BENİGN HEMATOLOJİDE YENİLİKLER

UZM. DR. S. GÜLKAN ÖZKAN

YEDİTEPE ÜNİVERSİTESİ İHTİSAS HASTANESİ

HEMATOLOJİ KLİNİĞİ

BENİGN HEMATOLOJİDE YENİLİKLER

- Anemi ve diğer eritrosit hastalıkları
- Hemostaz ve tromboz
- Transfüzyon
- Diğer benign hematolojik hastalıklar

Anemi ve Diğer Eritrosit Hastalıkları

OTOİMMUN HEMOLİTİK ANEMİ (OİHA)

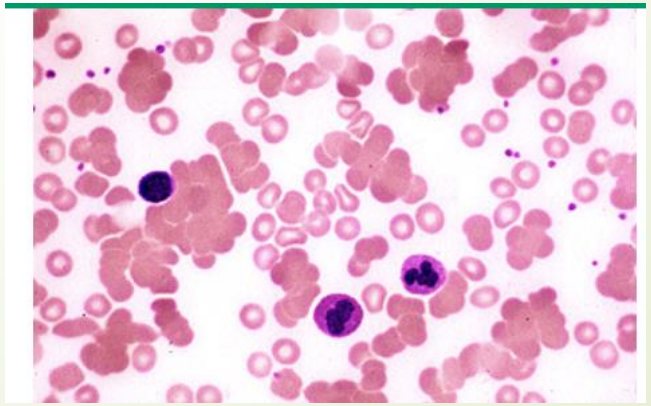
Sarılık, koyu renkli idrar, hızla gelişen anemi semptomları, LDH yüksekliği, haptoglobin düşüklüğü,retikulositoz, periferik yaymada polikromazik eritrositler-normoblastların varlığı ve **coombs pozitifliği**

Sıcak tip otoimmun hemolitik anemi((Rh proteins or glycophorins A-D)

Soğuk tip otoimmun hemolitik anemi(I antijene karşı oligoklonal veya monoklonal IgM)

Otoimmun Hemolitik Anemi

- Sıcak tip OİHA; normal vücut ısısında aktive olan genellikle Ig G tipi antikor ilişkili otoimmun hemolitik anemi tipidir. Primer, ilaç ilişkili veya sekonder nedenlerle olabilir.
- Soğuk tip OIHA; normal vücut sıcaklığının altında aktive olan eritrositlerdeki ''ı'' veya ''İ'' antijenlerine karşı gelişen IgM tipi antikor ilişkilidir. Primer veya sekonder nedenlerle gelişebilir.
- SLE tanılı hastalarında %10 - KLL hastalarında %5-10 OIHA ye rastlanır. Sıcak antikor ilişkili OIHA ye daha sık rastlanır.Akut, geçici ve kronik OIHA olarak tanımlanabilir.



Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting

Ulrich Jäger[1], Wilma Barcellini[2], Catherine M. Broome[3], Morie A. Gertz[4], Anita Hill[5], Quentin A. Hill[5], Bernd Jilma[6], David J. Kuter[7], Marc Michel[8], Marco Montillo[9], Alexander Röth[10], Sacha S. Zeerleder[11], Sigbjørn Berentsen[12,*]

- LDH,bilirubin, haptoglobin, retikulosit, periferik yayma değerlendirmesi her hastada yapılmalı
- DAT mümkün ise IgG,Ig A IgM e karşı
- Tüm OIHA hastaları altta yatan sekonder nedenler için detaylı araşatırılmalı
- Soğuk agglutinin hastalığı için C3d pozitifliği olmalı,soğuk agglutinin titresi ve kemik iliği değerlendirmesi yapılmalıdır
- IgG ve C3 pozitif fakat soğuk agglutinin hastalığı semptomları olan hastalarda mixt OIHA düşünülmeli ve soğuk agglutinin titresi istenmelidir
- DAT negatif hemoliz varlığında non immun hemoliz nedenleri dışlanmalıdır
- Tromboz proflaksisi hemoliz döneminde unutulmamalıdır(özellikle splenektomize hastalarda)

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- Tedavide ilk seçenek oral steroid 1 mg/kg /gün (prednisolone) seçilmiş hastalarda rituksimab+ steroid kullanılabilir
- Steroid tedavisine yanıtlı hastalarda doz 14-21 günde azaltılmalı yanıt sonrası 3 ay tedaviye devam edilmelidir
- İkinci basamak tedavide rituksimab 375 mg/m2 4 hafta süre ile haftalık veya 1-15. gün kullanılabilir.
- 3. basamak tedavi splenektomi, azatiopirin, siklosporin, mikofenolat mofetil kar zarar oranına göre kişisel tedavi düşünülerek seçilmelidir
- 3 ajana yanıtsız kronik OIHA varlığında özellikli merkeze sevk ve klinik çalışmaya alın
- Diğer tedavi seçenekleri siklofosfamid,sürekli düşük doz prednizolon, kök hücre nakli danazol, bortezomib
- Transfüzyon refrakter ve ilk seçenek tedaviler tüketilmesine rağmen etkinlik sağlanamaz ise plazma değişimi, IVIG tedavileri planlanmalı ve yoğun bakım ünitesinde takip edilmeli

blood
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Red cell bound antibodies and transfusion requirements in hospitalized patients with COVID-19

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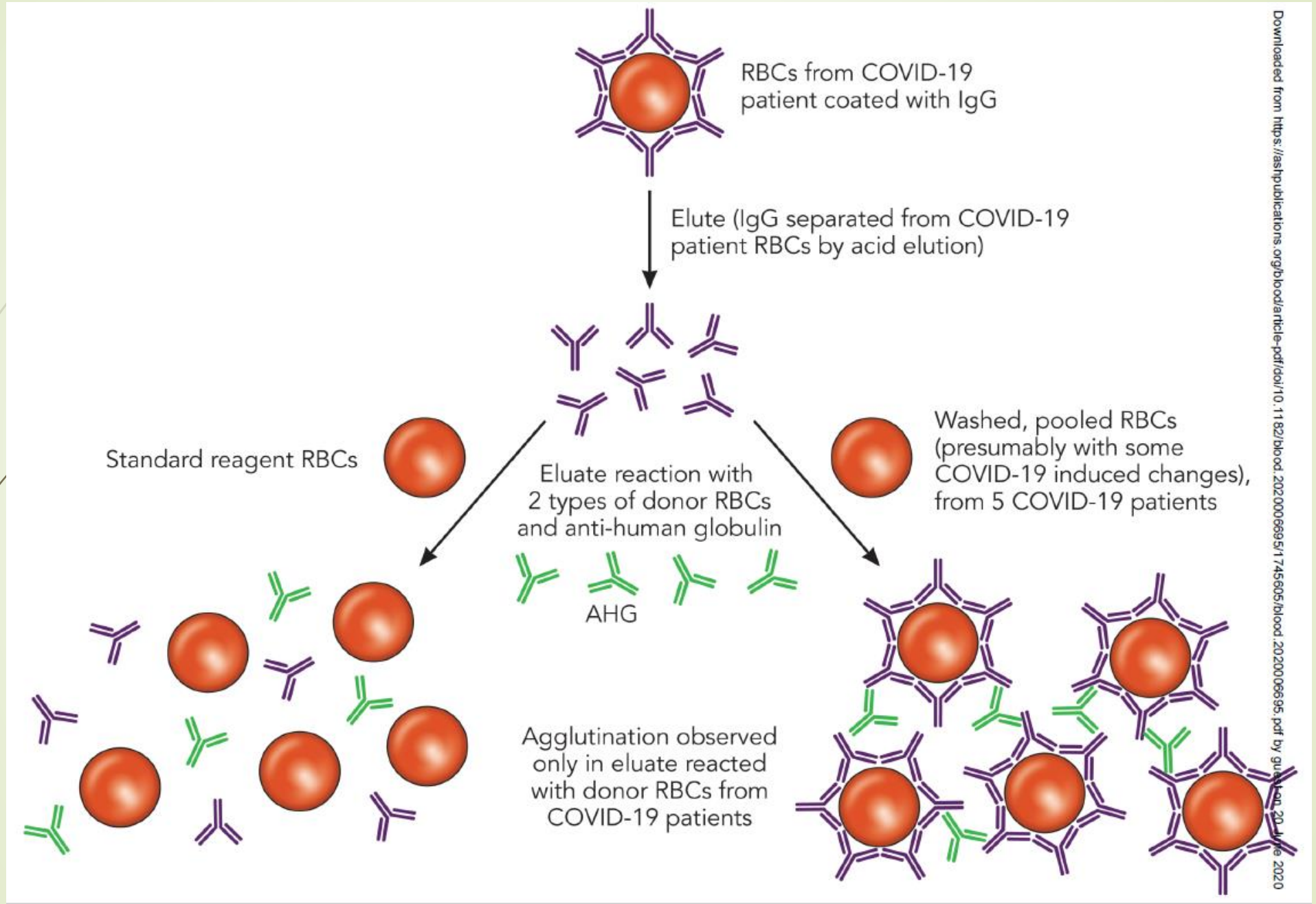
- İtalya, 3 merkezli
- SARS-COV-2 pozitif ve transfüzyon istemi yapılan **113** hasta değerlendirilmiş
- Hidroksiklorokin, heparin,steroid,anti interlökin 1, antiviral, antibiyotikler ve ventilatör desteği alan ve hiçbiri immun plazma almamış hastalar
- 52/113 hastada DAT pozitifliği (48 hastada IgG, 4 hastada IgG veC3, 2 hastada C3)
- 10 hastanın plazmasında SARS-Cov-2 viremisi gösterilmiş(SARS-CoV-2 RNA Droplet Digital PCR System)
- DAT pozitif hastalarda hemoglobin daha düşük, transfüzyonun birden fazla fakat LDH, bilirubin farksız
- Hastalığın trombotik süreci ile ilişkisi?? Ağır hastalık ilişkisi??



