



ACİL SERVİSTE KANAMA KONTRÖLÜ

Doc.Dr. Kenan Ahmet TÜRKDOĞAN
Sağlık Bilimleri Üniversitesi Bağcılar SUAM
Acil Tıp Kliniği

Amaçlar



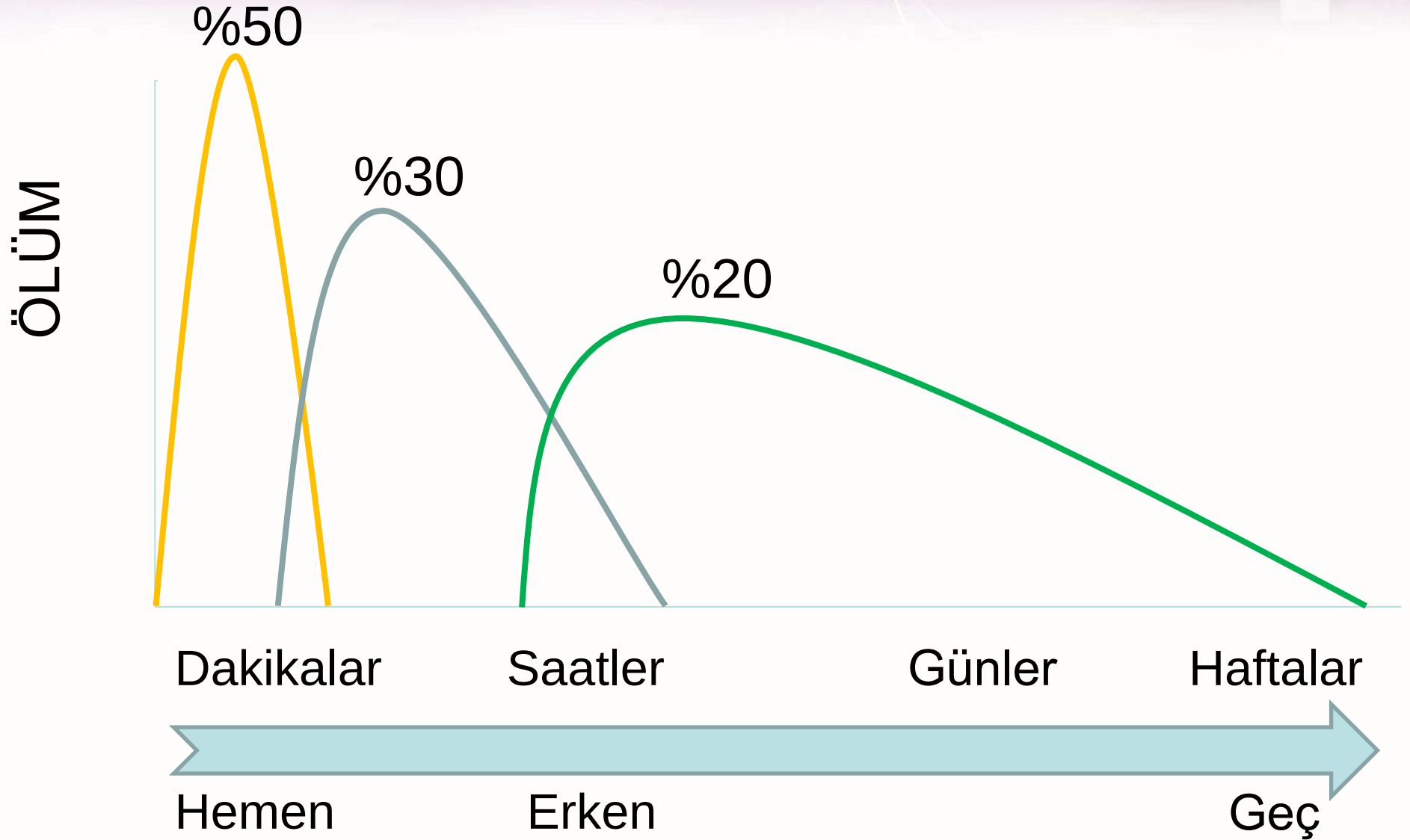
Bu sunumun sonunda;

