Anticoagulation, Bleeding and Transfusion

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Anticoagulation

Anticoagulants

- medicines that help prevent blood clots
- interrupting the process involved in the formation of blood clots
  (= blood-thinning)
- different to antiplatelet medicines(aspirin and clopidogrel)
- Drug; Heparin(UFH, LMWH), Warfarin,…
  NOAC(Non-Vit K antagonist Oral AntiCoagulants,
  New Oral AntiCoaulants) = DOAC(Direct acting Oral AntiCoagulants)
- For prevent; strokes or transient ischemic attacks ("mini-strokes"),
  heart attacks, deep vein thrombosis, pulmonary embolism

USE

- Extracorporeal circulation; Heart-Lung pump,

  ECMO, CRRT,..
- Heart valve surgery (replace/plasty)
- Atrial Fibrillation
- developed blood clots in the past
- Coronary artery disease
- Immobilization due to recently surgery (THR, TKR,..)
- increased tendency to form clots, ...

ECMO

- Heparin(UFH); initial 50~100u/kg bolus and then continuous 10~50u/kg/hr infusion (ACT<300sec start)
- ACT(180~220sec), aPTT(1.5~2.5 times baseline)
- In HIT; direct thrombin inhibitor(DTI) 사용
- DTI; argatroban, bivalirudin, lepirudin
- Bleeding; frequent(체외순환, anticoagulation, consumption,..)
- Transfusion; Hct>35%, INR<1.5~2.0, PLT>100,000
- Thrombosis; low flow, venous side more common

After valve surgery (2020 ACC/AHA Guideline)

- Mechanical AV; INR 2.5(2.0~3.0) <high thrombo-risk 3.0>
- Tissue AV; aspirin 81mg(50~100mg) <high thrombo-risk INR 2.5>

- Mechanical MV; INR 3.0(2.5~3.5) c aspirin (75~100mg)
- Tissue MV; INR 2.5(2.0~3.0) postop. 3months and then aspirin (75~100mg) <high thrombo-risk warfarin, aspirin both use>
- Mitral annuloplasty ring; 3 months warfarin

- Different from prof. by prof.

HIT/HITT

- Immune Rx; Ig G + PF4(heparin platelet factor)
- Widespread arterial and venous thrombosis
- Sx; Stroke, MI, mesenteric thrombosis, deep vein thrombosis,..

  Finger/toe/ear/nose tip cyanosis
- Dx; thrombocytopenia, heparin/PF4 antibody(ELISA)
- Tx; heparin stop, no PLT transfusion,

  direct thrombin inhibitor(Argatroban, Lepirudin, Bivalirudin,..) 사용

  Argatroban 2ug/kg/min start to aPTT 1.5~3 times (until PLT>10만)

  이후 warfarin(2.5~5mg)과 5일 정도 병용 투여 후 PLT> 15만, INR>4 가 되면

  Argatroban stop하고 warfarin만 사용(3주정도, INR 3정도 유지)

NOACs

Advantages

Oral (vs. LMWH)

No monitoring of INR

Fast onset (within hours)

Standard dose (no weight adjustment)

Minimal drug/dietary interaction

Disadvantages

Expensive

No antidote (i.e Vit K, PCC, plasma with warfarin)

No means to determine compliance, anticoagulation effect

Renal failure prolongs half life (with CrCl)

NOACs

	다비가트란 프라닥사	리바록사반 자렐토	아픽사반 엘리퀴스	에독사반 릭시아나
작용기전	Oral direct thrombin inhibitor	Oral direct factor Xa inhibitor	Oral direct factor Xa inhibitor	Oral direct factor Xa inhibitor
생체 이용률, %	6	66 공복시, 80-100 음식물과 함께	50	62
최고 농도까지 도달시간	3	2-4	3	1-2
반감기 (시간)	12-17	5-13	9-14	10-14
배설	80% 신장	66% 간 33% 신장	27% 신장	50% 신장
용량	150mg 일일 2회 혹은 110mg 일일 2회	20mg 일일 1회	5mg 일일 2회	60mg 일일 1회 혹은 30mg 일일 1회
특정 환자에서의 감량		CrCl 30-49 mL/min일 경우 15mg 하루 한번	나이가 80이상, 몸무게가 60kg이하, 혈장 크레아티닌 1.5mg/dL이상중 2개 이상에 해당될 경우 하루 2.5mm 두 번 복용.	크레아틴 청소율이 30-50mL/min거나 몸무게 60kg이하거나, 베라파밀이나 퀴니딘, 드로네다론을 함께 사용할 경우, 60mg에 해당되는 환자는 30mg으로, 30mg에 해당되는 경우는 15mg으로 감량.
연구 디자인	무작위 단측 맹검	무작위 양측 맹검	무작위 양측 맹검	무작위 양측 맹검
환자수	18,113	14,264	18,201	21,105
추적 관찰 기간	2	1.9	1.8	2.8
대조군	Dose-adjusted warfarin vs. blinded doses of dabigatran (150mg twice daily, 110mg twice daily.)	Dose-adjusted warfarin vs. rivaroxaban 20mg once daily	Dose-adjusted warfarin vs. apixaban 5mg twice daily	Dose-adjusted warfarin vs. edoxaban (60mg once daily, 30mg once daily)

