (ICU, p=0.04) length-of-stay. Mortality rates remained comparable between treatment groups, despite the observed reductions in blood product transfusion. One additional RCT in an emergency surgery study was also identified for evaluation. Significant reductions in platelet and plasma transfusion (p=0.04 and p=0.02, respectively) were reported for TEG®-guided therapy compared to the control in the emergency surgery study, together with decreased mortality (p=0.049). Additionally, the number of ventilator-free and ICU-free days (p=0.10 and p=0.09, respectively) were increased in the TEG®-guided therapy group compared with the control. Higher complication rates were observed for TEG®-guided therapy versus control (p=0.06), potentially due to survival bias. Analysis indicated increased probability of survival at 28 days in the TEG®-guided therapy group (log-rank p=0.032, Wilcoxon p=0.027).

Conclusion: This systematic review and analysis indicates that using TEG® to guide haemostatic therapy can improve key patient outcomes and blood product resource management.
P57

Dynamic functional clot formation in patients undergoing endoscopic mucosal resection

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Introduction: Colonic cancers are the second most commonly diagnosed malignancies in Australian (Cancer Council, 2014). A majority of patients require surgery, which is associated with high morbidity and mortality, particularly in the elderly (McNicol et al. 2007). Endoscopic Mucosal Resection (EMR) is a cost-effective and minimally invasive electrosurgical technique for the removal of large sessile polyps (Moss, et al. 2011). Unfortunately, clinically significant post-endoscopic bleeding (CSPEB) is the most frequent adverse event associated with EMR (Burgess, et al. 2014; Elliott, et al., 2018). Previous studies show electrosurgery and burns can cause plasminogen activation and fibrinolysis (Shubina et al., 2000; Gibson et al., 2007). While others have attempted to reverse post-EMR bleeding with sub-mucosal injection of autologous platelet-rich plasma (PRP) (Lorenzo-Zúñiga, et al. 2018), underlying mechanisms for its effectiveness remain unclear. This study therefore examined the kinetics of haemostasis in patients undergoing EMR to characterise any disturbances in coagulation across time.

Methods: We evaluated dynamic clot formation in 23 patients undergoing EMR for large sessile intestinal polyps at the LMH. Blood samples were taken prior to EMR, an hour following the procedure and 2 days post-EMR. Rotational Thrombelastometry (ROTEM) was performed, plasminogen levels were measured and ELISA was used to quantify tissue-type plasminogen activator (tPA) antigen expression. Data were log-transformed and analysed using repeated-measure ANOVAs.

Results: Plasminogen levels decreased significantly post-EMR (p= 0.001) and returned to pre-EMR levels by day 2. FibTEM A10 (mm) and Maximum Clot Firmness (mm) were decreased an hour following EMR (F A10; p <0.001 and F MCF; p=0.001) compared to measures taken pre-EMR and 2 days post-EMR. Maximum lysis (%) was increased 2 days post-EMR (p=0.001). tPA expression was increased, but was not significant. There were no significant differences in any of these measures according to sex, age and BMI. One patient experienced CSEPB at one week post-EMR, with substantially decreased ROTEM values (FibTEM A10 and MCF) compared to 2 days post-EMR.

Conclusion: These findings show decreased post-EMR plasminogen corresponds with decreased clot firmness and enhanced lysis. In this context, plasminogen activation is suspected to lead to fibrinogen utilisation and therefore, the potential for a protective intervention needs to be explored. While larger investigation is required to confirm the overall risk of CSPEB and mechanisms for plasminogen activation, this study highlights the utility of ROTEM in assessing fibrinolytic activity in EMR.
Improvement in patient treatment with blood components after introduction of Rotem analysis

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Introduction: Rotem technology is based on the evaluation of viscoelastic properties of whole blood during blood clot formation and lysis. The objective of this study was evaluation of blood product consumption during 2017 and 2018, after introduction of Rotem analysis into clinical practice in our institution.

Methods: Thromboelastometry analysis was performed using a ROTEM sigma device following standard protocols using two types of cartridges, Rotem aptem and Rotem heptem. Data of blood components usage were available from our transfusion information system DATEC. We analysed usage of packed red blood cells (PRBC) and fresh frozen plasma (FFP) for main users of Rotem from 2016 to 2018.