- Hemorajik şok belirtilerini ve semptomlarını tanır
- Travma hastalarında erken kanama kontrolünün önemini farkederek
- Hemorajik şokun tedavisini ve devam eden değerlendirmesini tanımlar
- Hasar kontrolü resüsitasyonunun bileşenlerini listeler
- Kanama kontrolünde ilaç yönetimini düşünür

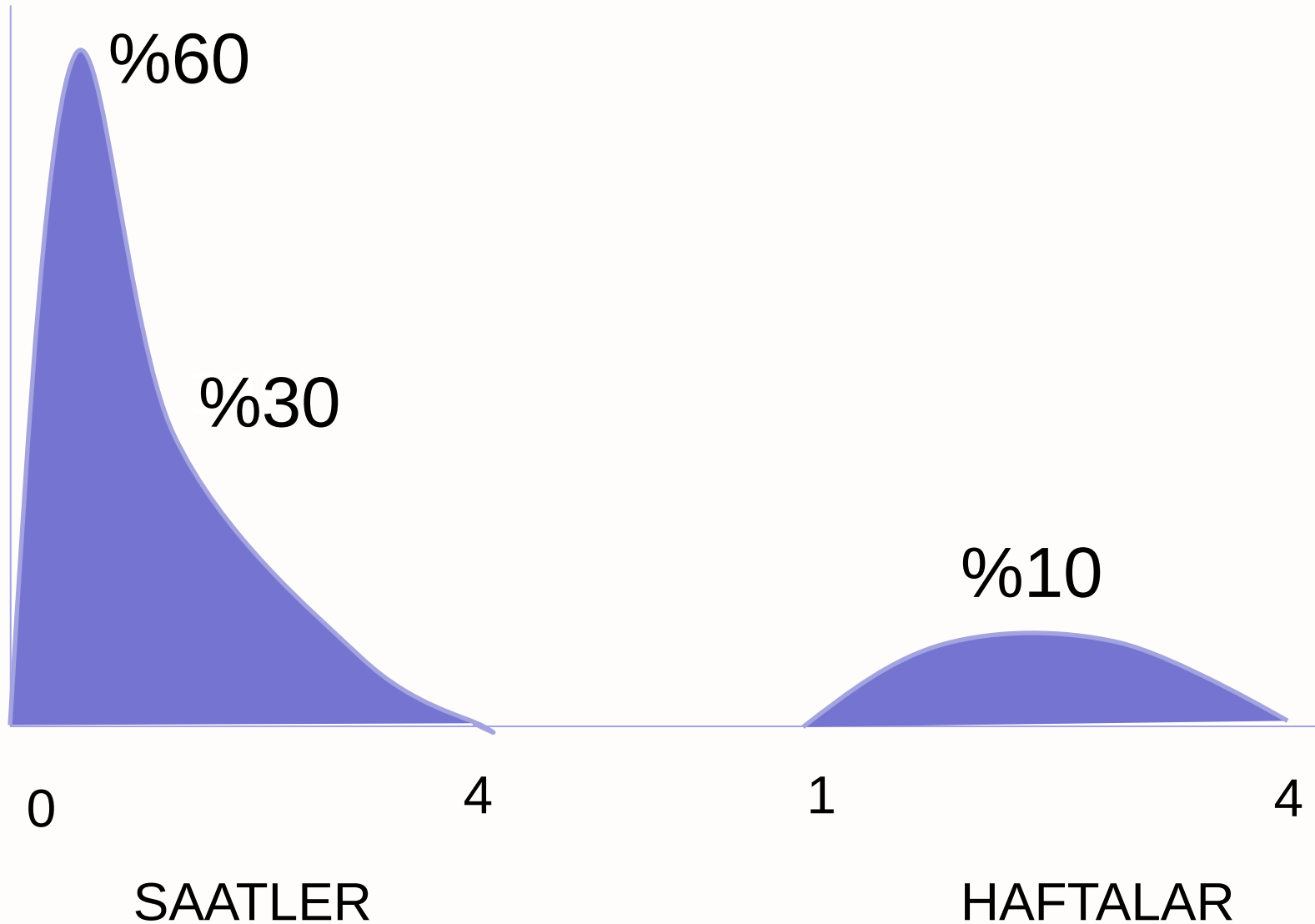
Hemorajik Şok



Tarihsel Travma Trimodal Ölüm Distribüsyonu



Yeni Bimodal Travma Ölüm Distribüsyonu



Hemorajiye Yol Açan Yaralanmalar

Vasküler	Solid Organ	Kemikler
Aort Vena Kava	Dalak Karaciğer	Pelvis Femur

Hızla Kan Kaybını Dışla

Göğüs Boşluğu – PAAC / FAST

Abdomen – FAST

Pelvis – Röntgen

Femur – FM / Röntgen