GFR 감소 시 감량 필요, 투석환자에서는 사용 못함

Bleeding

Published in final edited form as:
J Thromb Thrombolysis. 2013 April ; 35(3): 312–319. doi:10.1007/s11239-013-0899-7.

Assessing Bleeding Risk in Patients Taking Anticoagulants

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Abstract

Anticoagulant medications are commonly used for the prevention and treatment of thromboembolism. Although highly effective, they are also associated with significant bleeding risks. Numerous individual clinical factors have been linked to an increased risk of hemorrhage, including older age, anemia, and renal disease. To help quantify hemorrhage risk for individual patients, a number of clinical risk prediction tools have been developed. These risk prediction tools differ in how they were derived and how they identify and weight individual risk factors. At present, their ability to effective predict anticoagulant-associated hemorrhage remains modest. Use of risk prediction tools to estimate bleeding in clinical practice is most influential when applied to patients at the lower spectrum of thromboembolic risk, when the risk of hemorrhage will more strongly affect clinical decisions about anticoagulation. Using risk tools may also help counsel and inform patients about their potential risk for hemorrhage while on anticoagulants, and can identify patients who might benefit from more careful management of anticoagulation.

Risk factors for Anticoagulant-associated Hemorrhage

- Advanced age
- comorbid medical conditions; congestive heart failure, cerebrovascular disease, hepatic or renal disease, DM, HTN, malignancy, fall (AF)
- history of bleeding (especially in the gastrointestinal tract) and anemia
- Antiplatelet agents that are co-administered

  ; triple antithrombotic therapy > warfarin monotherapy X 3
- [INR > 3.0] > [INR 2.0~3.0] X 2
- NOAC; significant reduction in the risk of fatal bleeding and intracranial hemorrhage

Recommended Anticoagulation Regimens for Prosthetic Heart Valves		
	Warfarin	**Antiplatelet Drugs**
AVR - tissue	INR 2.0-3.0 for 3 months if risk factors (ACC/AHA)	Aspirin 75-100 mg alone if no risk factors
AVR - mechanical	INR 2.0-3.0 indefinitely	Aspirin 75-100 mg
Mitral valve repair	INR 2.0-3.0 for 3 months (use either warfarin or aspirin)	Aspirin 75-100 mg (use either warfarin or aspirin)
MVR - tissue	INR 2.0-3.0 for 3 months (ACCP) Continue indefinitely if risk factors	Aspirin 75-100 mg with warfarin if risk factors Aspirin 75-100 mg alone if no risk factors (ACC/AHA) Aspirin 75-100 mg after warfarin is stopped
MVR-mechanical	INR 2.5-3.5 indefinitely	Aspirin 75-100 mg
AVR-MVR -tissue	INR 2.0-3.0 for 3 months	Aspirin 325 mg after 3 months
AVR-MVR – mechanical	INR 3.0-4.5 indefinitely	Aspirin 75-100 mg
Atrial fibrillation with any of above	Continue warfarin indefinitely	

Risk factors: hypercoagulable state, history of systemic thromboembolism, ejection fraction<35%, history of anteroapical infarction, atrial fibrillation.
ACCP, American College of Chest Physicians recommendations 2008;[65] ACC/AHA, American Colege of Cardiology/American Heart Association recommendations 2008. [66]