Results: During the first year after introduction Rotem analysis 537 samples were tested. In the next year the number of tested samples rose from 537 to 951 (77%). Approximately 66% of assays were ordered by perioperative intensive care unit and cardiac surgery, 10% urgent trauma, 8% general surgery, 5% vascular surgery, 2.6% perinatology, 2.2% neurosurgery and rest for the other departments. Analysis of blood components consumption in perioperative care unit showed decrease in use of PRBC for 34% (from 1342 to 889) and 59% (from 971 to 398) for FFP. In cardiac surgery use of PRBC decreased for 21% (from 856 to 677) and 68% (from 802 to 253) for FFP. In urgent trauma cases use of PRBC decreased by only 8% (from 1406 to 1291), while for FFP decreased by 52% (from 657 to 314).

Conclusion: Transfusion of blood components is safe but still associated with some adverse reactions and increased morbidity and mortality in politransfused patients. Evaluation of blood components consumption after introduction a Rotem analysis in our institution showed a great improvement in patient treatment due to significantly reduced use of PRBC and FFP. Further analysis is necessary to estimate cost benefit and introduction a second Rotem sigma device in operation room and perioperative care unit.
Poster Abstracts

P59

Bleeding in cardiovascular surgery: Impact of interdisciplinary protocolization

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Introduction: Cardiovascular surgery (CVS) is considered one scenario where the use of fresh frozen plasma (FFP), and platelets (PL) are the best patients (PTS) option, a lot of times without enough evidence of coagulopathic bleeding, or without bleeding at all, only with "intention to prevent".

Objective: Demonstrate that we could reduce the exposure to blood components, establishing therapeutic rules based in scientific evidence.

Material and Methods: 88 first-time CVS PTS with cardiopulmonary bypass (CBP) were evaluated. Group A and Group B. Pre-surgical and peri-surgical haemostasis control was made in both groups by conventional laboratory tests (CLT), including Fibrinogen (FI) by Claus method and platelet count. Group B control also included rotational thromboelastometry (ROTEM). Haemostasis monitoring was performed in both groups at pump exit and in the ICU until parameters were normal and/or bleeding stopped. Group B also underwent a ROTEM study during CPB a minutes before heparin inactivation. Both Groups received antifibrinolytic agents: Tranexamic Acid (TXA) during CPB, medium dose 1 g. For Fibrinogen correction both groups use only FI concentrate (Haemocomplettan-CSL Behring). Group A was transfused with a liberal strategy during surgery period in spite of the CLT in really short time (no more than 15 min). Group B was on an interdisciplinary restrictive protocol, only transfusing bleeding patients and guiding by ROTEM, avoiding use of FFP to correct INR or low fibrinogen, and no Platelets as preventive measurement. Group B was on a severe control of basic haemostasis condition: pH, temperature and calcium in all perioperative periods.

Results: FFP Group A: 32% Group B: 5.9% of PTS (p:0001), Group A: 35% PL Group B: 2% PL (p <0.001) and Group A 45.9% both PL+FFP, and Group B: 7.5% (p <0.001). We could not reduce significantly the use of packed red blood cells in both groups due to not optimized anaemia conditions of the PTS. It is interesting that the statistical analysis of both groups of CABG shows a tendency to 26% lower bleeding in Group B (p 0.07) that received less FFP and PL.

Conclusion: We are convinced about the need to changing old paradigms in haemostasis management, not only in established bleeding, but also in the biggest surgeries, also understanding haemostasis as a complex system with a great reserve and multiple mechanism of compensations that prevent bleeding in a lot of extreme circumstances, optimizing anaemia conditions pre- and peri-operatively, remembering that haemostasis needs basic conditions, pH, temperature and calcium like all enzymatic reaction to function. And finally to be aware that transfusion can save lives...but it still has adverse‼‼effects!
Efficacy and safety of fibrinogen concentrate vs cryoprecipitate in pseudomyxoma peritonei surgery: a prospective, randomised, controlled phase 2 study

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Introduction: Maintaining adequate plasma fibrinogen levels during cytoreductive surgery for pseudomyxoma peritonei (PMP) may help control haemostasis. FORMA-05 compared the efficacy and safety of cryoprecipitate (cryo) with a new highly purified, double virus-inactivated human fibrinogen concentrate (HFC; Fibryga, Octapharma) in patients with acquired fibrinogen deficiency undergoing surgery for PMP.

