Midnight Journal Club 5th June 2023

大阪府済生会千里病院
千里救命救急センター
伊藤　裕介

Midnight Journal Club

- 第1，2，3月曜20時より開催
- サブスペシャリティを持つスタッフがその専門領域のup to dateな内容を提示
- 本年度から専攻医も参加！ちょっとした小ネタ集でもOK!
- 明日からのdecision makingに使えるものを
- 調べた知識を皆で共有
- もはや脳みそは筋肉ではない！

担当表

日時	担当者	専門分野
2023_06_05_20:00	伊藤	外傷/Acute care surgery
2023_06_12_20:00	淀キリ	
2023_06_19_20:00	橘高	外傷/Acute care surgery
2023_07_03_20:00	大医	
2023_07_10_20:00	澤野	集中治療
2023_07_17_20:00	淀キリ	
2023_08_07_20:00	福田	IVR/集中治療
2023_08_14_20:00	大医	
2023_08_21_20:00	加藤	外傷/Acute care surgery
2023_09_04_20:00	淀キリ	
2023_09_11_20:00	佐藤	外傷整形
2023_09_18_20:00	大医	
2023_10_02_20:00	渡邉	救急/集中治療
2023_10_09_20:00	淀キリ	
2023_10_16_20:00	金子	外傷整形

本日のテーマ

Damage Control Resuscitation

Damage Control Resuscitation?

- Permissive hypotension
- Restrictive fluid resuscitation
- Damage Control Surgery
- Tranexamic acid
- Avoid hypothermia
- Avoid acidosis
- Avoid Trauma induced coagulopathy

Traumatic coagulopathy

RESEARCH Open Access

The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition

Donat R. Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Jacques Duranteau[7], Daniela Filipescu[8], Beverley J. Hunt[9], Radko Komadina[10], Marc Maegele[11], Giuseppe Nardi[12], Louis Riddez[13], Charles-Marc Samama[14], Jean-Louis Vincent[15] and Rolf Rossaint[16*]

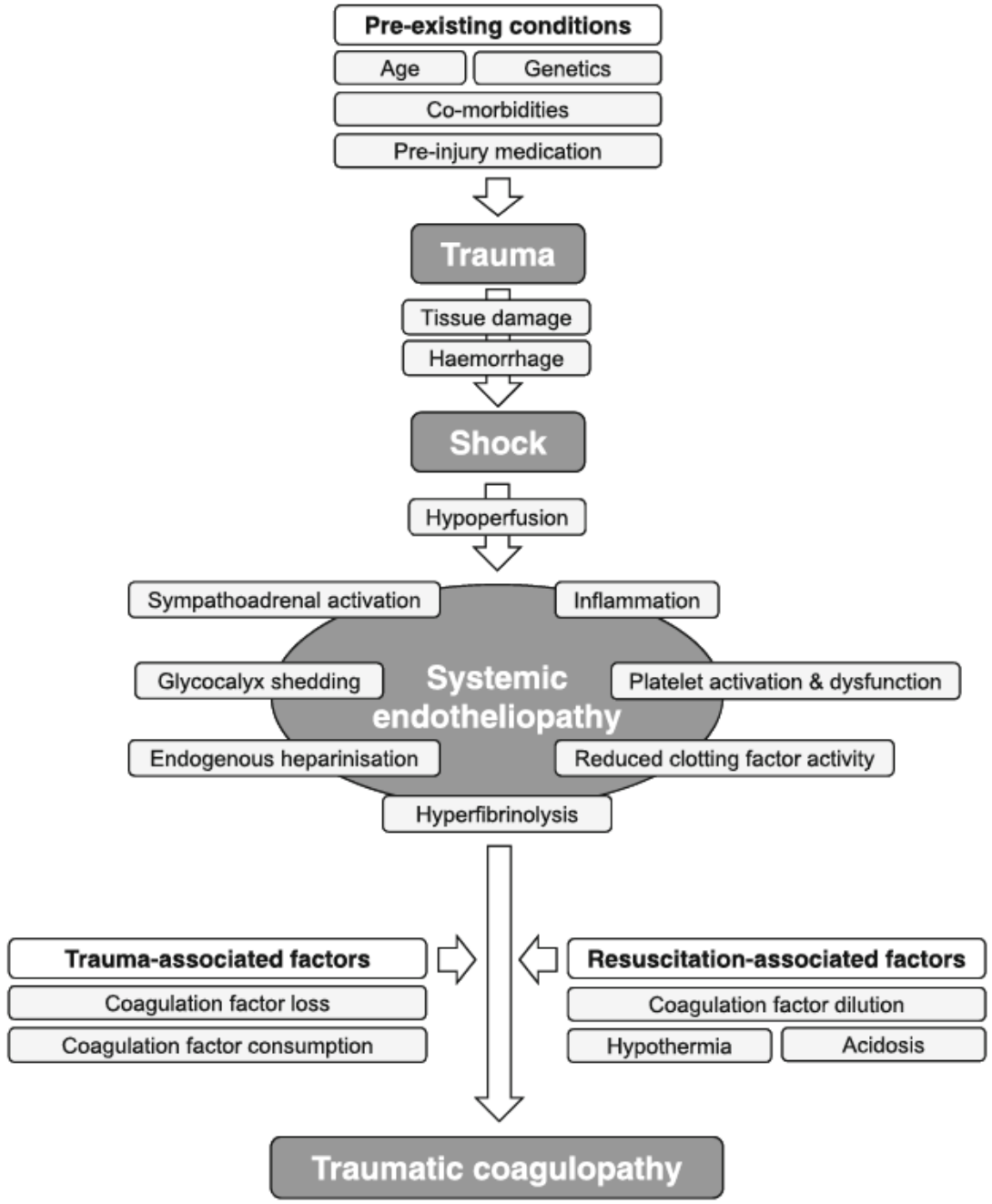


Fig. 1 Schematic drawing of the factors, including those that are preexisting as well as those related to both trauma and resuscitation measures, that contribute to traumatic coagulopathy. Adapted from [20, 24, 30–32, 38]