Protocol for Initiation of warfarin Doses

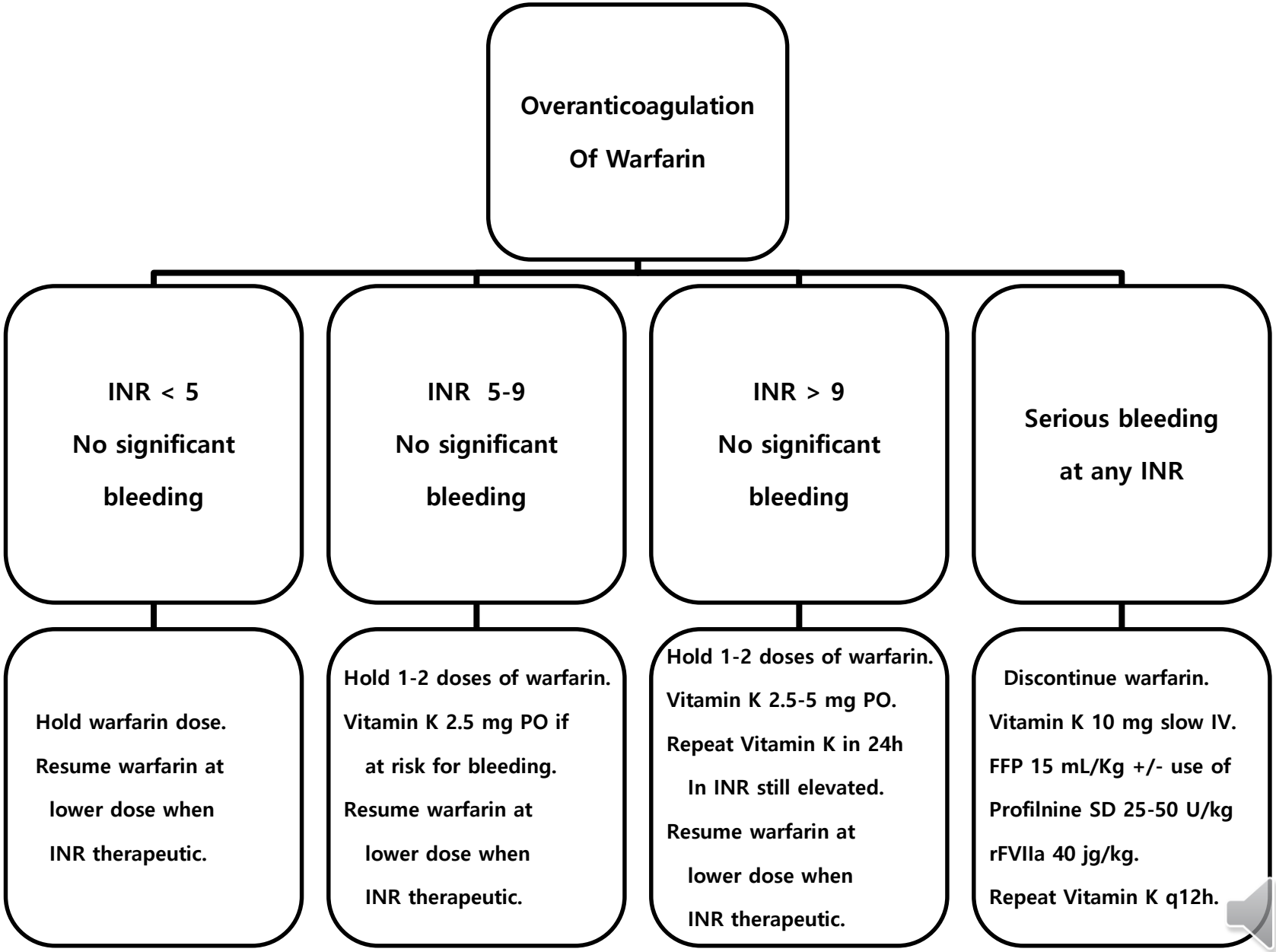
Assess whether patient is at greater risk for sensitivity to warfarin-if so, use low-dose protocol

a. Small, elderly females
b. Over age 75
c. Renal (creatinine > 1.5 mg/dL) or hepatic dysfunction
d. Interacting medications (amiodarone, antibiotics)

Day	INR	Standard	Low-Dose
1	WNL	5 mg	2.5 mg
2	<1.5 1.5-1.9 ≥2	5 mg 2.5 mg HOLD*	5 mg 1.25 mg HOLD*
3	<1.5 1.5-1.9 2-3 >3	7.5 mg 5 mg 2.5 mg HOLD*	5 mg 2.5 mg HOLD* HOLD*
4	<1.5 1.5-1.9 2-3 >3	10 mg 7.5 mg 5 mg HOLD*	7.5 mg 5 mg HOLD* HOLD*
5	<1.5 1.5-1.9 2-3 >3	10 mg 10 mg 5 mg HOLD*	10 mg 5 mg HOLD* HOLD*
6	<1.5 1.5-1.9 2-3 >3	12.5 mg 10 mg 5 mg HOLD*	10 mg 7.5 mg 2.5 mg HOLD*

*Restart warfarin when INR is less than 3

Algorithm for over-anticoagulation management.



Received: 23 October 2019 | Accepted: 18 February 2020

DOI: 10.1111/jth.14772

ORIGINAL ARTICLE

jth

Vitamin K versus warfarin interruption alone in patients without bleeding and an international normalized ratio > 10

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Funding information
This study was funded by the Kaiser Permanente Pharmacy Department.