Kanamaya Sebep Olan Kırıklar

- Humerus 750 ml
- Tibia 750 ml
- Femur 1500 ml
- Pelvis > 3 L

Çevre Yumuşak Doku Travması Sitokin Salınımı

- Geçirgenlik artışı
- Sıvı kaybında artış

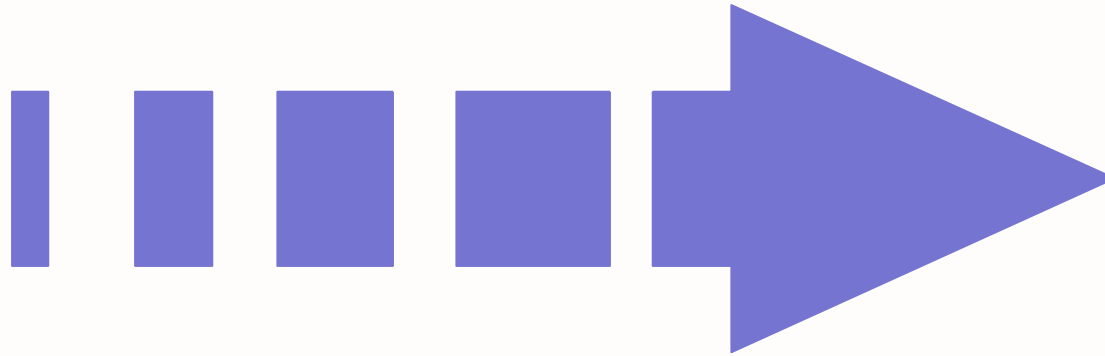


Hemorajik Yanıtı Kötüleştiren Faktörler

- Yaş
- Hastalık öyküsü / ilaçlar
- Yaralanmanın ağırlığı
- **Tedaviye ulaşım**
- **Şok süresi**
- Hastane öncesi sıvı tedavisi miktarı
- Hipotermi



Hemorajik Şok



Patofizyoloji

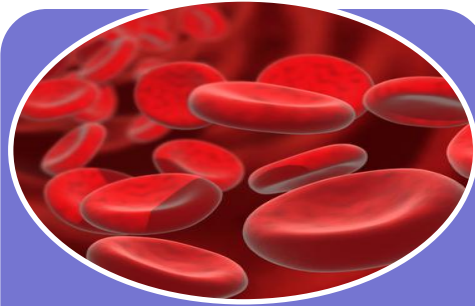
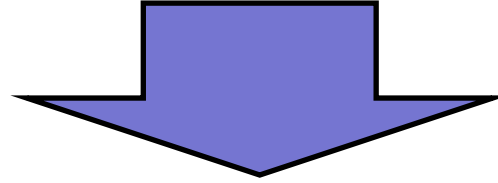
Kalp
Hızı
(atım/dk.)

X

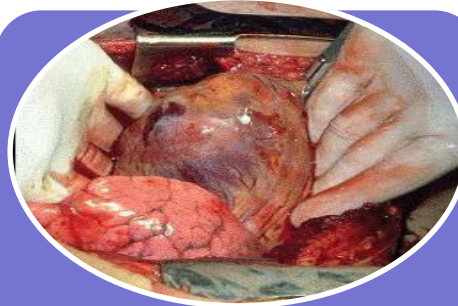
Atım
Hacmi
(ml/atım)

=

Kardiyak
Output
(L/min)