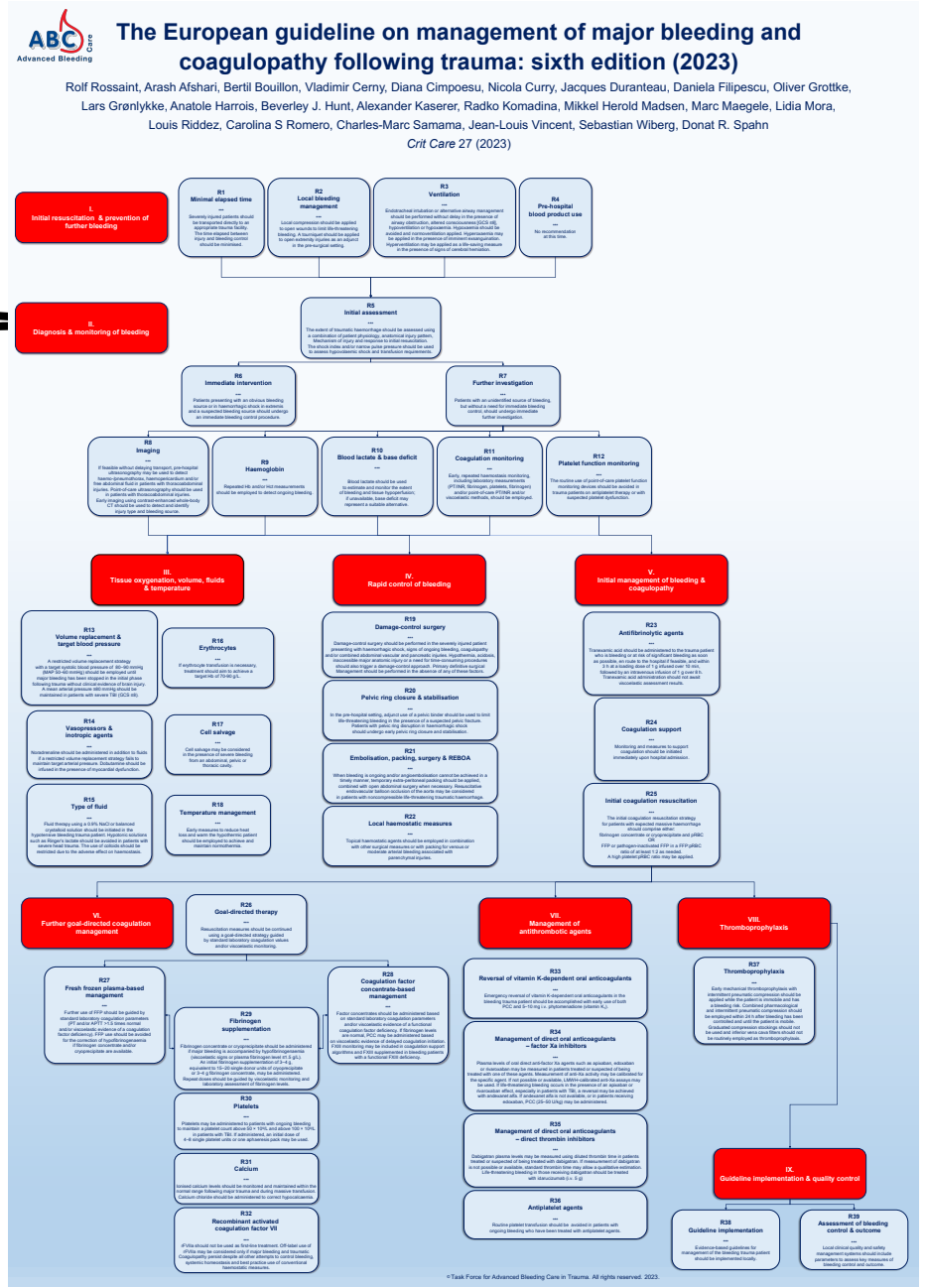
GUIDELINES Open Access

The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

Rolf Rossaint[1*], Arash Afshari[2], Bertil Bouillon[3], Vladimir Cerny[4,5], Diana Cimpoesu[6], Nicola Curry[7,8], Jacques Duranteau[9], Daniela Filipescu[10], Oliver Grottke[1], Lars Grønlykke[11], Anatole Harrois[9], Beverley J. Hunt[12], Alexander Kaserer[13], Radko Komadina[14], Mikkel Herold Madsen[2], Marc Maegele[15], Lidia Mora[16], Louis Riddez[17], Carolina S. Romero[18], Charles-Marc Samama[19], Jean-Louis Vincent[20], Sebastian Wiberg[11] and Donat R. Spahn[13]