Abstract

Background: Reversal of an international normalized ratio (INR) > 10 with vitamin K is recommended in patients experiencing bleeding; however, information on outcomes with reversal using vitamin K in non-bleeding patients is lacking.

Objective: To compare clinical and safety outcomes between non-bleeding patients receiving warfarin with an INR > 10 who did and did not receive a prescription for vitamin K.

Patients/Methods: This was a retrospective cohort study conducted in an integrated health-care delivery system. Adult patients receiving warfarin therapy who experienced an INR > 10 without bleeding between 01/01/2006 and 06/30/2018 were included. Patients were assessed for an outpatient dispensing or in-office administration of vitamin K on the day of or the day after an INR > 10 and then clinically relevant bleeding, thromboembolism, all-cause mortality, and time to INR < 4 within the next 30 days.

Results: A total of 809 patients was included with 332 and 477 who were and were not dispensed vitamin K, respectively. Overall, mean patient age was 71.7 years, 60.1% were female and the mean INR was 10.4 at presentation. There were no differences between groups in 30-day rates of bleeding or thromboembolism (both $P > .05$). Patients dispensed vitamin K had a higher likelihood of mortality (15.1% versus 10.1%, $P = .032$, adjusted odds ratio = 1.63, 95% confidence interval 1.03 to 2.57). Overall, time to an INR < 4 was similar between groups.

Conclusion: Vitamin K administration was not associated with improved clinical outcomes in asymptomatic patients with an INR > 10.

Managing life threatening bleeding in the anticoagulated patient

A) Warfarin Reversal in Life-threatening Bleeding

- **Vitamin K**: 10 mg IV(N/S 50mL mix) over 30 minutes
  (INR reversed within 24 hrs).
- **Plasma (FFP)**: 4-6 units required
  (단점; large volume, need time, ABO compatibility, risks of transfusion)
- **Prothrombin Complex Concentrate** (PCC)

Current Canadian recommendations:

INR 1.6-3: 1000 U PCC + Vit K

INR 3-5: 2000 U PCC + Vit K

INR >5: 3000 U PCC + Vit K

Managing life threatening bleeding in the anticoagulated patient

B) Bleeding with New Oral Anticoagulants

Dabigitran/Rivaroxaban: overall bleeding risk approximately equal to warfarin.

Increased risk of GI bleed, but decreased risk of intracranial bleed.

Apixaban: less major and clinically significant non-major bleeding vs. warfarin.

C) Reversal Strategies

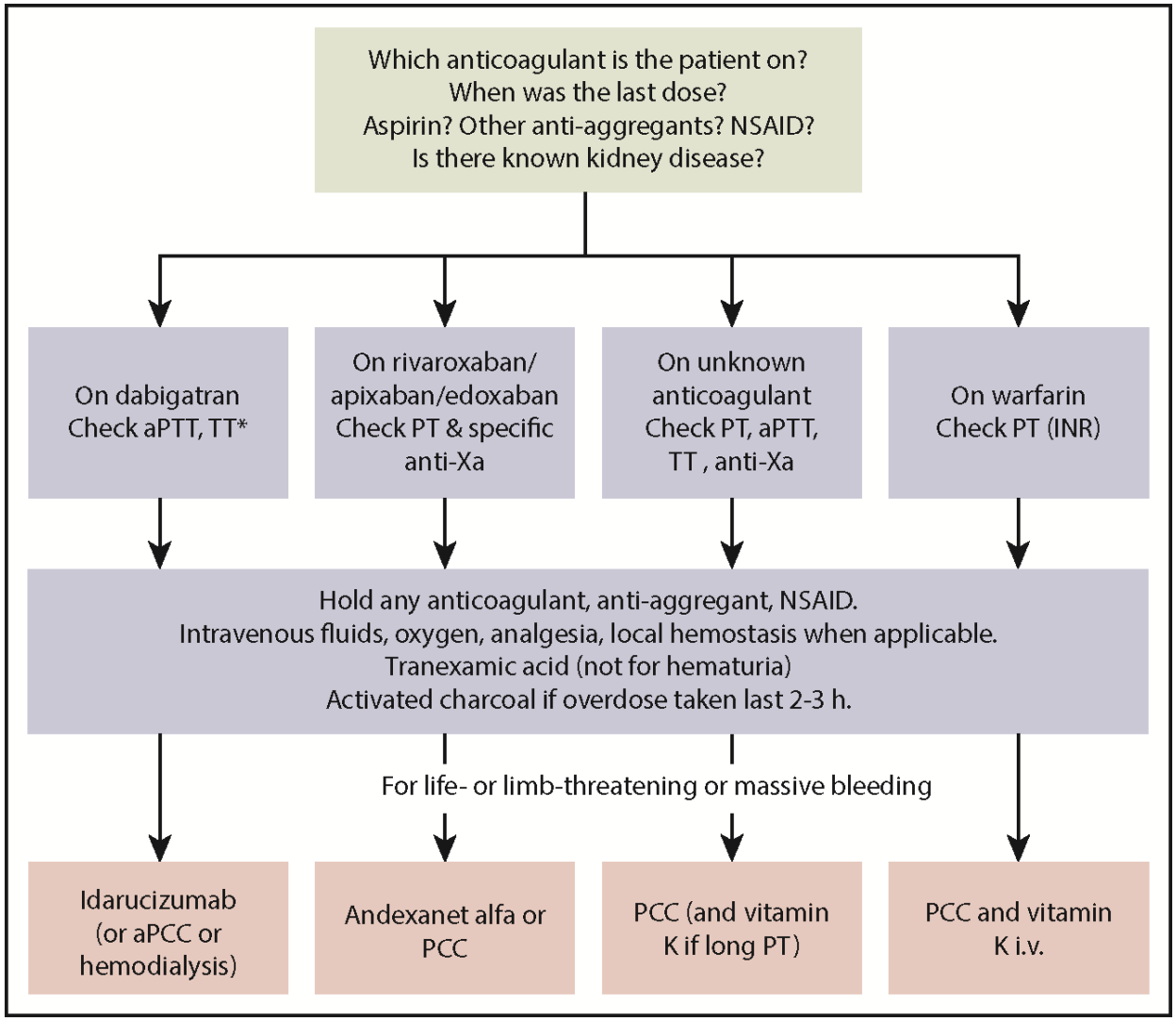
Supportive management, hydration, local control.