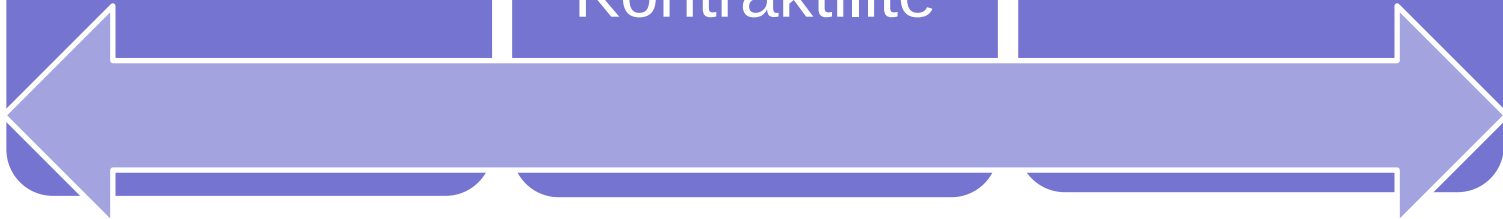
Ön yük



Miyokardiyal
Kontraktilite

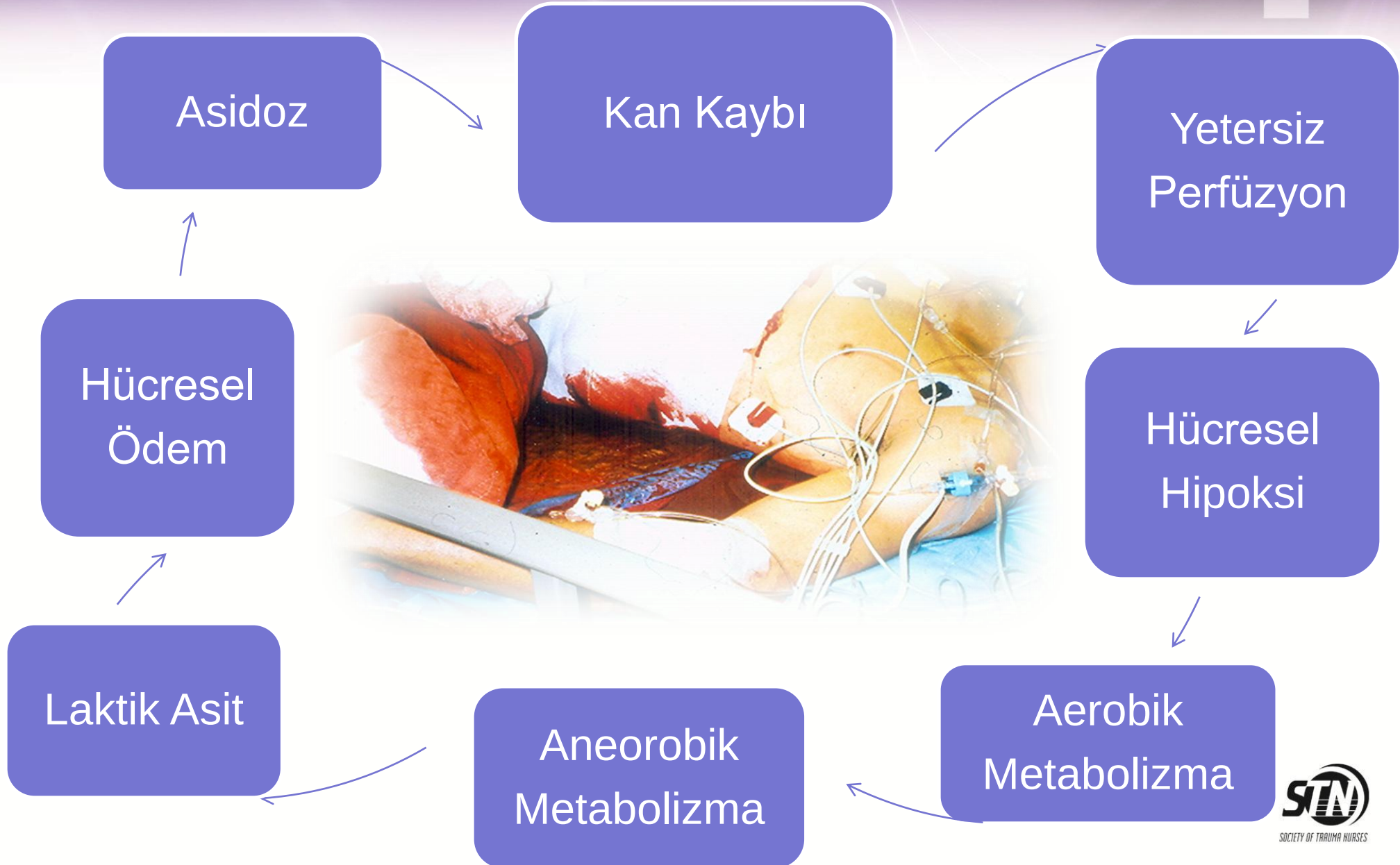


Arka yük

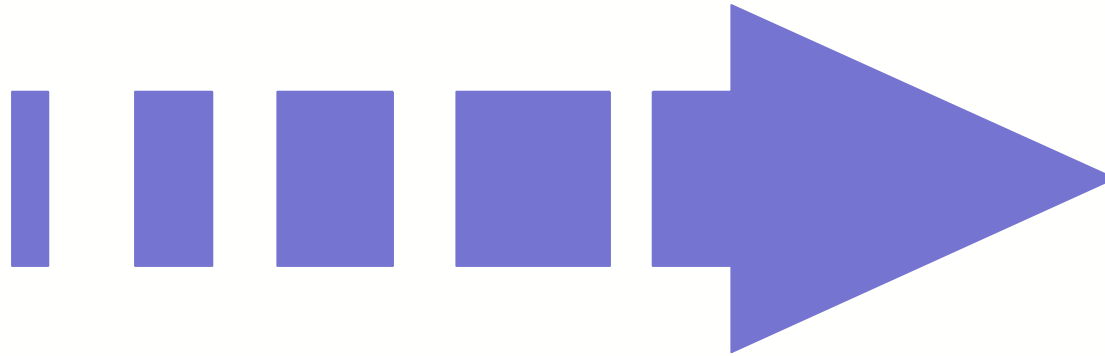


Kardiyak Output

Şokta Hücresel Yanıt



Hemorajik Şok



Değerlendirme

Şokun Klasik Bulgu&Belirtileri

- Mental durum değışikliđi
- Taşikardi
- Soğuk, nemli deri
- Uzamış kapiller geri-dolum zamanı
- Daralmış nabız basıncı
- Azalmış idrar çıkışı
- Hipotansiyon





Normal vital
bulgular okkült
hipoperfüzyonu
dışlamaz

Hemorajik Şokun ATLS Sınıflaması

TABLE 3-1 SIGNS AND SYMPTOMS OF HEMORRHAGE BY CLASS

PARAMETER	CLASS I	CLASS II (MILD)	CLASS III (MODERATE)	CLASS IV (SEVERE)
Approximate blood loss	<15%	15-30%	31-40%	>40%
Heart rate	↔	↔/↑	↑	↑/↑↑
Blood pressure	↔	↔	↔/↓	↓
Pulse pressure	↔	↓	↓	↓
Respiratory rate	↔	↔	↔/↑	↑
Urine output	↔	↔	↓	↓↓
Glasgow Coma Scale score	↔	↔	↓	↓
Base deficit*	0 to -2 mEq/L	-2 to -6 mEq/L	-6 to -10 mEq/L	-10 mEq/L or less
Need for blood products	Monitor	Possible	Yes	Massive Transfusion Protocol

* Base excess is the quantity of base (HCO_3^- , in mEq/L) that is above or below the normal range in the body. A negative number is called a base deficit and indicates metabolic acidosis.

Data from: Mutschler A, Nienaber U, Brockamp T, et al. A critical reappraisal of the ATLS classification of hypovolaemic shock: does it really reflect clinical reality? *Resuscitation* 2013;84:309-313.