Methods: FORMA-05 was a prospective, single centre, randomised, controlled phase 2 study. Patients undergoing surgery for PMP with predicted intraoperative blood loss ≥2 L pre-emptively received HFC (4 g) or cryo (2 pools of 5 units). The composite primary endpoint was intraoperative (assessed by surgeon/anaesthesiologist) and postoperative efficacy (assessed by haematologist), graded using objective 4-point scales and adjudicated by an Independent Data Monitoring & Endpoint Adjudication Committee (IDMEAC).

Results: The per-protocol set included 43 patients (HFC, n=21; cryo, n=22). The mean total intraoperative dose of HFC was 6.5 g, vs 4.1 pools of cryo (containing approx. 8.8 g of fibrinogen). Median duration of surgery was 7.7 h. Overall haemostatic efficacy of HFC was non-inferior to cryo and was rated excellent or good for 100% of patients receiving HFC and cryo (Farrington–Manning test with a non-inferiority margin of 0.2; p=0.0095), with similar blood loss. Intraoperatively, only red blood cells were transfused (median: 1 unit). Intraoperative efficacy was rated as ‘excellent’ or ‘good’ for the majority of patients by the surgeon and anaesthesiologist (HFC, 95.23%; cryo, 81.82%) and by the IDMEAC (HFC, 95.23%; cryo, 72.73%). Infusions were initiated 0.4 h earlier with HFC than cryo due to faster product availability. HFC led to a greater mean increase vs cryo in FIBTEM A20 (2.38 mm ±2.84, p=0.0088) and plasma fibrinogen (0.37 g/L ±0.39, p=0.0038).

There were 6 serious adverse events (SAEs) in the HFC group and 17 in the cryo group, including 7 thromboembolic events (TEEs; 2 deep vein thromboses, 5 pulmonary embolisms). No AEs or SAEs were deemed related to the study drug.

Conclusion: The data indicate that HFC is as efficacious as cryo in patients undergoing surgery for PMP, with a lower amount of fibrinogen administered, and faster availability. No related AEs and no TEEs occurred in patients treated with HFC.
Experience with factor XIII concentrate administration following acquired factor XIII deficiency in a tertiary university children’s hospital

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Introduction: Factor XIII (FXIII) promotes formation of cross-linked fibrin polymers and a stable haemostatic plug. Standard haemostasis assays are normal with FXIII deficiency, and thus the reason for bleeding in this condition may be overlooked. Transfusion of plasma does not adequately restore FXIII levels. We aimed to 1) determine the frequency of moderate (<60%) and severe (<30%) acquired FXIII deficiency for children receiving major paediatric surgery, and 2) determine whether infusing FXIII concentrate (FXIIIIC) improved FXIII levels and decreased subsequent transfusions.

Methods: This is a single centre retrospective analysis of 16,971 anaesthesia cases performed at a paediatric hospital from 2017-8. Basic demographics, laboratory and transfusion results, and clinical/anaesthesiology records were obtained from a PBM database. Inferential statistics were used to compare transfusion requirements between 1) patients with low vs normal FXIII levels and 2) those with low FXIII treated with FXIIIIC vs those who were not treated with FXIIIIC.

Results: 2317 transfusion events (mean 0.137/procedure) were analysed; in 246 (10.6%) of all documented transfusion events FXIII levels were <30% and in 953 (41.1%) <60%. FXIIIIC was administered 264 times (256 intraop/8 postop) at a mean dose of 28.2 IU/kg (21.1-43.8). FXIIIIC was given when FXIII levels dropped to <30% 52 times (19.7% of FXIIIIC infusions), when FXIII levels were 30-59% 169 times (64.0%), and when FXIII levels were ≥60% 43 times (16.3%). Mean increase in FXIII levels (If no other product was given) was 23.9% (0.5-42.3%), which corresponds to an increase of 0.8% per IU/kg FXIII given.
Increase in FIBTEM MCF was 0mm (0-6.5). No increase in FXIII levels could be detected after only platelet or fibrinogen concentrate infusion. For those that did not receive FXIIIIC replacement, the total number of blood products transfused was significantly higher in the group with FXIII level <30% vs 30-59% (p=0.042), while no difference was observed between the group with FXIII level 30-59% vs ≥60%. If FXIII concentrate was administered in patients with FXIII levels <60%, significantly less products were given subsequently (p=0.008).