Dabigitran:

Dialysis may be helpful: less drug bound to protein

No change in laboratory abnormalities with PCC (vs. change with Rivaroxaban)

Treatment of bleeding complications in patients on anticoagulant therapy



Siavash Piran,Sam Schulman, Treatment of bleeding complications in patients on anticoagulant therapy, Blood, 2019, Figure 1.

Transfusion

Contents

- Transfusion complication
  - TRALI
  - others
- Transfusion strategy
- Transfusion guideline

Complication of transfusion

- Most common adverse side effects are usually mild and non-life-threatening.
- Two categories:

1) Infectious complications
2) Non-infectious complications

Complication of transfusion

- Fever
- TACO (1/700)
- Transfusion related acute lung injury (TRALI, 1/10,000,
- Acute hemolytic transfusion reaction (1/40,000)
- Sepsis (bacterial infection, 1/250,000 for RBCs)
- Allergic reactions
- De-emphasize viral infections, which are much more rare:
  Hep B/C (1 in 2 million), HTLV (1 in 4 million), HIV (1 in 8 million).
- Bacterial Contamination: More common with platelet transfusions.

  Risk is less in single donor apheresis derived units.

Complication of transfusion (Non-infectious)

- Acute (< 24hrs)

  1) Immunologic ; Hemolytic, Anaphylactic, Urticarial / Allergic

  2) Non-immunologic;

     Transfusion-related acute lung injury (TRALI)

     Transfusion-associated Circulatory overload (TACO)

- Delayed (> 24hrs)

  1) Immunologic; Graft-versus-host disease (GVHD)

  2) Non-immunologic

Hemolytic

- Etiology

  1) 1:38,000 to 1:70,000

  2) Clerical and other human error

  3) most common causes of ABO- incompatible transfusion

  4) CAP survey – 3601 institution 834 HTR over 5 year period w/ 50 (6%) fatality

  5) Mortality estimated to be 1:1,000,000 transfusion

- Can occur after infusion of as little as 10-15 mL ABO- incompatible blood Etiology
- Mortality is high when more than 200 ml has been transfused

Hemolytic

- Clinical feature

1) Pain at the infusion site and along the vein
2) Facial burning
3) Chest and back pain
4) Fever, rigor and vomiting
5) Restlessness, breathlessness, flushing and hypotension
6) Bleeding from vascular access sites and wound

Hemolytic

- Treatment/Prevention

1) Stop transfusion
2) Supportive care to maintain renal function

   Adequate hydration and Forced diuresis

   Goal of urine output 100 mL/hr. in adults for at least 18- 24 hours

3) Low dose dopamine
4) Treatment of DIC
5) Prevention of clerical/human errors

Transfusion-related acute lung injury (TRALI)

- Between 2001 – 2003, FDA report on causes of transfusion related deaths

TRALI	16.3%
ABO/Hemolytic transfusion reaction	14.3%
Bacterial contamination	14.1%

- UK SHOT Data 7 years experience (from 1996)

Total 155 cases 32 Deaths

Transfusion-related acute lung injury (TRALI)

