

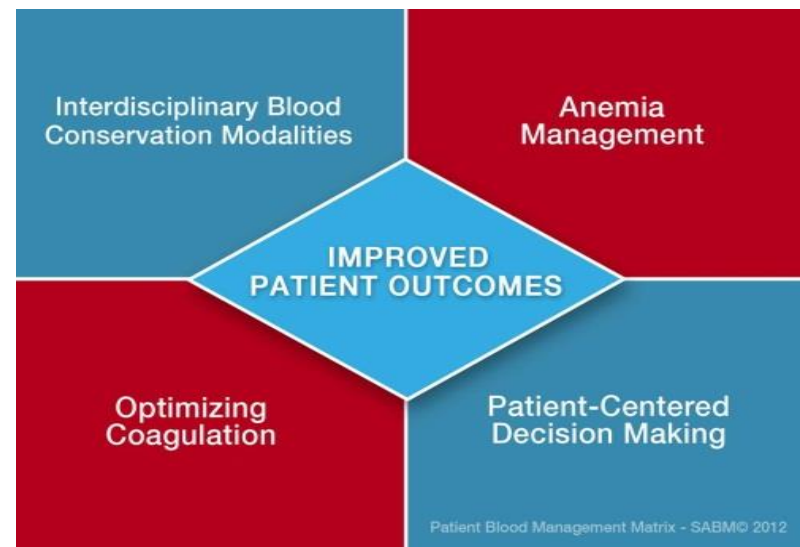
# Peri-Surgical Anemia and the TAVR Patient

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April, 2015

MIDWEST VALVE SYMPOSIUM, April 2015

# Credentials and Conflicts of Interest

- Pathologist (AP/CP/Tx. Med) and Director of Patient Blood Management and Pre-OP Anemia Clinic, Fairview Southdale Hospital
- AABB Standards Committee: Patient Blood Management
- Society for the Advancement of Blood Management (SABM) “Iron Corner” Expert Panel.
- Medtronic Speakers Bureau for “Rethinking Blood Conservation”
- Founder and Chief Medical Officer, Patient Readiness Institute.

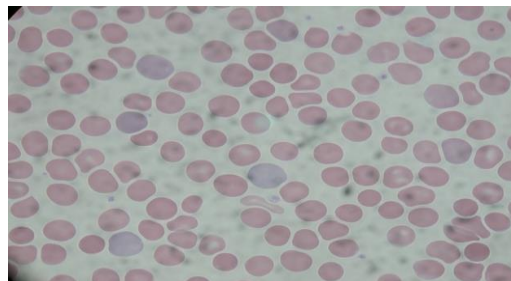
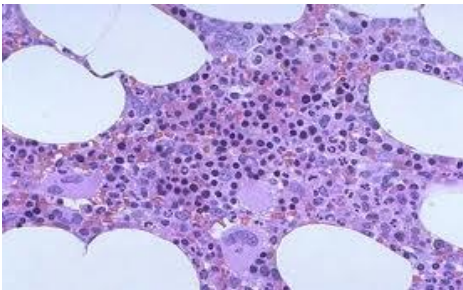


# Disclaimer

**No off-label use of medications or commercial products will be discussed in this presentation.**

# Anemia and the TAVR Patient

- What do we know?
- SAVR, TAVR, Pre-OP anemia, transfusion, Post-OP anemia
- What can we do?
- LOTS (do new things, do less of things we've commonly done)



# What we know from SAVR

reference 1

- Anemia prior to SAVR 30-40% (WHO criteria= Hgb <12 females; 13 males)
- STS-ACA guidelines ( since 2007)have recommended case start Hgb of 12.9 or > regardless of gender
- Mortality and composite morbidity 3 times higher in patients with pre-operative anemia, correlates directly with the degree of anemia
- Thresh-hold for increased M and M is Hgb 12

