Preoperative Anemia Management

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Introduction

- University of Colorado Hospital, a Level 1 Trauma Center located on the Anschutz Medical Campus in Aurora, Colorado
- Flagship hospital for the UCHealth hospital system, serving Colorado and surrounding states
- Received our fifth Magnet designation in 2021

- Preprocedure Services Clinic
  - Anesthesia optimization clinic staffed with advanced practice providers and Department of Anesthesia faculty
  - Referral based clinic offering in person clinic and telehealth appointments

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Anemia – Definition and Criteria

- Anemia is generally defined as a hemoglobin value of <13 gm/dl in males and <12 gm/dl in females
- For high blood loss procedures, preoperative anemia is defined as <13gm/dl in both men and women as women tend to have a greater loss of red cell mass
- Iron deficiency anemia is a common type of anemia and diagnosed by one of the following findings:
  - Serum ferritin <30 ng/ml
  - Anemia that resolves upon iron administration
  - Absence of stainable iron in the bone marrow
  - Transferrin saturation <19 percent

Lin Y. Preoperative anemia-screening clinics. Hematology Am Soc Hematol Educ Program. 2019 Dec 6;2019(1):570-576.

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Facts about Iron

- Iron
  - Mineral
  - Two types of iron
    - Heme – primarily sourced from animal protein and easily absorbed
    - Non heme – plant based, also found in enriched grains and fortified cereals
- Iron is required for major physiologic processes:
  - Oxygen transport (as hemoglobin)
  - Muscle oxygenation (as myoglobin)
  - Synthesis of DNA, RNA and proteins
  - Cellular respiration (as cytochromes)
  - Immune function
  - Myelin sheath formation

https://medschool.co/tests/ironstudies

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Facts about Iron

- Absorption occurs in the duodenum, converts to the ferrous form (FE2+)
- Primarily stored as ferritin, found in macrophages and in the liver
- Regulation is provided by hepcidin
  - Intestinal absorption
  - Storage within the liver
  - Recycling by macrophages
- Hepcidin levels are controlled by several factors
  - Serum iron levels
  - Anemia
  - Hypoxia
  - Inflammation
- Overexpression of hepcidin may be a marker for anemia of chronic disease

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Prevalence of Iron Deficiency Anemia

- Iron deficiency impacts over 2 billion people globally and is the most common cause of anemia worldwide.
- Depending on the population, rates of anemia may be as high as 40%
- High risk populations include:
  - Preschool age children
  - Menstruating women
  - Pregnant women
- Preoperative anemia is not uncommon and is known to be correlated with postoperative mortality and morbidity

Camaschella, C. Iron-Deficiency Anemia. N Engl J Med 2015;372:1832-43.
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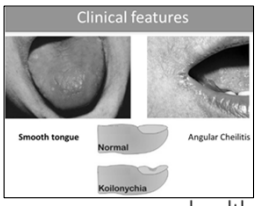
Clinical Features of Iron deficiency

- Common symptoms of anemia include:
  - Fatigue and lethargy
  - Shortness of breath and lightheadedness
  - Tachycardia
  - Headache
  - Pica - craving of non-food items such as ice, chalk and dirt
- Signs of anemia include:
  - Conjunctival pallor
  - Alopecia
  - Koilonychia or spoon-shaped nails
  - Atrophic glossitis or smooth tongue
  - Angular stomatitis/cheilitis



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Iron Deficiency Anemia

- Bleeding is known to be the most common contributing factor
  - Gastrointestinal
  - Gynecological
- Iron absorption issues
  - Celiac disease
  - Gastric surgery
  - Irritable bowel disease
  - Kidney failure and difficulty producing red blood cells
  - Use of antacids, proton pump inhibitors
  - Foods containing calcium, tannins, and phytates

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Iron Deficiency Anemia

- Medications: Aspirin, clopidogrel, warfarin, heparin
- Increased iron requirements:
  - Pregnancy
  - Rapid growth in pediatric patient population
  - Use of erythropoiesis-stimulating agents
- Insufficient dietary iron intake
  - Vegetarian
  - Vegan