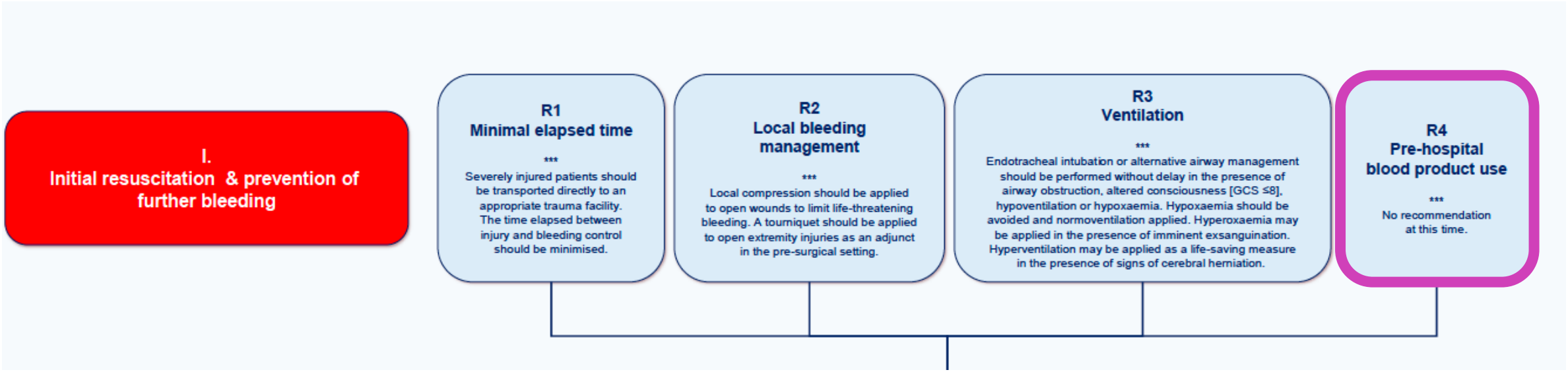
覚えておくべき数字

- a target systolic blood pressure 80-90 mmHg
- a target hemoglobin of 7.0-9.0 g/dl
- a target platelet of 50×10^9/L
- FFP: pRBC ratio of at least 1:2
- 1g Tranexamic acid within 3hr
- plasma fibrinogen level ≧ 150 mg/dl
- Ca^{2+} level ≧ 0.9 mmol/L



Rossaint *et al. Critical Care* (2023) 27:80

Initial resuscitation & prevention of further bleeding



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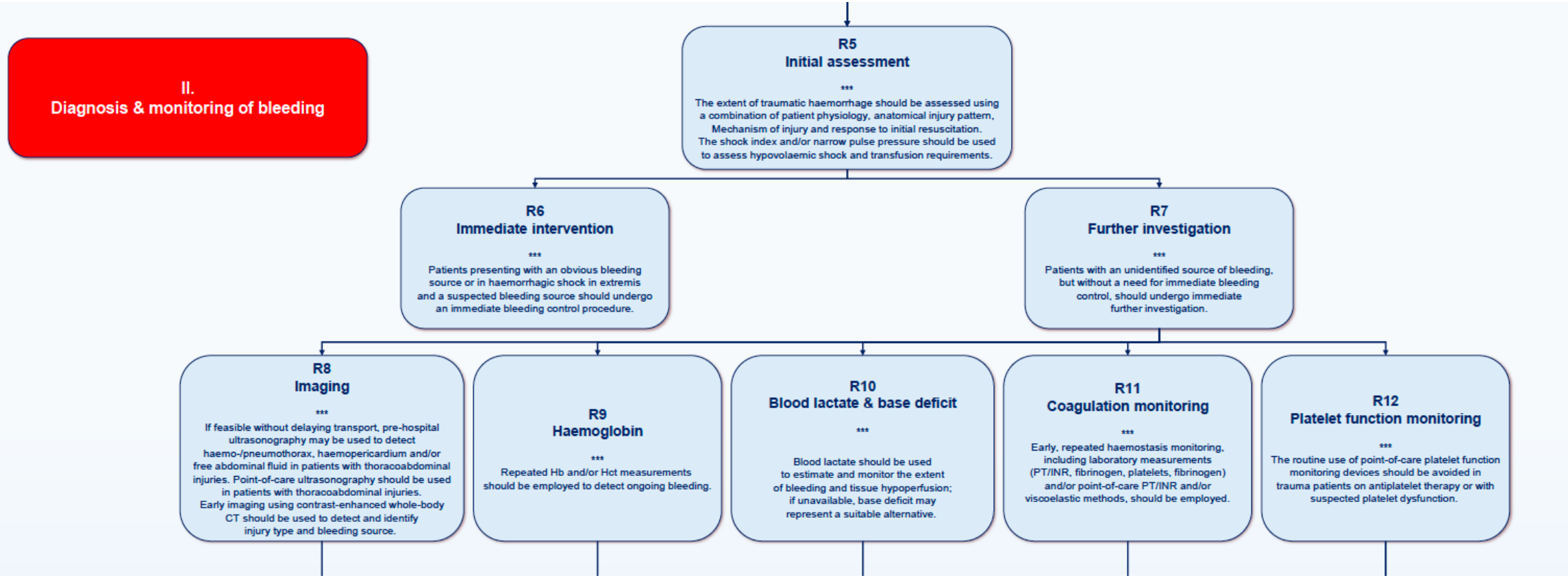
Diagnosis & monitoring of bleeding