**Table 2:** Unadjusted outcomes

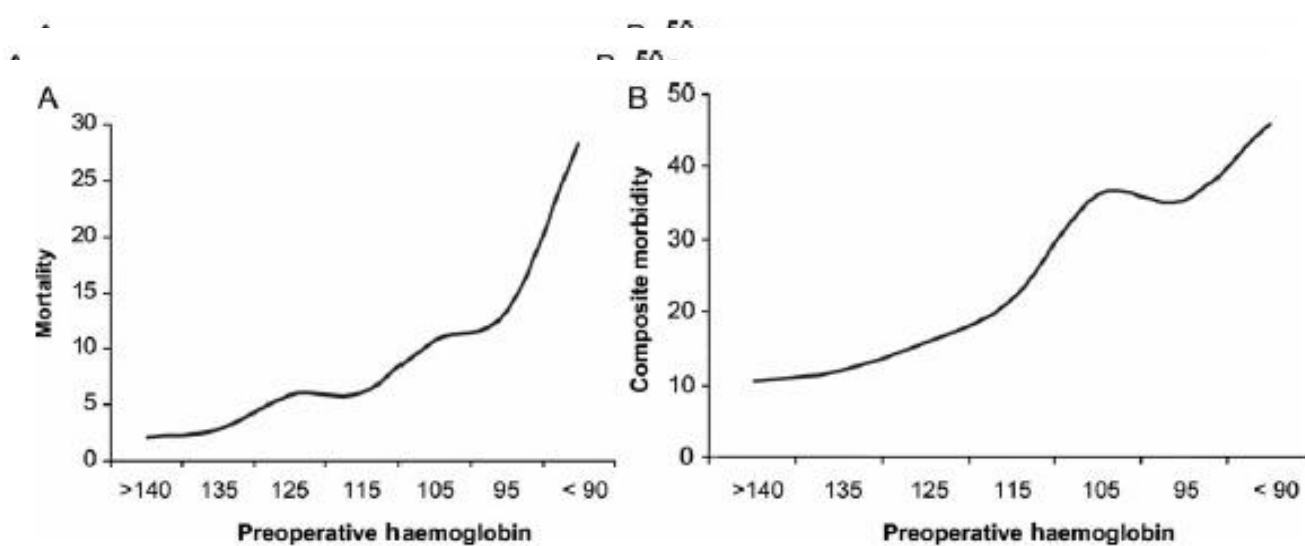
Variable	Non-anaemic patients (n = 1830)	Anaemic patients (n = 868)	*P-value
Mortality	2.8%	8.0%	<0.0001
Periop. MI	1.8%	2.3%	0.29
Stroke	1.6%	3.2%	0.007
RRT	3.0%	11.4%	<0.0001
Prolonged ventilation	9.5%	23.8%	<0.0001
Deep sternal infection	0.4%	0.9%	0.08
Composite morbidity	11.2%	28.0%	<0.0001

RRT: renal replacement therapy; periop.: perioperative; MI: myocardial infarction.  
\*P-value between anaemic and non-anaemic patients.

**Table 4:** Multivariable analysis: predictors of composite morbidity

Variable	Odds ratio	95% CI	P-value
Preop. Hb <sup>a</sup>	1.35	1.04–1.76	0.021
Age	1.025	1.14–1.036	<0.0001
Preop. creatinine	1.006	1.004–1.008	<0.0001
Total CPB time	1.011	1.009–1.014	<0.0001
Redo surgery	0.625	0.45–0.869	0.0052
Diabetes	1.642	0.496–0.832	0.0008
Urgent surgery	1.551	0.425–0.715	<0.0001
Peripheral vascular disease	0.631	0.543–0.879	0.0065
Intraoperative blood transfusion	1.977	1.49–2.61	<0.0001

Preop.: preoperative; CPB: cardiopulmonary bypass.  
<sup>a</sup>Per 10 g decrease of Hb.



**Figure 1:** The effect of Hb level on mortality (A) and composite morbidity (B). This figure illustrates the dose-dependent effect with a higher incidence of mortality and composite morbidity observable at an Hb level <120 g/L.

# What we know from SAVR

reference 1

- Anemic patients have higher burden of comorbid disease ( recent MI, CKD, DM, impaired LV function)
- Pre-operative anemia is the single most important determinant of blood transfusion (and the only thing that can be made better)
- Transfusion and pre-operatively are each independently associated with increased M and M and decreased long term survival

# What we know from TAVR

reference 2

- 10 center cohort, 1696 patients, Netherlands
- Pre-Operative Anemia (POA) in 57% (WHO Criteria)
- POA not associated with 30 day mortality but was associated with mortality and 1 and > years compared to initially non anemic patients
- POA patients transfused more and received more blood when transfused
- POA NOT associated with more bleeding than patients without POA
- Transfused patients- had increased mortality at 30 days and beyond



# What we know from TAVR

reference 2

## WHAT IS KNOWN

- Preoperative anemia is a common finding in elderly patients, in patients with heart disease, and in patients undergoing percutaneous and surgical cardiac interventions.