- Non cardiogenic edema after blood transfusion was first described by Banard (1951) & Brittingham (1957)
- Term " transfusion related acute lung injury" by Popovsky. (1983)
- A series of 36 TRALI patients is analyzed by Popovsky (1985)

1) Acute respiratory distress & new bilateral lung infiltrate within 6 hrs of blood transfusion, absence of volume overload or cardiac dysfunction

2) Leukocyte antibodies in the blood of 89% of implicated donors

Transfusion-related acute lung injury (TRALI)

- TRALI criteria

  a. ALI (acute lung injury): onset, P/F ratio, CXR,..

  b. No preexisting ALI before transfusion

  c. During or within 6 hr of transfusion

  d. No temporal relationship to an alternative risk factor for ALI

- Risk factor: Aspiration, multiple trauma, pneumonia, cardiopulmonary bypass, burn injury, toxic inhalation, lung contusion, pancreatitis, drug overdose, near drowning, shock, severe sepsis

Transfusion-related acute lung injury (TRALI)

- Incidence: ~8% of transfused pts.
- Pulmonary microvascular occlusion by platelets, leucocytes and fibrin
- Clinical feature

1) Rapid onset of respiratory distress

a. symptoms appear within the first 2–6 hrs from initiation of blood transfusion.

b. some cases occur much later, even up to 48 hrs

2) Common clinical presentation: rapid onset of severe hypoxemia, marked hypovolemia, hypotension

3) Fever, Breathlessness, Non-productive cough, Hypoxia

Transfusion-related acute lung injury (TRALI)

- Clinical course

1) Symptoms generally resolve in 48 to 96 hours
2) Resolution of pulmonary infiltrates within 1-4 days with no long term sequelae (80%)
3) Mortality rate : 5% to 10%
4) However, higher mortality rate in a critically ill patients population(up to 67%)

- TRALI has been associated with all plasma-containing products (Whole blood, PRBCs, FFP, platelets, cryoprecipitate, IV IG)
- High plasma volume products (FFP and platelets, esp multiparous female donors) are the most implicated products.

Transfusion-related acute lung injury (TRALI)

- Treatment of TRALI

1. Treatment is largely supportive.
2. Monitor Oxygen saturation, Provide supplemental oxygen to maintain saturation above 92%
3. Hypoxemia severe enough to require: Endotracheal Intubation and PPV occurs in 70-75% of patients.
4. No evidence supports the routine use of Corticosteroids.

Transfusion-related acute lung injury (TRALI)

- Prevention of TRALI

1) Use plasma from male donor or female donor with negative leukocyte screening test

- SHOT recommendation: obtain the all the FFP from male donors and HLA-pre-screening for female donors who are giving platelets

2) Leukocyte depleted blood

- Reduce TRALI due to lekcocyte Ab in the recipient

3) Use fresh blood

- Biologically active lipids accumulate with storage
- RBC less than 14 days
- Platelet less than 2 days

Transfusion-associated Circulatory overload (TACO)

- Definition

1) no universally agreed-upon definition

2) Serious Hazards Of Transfusion (SHOT) definition: TACO includes any 4 of the following that occur within 6 hours of transfusion

a. Acute respiratory distress

b. Tachycardia

c. Increased blood pressure

d. Acute or worsening pulmonary edema

e. Evidence of positive fluid balance

Transfusion-associated Circulatory overload (TACO)

- Risk Factors

  1) Young children and elderly at risk (esp, age > 70)

  2) Cardiac and pulmonary compromise (esp, CHF history)

  3) Renal failure

  4) Positive fluid balance

- Signs/Symptoms: Dyspnea, cyanosis, orthopnea, HTN

  CHF during or soon after transfusion

Transfusion-associated Circulatory overload (TACO)