Değerlendirmeye Karşılık Resüsitasyon Hedefleri

İlk Değerlendirme

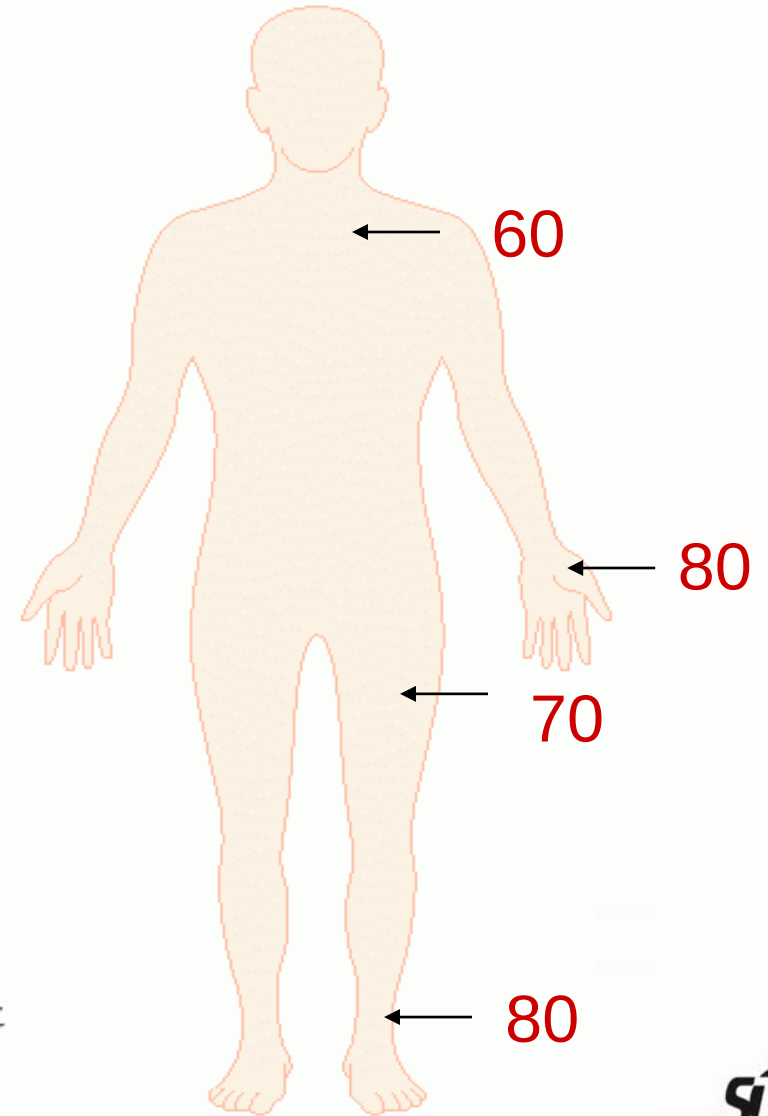
Geleneksel ↔ Yeni
Akut ↔ Süregelen
Statik ↔ Dinamik
Global ↔ Hedef Organ

- Mental Durum
- Cilt Perfüzyonu
- Nabız
- Kan Basıncı
- Nabız Basıncı
- Şok İndeksi
- İdrar Çıkışı
- pH
- Serum Laktat Seviyesi
- Baz Açığı
- Ekokardiyografi
- Arteriyel Dalga Analizi
- StO2 (NIRS/yakın kızıl ötesi)