## WHAT THE STUDY ADDS

- Preoperative anemia is prevalent in more than half of patients undergoing transcatheter aortic valve implantation.
- Various baseline factors are associated with anemia, which in turn is strongly associated with 1-year mortality but not with early mortality.
- Patients with anemia receive more transfusions mostly for indications unrelated to overt bleeding, whereas transfusion is independently associated with both early and 1-year mortality.

# Data from 1 center in cohort

reference 3

- Anemia in 49% ( WHO criteria), blood collected 1 day prior to surgery, all Medtronic CoreValve, 118 patients, 115 TA-TF, 3 TA-TS, follow-up at 1 month, 1 year and yearly thereafter
- Transfusion criteria at discretion of care team (59% of all patients within 24 hours, 70% of all patients during hospital stay, no excess blood loss in POA patients).

Clinical outcome after TAVI (Valve Academic Research Consortium VARC) stratified for the presence of baseline anemia	Entire cohort (n=118)	No anemia n=60	Anemia n=58	P-value
Vascular complications- Any	22(19)	8(13)	14(24)	0.13
Bleeding complications-any	34(29)	14(23)	20(35)	0.18
Acute kidney injury	21(18)	13(22)	8(14)	0.34
30 day mortality	13(11)	7(12)	6(10)	0.82
1 year mortality	21(28)	6(25)	15(44)	0.006
Prolonged LOS > 14 days	32(27)	10(17)	22(38)	0.009)

Cause of death stratified for presence of anemia		
Cause of death	No anemia (60)	Anemia (58)
All cause mortality	15(25)	22(38)
Cause of death		
Cardiac < 30 days	3(5)	3(5)
Cardiac > 30 days	5(8)	6(10)
Non cardiac < 30 days	3(5)	3(5)
Non Cardiac > 30 days	4(6)	10(17)
Independent predictors of late mortality in patients undergoing TAVI	Hazard ration(%95 CI)	p-value
Pre-procedural anemia	2.10 (1.06-4.18)	0.034
Acute kidney injury	2.88 (1.4-5.93)	0.004

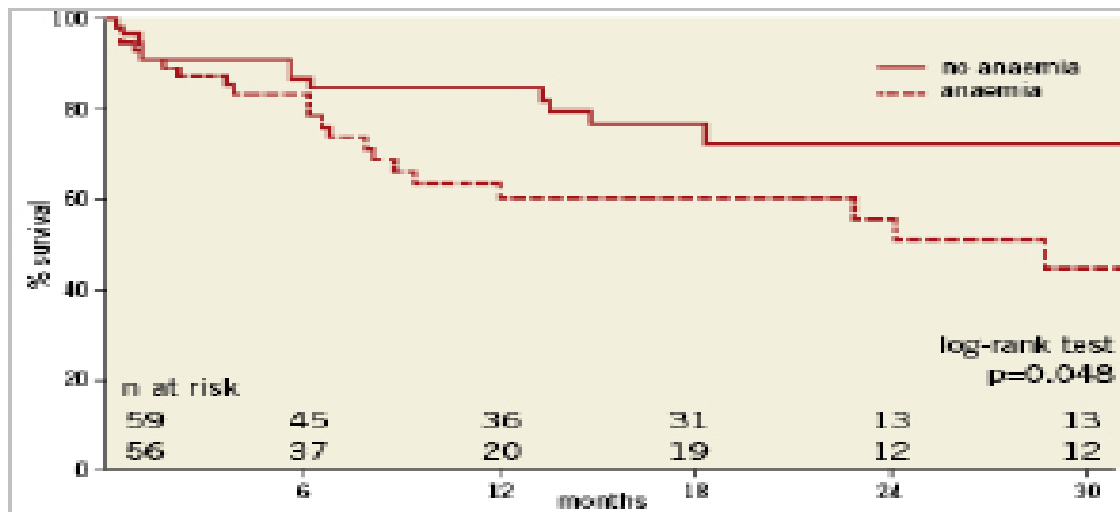


Figure 1. Kaplan-Meier survival curves with or without baseline anaemia.