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Letter to the Editor

Severe Autoimmune Hemolytic Anemia in COVID-19 İnfection, Safely Treated with Steroids

Keywords: Autoimmune hemolytic anemia; Covid-19; Corticosteroids.

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CASE REPORT

Cold agglutinin disease and autoimmune hemolytic anemia with pulmonary embolism as a presentation of COVID-19 infection

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Autoimmune haemolytic anaemia associated with COVID-19 infection

Gregory Lazarian [1], Anne Quinquenel [2], Mathieu Bellal [3], Justine Siavellis [1], Caroline Jacquy [4], Daniel Re [5], Fatiha Merabet [6], Arsene Mekinian [7], Thorsten Braun [1], Gandhi Damaj [3], Alain Delmer [2], Florence Cymbalista [1]

Patient	Age	Gender	Comorbidity	CT-scan*	Oropharyngeal swab (tested by PCR)	Haemoglobin (g/l)	Reticulocyte count (10^9/l)	Lymphocyte count (10^9/l)	Lactate dehydrogenase (U/l)	Haptoglobin (g/l)	DAT specificity	Optimum temperature	Day between COVID-19 symptoms and AIHA	Related pathology	AIHA treatment	Response
#1	61	M	Hypertension, chronic renal failure	Moderate	Positive	60	477	250	1000	<0·1	IgG + C3d	warm	13	CLL	Steroids	Ongoing
#2	89	F	Hypertension, chronic renal failure, atrial fibrillation	Mild	Positive	84	103	1·7	598	<0·1	IgG + C3d	warm	7	MGUS	Steroids	Ongoing
#3	62	F	Hypertension, cirrhosis	Severe	Positive	108	101	1·3	357	<0·1	C3d	cold	4	MZL†	1. Steroids 2. Rituximab	PR Planed
#4	69	F	Obesity	Moderate	Positive	38	215	5·9	2610	<0·1	IgG + C3d	cold	10	MZL	Steroids	PR
#5	61	M	Hypertension, chronic renal failure, diabetes, hypercholesterolaemia	Mild	Positive	72	145	3	807	0·8	C3d	cold	11	Prostate cancer	RBC infusion	Ongoing
#6	61	M	Diabetes	Severe	Positive	70	155	1·2	1800	<0·1	IgG	warm	9	None	1. Steroids 2. Rituximab‡	Failure Ongoing
#7	75	M	Diabetes, hypercholesterolaemia, cardiopathy, obesity, chronic obstructive bronchopneumopathy	Moderate	Positive	71	98	108	2000	<0·1	IgG	warm	6	CLL	RBC infusion	Ongoing

Perioperatif Anemi Yönetimi

GUIDELINES

Blood transfusion: summary of NICE guidance

Smita Padhi *senior research fellow*[1], Sophia Kemmis-Betty *senior health economist*[1], Sharangini Rajesh *research fellow*[1], Jennifer Hill *operations director*[1], Michael F Murphy *professor of transfusion medicine, consultant haematologist*[2], On behalf of the Guideline Development Group

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Intravenous and oral iron

- Offer oral iron before and after surgery to patients with iron deficiency anaemia. [*Based on very low to low quality evidence from RCTs, cost effectiveness evidence, and the experience and opinion of the Guideline Development Group (GDG).*]
- Consider intravenous iron before or after surgery for patients who:
  -Have iron deficiency anaemia and cannot tolerate or absorb oral iron or are unable to adhere to oral iron treatment[4]

  -Are diagnosed as having functional iron deficiency, or

  -Are diagnosed as having iron deficiency anaemia and the interval between the diagnosis of anaemia and surgery is predicted to be too short for oral iron to be effective.

[*Based on very low to low quality evidence from RCTs, cost effectiveness evidence, and the experience and opinion of the GDG.*]

- For patients with anaemia and chronic kidney disease, consult the NICE guideline on management of anaemia in chronic kidney disease.[5]

Intravenous ferric carboxymaltose versus standard care in the management of postoperative anaemia: a prospective, open-label, randomised controlled trial

Alhossain A Khalafallah, Carl Yan, Raghad Al-Badri, Ella Robinson, Brooke E Kirkby, Emily Ingram, Zara Gray, Vinod Khelgi, Iain K Robertson, Brian P Kirkby

Summary

Background Despite increasing efforts in perioperative management, postoperative iron deficiency anaemia persists, and few data are available about the management of this condition. In this study, we aimed to determine whether giving postoperative intravenous iron (in the form of ferric carboxymaltose) improved iron stores, haemoglobin concentrations, and outcomes following surgery.

Methods We did a prospective, open-label, randomised, controlled study of patients at two centres (a general hospital and a private health-care centre) in Tasmania, Australia, undergoing elective surgery with functional iron deficiency anaemia (haemoglobin 70–120 g/L and ferritin ≤100 µg/L or iron saturation ≤20%), measured at day 1 postoperatively. Consecutive routine elective surgical patients who were having major orthopaedic surgery, abdominal, and genitourinary surgery, and other surgeries were recruited. Via computer-generated randomisation, patients were randomly assigned (1:1) to either a single dose of intravenous 1000 mg ferric carboxymaltose (intervention group) or standard care, consisting of observation (control group). The primary endpoints were changes in haemoglobin concentrations and iron stores at 4 weeks postoperatively, and the number of transfused units of blood required postoperatively until discharge. Analyses were done on an intention-to-treat basis. This trial is registered with the Australian New Zealand Clinical Trials Registry and the WHO International Clinical Trials Registry platform (number ACTRN12614001261606).

Findings Between Dec 17, 2014, and May 7, 2015, we recruited 201 eligible patients, assigning 103 to intravenous ferric carboxymaltose and 98 to standard care only. Baseline mean haemoglobin was 105·5 g/L (SD 13·8) in the standard care group versus 106·2 g/L (11·9) in the ferric carboxymaltose group, improving at 4 weeks to 121·5 g/L (SD 14·5) in the standard group and 130·1 g/L (11·3) in the ferric carboxymaltose group (mean difference of 7·84 g/L, 95% CI 3·79–11·9; p<0·0001 in favour of the ferric carboxymaltose group). Significant improvements in serum iron (5·36 µmol/L, 95% CI 3·62–7·09; p<0·0001), iron saturation (11·40%, 95% CI 8·33–14·50; p<0·0001), and serum ferritin concentrations (468 µg/L, 95% CI 355–582; p<0·0001) were also noted in the ferric carboxymaltose group at 4 weeks compared with standard care, although no differences were noted in transferrin concentrations (0·06 g/L, 95% CI –0·97 to 1·09; p=0·62). Fewer transfused blood units were given in the ferric carboxymaltose group (to one of 103 patients [<1%]) than in the standard care group (to five of 98 patients [5%]; incidence rate ratio 0·10; 95% CI 0·01–0·85; p=0·035). No adverse events were observed with ferric carboxymaltose treatment.

Interpretation Postoperative intravenous ferric carboxymaltose is a feasible and pragmatic management approach in surgical patients with functional iron deficiency anaemia. Our study suggests that patient blood management guidelines should be updated, incorporating the use of postoperative intravenous iron infusion to optimise patient outcomes. Further trials to assess our approach are warranted.

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See Comment page e401

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- Tazmanya'da 2 merkez
- Prospektif açık etiketli, randomize 201 hasta
- Mojor cerrahi op +1. günde

1. Grup(n=103) :IV 1000 mg ferric karboksimaltoz
2. Grup(n=98) : standart tedavi veya takip

Birincil sonlanım noktası postop 4. hafta hemoglobin konsatrasyonu ve demir deposu

Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, double-blind, controlled trial

Toby Richards, Ravishankar Rao Baikady, Ben Clevenger, Anna Butcher, Sandy Abeysiri, Marisa Chau, Iain C Macdougall, Gavin Murphy, Rebecca Swinson, Tim Collier, Laura Van Dyck, John Browne, Andrew Bradbury, Matthew Dodd, Richard Evans, David Brealey, Stefan D Anker, Andrew Klein

Summary

Background Preoperative anaemia affects a high proportion of patients undergoing major elective surgery and is associated with poor outcomes. We aimed to test the hypothesis that intravenous iron given to anaemic patients before major open elective abdominal surgery would correct anaemia, reduce the need for blood transfusions, and improve patient outcomes.

Methods In a double-blind, parallel-group randomised trial, we recruited adult participants identified with anaemia at preoperative hospital visits before elective major open abdominal surgery at 46 UK tertiary care centres. Anaemia was defined as haemoglobin less than 130 g/L for men and 120 g/L for women. We randomly allocated participants (1:1) via a secure web-based service to receive intravenous iron or placebo 10–42 days before surgery. Intravenous iron was administered as a single 1000 mg dose of ferric carboxymaltose in 100 mL normal saline, and placebo was 100 mL normal saline, both given as an infusion over 15 min. Unblinded study personnel prepared and administered the study drug; participants and other clinical and research staff were blinded to treatment allocation. Coprimary endpoints were risk of the composite outcome of blood transfusion or death, and number of blood transfusions from randomisation to 30 days postoperatively. The primary analysis included all randomly assigned patients with data available for the primary endpoints; safety analysis included all randomly assigned patients according to the treatment received. This study is registered, ISRCTN67322816, and is closed to new participants.