- Treatment/Prevention

  1) Stop transfusion

  2) Supportive care

  3) Phlebotomy

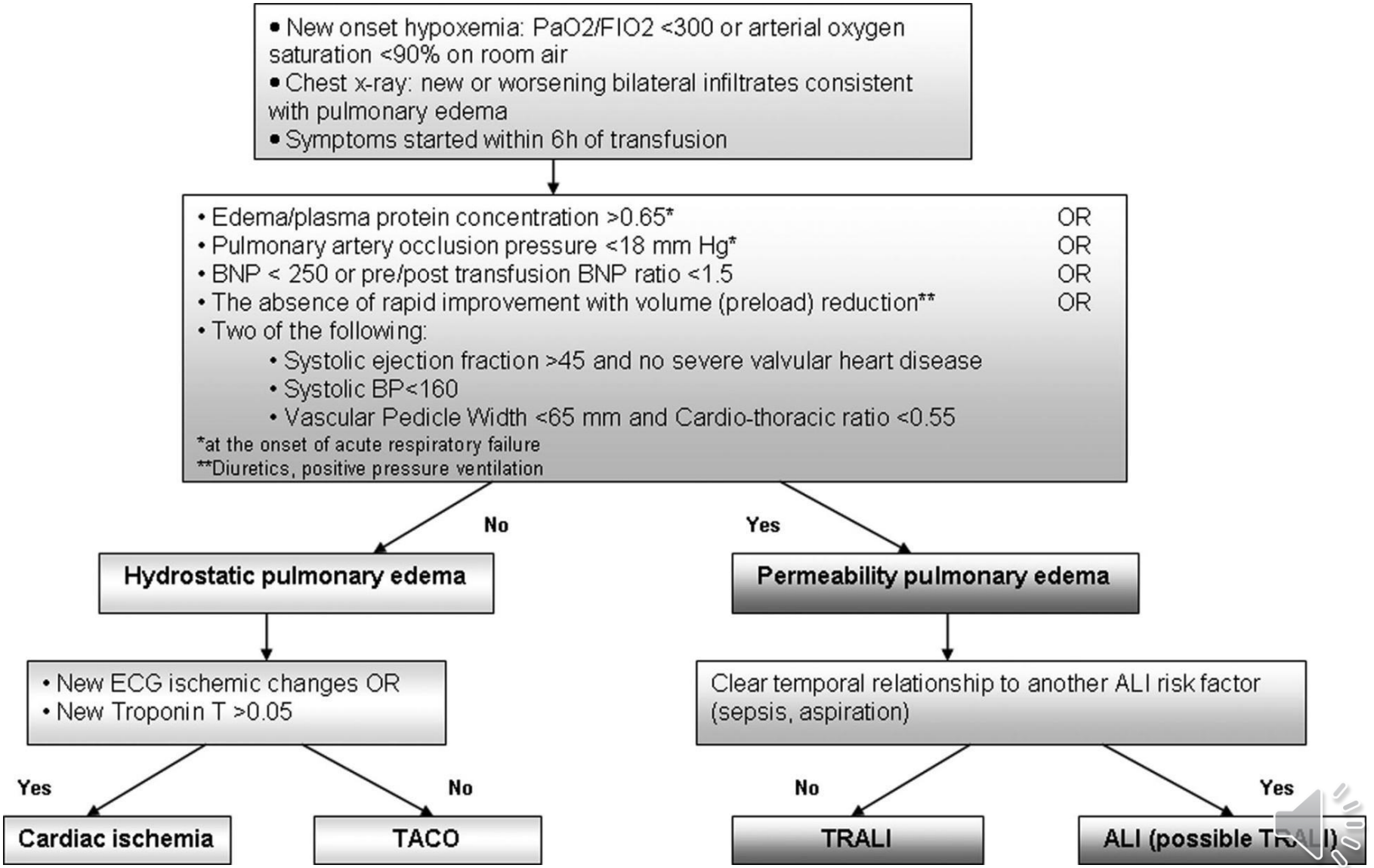
  4) Diuretic

  5) Slow transfusion

     a) Usually 4 hours, can be extended to 6 hours

     b) Other strategies

Transfusion-associated Circulatory overload (TACO)



Gajic O, et al. Crit Care Med 2006: 34:5

TACO Vs TRALI

1) TRALI is **non-cardiogenic** pulmonary edema, with onset within 6h of transfusion.

2) **TRALI does not respond to furosemide.**

Graft-versus-host disease (GVHD)

1) Rare but high mortality.
2) Can damage liver, skin, mucosa, GI tract causing diarrhea.
3) Preventable by using **irradiated** blood in at-risk immunosuppressed patients

Transfusion strategy

Transfusion Requirements After Cardiac Surgery

The TRACS Randomized Controlled Trial

JAMA. 2010;304(14):1559-1567

Ludhmila A. Hajjar, MD, PhD
Jean-Louis Vincent, MD, PhD
Filomena R. B. G. Galas, MD, PhD

Context Perioperative red blood cell transfusion is commonly used to address anemia, an independent risk factor for morbidity and mortality after cardiac operations; however, evidence regarding optimal blood transfusion practice in patients undergoing cardiac surgery is lacking.

- liberal strategy of blood transfusion (to maintain a hematocrit 30%) or to a restrictive strategy (hematocrit 24%).(n=502)
- Among patients undergoing cardiac surgery, the use of a restrictive perioperative transfusion strategy compared with a more liberal strategy resulted in noninferior rates of the combined outcome of 30-day all-cause mortality and severe morbidity.