# Transfusion in TAVR patients

reference 4

	Transfusion N=124	No Transfusion (N=208)	P Value
In-Hospital All-Cause Death	9%	1%	<.001
In Hospital Cardiac Death	8%	0.5%	<.001
Mortality at 30 days	11%	2%	< .001

30 day mortality was tripled when transfusion was due to bleeding complications rather than to other causes ( 18% vs 6%; P=.03)

Conclusions: In patients with anemia prior to undergoing TAVR, the Risk of short term mortality is heightened by the use of blood transfusions

# What we can do

- Identify and correct Hgb ( to  $> 12$ ) before procedure
- Transfuse less during procedure
- Identify and manage anemia post-hospital
- (40% of patients with baseline anemia will have this correct, those that don't do worse, we can help both) reference 5
- Transfusion impairs early hematopoiesis, transfused patients recover from anemia later ( ie transfusion is not helping unless alleviating syx)

# Why are our patients anemic?

- Anticoagulant medications
- Medications interfering with hematopoiesis (antacids, beta-blockers, ARB's, others)
- Underlying medical conditions (CKD)
- Inflammatory states ( iron sequestration), DM, autoimmune, CHF, obesity, others
- Bleeding (including after angiogram)
- Often multifactorial



# Lab Testing

## Initial Panel

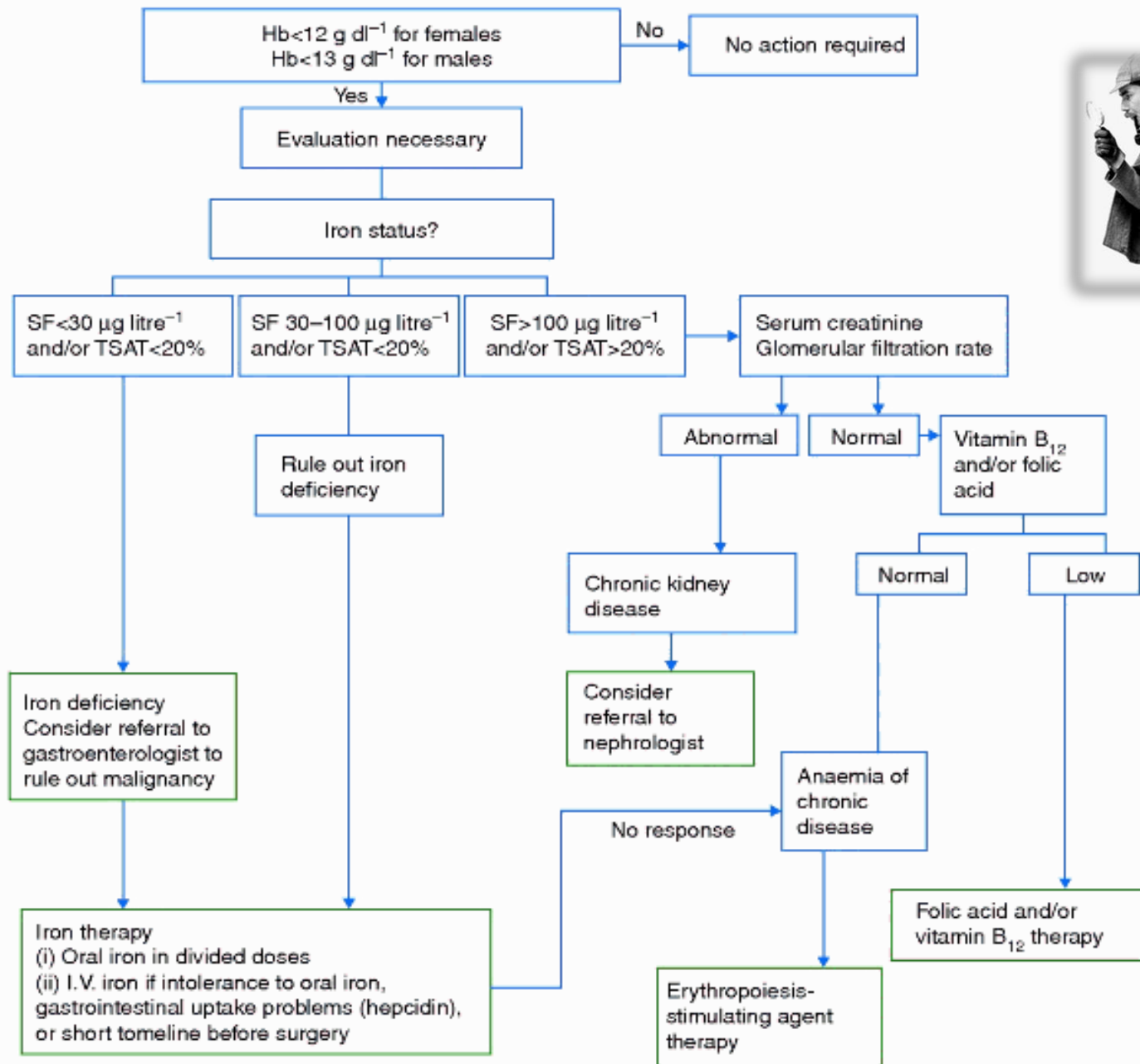
- CBC (need more than just Hgb)
- Reticulocyte count, Reticulocyte Hgb
- Creatinine with GFR
- Serum Iron, % saturation  
TIBC
- Ferritin