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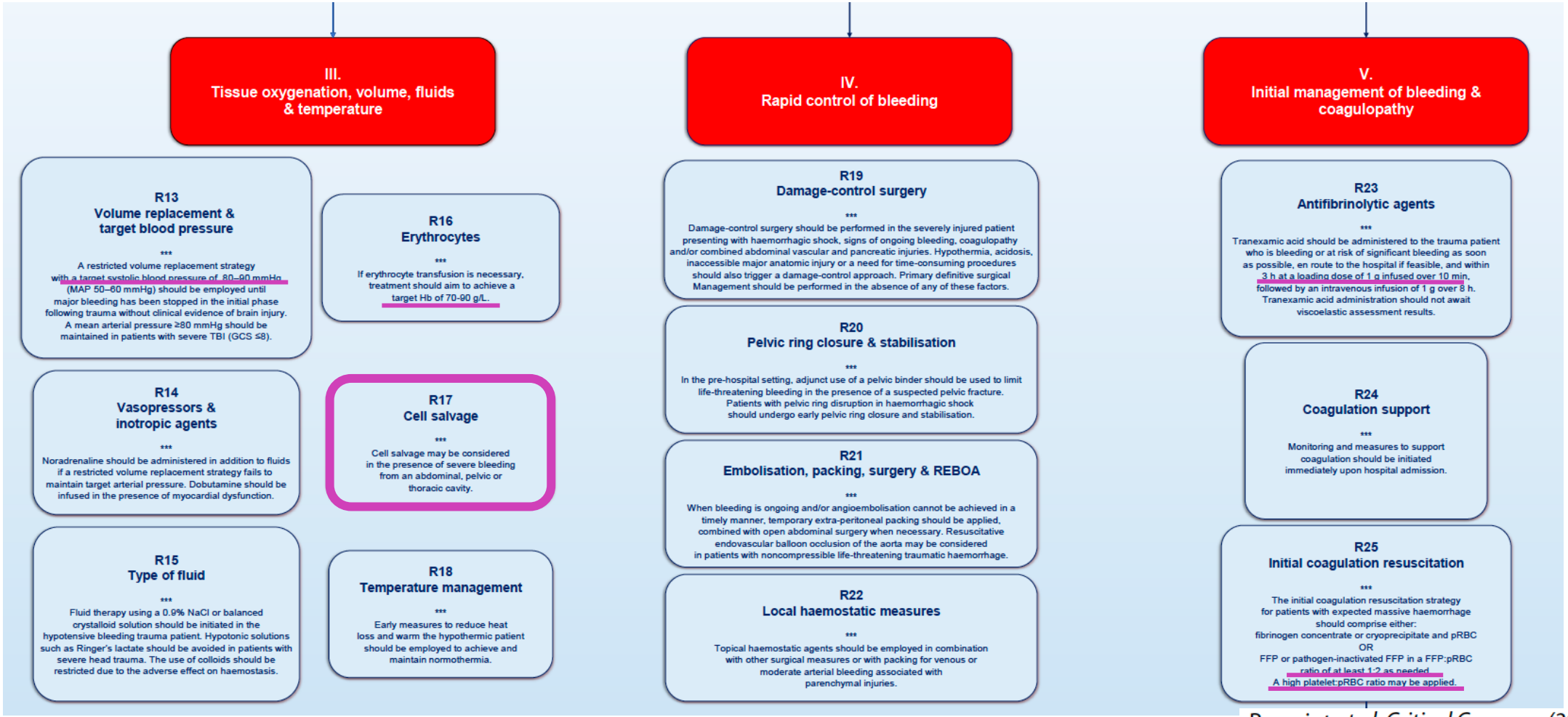
Tissue oxygenation, Rapid control & initial management of bleeding & coagulopathy