Conclusion: Acquired FXIII deficiency is common in major paediatric surgery. Replacing with FXIIIIC effectively improves FXIII levels and decreases subsequent transfusion requirements.
Tranexamic acid administration in total hip arthroplasty within a blood patient management programme

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Introduction: The aim of this study was to evaluate the use of tranexamic acid (TXA) in total hip arthroplasty (THA) and its effectiveness on reducing blood loss and transfusion rate.

Methods: Retrospective and observational study of patients who underwent primary THA during 24 months. Patients were divided in two groups: control and tranexamic acid group (TXA). The TXA regimen consisted of a TXA bolus 10 mg/kg iv followed by a continuous infusion at 2 mg/kg/h. Demographic and analytical data, perioperatively blood and transfusion rate were measured. Thromboembolic events were registered with a follow-up of 6 months.

Results: 438 patients were enrolled, 286 in TXA group and 152 in the control group. Transfusion rate was lower in the TXA group 13% vs 29% in the control group, p=0.04, total blood loss was higher in the control group, 1360 mL vs 760 mL in TXA group, p=0.02. There were no thromboembolic complications in either groups.

Conclusion: TXA group showed a significant reduction of perioperatively blood loss and transfusion rate without an increased incidence of adverse events. TXA has become a very effective measure as part of a patient blood management programme.
Transfusion rate in a monographic hospital of orthopaedic surgery after implementing a protocol of perioperative use of tranexamic acid

Hospital Complex of Navarra, Pamplona, Spain

Introduction: Perioperative use of tranexamic acid has been shown to reduce intraoperative bleeding in several types of surgery.

Methods: We describe the experience after 8 months using a perioperative protocol of intravenous tranexamic acid (TXA) to reduce bleeding in major orthopaedic surgery adapted to the target population, frequently elderly, obese patients with multiple cardiovascular pathology.

Results: We have studied prospectively 885 patients, with mean demographic characteristics of 65.7±12.8 yr., 77.9±15.4 kg, 164.2±13.4 cm, BMI 28.8±5.2, sex distribution (56.2% male and 43.8% female) and the following physical state classification of the American Anaesthesiologists Association: I 10.4%, II 44.6%, III 40.8% and IV 4.2%) underwent programmed surgeries of hip replacement (39%), knee arthroplasty (45.1%), vertebral arthrodesis (12.7%), cervical spine surgery (1%) and scoliosis correction (1.3%). All patients received postoperative CBCII blood conservation system excepting surgeries with suspicion of infection. The mean use of TXA was 0.76±0.45 g IV intraoperative and 0.48±0.46 g iv postoperative. We have no cases of adverse effects related to the use of intravenous TXA. Bleeding was considered to be greater than usual in 12.9% of patients. Our patients had a mean preoperative haemoglobin (Hb) levels of 13.9±1.7 g/dL (14.6±4.8 men and 13.1±4.2 women) and values at discharging of the Postoperative Care Unit (24 h later) of 11.1±1.5 g/dL (11.7±3.9 men and 10.4±3.4 women). We observed preoperative Hb levels lower than 13 g/dL in 28.99% of the patients (7.25% men and 21.98% women). A 7.97% of women had preoperative Hb levels below 12 g/dL.

The transfusion rate was 8.2% and it is mainly due from the surgical point of view to the presence of extensive vertebral surgery and replacements of hip and knee prostheses, and from the point of view of the patients to the presence of heart disease ischaemic or history of stroke or thrombosis, which contraindicated the use of TXA. The ratio of transfusion was 2.91 times higher with Hb <13 g/dL (1.5 in men and 4.6 times in women), but there were no differences in women when the cut-off point was set at 12 g/dL.