Findings Of 487 participants randomly assigned to placebo (n=243) or intravenous iron (n=244) between Jan 6, 2014, and Sept 28, 2018, complete data for the primary endpoints were available for 474 (97%) individuals. Death or blood transfusion occurred in 67 (28%) of the 237 patients in the placebo group and 69 (29%) of the 237 patients in the intravenous iron group (risk ratio 1·03, 95% CI 0·78–1·37; p=0·84). There were 111 blood transfusions in the placebo group and 105 in the intravenous iron group (rate ratio 0·98, 95% CI 0·68–1·43; p=0·93). There were no significant differences between the two groups for any of the prespecified safety endpoints.

Interpretation Preoperative intravenous iron was not superior to placebo to reduce need for blood transfusion when administered to patients with anaemia 10–42 days before elective major abdominal surgery.

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- Çift kör, paralel-grup randomize
- 46 merkez, 487 hasta

(244 hasta ıv demir grubu)

(243 hasta plasebo grubu)

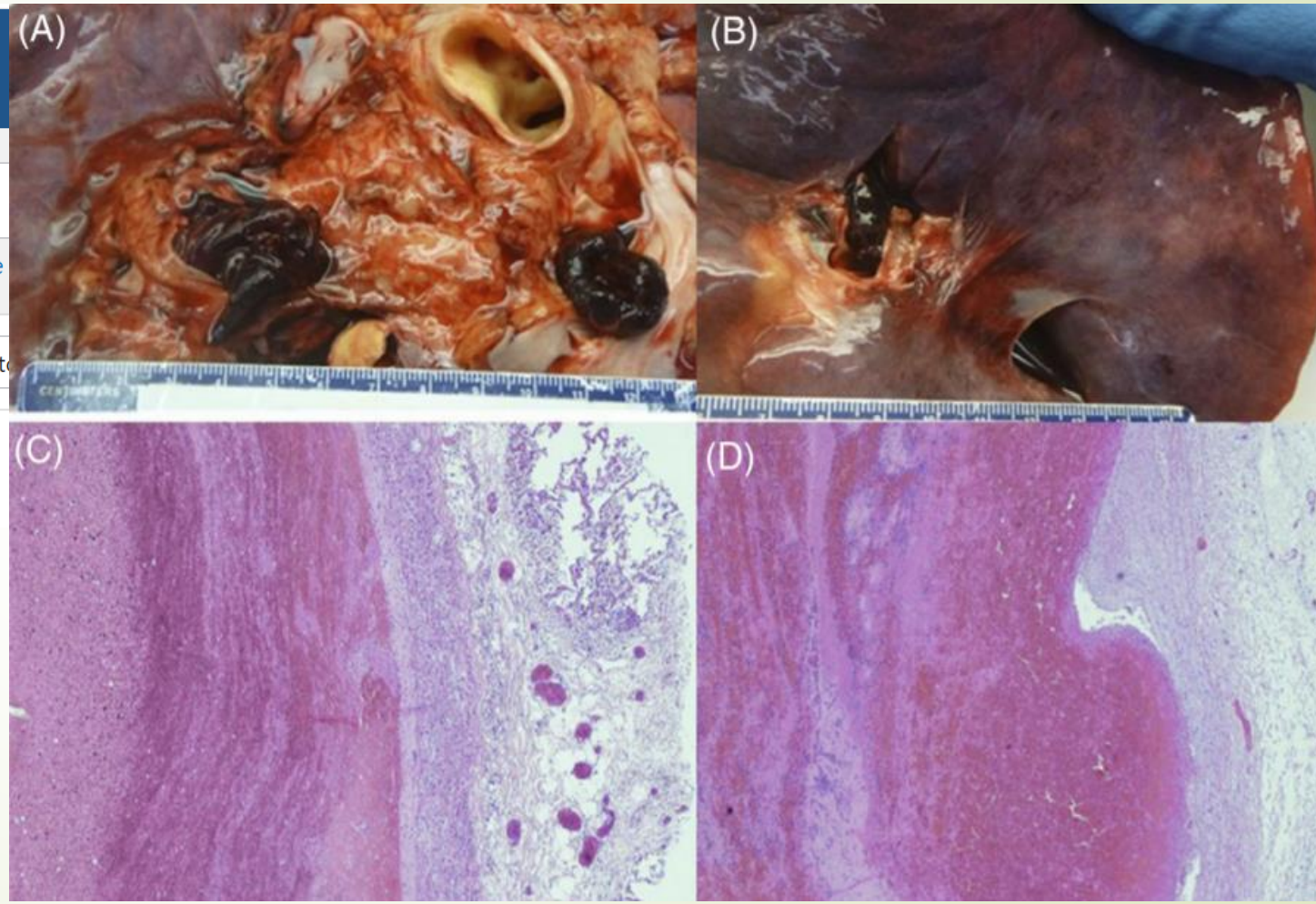
- IV 1000 mg ferric karboksimaltoz
- Preop 10-42 gün arasında
- ölüm ve kan transfüzyonları arasında anlamlı fark yok

Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, double-blind, controlled trial

	Placebo (n=243)	Intravenous iron (n=244)	Treatment effect (95% CI)	Interaction p value
Blood transfusion or death within 30 days				
Age (years)				
<70	44/156 (28%)	41/157 (26%)	0·93 (0·64–1·33)	--
≥70	23/81 (28%)	28/80 (35%)	1·23 (0·78–1·95)	0·34
Central laboratory haemoglobin (g/L)				
<100	23/42 (55%)	23/41 (56%)	1·02 (0·70–1·51)	--
≥100	44/187 (24%)	45/190 (24%)	1·01 (0·70–1·45)	0·95
Sex				
Female	42/139 (30%)	39/122 (32%)	1·06 (0·74–1·52)	--
Male	25/98 (26%)	30/115 (26%)	1·02 (0·65–1·62)	0·91
Body-mass index (kg/m^2)				
<30	52/178 (29%)	51/161 (32%)	1·08 (0·79–1·50)	--
≥30	15/57 (26%)	18/75 (24%)	0·91 (0·50–1·65)	0·62
Central laboratory ferritin (ng/mL)				
<100	34/132 (26%)	34/128 (27%)	1·03 (0·69–1·55)	--
≥100	32/98 (33%)	31/94 (33%)	1·01 (0·67–1·51)	0·94
Central laboratory TSAT (%)				
<20	55/174 (32%)	49/163 (30%)	0·95 (0·69–1·31)	--
≥20	8/50 (16%)	15/53 (28%)	1·77 (0·82–3·81)	0·13
Type of surgery				
Complex major	25/83 (30%)	20/87 (23%)	0·76 (0·46–1·26)	--
Major	17/86 (20%)	22/85 (26%)	1·31 (0·75–2·29)	--
Major plus	25/68 (37%)	27/65 (42%)	1·13 (0·74–1·73)	0·32

	Placebo (n=243)	Intravenous iron (n=244)	Treatment effect (95% CI)	Interaction p value
Blood transfusion episodes within 30 days				
Age (years)				
<70	0·5 (1·0)	0·4 (0·8)	0·79 (0·50–1·24)	--
≥70	0·4 (0·7)	0·6 (1·1)	1·48 (0·79–2·77)	0·11
Central laboratory haemoglobin (g/L)				
<100	0·8 (1·1)	0·8 (1·2)	1·07 (0·51–2·24)	--
≥100	0·4 (0·9)	0·4 (0·8)	0·93 (0·61–1·41)	0·74
Sex				
Female	0·5 (0·9)	0·4 (0·7)	0·92 (0·55–1·51)	--
Male	0·4 (0·9)	0·5 (1·1)	1·07 (0·61–1·86)	0·69
Body-mass index (kg/m^2)				
<30	0·5 (0·9)	0·5 (1·0)	1·12 (0·73–1·72)	--
≥30	0·5 (1·0)	0·3 (0·6)	0·68 (0·32–1·42)	0·25
Central laboratory ferritin (ng/mL)				
<100	0·5 (1·0)	0·4 (0·9)	0·92 (0·55–1·52)	--
≥100	0·5 (0·8)	0·5 (0·9)	1·07 (0·61–1·88)	0·70
Central laboratory TSAT (%)				
<20	0·5 (1·0)	0·5 (1·0)	0·92 (0·60–1·41)	--
≥20	0·3 (0·7)	0·4 (0·7)	1·55 (0·64–3·75)	0·29
Type of surgery				
Complex major	0·6 (1·1)	0·4 (1·0)	0·77 (0·43–1·40)	--
Major	0·3 (0·7)	0·3 (0·6)	1·24 (0·62–2·45)	--
Major plus	0·6 (0·9)	0·6 (1·0)	1·09 (0·57–2·08)	0·56

Hemostaz ve Tromboz



COVID-19 ve Tromboz

- Trombotik komplikasyonlar COVID-19 enfeksiyonu sürecinde sıklıkla görülmekte olup artmış morbidite ve mortalite ilişkilidir
- İlk hiperkoagulabilite ilişkili yayınlar sonrasında antikoagulan kullanımı ile ilgili yerel tedavi politikaları oluşturulmuştur
- D-Dimer artışı mortalite ilişkisi gösterilmiştir.
- Henüz doz ve süre ile ilgili karşılaştırmalı çalışma sonuçları literatürde yoktur.