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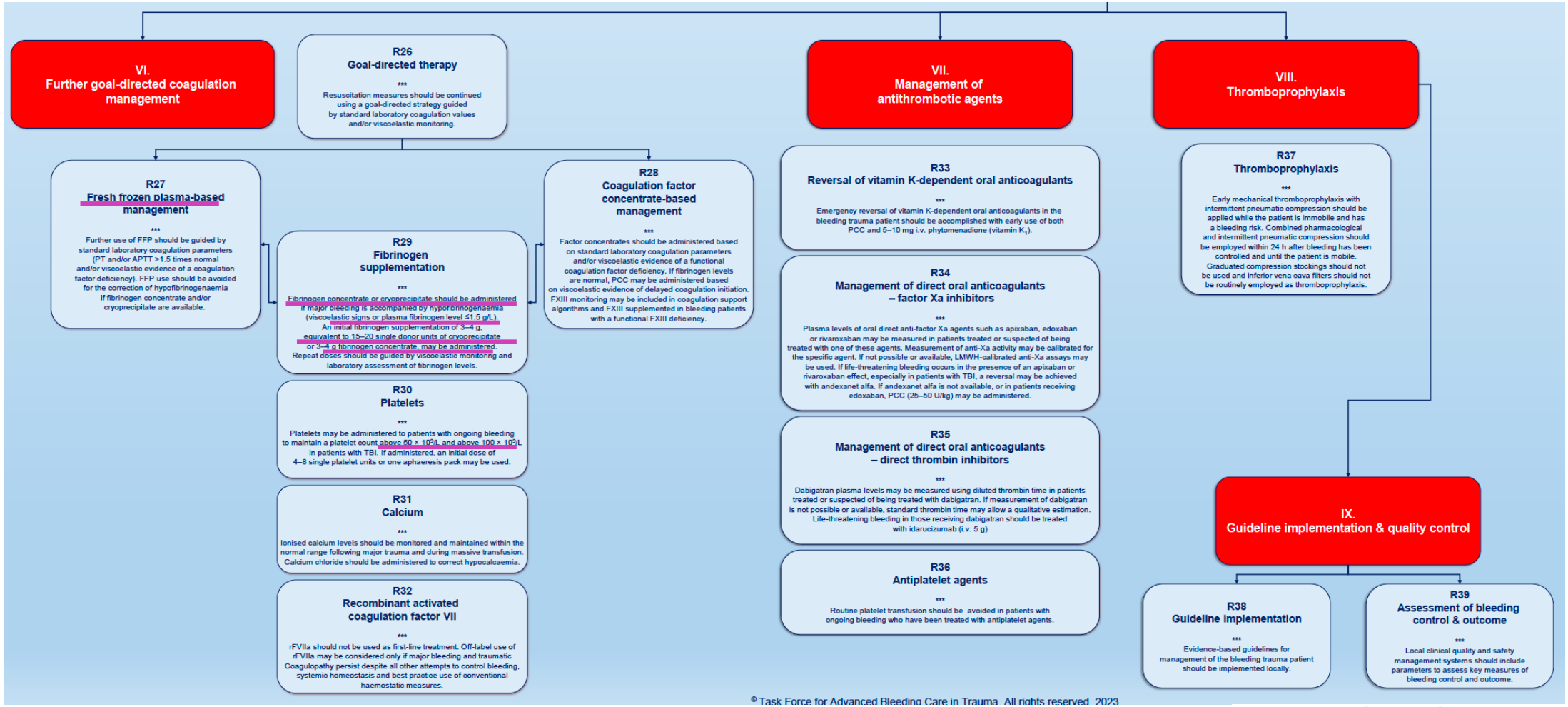
Coagulation and antithrombotic agents and thromboprophylaxis



Rossaint *et al. Critical Care* (2023) 27:80

本日の論文

JAMA Surgery | Original Investigation

Association of Whole Blood With Survival Among Patients Presenting With Severe Hemorrhage in US and Canadian Adult Civilian Trauma Centers

Crisanto M. Torres, MD, MPH; Alistair Kent, MD, MPH; Dane Scantling, DO, MPH; Bellal Joseph, MD; Elliott R. Haut, MD, PhD; Joseph V. Sakran, MD, MPH, MPA

JAMA Surgery Published online January 18, 2023

Background

- Trauma-induced coagulopathy(TIC) は致死率50%に及ぶ出血関連死の重要な要素である
- 近年の外傷蘇生戦略はTICに対し、バランスを重視した成分輸血製剤の使用を行っている
- Massive transfusion protocol(MTP)は、全血輸血に似せた比率で外傷出血患者の予後の改善に寄与した

J Trauma Acute Care Surg. 2017;82(3):605-617.

➡ 論理的には、全血輸血療法も同じ結果をもたらす

Background

- 全血輸血の使用は、抗凝固剤の出現により保存が可能となった、第１次世界大戦において使用された
- その後、合併症の問題から成分輸血製剤の開発が進み、全血輸血の使用は減少していった
- 戦地において、成分輸血製剤の貯蔵は難しく、元気な兵士から採取した全血輸血が復活した
- 戦場での使用により、全血輸血の止血機能と生存率の改善が注目されるようになった

J Trauma Acute Care Surg. 2012;73(6)(suppl5):S445-S452.

そもそも全血輸血とは？

- 全血製剤は、血液に保存液を加えたもので、大量出血などすべての成分が不足する状態で、赤血球と血漿の同時補給を要する場合に使用されますが、現在では患者さんが必要とする成分だけを輸血する「成分輸血」が主流となったため、ほとんど使われていません。
- 採血後21日間使用できます。
- 現在も全輸血製剤使用のうち0.01%で使用されている
- アメリカのlevel Ⅰ外傷センターの半数が使用

Transfus Med.2016;26(6):406-414.

日本赤十字社ホームページより

Objective

- To analyze survival associated with WB as an adjunct to MTP (WB-MTP) compared with MTP alone in patients presenting with severe hemorrhage in US and Canadian adult civilian trauma centers over a 2-year period.
- Hypothesis=WB-MTP would be associated with improved survival at 24 hours and 30 days without an increase in major complications.