Conclusion: The use of a perioperative protocol of intravenous TXA adapted to the target population in a monographic hospital of orthopaedic surgery has significantly reduced the consumption of blood products. The next two phases of perioperative care for patients include the topical use of TXA in cases that are contraindicated intravenously and the optimization of perioperative haemoglobin levels with a Patient Blood Management program.
Transfusion rate in hip prosthetic surgery after implementing a protocol of perioperative use of tranexamic acid

Hospital Complex of Navarra, Pamplona, Spain

Introduction: Perioperative use of tranexamic acid has been shown to reduce intraoperative bleeding in several types of surgery.

Methods: We describe the experience after 8 months using a perioperative protocol of intravenous tranexamic acid (TXA) to reduce bleeding in hip prosthetic surgery adapted to the target population, frequently elderly, obese patients with multiple cardiovascular pathology.

Results: We have included prospectively 123 patients underwent programmed surgeries of replacement hip prosthesis (6.5%) and total hip arthroplasty (92.7%). Their mean demographic characteristics were: 63.8±14.5 yr., 76.3±16.5 kg, 166.1±18.0 cm, BMI 27.6±5.2, sex distribution 59.3% male and 40.7% female) and the following physical state classification of the American Anaesthesiologists Association: I 17.1%, II 40.7%, III 39.0% and IV 3.3%)

Our patients had a mean preoperative haemoglobin (Hb) levels of 14.0±2.0 g/dL (14.6±3.6 men and 13.1±2.7 women) and values at discharging of the Postoperative Care unit (24 hours later) of 11.1±1.8 g/dL (11.8±2.9 men and 10.2±2.1 women). We observed preoperative Hb levels lower than 13 g/dL in 28.46% of the patients (11.38% men and 17.07% women). A 4.88% of women had preoperative Hb levels below 12 g/dL. The mean use of TXA was 0.75±0.44 g IV intraoperative and 0.48±0.43 g iv postoperative. We have no cases of adverse effects related to the use of intravenous TXA. Bleeding was considered to be greater than usual in 6.5% of patients. All patients received postoperative CBCII blood conservation system excepting surgeries with suspicion of infection.

The transfusion rate was 8.1% (0.67±0.58 auto-donation units and 1.33±0.9 RBC units) and it is mainly due to the presence of heart disease ischemic or history of stroke or thrombosis, which contraindicated the use of TXA. The ratio of transfusion was 4.0 times higher with Hb < 13 g/dL (2.5 times in women), but there were no differences in women when the cut-off point was set at 12 g/dL.

Conclusion: The use of a perioperative protocol of intravenous TXA adapted to the target population in hip prosthetic surgery has significantly reduced the consumption of blood components. The next two phases of perioperative care for patients include the topical use of TXA in cases that are contraindicated intravenously and the optimization of perioperative Hb levels with a Patient Blood Management program.
Abstracts of the 20th Annual NATA Symposium

Poster Abstracts

P65

Transfusion rate in prosthetic knee surgery after implementing a protocol of perioperative use of tranexamic acid

Hospital Complex of Navarra, Pamplona, Spain

Introduction: Perioperative use of tranexamic acid has been shown to reduce intraoperative bleeding in several types of surgery.

Methods: We describe the experience after 8 months using a perioperative protocol of intravenous tranexamic acid (TXA) to reduce bleeding in prosthetic knee surgery adapted to the target population, frequently elderly, obese patients with multiple cardiovascular pathology.

Results: We have studied prospectively 159 patients, with mean demographic characteristics of 70.2±9.9 yr., 79.9±16.0 kg, 162.2±16.2 cm, BMI 30.0±5.6, sex distribution (46.5% male and 53.5% female) and the following physical state classification of the American Anaesthesiologists Association: I 6.3%, II 48.4%, III 42.1% and IV 3.1%) underwent programmed surgeries of total knee replacement (8.1%) and total knee arthroplasty (91.3%). Our patients had a mean preoperative Hb levels of 14.0±1.8 g/dL (14.7±3.2 men and 13.5±3.2 women) and values at discharging of the Postoperative Care unit (24 hours later) of 11.3±1.6 g/dL (11.6±2.6 men and 10.8±2.5 women). All patients received postoperative CBCII blood conservation system excepting surgeries with suspicion of infection. The mean use of TXA was 0.75±0.38 g IV intraoperative and 0.54±0.44 g iv postoperative. We have no cases of adverse effects related to the use of intravenous TXA. Bleeding was considered to be greater than usual in 7.5% of patients.