RECOMMENDATIONS AND GUIDELINES

jth

ISTH interim guidance on recognition and management of coagulopathy in COVID-19

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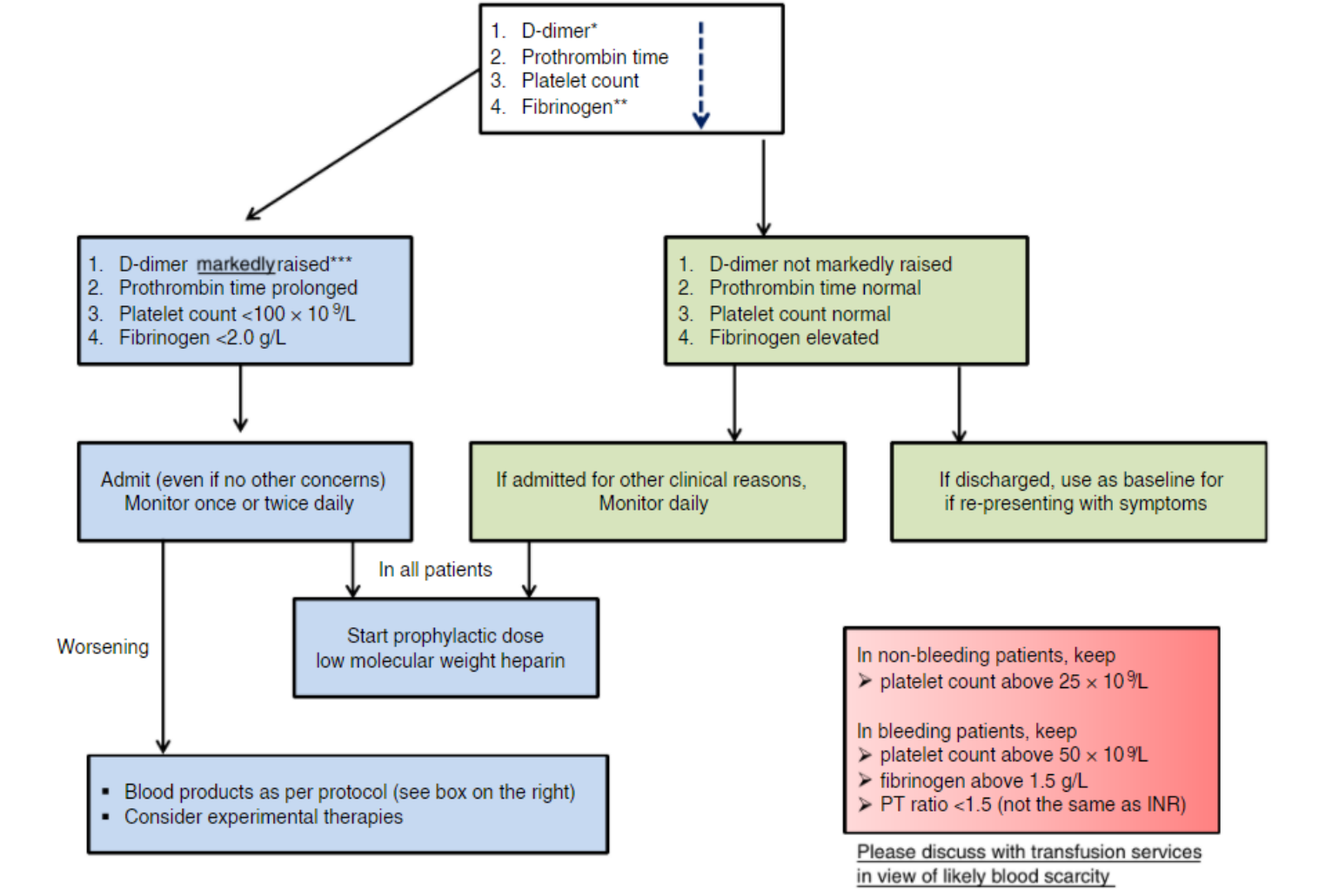

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ISTH interim guidance on recognition and management of coagulopathy in COVID-19: A comment

- Hiperkoagulabiliteye dikkat çekilmiş
- ISTH DIC kriterini karşılayan ¾ hastada venöz tromboz,D-dimer , fibrinojen artışı ve ATIII düşüklüğü
- Yüksek fibrinejen (900 üzeri) düzeyinin ATIII eksikliği nedeni ile heparin direnci oluşturabileceği
- Oral antikoagulan- DMAH tedavilerinin hastanede yatan hastalarda erken evrede başlanması önerilmiş.

Received: 29 June 2020 | Revised: 18 August 2020 | Accepted: 24 August 2020

DOI: 10.1002/ajh.25982

CRITICAL REVIEW

Thrombosis in COVID-19

Thomas C. Hanff[1,2] | Amir M. Mohareb[3,4] | Jay Giri[1] | Jordana B. Cohen[2,5] | Julio A. Chirinos[1]

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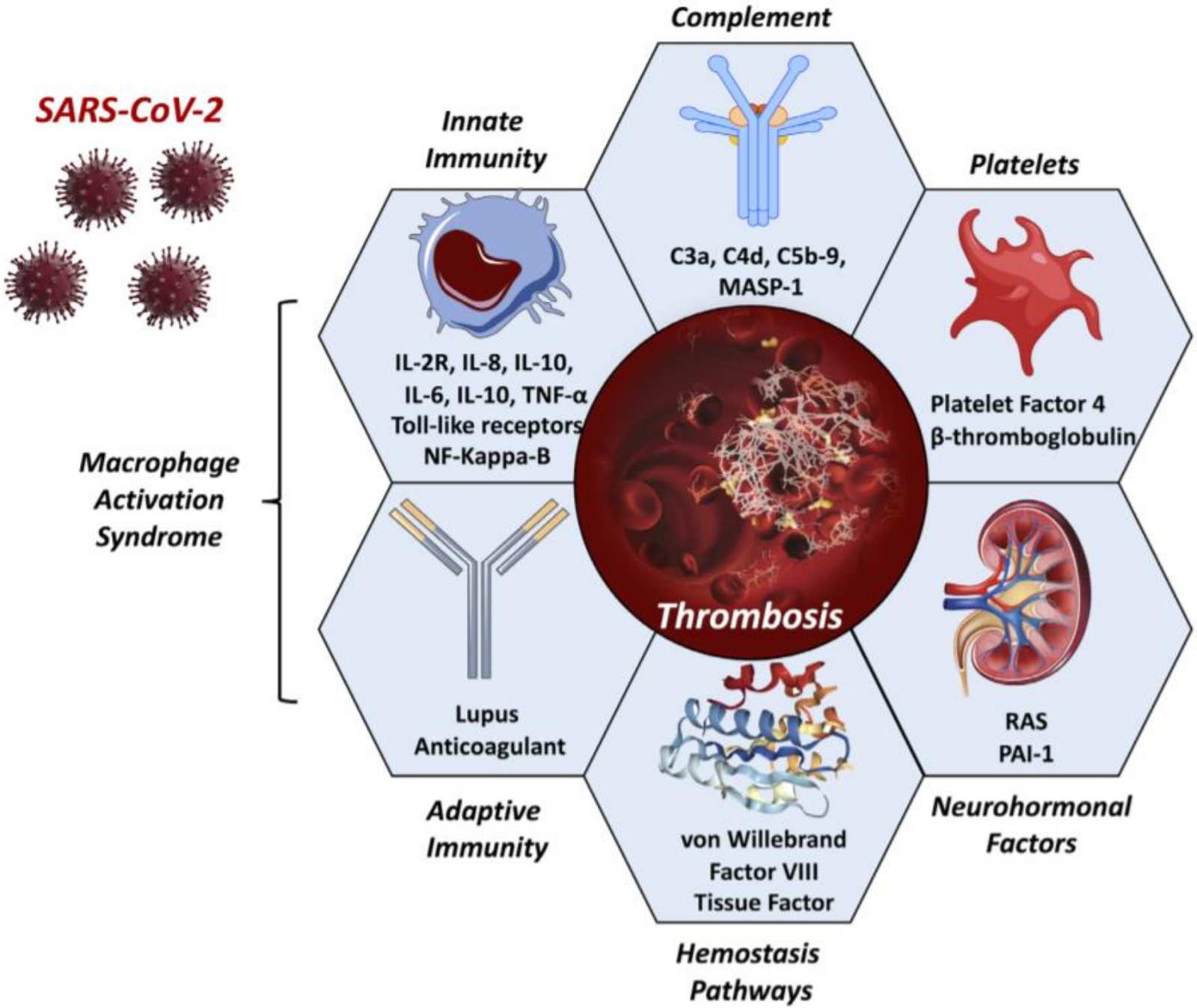
[5]Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

- Erken raporlarda lupus antikoagulan ilişkili tromboz?
- Hem erken evrede hem de geç evrede arterial-venöz mikro-makrovasküler komplikasyonlar
- En sık PE, DVT (kritik hastalarda %20-30)
- Alman grubu yoğun bakım hastalarında kümülatif geniş damar tromboz oranını %49 olarak tespit etmiştir. PE en sık hastada nandoparin altında tromboz geliştiğine dikkat çekmiş
- İtalyan grup tromboz kümülatif insidansı %21 tespit etmiş
- Fransız grup ise tromboz riskini diğer yoğun bakım hastalarından farklı bulmamış


SARS-CoV-2
Complement
C3a, C4d, C5b-9,
MASP-1
Innate
Immunity
IL-2R, IL-8, IL-10,
IL-6, IL-10, TNF-α
Toll-like receptors
NF-Kappa-B
Platelets
Platelet Factor 4
β-thromboglobulin
Macrophage
Activation
Syndrome
Thrombosis
Lupus
Anticoagulant
Adaptive
Immunity
von Willebrand
Factor VIII
Tissue Factor
Hemostasis
Pathways
RAS
PAI-1
Neurohormonal
Factors

Received: 29 June 2020 | Revised: 18 August 2020 | Accepted: 24 August 2020
DOI: 10.1002/ajh.25982

CRITICAL REVIEW

AJH WILEY

Thrombosis in COVID-19

Inflammation	Coagulopathy	Renin angiotensin system activity
IL-2R	Prothrombin time	Angiotensin II
IL-6	Activated partial-thromboplastin time	Angiotensin converting enzyme 2
IL-8	D-dimer	
IL-10	Plasminogen activator inhibitor 1	
TNF-α	Platelet count	
Ferritin	Fibrinogen (↑ or ↓)[a]	
Transforming growth factor-β	Fibrin degradation products	
Erythrocyte sedimentation rate	von Willebrand factor	
C-reactive protein	Factor VIII	