Study Design

- Retrospective cohort study
- ACS-TQIPに参加したアメリカ・カナダのlevel Ⅰ・Ⅱの外傷センター
- 2017年1月1日から2018年12月31日まで2年間

Study participants

- Inclusion

  aged ≧18 years

  severe hemorrhage who received MTP within the first 24 hours

- Exclusion

  burns

  died within 1 hour of ED arrival

  interfacility transfers

PICO

P　：MTPが必要な成人外傷患者

I　：全血輸血とMTPを行った群

C　：MTPのみを行った群

O　：24時間と30日生存時間

Statistical Analysis

- 欠損値はMultiple imputation（多重代入法）で補足
- 主要評価項目はCox比例ハザード回帰分析を使用
- Propensity score matchingを行い、再度主要評価項目を分析

Result

characteristics

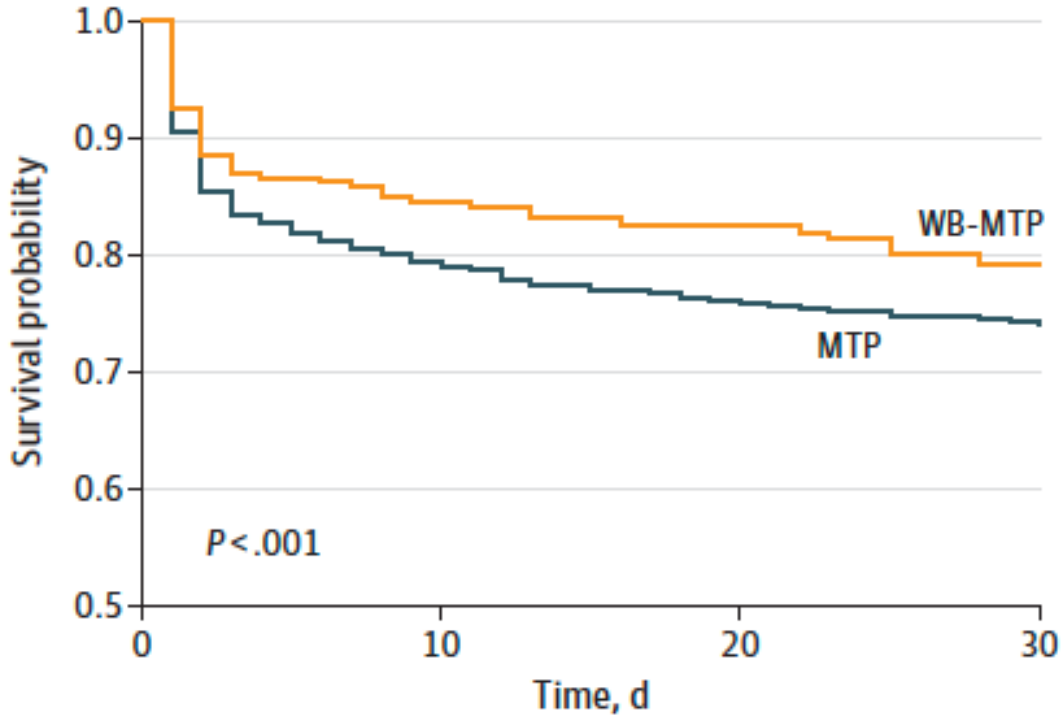
Table 1. Baseline Characteristics of the Study Population and Trauma Centers by Transfusion Group

Characteristic	Patients[a]			
	Unmatched		Propensity score matched	
	WB-MTP (n = 432)	MTP (n = 2353)	WB-MTP (n = 263)	MTP (n = 263)
Demographics				
Age, median (IQR), y	38 (27-57)	38 (27-56)	37 (27-51)	38 (27-53)
Race				
Asian	6 (1)	67 (3)	4 (2)	5 (2)
Black	120 (28)	700 (30)	72 (27)	68 (26)
White	242 (56)	1237 (53)	149 (57)	145 (55)
BMI, median (IQR)	28 (24-32)	28 (24-32)	28 (24-31)	26 (22-30)
Sex				
Female	97 (22)	531 (23)	62 (24)	59 (22)
Male	335 (78)	1822 (77)	201 (76)	204 (78)
ED vital sings, median (IQR)				
Systolic blood pressure, mm Hg	70 (60-79)	69 (59-77)	70 (60-79)	70 (59-79)
Heart rate, beats/min	112 (97-129)	117 (99-133)	117 (100-129)	117 (100-134)
Glasgow Coma Scale score[b]	14 (13-15)	8 (3-15)	14 (13-15)	14 (13-15)
Injury				
Penetrating	150 (35)	908 (39)	87 (33)	102 (39)
ISS[c]				
Median (IQR)	26 (17-35)	27 (19-36)	26 (17-34)	27 (19-34)
1-8	14 (3)	46 (2)	6 (2)	8 (3)
9-15	56 (13)	243 (10)	33 (13)	23 (9)
16-24	112 (26)	616 (26)	75 (29)	84 (32)
25-75	250 (58)	1448 (62)	149 (57)	148 (56)
AIS, median (IQR)[d]				
Head	0 (0-1)	0 (0-3)	0 (0-1)	0 (0-1)
Chest	3 (1-4)	3 (1-4)	3 (2-4)	3 (0-4)
Abdomen	3 (0-4)	3 (0-4)	3 (0-4)	3 (0-4)
Spine	0 (0-2)	0 (0-2)	0 (0-2)	0 (0-2)
Comorbidities				
Hypertension	70 (16)	333 (14)	47 (18)	43 (16)
Diabetes	32 (7)	149 (6)	24 (9)	14 (5)
COPD	14 (3)	57 (2)	11 (4)	11 (4)
Myocardial infarction	2 (1)	16 (1)	1 (1)	1 (1)
Stroke	7 (2)	17 (1)	3 (1)	1 (1)
Trauma center				
ACS trauma center				
Level I	301 (70)	1758 (75)	171 (65)	171 (65)
Level II	131 (30)	595 (25)	92 (35)	92 (35)
Intervention for hemorrhage control	324 (75)	1905 (81)	197 (75)	197 (75)
Time to intervention, median (IQR), min	62 (41-115)	60 (37-109)	66 (43-115)	59 (38-109)
Time to first blood product transfusion, median (IQR), min	37 (17-76)	37 (17-72)	37 (17-76)	37 (17-76)
Transfusion amount, median (IQR), U				
24 h				
pRBCs	8 (4-14)	14 (9-22)	9 (5-14)	9 (5-14)
Plasma	6 (3-10)	10 (6-17)	6 (3-10)	8 (5-12)
Platelets (pooled pack)	1 (0-3)	4 (2-7)	3 (1-5)	4 (2-6)
Cryoprecipitate	0 (0-1)	0 (0.3-2)	0 (0-1)	0 (0-1)
WB	1 (1-1)	NA	NA	NA
4 h				
pRBCs	7 (4-11)	11 (6-18)	7 (4-11)	7 (5-11)
Plasma	4 (2-8)	8 (4-14)	5 (2-8)	6 (4-9)
Platelets (pooled pack)	1 (0-2)	3 (2-5)	1 (0-3)	2 (1-4)
Cryoprecipitate	0 (0-0.5)	0 (0-1)	0 (0-0)	0 (0-0)
WB	1 (1-1)	NA	NA	NA