The transfusion rate was 3.8% (1.33±0.76 RBC units) and it is mainly from the point of view of the patients to the presence of heart disease ischaemic or history of stroke or thrombosis, which contraindicated the use of TXA. We observed preoperative Hb levels lower than 13 g/dL in 23.9% of the patients (4.4% men and 19.5% women). A 6.29% of women had preoperative Hb levels below 12 g/dL. The ratio of transfusion was 5.0 times higher with Hb <13 g/dL and also 2.0 times higher in women when the cut-off point was set at 12 g/dL.

Conclusion: The use of a perioperative protocol of intravenous TXA adapted to the target population in prosthetic knee surgery has significantly reduced the consumption of blood components. The next two phases of perioperative care for patients include the topical use of TXA in cases that are contraindicated intravenously and the optimization of perioperative Hb levels with a Patient Blood Management program.
P66

Use of a fibrin sealant (EVICEL®) within a blood-sparing protocol in patients undergoing total hip arthroplasty revision: effects on post-operative blood transfusion and health-care related cost analysis

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**Background:** Blood transfusion and haemostasis are important aspects of preoperative planning and intraoperative decision making in orthopaedic surgery. Humanitas Research Hospital adopted a new blood-sparing protocol. Strategies include the use of autologous blood donation and administration of erythropoietin, acute normovolemic haemodilution, hypotensive anaesthesia, tranexamic acid, intraoperative and postoperative blood salvage, and a fibrin sealant (EVICEL®) in selected case. Objectives of the study were: 1) to compare the total number of transfusions and the length of hospital stay in patients undergoing total hip arthroplasty (THA) revisions with and without the use of EVICEL® and 2) to evaluate the possible role in cost savings of EVICEL® in association with the blood-sparing protocol.

**Methods:** Retrospective observational study evaluating patients undergoing THA revision with the blood-sparing protocol with (n=50) and without EVICEL® (n=60). The outcome measures were: number of patients transfused (allogeneic red blood cells – RBC - and plasma), amount of blood/plasma transfusions, quantity of re-infused recycled blood, and length of hospital stay. An economic model was developed to quantify the differences in costs between the two groups.

**Results:** EVICEL® reduced the number of transfused red blood cells and plasma (p <.001), and the hospital stay (p=.01). EVICEL® can induce a reduction in resource consumption with an average cost-savings of €1.676 per patient.

**Conclusion:** EVICEL® may be effective in reducing red blood cells and plasma transfusion as well as hospital stay. The inclusion of EVICEL® in the blood-saving protocol seems to produce clinical appropriateness and cost savings.

**Key words:** Total hip arthroplasty, Revision, Blood management, Transfusion, Fibrin sealant, Evicel.
Heparin induced thrombocytopenia in critical ill patient. Case report

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Introduction: Heparin-induced thrombocytopenia (HIT) is a prothrombotic state that affects roughly 1 in 5000 hospitalized patients and is caused by antibodies directed against platelet factor 4-heparin complexes. The diagnosis is often difficult and is based on a combination of clinical criteria and laboratory tests. Treatment involves suspension of all forms of heparin and institution of an alternative anticoagulant. The aim of this report is to analyse the management of anticoagulation in an intensive care patient setting.

Methods: We present the case of a 56-year-old male patient, who was admitted to our hospital with acute necro-haemorrhagic pancreatitis. He had hypertension, stage III chronic renal disease, cholecystectomy and familiar hypertriglyceridemia with 3 previous episodes of pancreatitis. On arrival the patient showed multiple organ failure, needing intensive care unit admission.