Received: 20 March 2020 | Accepted: 24 March 2020

DOI: 10.1111/jth.14817

ORIGINAL ARTICLE

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

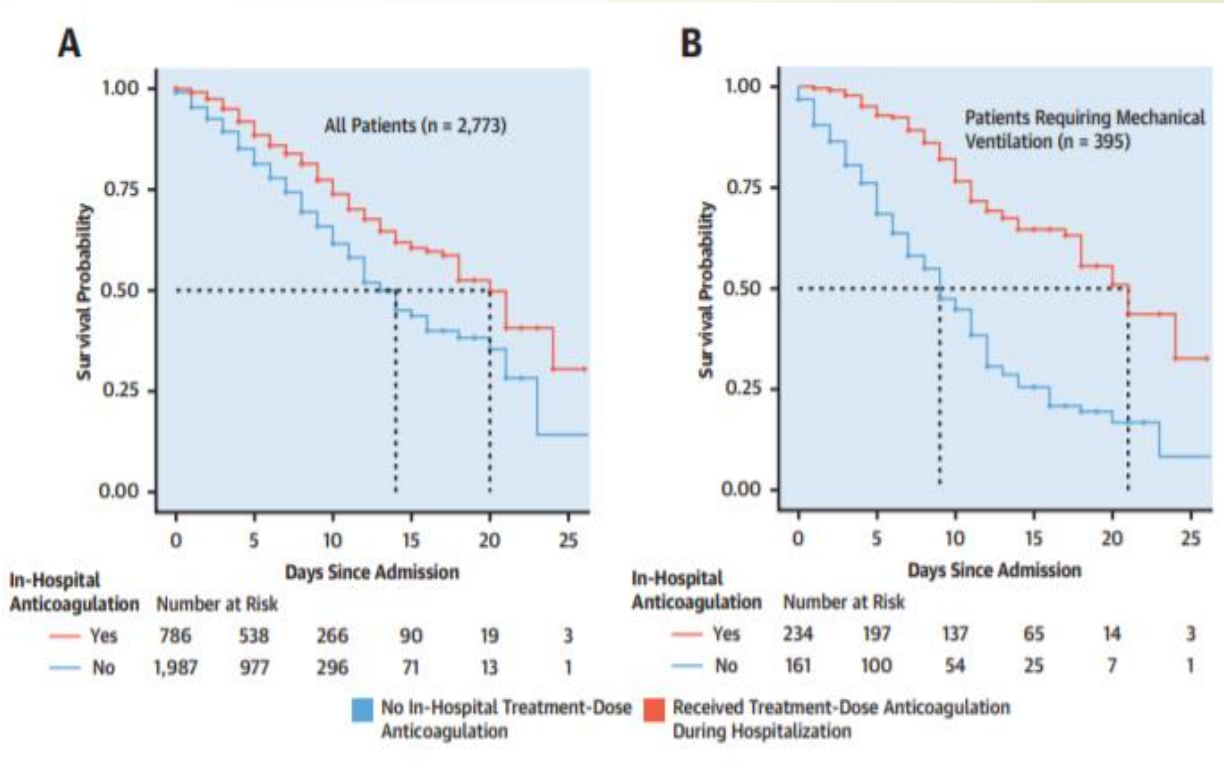
Ning Tang[1] | Huan Bai[1] | Xing Chen[1] | Jiale Gong[1] | Dengju Li[2] | Ziyong Sun[1]

	Multivariate analysis	
	Odds ratio (95% CI)	*P* value
Age	1.033 (1.013-1.055)	.002
Sex ratio	0.677 (0.425-1.078)	.100
With underlying diseases	0.861 (0.538-1.379)	.534
Treating with heparin	1.647 (0.929-2.921)	.088
Prothrombin time	1.107 (1.008-1.215)	.033
Platelet count	0.996 (0.993-0.998)	.001
D-dimer	1.058 (1.028-1.090)	<.001

Letters

Association of Treatment Dose Anticoagulation With In-Hospital Survival Among Hospitalized Patients With COVID-19

Paranjpe, I., Fuster, V., Lala, A., Russak, A., Glicksberg, B. S., Levin, M. A., ... Nadkarni, G. N. (2020). *Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19. Journal of the American College of Cardiology.* doi:10.1016/j.jacc.2020.05.001



COVID-19
(SARS-CoV-2 ENFEKSİYONU)

ANTİSİTOKİN-ANTİİNFLAMATUAR TEDAVİLER, KOAGÜLOPATİ YÖNETİMİ

Bilimsel Danışma Kurulu Çalışması

T.C. SAĞLIK BAKANLIĞI
7 Kasım 2020

Hastaneden çıkışta antikoagulasyon profilaksi süresi:

Tromboembolizm riski	**Düşük**	**Yüksek** (D-dimer >X 2, hareketsiz, aktif kanseri var)
Rivaroxaban	31–39 gün	45 gün
Betrixaban	35–42 gün	45 gün
Enoxaparin	14 – 30 gün	45 gün
Aspirin* (*bazı gruplarda önerilmemektedir)	30 gün	

ÖNERİ 2: TROMBOZ PROFİLAKSİSİ VE TEDAVİSİ

Tüm hastanede yatırılan COVID-19 hastalarında aktif kanama veya trombositopeni (<25-30.000/µl) olmadığı sürece tromboz profilaksisi uygulanmalıdır.

Profilakside önerilen tedavi: DMAH (enoksaparin)

Tromboz profilaksisinde düşük moleküler ağırlıklı heparin (DMAH) standart heparine tercih edilerek önerilmektedir. Çünkü DMAH daha nadir trombositopeni yapar ve daha seyrek injeksiyon gerektirir (DMAH 1x1, standart heparin 3x1).

Profilakside oral antikoagulan rutin önerilmemektedir. Çünkü ilaç etkileşimi, böbrek ve karaciğer işlev kusuru ile farmakodinamik etkilenmesi, uzun yarı ömür, maliyet, ve etkisinin geri döndürülmesi için gerekli etken maddelerin her hastanede bulunmaması gerekçe olarak gösterilmektedir.

ENOKSAPARİN **40MG: 4000 anti-Xa IU/O.4ML**

HEPARİN **25000u/5ML**

Ağır dereceli olmayan COVID-19

BMI <40kg/m2: Enoksaparin 40mg/gün sc

BMI > 40/kg/m2 Enoksaparin 40mg 2x1 sc

CrCl < 30ml/dak. : Enoksaparin kullanılması önerilmez.

Standat heparin önerilir. 5000 U sc 2x1 veya 3 x1

Ağır dereceli COVID-19:

CrCl> 30 ml/dak enoxaparin 40 mg 2x1sc, veya standart heparin 7500 U/; 3x1 (öneri ACF'e ait)

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site | PRS Login

Home > Search Results

Modify Search | Start Over

46 Studies found for: **anticoagulation | covid-19**

Also searched for **COVID** and **SARS-CoV-2**. See Search Details

Your search included: **covid-19**

Learn more about clinical studies related to COVID-19:

- **ClinicalTrials.gov**: Federally-funded clinical studies related to COVID-19
- **WHO Trial Registry Network**: COVID-19 studies from the ICTRP database
- **NIH**: COVID-19 Treatment Guidelines
- **ClinicalTrials.gov**: Views of Listed COVID-19 Studies (Beta)

Journal of Hematopathology
https://doi.org/10.1007/s12308-020-00419-3

ORIGINAL ARTICLE

Elevated eosinophil count is related with lower anti-factor Xa activity in COVID-19 patients

Selma Ari[1] · Veysi Can[1] · Ömer Furkan Demir[1] · Hasan Ari[1] · Fahriye Vatansever Ağca[1] · Mehmet Melek[1] · Sencer Çamci[1] · Özlem Şengören Dikiş[2] · Kağan Huysal[3] · Tamer Türk[4]