Result

unadjusted outcomes

Figure 1. Unadjusted Kaplan-Meier Survival Estimates by Transfusion Group



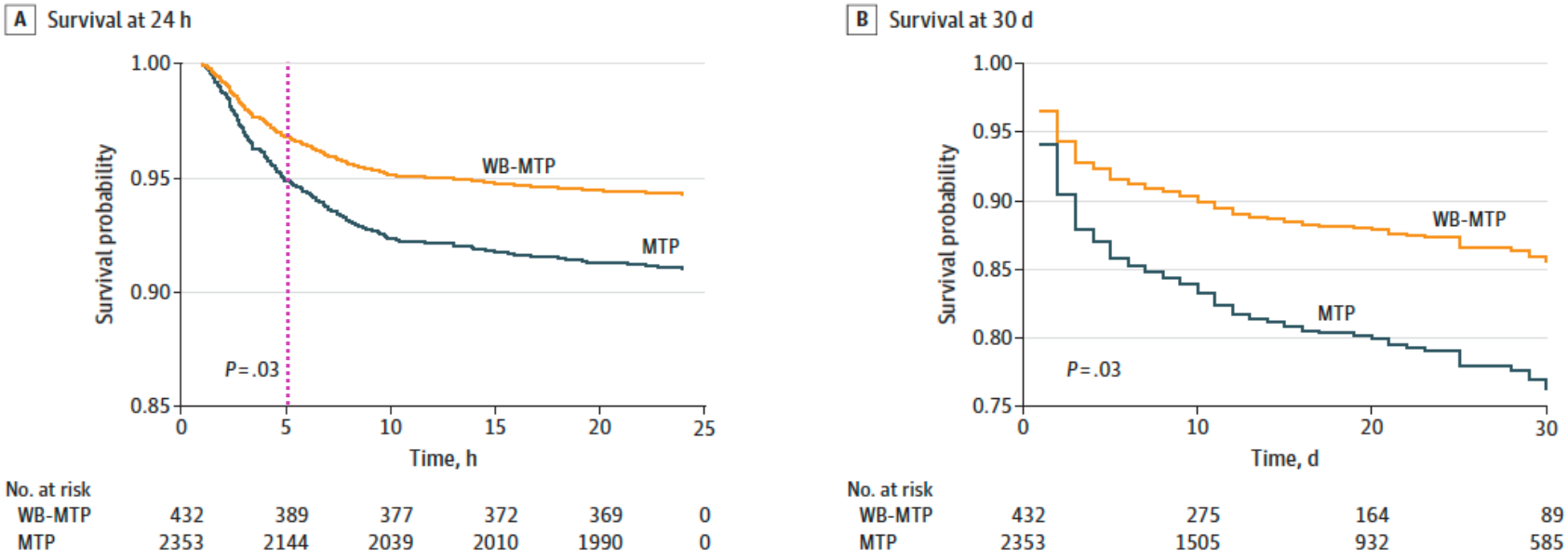
No. at risk				
MTP	2353	1505	932	585
WB-MTP	432	275	164	89

MTP indicates massive transfusion protocol and WB-MTP, whole blood as an adjunct to component therapy–based MTP.

Result

adjusted outcomes

Figure 2. Adjusted Kaplan-Meier Survival Estimates by Transfusion Group



MTP indicates massive transfusion protocol and WB-MTP, whole blood as an adjunct to component therapy–based MTP.