Results: On day 21 of hospitalization, thrombosis of the splenic and superior mesenteric vein was diagnosed, and 2 days later a thrombus in the left main pulmonary artery without associated ventricular dysfunction. An infusion of unfractionated heparin (UFH) was initiated, and after seven days Immunohemotherapy department was contacted due to a thrombocytopenia of 24 x 10.9 platelets/L. (initial count 134 x 10.9 platelets/L). The patient had an intermediate 4Ts score for HIT based upon the timing and magnitude of platelet count fall and the possibility of alternative explanations for his thrombocytopenia. Both the Heparin/PF4 antibody assays performed were strongly positive. The heparin infusion was immediately stopped; however, the high haemorrhagic risk did not allow to start an alternative anticoagulant (argatroban), which was only possible on day 44. After heparin discontinuation the platelet count quickly began to rise, and argatroban was started (dose of 2 mcg/kg/min via continuous infusion and adjusted based on routine laboratory values) and maintained for 12 days (count 179 x 10.9 platelets/L). On day 56 he developed a haemorrhagic shock requiring hemodynamic resuscitation with a high transfusion profile, emergent embolization of the gastroduodenal artery. Since then it was not possible to restart the anticoagulation due to the multifactorial instability and high haemorrhagic risk however the platelet count remained normal. The patient remains hospitalized in the Intensive Care Unit (ICU) and after more than 90 days he is slowly improving his medical condition. No new thrombotic episodes were recorded.

Conclusion: Thrombocytopenia is one of the most common laboratory abnormalities in critically ill patients. HIT is an important aetiology of thrombocytopenia in critical illness that is associated with high mortality. In this case, and despite the patient presenting with other possible causes of thrombocytopenia, clinical suspicion and laboratory diagnosis were supported by the rapid increase in platelet count once heparin was stopped. The severity of the patient’s condition did not allow to maintain any anticoagulation emphasizing the common difficulties that critical care patients to hold the correct antithrombotic therapy.
Impact of direct oral anticoagulant therapy on the management of hip fracture patients

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Introduction: Management of patients with hip fracture can be complicated by preoperative direct oral anticoagulant (DOAC) therapy. This retrospective analysis aimed at assessing the impact of such treatment on the anaesthetic management of elderly patients undergoing surgical treatment of their hip fracture.

Methods: We retrospectively reviewed all hip fractures operated from December 2017 to May 2018 (N=184) at our institution. Of these, 16 were treated with DOAC for atrial fibrillation. These patients (DOAC group; N=16) were matched on 1:2 ratio with patients not taking any anticoagulant (Control group; N=32) on the basis of the following criteria: age, type of surgery and anaesthesia (general vs. neuraxial) and time of admission (working days vs. week-end). Normally distributed variables (mean ± SD) were compared using a student t test. Non-normally distributed data (median [25-75 percentiles]) were compared using a Mann-Whitney U test. Non continuous variables were compared with a Chi square and presented as percentage.

Results: In the DOAC group, 15 patients received anti-Xa and one anti-IIa treatment. None received direct antagonist or PCC. Patients under DOACs had higher ASA status, with a higher incidence of ischemic heart and chronic kidney diseases. They took more frequently beta-blocking agents and diuretics. Preop and final Hb were not different between groups. Time from admission to operation was significantly higher in the DOAC group (Table). Number of units transfused was not different between groups (2 [1.8-2.0] versus 2 [2.0-2.0]; p=0.805).

<table>
<thead>
<tr>
<th>Preop variables</th>
<th>DOAC group</th>
<th>Control group</th>
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<tr>
<td>Age (y)</td>
<td>88 [64-89]</td>
<td>88 [62-69]</td>
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<tr>
<td>Gender (M/F)</td>
<td>11/5</td>
<td>27/5</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>28 ± 5</td>
<td>23 ± 4</td>
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<tr>
<td>aPTT (s)</td>
<td>25 [23-32]</td>
<td>23 [22-25]</td>
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<tr>
<td>F1 (%)</td>
<td>73 [63-86]</td>
<td>91 [84-100]</td>
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<tr>
<td>Fibrinogen (mg/dl)</td>
<td>3.45±0.68</td>
<td>3.34±0.57</td>
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</table>

<table>
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<th>Outcome variables</th>
<th>DOAC group</th>
<th>Control group</th>
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<tr>
<td>Admission to operation (h)</td>
<td>42 [31-61]</td>
<td>7 [4-24]</td>
<td>0.009</td>
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<tr>
<td>Blood loss (ml)</td>
<td>683±442</td>
<td>685 ± 231</td>
<td>0.458</td>
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<td>Patients transfused (%)</td>
<td>62.5</td>
<td>34.4</td>
<td>0.064</td>
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<tr>
<td>Complications (%)</td>
<td>63</td>
<td>44</td>
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<tr>
<td>30-day mortality (%)</td>
<td>12.5</td>
<td>6.3</td>
<td>0.460</td>
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<tr>
<td>90-day mortality (%)</td>
<td>25</td>
<td>6.3</td>
<td>0.064</td>
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</tbody>
</table>