Liberal versus restrictive blood transfusion strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial

Jeffrey L Carson, Frederick Sieber, Donald Richard Cook, Donald R Hoover, Helaine Noveck, Bernard R Chaitman, Lee Fleisher, Lauren Beaupre, William Macaulay, George G Rhoads, Barbara Paris, Aleksandra Zagorin, David W Sanders, Khwaja J Zakriya, Jay Magaziner

Summary

Background Blood transfusion might affect long-term mortality by changing immune function and thus potentially increasing the risk of subsequent infections and cancer recurrence. Compared with a restrictive transfusion strategy, a more liberal strategy could reduce cardiac complications by lowering myocardial damage, thereby reducing future deaths from cardiovascular disease. We aimed to establish the effect of a liberal transfusion strategy on long-term survival compared with a restrictive transfusion strategy.

Lancet 2015; 385: 1183–89
Published Online
December 9, 2014
http://dx.doi.org/10.1016/S0140-6736(14)62286-8

- no evidence to suggest that a liberal transfusion strategy has a moderate adverse effect on long-term mortality or affects cause of death.
- Mobidity? (liberal > restrictive x 3 transfusion)

Thresholds for red blood cell transfusion in adults

Condition	Hgb threshold for transfusion
Symptomatic patient (eg, myocardial ischemia, tachycardia)	10 g/dL*[1,2]
Hospitalized patient	
Preexisting coronary artery disease	8 g/dL*[2]
Acute coronary syndromes	8 to 10 g/dL¶[2,3]
Heart failure	7 to 8 g/dL¶
Intensive care unit (hemodynamically stable)	7 g/dL*[4,5]
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL*[6]
Non-cardiac surgery	8 g/dL*[1]
Cardiac surgery	7 to 8 g/dL*[7]
Ambulatory outpatient	
Oncology patient in treatment	7 to 8 g/dL¶
Palliative care setting	As needed for symptoms; hospice benefits may vary

2016년 수혈가이드라인 개정(안)

□ 배경 및 필요성

○ 수혈가이드라인은 2002년 대한수혈학회에서 국내최초로 발간하고 2009년 대한수혈학회와 질병관리본부가 공동으로 제정한 이후 2011년, 2013년에 오류 수정과 일부 내용을 보완하는 부분개정을 한 바 있음

○ 수혈가이드라인이 각 의료기관에서 수혈에 대한 기본 지침으로 활용되고 있는 만큼 초판 발행 후 약 7년이 지난 현재 발전하는 수혈의학의 최신지견과 변화하는 의료현실을 반영한 수혈가이드라인이 필요함

○ 또한, 적정수혈 강화를 위해 최신경향이 반영된 수혈가이드라인 개정이 필요함

적혈구수혈

- 혈류역학적(hemodynamic)으로 안정된, 내과적 질환을 가진 중환자실(ICU) 환자에서는 적혈구 수혈의 제한적 지침(혈색소 7 g/dL에서 수혈, 수혈 후 목표치 7-9 g/dL)이 권장된다.
- 수술로 인한 출혈환자에서는 기본적으로 증상이 있거나 혈색소 수치가 8 g/dL 미만으로 떨어지면 적혈구 수혈을 실시한다.

적혈구수혈

- 관상동맥질환 환자 중 안정된 상태이고 증상이 없는 경우에는 혈색소 8 g/dL 미만에서 수혈을 고려한다. 하지만 급성관상동맥증후군(예를 들어 급성심근경색(acute myocardial infarction)이나, 불안정형협심증(unstable angina))환자, 폐기능 이상 혹은 뇌순환 이상이 있는 환자에서는 혈색소 수치가 8-10 g/dL이라도 수혈을 고려할 수 있으며 특히 심근허혈이 진행 중이거나 증상이 있는 경우에는 혈색소 10 g/dL을 유지하도록 권장한다.

신선동결혈장제제 수혈

- 비타민 K, 동결침전제제, 제8응고인자 농축액, 프로트롬빈 복합체 농축제제나 섬유소원 농축제제가 더 효과적인 경우는 신선동결혈장보다 우선적으로 사용할 것을 권장한다. 이와 같은 대안적인 치료가 가능하지 않은 경우에만 신선동결혈장제제의 적응증이 된다.

신선동결혈장제제 수혈

- 투여 전 PT, aPTT 를 측정하고, 대량출혈 시에는 섬유소원 수치도 측정한다.
- 응고인자 결핍이나 섬유소원 결핍 때 사용한다.

혈소판수혈

- 출혈이 없는 안정상태: 혈소판 수를 10,000/uL 이상으로 유지한다.
- 출혈은 없으나 불안정상태: 혈소판 수를 20,000~50,000/uL으로 유지한다.
- 활동성 출혈이 있거나 침습적인 처치를 시행하는 경우:

  혈소판 수를 50,000~ 100,000/uL으로 유지한다.
- 혈소판 기능에 이상이 있는 경우 수혈한다.


Thank you
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