Result

adjusted cox proportional hazards regression

Table 2. Adjusted Cox Proportional Hazards Regression Treatment Effect Estimates by Transfusion Group for Unmatched and Matched Results

Treatment characteristic	Unmatched				Propensity score matched			
	Mortality at 24 h		Mortality at 30 d		Mortality at 24 h		Mortality at 30 d	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
MTP alone	1 [Reference]	NA	NA	NA	NA	NA	NA	NA
WB-MTP	0.63 (0.41-0.96)	.03	0.53 (0.31-0.93)	.02	0.76 (0.62-0.95)	.02	0.48 (0.25-0.91)	.03
ISS, each category increase	1.02 (1.02-1.03)	<.001	1.02 (1.01-1.02)	<.001	1.00 (0.99-1.06)	.10	1.03 (1.01-1.05)	.001
Total GCS score, 1-point increase	0.90 (0.85-0.97)	.001	0.93 (0.88-0.97)	.002	0.86 (0.75-1.01)	.06	0.91 (0.82-0.99)	.04
Penetrating injury	1.67 (1.02-2.76)	.04	1.08 (0.77-1.51)	.65	0.99 (0.30-3.38)	.10	1.11 (0.48-2.60)	.80
Time to bleeding control, per min increase	0.99 (0.99-1.01)	.07	0.99 (0.99-1.01)	.53	0.99 (0.98-1.01)	.14	0.99 (0.99-1.01)	.36
Intervention for bleeding control	0.87 (0.78-0.97)	.01	0.80 (0.69-0.92)	.002	0.74 (0.49-1.10)	.14	0.61 (0.42-0.88)	.009
Trauma center								
Level I	0.91 (0.51-1.67)	.78	0.73 (0.49-1.49)	.12	0.81 (0.33-2.01)	.66	0.96 (0.86-1.08)	.55
Level II	1.29 (1.10-1.51)	.002	1.46 (0.99-2.12)	.051	1.07 (0.39-2.90)	.14	1.84 (1.00-3.37)	.048
Time to first blood product transfusion	1.00 (1.00-1.00)	.003	1.00 (1.00-1.00)	<.001	0.99 (0.99-1.01)	.19	1.00 (1.00-1.00)	.008
Delay WB transfusion ≥2 h	1.00 (1.00-1.01)	.007	2.10 (0.77-5.73)	.14	1.00 (1.00-1.01)	.008	2.16 (0.76-6.15)	.15
Age, 10-y increase	1.26 (1.16-1.39)	<.001	1.45 (1.30-1.63)	<.001	1.80 (1.28-2.55)	.001	1.90 (1.46-2.47)	<.001
Male	1.38 (1.01-1.90)	.04	1.58 (1.06-2.34)	.02	2.36 (0.87-6.43)	.09	1.36 (0.68-2.73)	.39
Systolic blood pressure, 1-mm Hg increase	0.97 (0.96-0.97)	<.001	0.99 (0.99-1.01)	.60	0.99 (0.98-1.01)	.49	0.99 (0.98-0.99)	.04
Pulse, 10-point increase, beats per min	1.01 (1.01-1.02)	<.001	1.06 (0.97-1.16)	.18	1.01 (0.99-1.03)	.10	1.11 (0.92-1.34)	.28

Abbreviations: GCS, Glasgow Coma Scale; HR, hazard ratio; ISS, Injury Severity Score; MTP, massive transfusion protocol; NA, not applicable; WB, whole blood; WB-MTP, WB as an adjunct to component therapy–based MTP.

Result

complications

Table 3. Adjusted Odds Ratios for Major Complications in the WB-MTP Group Compared With the MTP-Only Group as Reference

Outcome	Odds ratio (95% CI)	*P* value
Acute kidney injury	0.47 (0.22-1.01)	.055
Pulmonary embolism	0.84 (0.32-2.19)	.73
Deep vein thrombosis	2.11 (0.99-4.45)	.06
ARDS	1.58 (0.72-3.51)	.25
Stroke	0.61 (0.17-2.16)	.44
Overall	0.82 (0.37-1.81)	.63

Abbreviations: ARDS, acute respiratory distress syndrome; MTP, massive transfusion protocol; WB-MTP, WB as an adjunct to component therapy–based MTP.

Discussion

- a survival benefit at 24 hours and 30 days associated with WB-MTP compared with MTP alone among patients presenting with or at risk of severe hemorrhage in adult civilian trauma centers in the US and Canada.
- WB is associated with an early beneficial effect in blunting the pathophysiology of TIC.

Limitation

- A retrospective analysis
- An observational study
- Indication
- Lack of laboratory data, practitioner-level and data on tranexamic acid administration
- The total amount of WB given was low (1 unit; IQR,1-1 unit)

知見

- 論理的にも真っ当な結果
- あとは実現性があるかないか。。。値段はお手頃。
- 血液型が合わないと投与できないのかな？

全血製剤	人全血液-LR「日赤」 （人全血液）	WB-LR-1	血液200mLに由来する 血液量　1袋	8,350	200
		WB-LR-2	血液400mLに由来する 血液量　1袋	16,700	400
	照射人全血液-LR「日赤」 （人全血液）	Ir-WB-LR-1	血液200mLに由来する 血液量　1袋	9,084	200
		Ir-WB-LR-2	血液400mLに由来する 血液量　1袋	18,164	400

照射洗浄赤血球液-LR「日赤」 （洗浄人赤血球液）	Ir-WRC-LR-1	血液200mLに由来する 赤血球　1袋	10,261	140
	Ir-WRC-LR-2	血液400mLに由来する 赤血球　1袋	20,522	280