Conclusion(s): In the conditions of our study, management of hip fracture patients treated with DOAC resulted in a delayed surgical repair with no apparent increase in the immediate postoperative complications rate.
Pharmacokinetics of enoxaparin after coronary artery bypass grafting. Randomized clinical trial

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Introduction: The aim of the study was to investigate pharmacokinetics of enoxaparin in elective coronary artery bypass grafting (CABG) patients by comparing the plasma anti-FXa activity levels when low molecular weight heparin (LMWH) enoxaparin is administered in continuous intravenous infusion or as in single subcutaneous shot.

Methods: This was a clinical, prospective, randomized, single blinded, controlled trial. 39 elective, on-pump CABG patients were randomized to receive 40 mg enoxaparin per day as in continuous intravenous infusion (IV-group) or 40 mg of enoxaparin once a day as a single subcutaneous shot (SC-group). Enoxaparin was initiated six to ten hours after the end of the surgery. Plasma anti-FXa activity levels were studied from blood samples 12-14 times during the study period of 72 hours. The maximum concentration of enoxaparin (anti-FXa C\textsubscript{max}) within 0-24 hours and 0-72 hours was recorded in both study groups. Compression ultrasound was made during the study period to detect deep vein thrombosis.

Results: 20 patients in IV-group and 18 in SC-group were included in the analysis of C\textsubscript{max}0-24h. C\textsubscript{max}0-24h were 0.15 IU/mL (IQR 0.13-0.19) vs. 0.25 IU/mL (IQR 0.18-0.32), p <0.005, in the IV- and SC-groups, respectively. C\textsubscript{max}0-72h were 0.15 IU/mL (IQR 0.11-0.20) vs. 0.27 IU/mL (IQR 0.20-0.32), p <0.005. One patient in IV-group and two in SC-group had clinically significant bleeding. Deep vein thrombosis or pulmonary embolism was not detected during the study or follow up period of 90 days. There was no 90 days mortality.

Conclusions: The anti-FXa concentrations were statistically significantly lower in IV-group compared to SC-group. In both study groups anti-FXa maintained in the level that is considered sufficient for postoperative thromboprohylaxis (0.1-0.3 IU/mL) in the literature. IV-infusion may offer a choice for thromboprohylaxis by providing more steady anticoagulation effect without high concentration peaks. More studies are needed of this matter.
A systematic review and meta-analysis of incidence of venous thromboembolism in pregnancy

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Introduction: Literature on venous thromboembolism (VTE) in pregnancy is disparate and has not assessed the impact of VTE events based on existing risk stratification systems, which guide prophylaxis. Our objective was to systematically assess the incidence of VTE during pregnancy according to varying risk factors and determine if VTE events influence pregnancy outcomes.

Methods: Systematic searches of electronic databases were conducted to identify studies of VTE events in pregnant women with and without risk factors. EMBASE, MEDLINE, CINHAL, AMED and BNI were searched from inception until 2018. Included studies were grouped into three categories: those without risk factors (all pregnant women), those with risk factors for VTE and those with pre-existing thrombophilia. Where possible data were pooled using analysis of proportions, with a random effects model, assuming binomial distribution of study level data.

Results: Fourteen studies met the inclusion criteria: four studies in all pregnant women (3,654,396 women), six in women with risk factors (24,997 women) and four in studies of women with pre-existing thrombophilia (6,209 women). The incidence of VTE events in the ‘all pregnant women’ group ranged from 4.9-8.7 per 10,000 women. In the ‘women with risk factors’ group the incidence ranged from 42-480 per 10,000 women. In the ‘women with thrombophilia’ group, the incidence ranged from 8.2-42.4 per 10,000 women, with a pooled incidence of VTE of 18 per 10,000 women.

Conclusion: Incidence of VTE events in pregnancy do not correlate with existing risk classification systems. Future research should determine how VTE events impact pregnancy outcomes.
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