## Add on tests as needed

- CRP (i)
- Red cell folate
- Serum B12
- Soluble transferrin receptor
- LDH
- Haptoglobin
- DAT
- Differential
- blood morphology





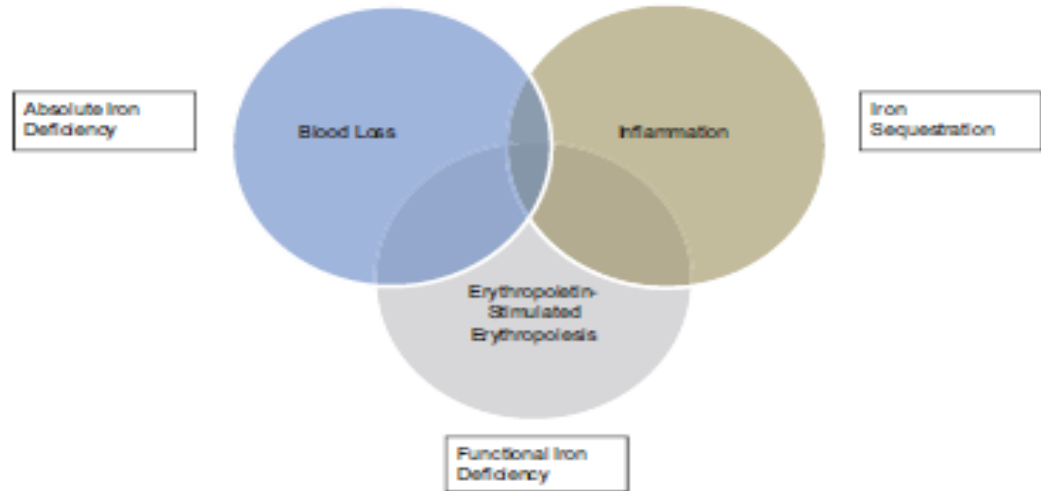
# Anemia Treatment

Safely increase Hgb 0.5-1 gm/week

- Treatment Options: IV iron, enteric iron, Erythropoietin stimulating agents (ESA's), Vitamin B-12, folate, treat co-morbidities, delay and defer
- IV iron, effect at 1 week, max effect at 2 weeks, several doses needed (1 gram divided dose common)
- ESA action onset 4-6 days, max at 10 days, must give with iron

# Iron Restricted Erythropoiesis

**Figure 1.** Iron deficiency syndromes. The relationships between absolute iron deficiency, iron sequestration, and functional iron deficiency are illustrated. Patients can have  $\geq 1$  combinations that all result in iron-restricted erythropoiesis. Adapted from Goodnough LT.<sup>61</sup>



**Table 3. Potential Role of Iron Therapy in Management of Anemia**

Condition	Expected hepcidin levels	Iron parameters	Iron therapy strategies	Potential hepcidin therapy
Absolute iron deficiency anemia (IDA)	Low	Low Tsat and ferritin	Orally or IV if poorly tolerated or malabsorbed	No
Functional iron deficiency (ESA therapy, CKD)	Variable, depending on $\pm$ CKD	Low Tsat, variable ferritin	IV	Antagonist (if hepcidin levels not low)
Iron sequestration (anemia of inflammation[AI], mixed anemia [AI/IDA, or AI/functional iron deficiency anemia])	High	Low Tsat, normal-to-elevated ferritin	IV	Antagonist
	Variable	Low Tsat, low-to-normal ferritin	IV <sup>a</sup>	Antagonist (if hepcidin levels not low)

Tsat = transferrin saturation; CKD = chronic kidney disease; ESA = erythropoiesis-stimulating agent.