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Iron Profile

Lab Exams	Comments	In IDA
Serum Fe (50-100 mcg/dL)	1. It is the **concentration bound to transferrin** 2. Approximately one-third transferrin bound to iron 3. **Levels are decreased by infection and inflammation** 4. **Best interpreted in conjunction with TIBC**	Low
Serum ferritin (>10-20 mcg/L)	1. **Ferritin (storage iron) is proportional to total iron stores** 2. **Best indicator of iron deficiency or overload** 3. Infection or inflammation can increase the concentration, independent of iron status	Low
Total iron binding capacity (TIBC) (250-410 mcg/dL)	1. Indirect measurement of the iron-binding capacity of serum transferrin (protein) 2. **Levels don't fluctuate** over hours or days unlike serum iron	High
% Saturation of transferrin (>20%)	1. Ratio of serum iron level to TIBC in percentage 2. Reflects the extent to which iron-binding sites are occupied on transferrin and **indicates the availability of iron for erythropoiesis** 3. Less sensitive and specific for IDA than ferritin	Low

DiPiro J. Anemia. In: Pharmacotherapy: A Pathophysiological Approach, 2011

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Negative Effects of Blood Transfusions

- Risk of transfusion has been found to be dose dependent with as little as **a single transfusion of one unit increasing the risk of adverse outcomes**
- Two leading causes of transfusion related morbidity and mortality
  - TRALI Transfusion related acute lung injury
  - TACO Transfusion associated circulatory overload
- Other adverse effects:
  - Increased mortality
  - Increased hospital length of stay
  - Surgical site infections
  - Multisystem organ failure

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Why Iron Replacement?

- Preoperative iron deficiency anemia is associated with:
  - Increased risk of transfusion
  - Increased postoperative mortality
  - Increased risk of major cardiac and cerebrovascular events
  - Postoperative ICU admission
  - Prolonged hospital length of stay
- Iron deficient patients are known to have poorer outcomes, adding transfusion increases the risk of an adverse outcome
- Improving hemoglobin levels preoperatively will decrease blood transfusions and overall improve surgical outcomes.

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Jin L, Kapadia TY, Von Gehr A, et al. Feasibility of a Preoperative Anemia Protocol in a Large Integrated Health Care System. *Perm J.* 2019;23:17-200.

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Treatment Modalities – Oral Iron

- Oral iron therapy is ineffective in treating preoperative iron deficiency
  - Propensity for GI side effects and noncompliance with therapy
  - Poor absorption due to inflammatory bowel disease, celiac disease, previous bowel resections
- Oral therapy also requires a 3 to 6 month window for optimal treatment
- Side effects of oral iron include:
  - Nausea
  - Constipation
  - Diarrhea
  - Abdominal pain and flatulence
  - Heartburn

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Treatment Modalities – IV Iron

- Indications include:
  - Intolerance to oral iron therapy
  - Less than 4 to 6 weeks to surgery
  - Severe anemia as indicated by hemoglobin <10 g/dL
- Side effects may include:
  - Anaphylaxis
  - Hypotension
  - Fever
  - Arthralgia
  - Myalgia
  - Back pain
  - Headache

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Types of IV Iron and Indications for Use

Drug	Trade Name	Indication	Test Dose
LMW Iron dextran	INFeD	If oral iron cannot be used	Yes, before first dose
Ferric gluconate	Ferrlecit	Hemodialysis patients with erythropoietin therapy	Not required; recommend if multiple allergies
Iron sucrose	Venofer	Chronic Kidney Disease	Not required; recommend if multiple allergies
Ferumoxytol	Feraheme	Chronic Kidney Disease	No
Ferric carboxymaltose	Injectafer	If oral iron cannot be used	No
Ferric derisomaltose	Monofer	If oral iron cannot be used	No

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https://www.uptodate.com/contents/image?imageKey=HEME%2F106130

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IV Iron Adverse Effects

- IV iron infusions may cause a true allergic reaction
- Self-limiting non-allergic reactions are a known risk with IV iron infusions
- Less than 1% of patients may experience a non-allergic reaction with symptoms such as urticaria, heart palpitations, dizziness, neck/back spasms
- Some experience a Fishbane reaction or non-allergic reaction with facial flushing, muscle aches in the chest and back
- Higher rates of allergic and non-allergic reactions were associated with high molecular weight iron dextran, which is no longer available

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Hypersensitivity Symptoms

Mild	Moderate	Severe
• Hypertension • Itching • Flushing • Slight chest tightness • Joint pain	• Urticaria • Chest tightness • Shortness of breath • Cough • Nausea • Vomiting	• Wheezing • Stridor • Cyanosis • Loss of consciousness • Cardiopulmonary arrest

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Potential Return on Investment