Received: 17 August 2020 / Accepted: 30 September 2020

Abstract

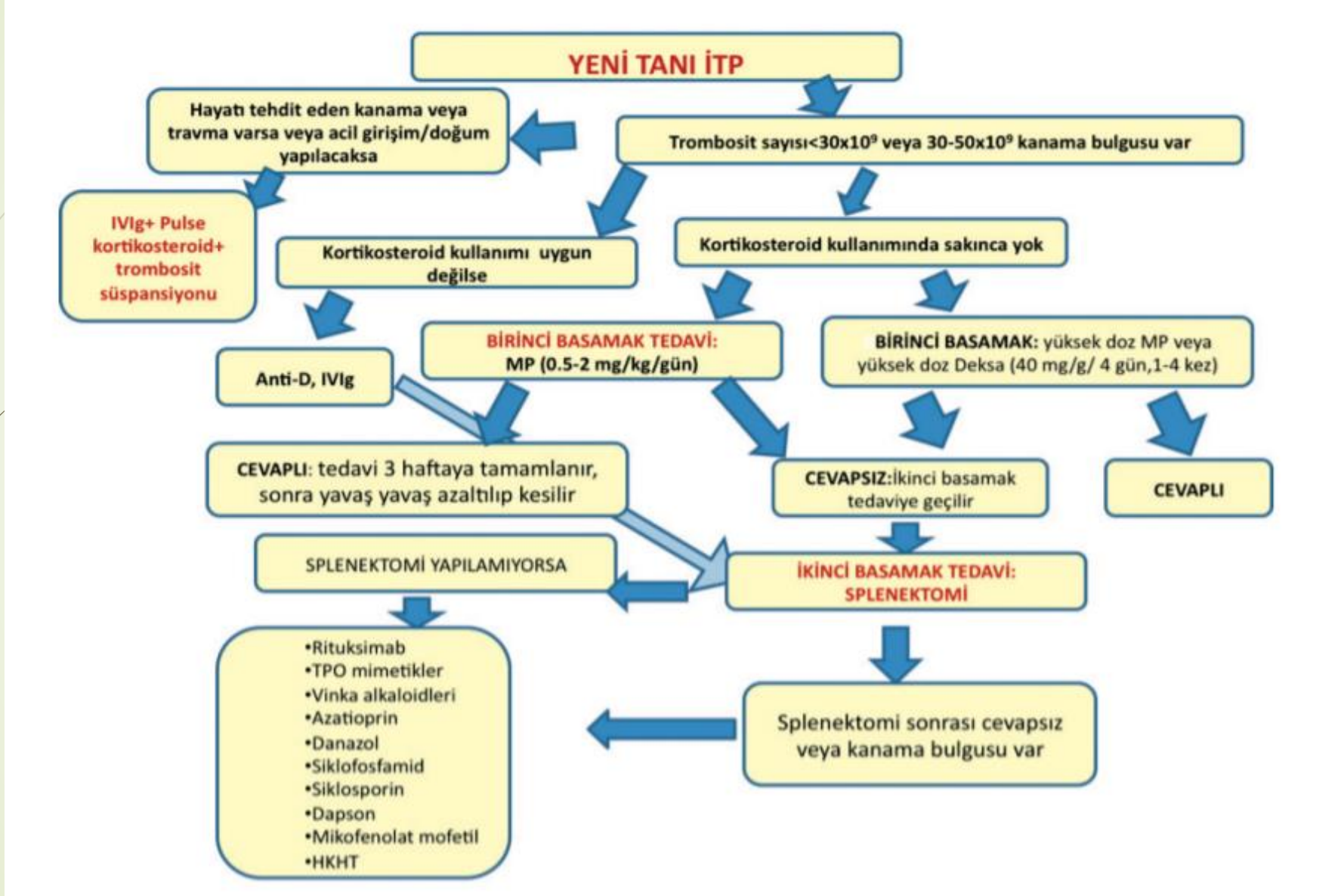
Despite prophylactic anticoagulant treatments, thrombotic complications may develop in patients with coronavirus disease 2019 (COVID-19). This study aimed to evaluate the factors influencing anti-factor Xa activity in COVID-19 patients receiving low molecular weight heparin (LMWH). We prospectively evaluated 80 COVID-19 patients, diagnosed using polymerase chain reaction test, who were admitted to our clinic and administered LMWH; LMWH (enoxaparin) was applied according to the weight, D-dimer levels, and clinical condition of patients. Anti-factor Xa activity in blood, drawn 4 h after the 3rd dose of LMWH, was measured and an activity of < 0.2 IU/mL was considered subprophylactic. Patients were followed up clinically, and anti-factor Xa activity was re-examined before discharge. Groups 1 and 2 included 13 and 67 patients with subprophylactic (mean ± SD: 0.18 ± 0.06) and prophylactic (mean ± SD: 0.43 ± 0.23) anti-factor Xa activity, respectively. The proportion of eosinophils in patients was significantly higher in group 1 than in group 2 (mean ± SD; 2.96 ± 2.55 vs 0.90 ± 1.28; $p = 0.001$). At the time of discharge, the eosinophilic proportion of patients was significantly higher (eosinophil %, mean ± SD; 3.06 ± 1.49 vs 2.07 ± 1.92; $p = 0.001$), but the activated partial thromboplastin time was significantly lower (22.34 ± 1.38 vs 24.38 ± 3.58; $p = 0.01$) in group 1 than in group 2. Of 14 patients with eosinophil content > 4%, 6 were in group 1 ((6/13) 46.2%), while 8 were in group 2 ((8/63) 11.9%); ($p = 0.009$), and all had a D-dimer level < 1 µg/mL ($p = 0.03$). ROC analysis for the presence of anticoagulation at subprophylactic level revealed an area under curve of 0.79 (95% CI: 0.64–0.93); $p = 0.001$). In conclusion; Elevated eosinophil count is related to lower anti-factor Xa activity in patients with COVID-19 receiving LMWH. The clinical significance of the subprophylactic anti-factor Xa activity should be studied in COVID-19 patients (NCT04507282).

İmmun Trombositopeni (ITP)

- Diğer trombositopeni nedenlerinin dışlanması ile tanı koyulmakta olup primer veya sekonder nedenli olabilir.
- Sekonder nedenler; otoimmun hastalıklar, immunyetmezlikler, viral enfeksiyonlar, lenfoid maligniteler, ilaç ve aşılardır.
- ITP, yeni tanı, persitan veya kronik olarak tanımlanır. Trombosit sayısı 30.000(20.000) /mm3 altında olması ağır trombositopeni olarak tanımlanır.
- Enfeksiyon ilişkili sekonder ITP de tetikleyici mekanizma virüs antijenlerine karşı oluşmuş antikorların trombosit yüzey antijenleri ile çapraz reaksiyon oluşturması sonucu trombosit yaşam ömrünün azalmasıdır.
- Trombosit destrüksiyonu sıklıkla dalakta olup bunun dışında karaciğer, lenf nodu ve kemik iliğinde de gerçekleşebilir.

İmmun Trombositopeni (ITP)

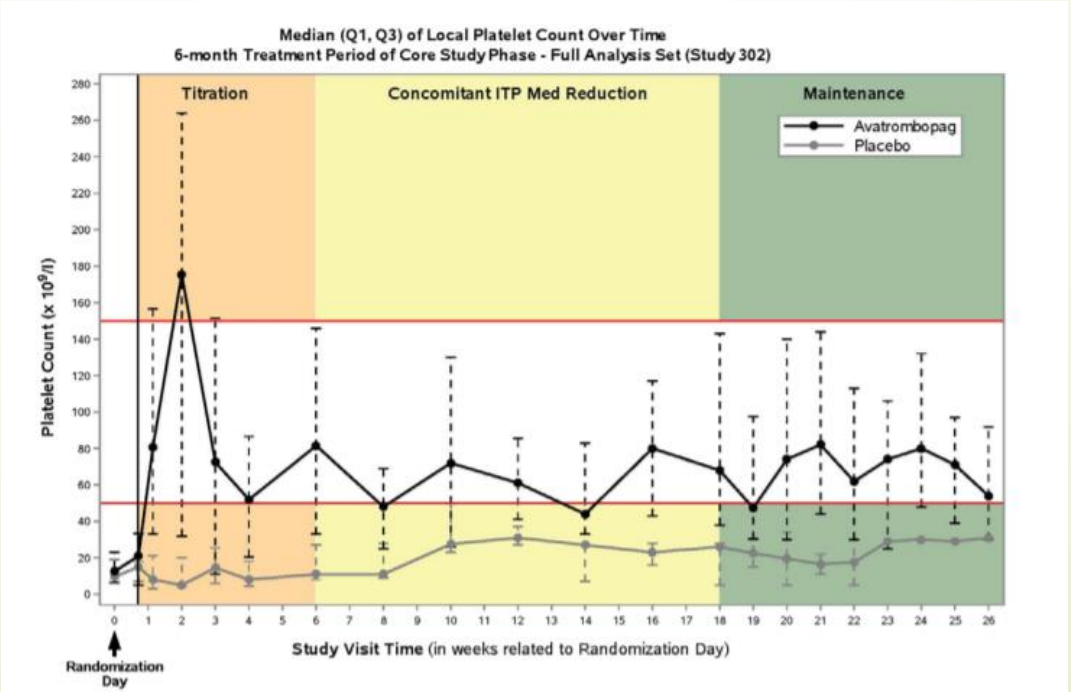
- ITP 0-14 yaş ve 60 yaş üstü iki pik yapar
- İnsidans 1-6/100.000
- Peteşi, purpura, ciddi kanama ,halsizlik veya asemptomatik klinik
- Hikaye, fizik muayene ve laboratuvar analizleri(periferik yayma, HIV,HCV, H. Pylori, B12, folat, TSH, kemik iliği analizi, immünolojik testler)
- Trombosit sayısı kanamasız hastada 30.000(20.000)/mm3 atında ise tedavi başlanmalıdır.
- Tedavide ilk sırada kontendike bir durum yok ise erişkinde steroid başlanmalıdır.
- Diğer tedavi seçenekleri ;IVIG, Anti-D, immunsupresif tedaviler, splenektomi, TPO mimetikler(eltrombopag,**avatrombopag**, romiplostim), danazol, **Fosfamatinib** , azatiopirin, siklosporin, MMF, vincristine


YENİ TANI İTP
Hayatı tehdit eden kanama veya travma varsa veya acil girişim/doğum yapılacaksa
Trombosit sayısı<30x10⁹ veya 30-50x10⁹ kanama bulgusu var
IVIg+ Pulse kortikosteroid+ trombosit süspansiyonu
Kortikosteroid kullanımı uygun değilse
Kortikosteroid kullanımında sakınca yok
Anti-D, IVIg
BİRİNCİ BASAMAK TEDAVİ: MP (0.5-2 mg/kg/gün)
BİRİNCİ BASAMAK: yüksek doz MP veya yüksek doz Deksa (40 mg/g/ 4 gün,1-4 kez)
CEVAPLI: tedavi 3 haftaya tamamlanır, sonra yavaş yavaş azaltılıp kesilir
CEVAPSIZ:İkinci basamak tedaviye geçilir
CEVAPLI
SPLENEKTOMİ YAPILAMIYORSA
İKİNCİ BASAMAK TEDAVİ: SPLENEKTOMİ
•Rituksimab
•TPO mimetikler
•Vinka alkaloidleri
•Azatioprin
•Danazol
•Siklofosfamid
•Siklosporin
•Dapson
•Mikofenolat mofetil
•HKHT
Splenektomi sonrası cevapsız veya kanama bulgusu var

bjh research paper

Phase 3 randomised study of avatrombopag, a novel thrombopoietin receptor agonist for the treatment of chronic immune thrombocytopenia