<sup>a</sup>Mixed anemia is a diagnosis of exclusion without a therapeutic trial of iron.

Adapted from Goodnough LT.<sup>61</sup>

# Effects of Preoperative Intravenous Erythropoietin Plus Iron on Outcome in Anemic Patients After Cardiac Valve Replacement

Cladellas M, Am J Cardiol. 2012 Oct 1; 110(7): 1021-6.

- **75 consecutive patients- EPO + IV iron x 5 doses** (2006-2011)
- **59 observational cohort**
  
- **Decreased Post op morbidity** OR 0.13 p = 0.008
- **Decreased in hospital mortality** OR 0.16 p = 0.04
- **Decreased postop renal failure** OR 0.23 p = 0.03
- **Decreased Transfusion rate** 67 v 93% p=0.01
- **LOS (median)** 10 v 15 p= 0.01
  
- **Adjusted for Operative Risk Score, type of intervention, time on CPB, year of surgery**

# Anemia Treatment

- Standardized order sets, including coding for pharmacy approval and reimbursement
- IV iron is the most commonly used agent
- ESA use: Non CV or vascular surgery, anemia's with inflammatory or renal components, no autologous blood donation
- Patients getting ESA need DVT prophylaxis in hospital

# Is anemia treatable, including in a short timeframe?

## Yes – BUT!

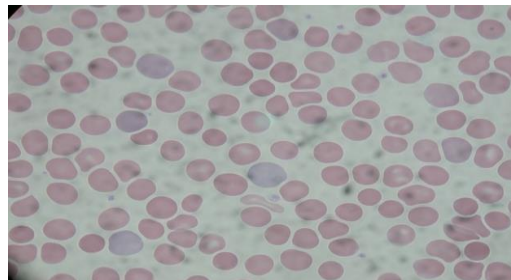
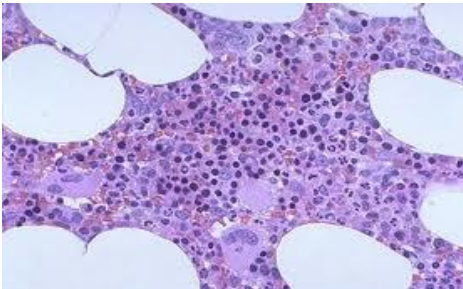
- Requires knowing the cause
- Requires knowing the absolute surgical timeframe (flexibility to delay surgery in select cases)
- Requires evaluating the patient as early as possible
- Requires knowing more than just lab values
- Requires understanding the treatment/medication options including risks, benefits, effectiveness and reimbursement rules
- Requires a standardized approach that integrates this information and reliably outputs treatment plans, gets patients treated quickly and safely and measures the results

# Manage post discharge anemia the same way

- Test, identify cause, treat, measure response, treat again if inadequate
- Pre-op consider akin to pre-operative Dental Clearance, consider part of the post-operative/hospital care process
- For Pre and Post hospital anemia “our care starts BEFORE you arrive and continues AFTER you leave” ...it does not occur only when you are within our walls.”

# Patients do best

- When their Hgb is adequate for the procedure
- When post procedure anemia is temporary and short lived
- When they are NOT transfused ( an UNDESIRABLE EVENT)





# References

- Elmistekawy, E. et al “Preoperative anaemia is a risk factor for mortality and morbidity following aortic valve surgery”. European Journal of Cardio-Thoracic Surgery 44(2013) 1051-56
- Nuis, R-J. et al. “Prevalence, factors associated with, and prognostic effects of pre-operative Anemia on short and long-term mortality in patients undergoing trans-catheter aortic valve implantation”. Circ Cardiovasc Interv, 2013;6:625-34
- Van Meighem N. et al. “Prevalence and prognostic implications of baseline anemia in patients undergoing trans-catheter aortic valve implantation”.  
[www.pcronline.com/eurointervention/37th\\_issue/32/](http://www.pcronline.com/eurointervention/37th_issue/32/)
- Alarcon, R. et al. “Blood transfusion increases mortality independent of hemoglobin levels in elderly patients undergoing trans-catheter aortic valve replacement”. J Am Coll Cardiol. 2014;63(12\_S)
- De Backer, O. et al. “Recovery from anemia in patients with severe aortic stenosis undergoing trans-catheter aortic valve implantation-prevalence, predictors and clinical outcome”. Open access. PLoS ONE 9(12):e114038. doi:10.1371/journal.pone.0114038