- Clinical trials have proven that a focused approach to the preoperative treatment of iron deficiency anemia amplifies hemoglobin concentrations thus decreasing perioperative transfusions
- Despite those benefits, minimal data has been gathered to reflect the impact on hospital costs and reimbursement, thus very few patients are offered this treatment
- Study conducted over 2 year period after implementation of an anemia management clinic found the following in a cohort of elective colorectal cases:
  - The number of patients screened increased from 13% to 73%
  - Decreased RBC transfusion by 50%
  - Reduction in cost for colorectal surgery

Trentino K, Mace H, Symons K, et al.. Associations of a Preoperative Anemia and Suboptimal Iron Stores Screening and Management Clinic in Colorectal Surgery With Hospital Cost, Reimbursement, and Length of Stay: A Net Cost Analysis. *Anesthesia & Analgesia*. 2021; 132 (2): 344-352.

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Background:

Cardiac patients given a unit of PRBCs intraop (Hgb 9-12)

- higher length of stay
- acute kidney injuries
- higher rate of postoperative cognitive dysfunction
- higher cost of care in comparison to reimbursement

ROL: Preop IV Iron can increase Hgb in iron deficient patients.

Goal: Reduce the rate of periop transfusions for iron deficient/anemic patients undergoing CABG surgery.

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Process

- Population: **Isolated CABG***, Spine, Total Joints, Ortho Limb, Bowel, Gyn-Onc
- AgileMD pathway – labs to be ordered and IV Iron orders
- Preprocedure Services – screening and identification
- Outpatient Infusion Center – schedule appointment for infusion (2 - 3 weeks)

Data

Postoperative cognitive delay, perioperative Hgb levels, transfusion rates, renal dysfunction, length of stay, reimbursements, and cost of care.

GO LIVE: March 8, 2021

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- Lead by anesthesiology department
- Go Live March 8, 2021
- Stakeholders
  - Anesthesiologists
  - Surgical Team
  - Advanced Practice Providers
  - Pharmacists
  - Nurses
  - Schedulers
- CABG Surgery
- Referral to Preprocedure Services (PPS)
- Coordinate appointments (Surgery clinic and Preprocedure clinic)

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Initial laboratory criteria

- Hgb < 12 g/dl
- Order Iron Panel: Ferritin, TSat, TBIC, Serum Iron and Reticulocyte Count

Follow up laboratory criteria

- Ferritin <50
- Transferrin Saturation <20%
- TIBC >450
- Serum Iron <40

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Anemia Clinic Process

IV Iron and Oral Iron Treatment plan ordered by Preprocedure Services (PPS) Provider

PPS RN notified to inform Outpatient Infusion Center (OIC)

OIC reviews and verifies insurance coverage

OIC schedules patient for treatment

PPS RN keeps track of patient's activity until day of surgery

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Anemia Clinic Patient Tracking Tool

- Identification

Date of Referral Request	Patient Name	MRN/DOB	DOS (CABG or SPINE)	PPS appt	Hgb	City or Town in Colorado	Anemia labs (Iron/Ferritin) Ordered and Completed-	Anemia Lab- WNL or Abnormal	Comments before Infusion is scheduled	Does patient need an Infusion (YES/NO)

- Infusion

EM sent to Outpatient Infusion Center (OIC)	Infusion Date	Comments after Infusion

- Evaluation

Return Visit (PPS/VV-1 week after Infusion or before surgery date if less than a week)	Comments	Instructions to CR	Status

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Patient Experience

- Patient A – Spine Surgery (5/23/2021)
- Screening (4/17/2021) Initial Hgb = 11.8
- PPS Evaluation (4/19/2021)

Component	Ref Range & Units	5/11/21 1312	4/19/21 1553
White Blood Cell Count	4.0 - 11.1 10*9/L	7.0	11.4
Red Blood Cell Count	4.18 - 5.64 10*12/L	4.86	5.10
Hemoglobin	12.1 - 16.3 g/dL	12.7	11.8
Hematocrit	35.7 - 46.7 %	40.9	39.8

Component	Ref Range & Units	5/11/21 1312	4/23/21 1459	4/19/21 1553
Ferritin Serum/Plasma	11 - 307 ng/mL	210	6	7
Resulting Agency		AMC Lab	AMC Lab	AMC Lab

Component	Ref Range & Units	5/11/21 1312	4/23/21 1459	4/19/21 1553
Total Iron Binding Capacity	284 - 507 ug/dL	332	480	512
Iron Serum/Plasma	45 - 160 ug/dL	73	20	14
Iron % Saturation	15 - 56 %	22	4	3
Unsat. Iron Binding Capacity	124 - 462 ug/dL	259	460	498
Transferrin	203 - 362 mg/dL	237	343	366