- Avatrombopag; 3. kuşak oral TPO mimetik, yemek etkileşimi yok
- 2018 de ITP ve kronik karaciğer hastalığı ilişkili trombositopenide FDA onayı aldı
- En sık yan etki baş ağrısı -konfüzyon

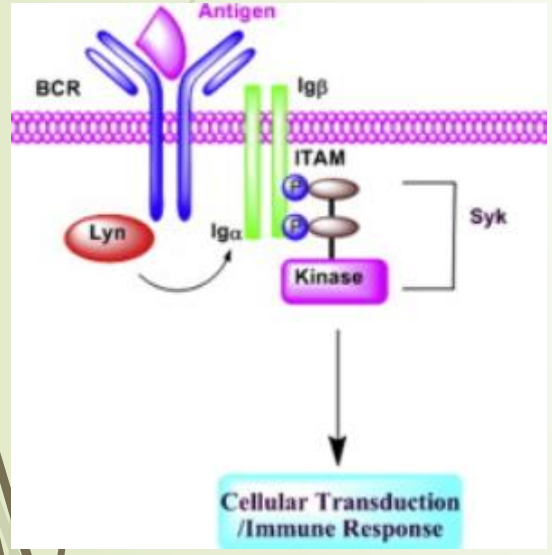


Fostamatinib for the treatment of chronic immune thrombocytopenia

Nathan T. Connell[1,2] and Nancy Berliner[1,2]

[1]Hematology Division, Brigham and Women's Hospital, Boston, MA; and [2]Harvard Medical School, Boston, MA

Fostamatinib is a spleen tyrosine kinase inhibitor recently approved for the treatment of chronic immune thrombocytopenia (ITP) in patients without adequate response to at least 1 prior line of therapy. This article reviews fostmatinib's mechanism of action and its clinical safety and efficacy in 2 industry-sponsored multicenter phase 3 randomized controlled trials in North America, Australia, and Europe (FIT1 and FIT2). Cost comparisons are discussed as well as the role of fostamatinib in relation to other options for chronic ITP. (*Blood*. 2019;133(19):2027-2030)



- Fostamatinib, oral Syk inhibitörü olan prodrug
- Kronik ITP hastalarında Nisan 2018 de FDA onayı almıştır
- 2x100 mg olarak başlanarak 2x150 mg olarak düzenlenebilir
- %43 yanıt(50.000 /mm3 ve üzeri trombosit sayısı)

Therapy	Response rate	Time to response	Toxicity	Duration of response
Splenectomy	80% overall, 66% stable	1-24 d	Surgical complications Infection (2-3 times baseline risk) Thrombosis (~2 times baseline risk)	Approximately 2/3 of patients will require no further therapy
Rituximab	60% overall, 40% stable	1-8 wk	Hypersensitivity reactions Immune suppression Hepatitis B reactivation	20-25% sustained at 5 y, although patients may be retreated
TPO mimetics (eg, romiplostim, eltrombopag)	>80% overall, 40-50% stable	2-3 wk	Rebound thrombocytopenia Thrombosis Hepatotoxicity (eltrombopag) Increased marrow reticulin deposition (1.8-7%)	Continuous as long as drug is administered In patients who have an initial response, >90% maintain that response at 5 y
Syk inhibitor (fostamatinib)	43% overall, 18% stable	2-8 wk	Diarrhea, nausea Hypertension Neutropenia	Unknown, but assumed to be continuous as long as drug is administered

bjh guideline

Practical guidance for the management of adults with immune thrombocytopenia during the COVID-19 pandemic

Sue Pavord,[1] Jecko Thachil,[2] Beverley J. Hunt,[3] Mike Murphy,[4] Gillian Lowe,[5] Mike Laffan,[6] Mike Makris,[7] Adrian C. Newland,[8] Drew Provan,[9] John D. Grainger[10] and Quentin A. Hill[11]

- COVID-19 enfeksiyonunda %36 hafif trombositopeni, %5 hastada 100.000 /mm3 altında ,multifaktöryel
- Immun sebepler dışında ilaçlar, sekonder enfeksiyonlar, hemodiyaliz, ECMO, heparin, trombopoetin baskılanması ile trombosit üretiminin azalması
- Ağır –orta trombositopeni genellikle geç dönemde multiorgan yetmezlik fazında, trombositopeni artmış mortalite ilişkili
- Ağır trombositopeni (30.000/mm3 altı) ve 24 saat içinde hızla azalan trombosit sayısı genellikle immun mekanizma ilişkili
- HIT, MAHA ve ilaç ilişkili trombositopeni dışlanmalı

bjh guideline

Practical guidance for the management of adults with immune thrombocytopenia during the COVID-19 pandemic

Sue Pavord,[1] Jecko Thachil,[2] Beverley J. Hunt,[3] Mike Murphy,[4] Gillian Lowe,[5] Mike Laffan,[6] Mike Makris,[7] Adrian C. Newland,[8] Drew Provan,[9] John D. Grainger[10] and Quentin A. Hill[11]

Relaps/yeni tanı ITP yönetimi;

- COVID-19 negatif ise ilk tercih TPO-mimetik olabilir
- COVID-19 pozitif hastalarda TPO-mimetiklerden tromboz riski ve hepatotoksisite nedeniyle kaçınılmalı
- Eğer ilk tercih steroid olursa doz azaltılmış ve süre kısaltılmış olarak tercih edilmeli
- Kanamasız hastada 20 mg/gün dozunda başlayıp 3-5 gün sonra yanıt alınmaz ise doz arttırılmalı yanıtlı ise düşük doz tercih edilmeli
- Steroid yanıtsızsa hızlıca doz azaltılıp kesilmeli yanıtlı ise 2 haftada yavaş doz azaltımı yapılmalı
- Hızlı yanıt isteniyorsa ilk seçenek IVIG olmalı,yoksa 2. tercih olarak seçilmeli
- Traneksamik asit COVID-19 tanılı hastada DIC varsa kullanılmamalı

bjh guideline

Practical guidance for the management of adults with immune thrombocytopenia during the COVID-19 pandemic

Sue Pavord,[1] Jecko Thachil,[2] Beverley J. Hunt,[3] Mike Murphy,[4] Gillian Lowe,[5] Mike Laffan,[6] Mike Makris,[7] Adrian C. Newland,[8] Drew Provan,[9] John D. Grainger[10] and Quentin A. Hill[11]

Kronik ITP yönetimi;

- Kronik ITP hastaları mevcut tedavilerine devam etmeli
- İzolasyonlarına dikkat etmeli
- Mümkün ise online platformdan takipleri yapılmalı
- Splenektomize hastalar aşılanma sürecine kadar antibiyotik proflaksisi almalı

bjh guideline

Practical guidance for the management of adults with immune thrombocytopenia during the COVID-19 pandemic

Sue Pavord,[1] Jecko Thachil,[2] Beverley J. Hunt,[3] Mike Murphy,[4] Gillian Lowe,[5] Mike Laffan,[6] Mike Makris,[7] Adrian C. Newland,[8] Drew Provan,[9] John D. Grainger[10] and Quentin A. Hill[11]

ITP hastalarında trombotik risk;

- ITP ilişkili tromboz riski artmış olup COVID-19 pozitif hastalarda bu durum gözden kaçmamalıdır
- Kanama bulgusu olmayan ve trombosit sayısı 30.000/mm3 ve üzerinde olan tüm ITP hastalarına DMAH proflaksisi verilmelidir
- Trombosit sayısı 30.000/mm3 altında olan hastalarda aralıklı pnömatik kompresyon uygulanmalıdır

DOI: 10.1002/jmv.26138

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

COVID-19 presenting with immune thrombocytopenia: A case report and review of the literature

Patient (reference)	Age	Sex	Presenting symptoms	COVID symptoms	Days from symptoms to referral	Viral serology and autoimmune profile	Days from admission to thrombocytopenia/ COVID course	Platelet Nadir	Prior drugs	IVIg dose/ response	Further treatment	Platelets increased to (after treatment), d	Outcome
P#1[4]	50	M	Epistaxis, generalized rash	None	Not reported	Negative	On presentation, stable COVID course	0	None	1 g/kg: 2 doses/ responsive	None	25×10^9/L, (2), 103×10^9/L, (14)	Discharged
P#2[4]	49	F	Bruises, gum bleed	None	3	Negative	On presentation, stable COVID course	4×10^9/L	None	1 g/kg: Single dose/ responsive	None	52×10^9/L (2)	Discharged
P#3[4]	96	F	Shortness of breath	Shortness of breath	Not reported	Negative	5th d, deteriorated	3×10^9/L	None	0.4 g/kg: 5 doses/ not known	None	16×10^9/L (2)	Died
P#4[6]	65	F	Fatigue, fever, dry cough	Fatigue, fever, dry cough	4	Anti-TPO (+)	4th d, complicated with subarachnoid hemorrhage	8×10^9/L	Amo-Clav, LMWH	1 g/kg/ unresponsive	Prednisolone, TPO-RA	139×10^9/L (4)	Discharged
P#5[5]	59	M	Petecihae, skin hematoma	Cough, fever	10	GPIb (+) GPIIB IIIa (+) GPV (+)	On presentation, stable COVID course	3×10^9/L	None	1 g/kg: 2 doses/ responsive	Dexamethasone	47×10^9/L (2), 51×10^9 (17)	Discharged
P#6[5]	66	F	Petechiae, epistaxis	Fever, dyspnea, cough, diarrhea	21	Negative	On presentation, stable COVID course	2×10^9/L	High dose dexamethasone	1 g/kg: dose not shared/ responsive	None	32×10^9 /L (22)	Discharged
P#7[5]	67	M	Fever, cough, dyspnea	Fever, cough, dyspnea	9	Negative	12th d, deteriorated, pulmonary embolism	3×10^9/L	Unfractionated heparin	None	Platelet transfusion	None	Died
P#8[7]	38	M	Cough, dyspnea, fever	Cough, dyspnea, fever	13	Negative	16th d, stable COVID course	2×10^9/L	Interferon-α, umifenovir,	400 mg/kg: 7 doses-responsive	Dexamethasone	60×10^9/L (3)	Discharged
Present case	41	M	Petecihae and purpura	Cough and runny nose	4	Negative	On presentation, stable COVID course	9×10^9/L	High dose dexamethasone	1 g/kg: 2 d/ responsive	None	54×10^9/L (2)	Discharged

Transfüzyon

JAMA

American Medical Association

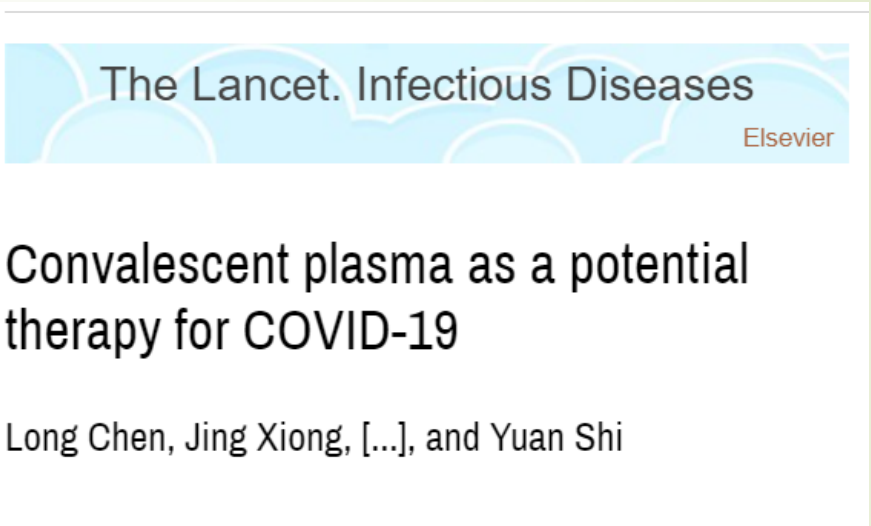
THIS ARTICLE HAS BEEN CORRECTED.

See JAMA. 2020 August 4; 324(5): 519.

Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19

A Randomized Clinical Trial

Ling Li, MD, PhD, Wei Zhang, MD, [...], and Zhong Liu, MD, PhD



The Lancet. Infectious Diseases

Elsevier

Convalescent plasma as a potential therapy for COVID-19

Long Chen, Jing Xiong, [...], and Yuan Shi

JCI The Journal of Clinical Investigation

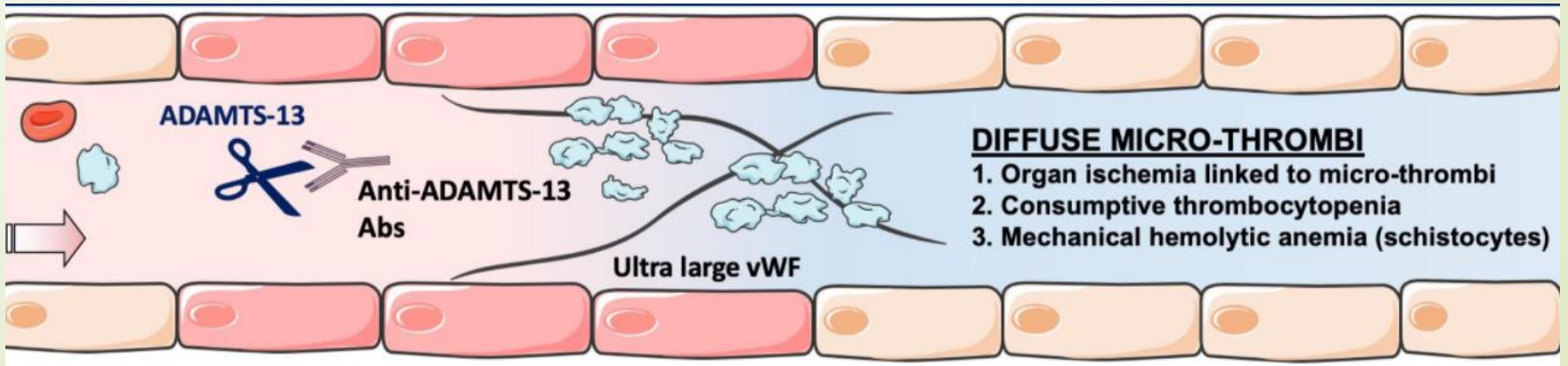
Deployment of convalescent plasma for the prevention and treatment of COVID-19

Evan M. Bloch, … , Jeffrey A. Bailey, Aaron A.R. Tobian

J Clin Invest. 2020;130(6):2757-2765. https://doi.org/10.1172/JCI138745.

Trombotik Trombositopenik Purpura

- Trombotik mikroanjiopati nedenlerinden biri olan TTP edinilmiş ve kalıtsal olarak ikiye ayrılır.
- Edinilmiş TTP: ADAMTS13 e karşı gelişen antikor aracılı ciddi ADAMTS13 aktivitesi azalır.
- İnsidans 3/1.000.000, median tanı yaşı 41, kadılarda ve siyah toplumda sık
- Nörolojik bulgular, GIS semptomları, renal yetmezlik, kardiyak semptomlar görülebilir
- Mikroanjiopatik hemolitik anemi ve trombositopeni/PY de şistositler
- Tanı ADAMTS13 aktivitesinin düşüklüğü(%10 altı) ve eşlik eden ADAMTS13 antikor varlığı ile konur



Trombotik Trombositopenik Purpura

PLASMIC SKOR

- Trombosit sayısı 30.000 /mcL altında olması (1 puan)
- Hemoliz (retikülosit sayısı %2.5 üzerinde olması, haptoglobin düşüklüğü veya indirek bilirubin yüksekliği)(1 puan)
- Aktif kanser olmaması (1 puan)
- Solid organ veya kök hücre nakli öyküsü olmaması(1 puan)
- MCV <90 fL(1 puan)
- INR <1.5(1 puan)
- Kreatinin <2.0 mg/dL(1 puan)

●0 to 4 puan – düşük

●5 puan – orta

●6 to 7 puan – yüksek

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ORIGINAL RESEARCH

TRANSFUSION

Diagnostic accuracy of the PLASMIC score in patients with suspected thrombotic thrombocytopenic purpura: A systematic review and meta-analysis

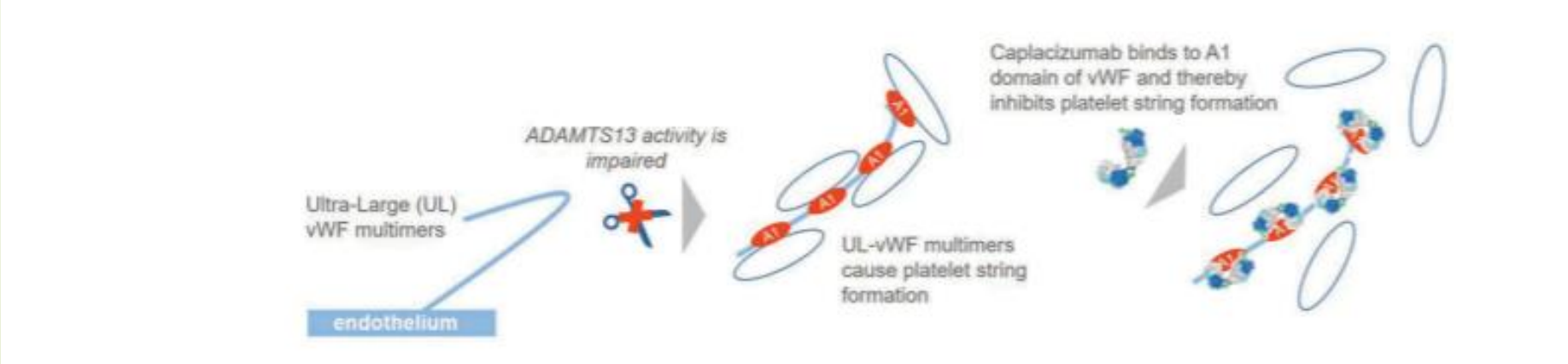
Koosha Paydary[1] | Emma Banwell[2] | Jiayi Tong[3] | Yong Chen[3] | Adam Cuker[4,5]

- 13 çalışmanın metanalizi (190 hasta)
- PLASMIC skor 5 ve üzeri olanlarda %99 sensitif,% 57 spesifik
- PLASMIC skor 6 ve üri olanlarda % 85 sensitif, % 89 spesifik
- Bu çalışma ile PLASMIC skor eşiği 5 olarak kabul edilmiştir.

- Bu skor sadece ön görü ve şüphe varlığında bir an önce tedaviye başlanması için önemlidir. **Kesin tanı koydurmaz**

Trombotik Trombositopenik Purpura

- Tedavide TDP ile plazma değişimi şüphe halinde hemen başlanmalıdır
- Edinilmiş TTP de immunsupresif ajanlar kullanılmalıdır
- Glukokortikoidler, rituksimab
- **Caplasizumab (anti-vonWillebrand antikoru**) ;10 mg ıv yükleme dozu sonrasu 10 mg SC, yüksek riskli hastalarda tercih edilmeli



TEŞEKKÜRLER