- Periop Course
  - EBL = 1600
  - PRBC = 2 units

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Outcomes

- Data: March 2021 to December 2021
- Patients – 32 identified based on initial Hgb criteria
- 14 completed the treatment plan
- 18 did not complete anemia clinic process
  - Follow ups were normal
  - Patients were managed by PCP and Nephrologist
  - Surgeries were escalated
  - Surgeries were cancelled
  - Patient refused treatment

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Postoperative Outcomes/Results

Surgical Service	PPS - Hgb	Preop Hgb (post iron transfusion)	EBL	Intraop PRBC (units)	Postop PRBC (units)	
Ortho- Spine	11.8	12.7	1600	2	0	
NSGY- Spine	10.3	10.3	1000	1	0	
Ortho- Spine	11.2	15.3	100	0	0	
Ortho- Spine	11.9	12.1	<50	0	3	
CT- Aortic Aneurysm	14.6	13.1	<50	1 (autologous)	0	
Ortho- Spine	11.7	12.2	1500	2	1	
Endocrine- Thyroid	7.5	7.5	<50	0	0	
Ortho- Spine	10.8	13.7	250	0	0	
Ortho- Joint- Knee	11.1	11.1	1000	1	2	
Ortho- Spine	10.9	9.8	600	2	0	
Gen Surg- Chole	11.0	11.0	<50	0	0	
Ortho- Joint- Knee	11.6	13.0	<50	0	0	
Ortho- Joint knee	8.3	9.0	600	1	0	
Transplant- Nephrectomy	9.7	9.7	<50	0	1	
Ortho - Joint Knee	9.8	9.8	300	0	0	
Other factors reviewed during study are comorbidities: DM II, HTN, CKD, obesity, anticoagulant therapy						

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Challenges and Barriers

- Not enough CABG patients enrolled
  - Spine and Total Joint surgeries
- Logistics
  - Patient lives far >2 hour drive
- Lack of insurance coverage
  - Pay out of pocket
- COVID Infection
  - Elective surgeries cancelled
  - Surgeries confirmed 2 weeks out with not enough time
- Gaps in Processes
  - Clinic providers were unaware of the processes and labs were not ordered in time
  - Timing of follow up labs – whose responsibility?

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Summary

- Treatment of anemia with IV iron infusions requires less time for treatment, has a greater absorption rate, and does not produce the side effects of oral iron.
- Clinical trials have shown that a focused approach to the preoperative treatment of iron deficiency anemia improves surgical outcomes by decreasing perioperative transfusions and associated sequela
- Despite these advantages, a minimal amount of data has been gathered to reflect the total impact on hospital costs and reimbursement, needed to justify program development.

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Resources

- Camaschella, C. Iron-Deficiency Anemia. N Engl J Med 2015;372:1832-43. DOI: 10.1056/NEJMra1401038
- Goot K, Hazeldine S, Bentley P, Olynyk J, Crawford D. Elevated serum ferritin - what should GPs know? Aust Fam Physician. 2012 Dec;41(12):945-9. PMID: 23210117.
- Lin Y. Preoperative anemia-screening clinics. Hematology Am Soc Hematol Educ Program. 2019 Dec 6;2019(1):570-576. doi: 10.1182/hematology.2019000061. PMID: 31808909; PMCID: PMC6913451.
- Jin L, Kapadia TY, Von Gehr A, et al. Feasibility of a Preoperative Anemia Protocol in a Large Integrated Health Care System. *Perm J*. 2019;23:17-200. doi:10.7812/TPP/17-200
- Spahn D, Goodnough L. Alternatives to blood transfusion. The Lancet. 2013 May;381(9880):1855-1865. doi.org/10.1016/S0140-6736(13)60808-9
- Trentino K, Mace H, Symons K, et al.. Associations of a Preoperative Anemia and Suboptimal Iron Stores Screening and Management Clinic in Colorectal Surgery With Hospital Cost, Reimbursement, and Length of Stay: A Net Cost Analysis. *Anesthesia & Analgesia.* 2021; 132 (2): 344-352. doi: 10.1213/ANE.0000000000005241.

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Thank you…
See you in Colorado

ASPAN's 42nd National Conference
April 27-30, 2023
Denver, Colorado

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