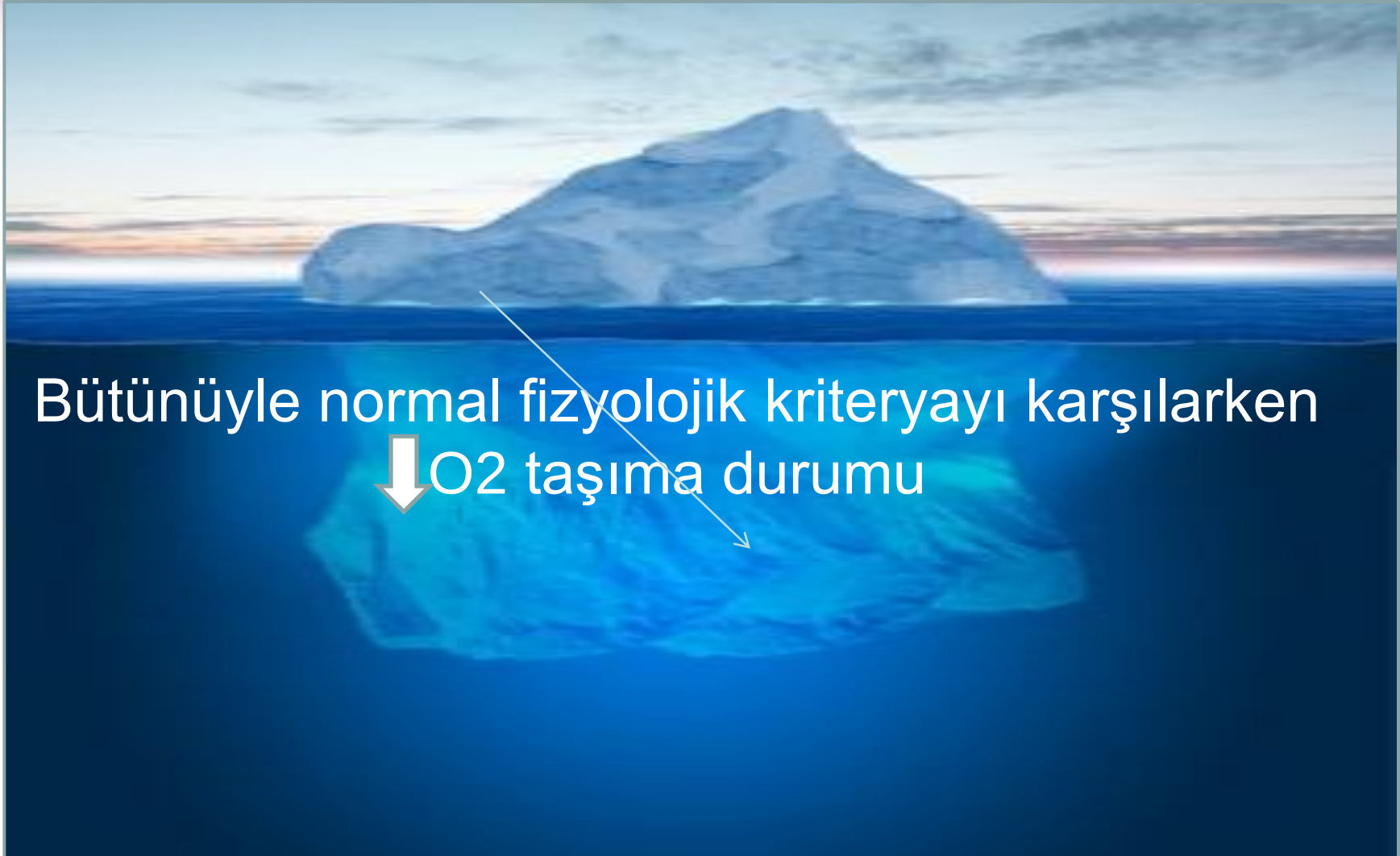
Resuscitation Endpoints

Nabız Palpasyonu İle KB Tahmini

- Eğer nabızı şemadaki noktalardan birinde palpe edebiliyorsanız, SKB'nın kabaca kaç olduğunu bilebilirsiniz.



Okkült Hipoperfüzyon



Bütünüyle normal fizyolojik kriteriyayı karşılarken
↓ O2 taşıma durumu

*Hastalar aniden kötüleşmezler, daha çok kötüleşme
aniden bizim dikkatimizi çeker...*

Mental Durum Deęişiklięi

- Perfüzyonun göstergesi
- İlaçlar & alkol durumu
- Hipoksi/Kafa travması
 - Aksi ispat edilene kadar



Cilt Perfüzyonu

- **Soluk, soğuk, alacalı**
 - Vazokonstüksiyon
- **En çok pediatrik hastalarda duyarlı**
 - Distal ekstremitelerde başlar
 - Gövdeye doğru uzanır
- **Kapiller Geridolum**
 - Ölçümü güvenilir değil
 - Normal < 2 saniye



Kan Basıncı



- **Volüm Kaybına KB Yanıtı**
 - Kompansatuar mekanizmalardan dolayı non-linear
 - Erken şok bulgusu olarak duyarsız
- **Az sıklıkta& yada yetersiz monitorizasyon**
 - İlk ölçülen KB her zaman manuel ölçülmelidir
 - Otomatik KB 10 mm Hg kadar fazla ölçer

Kan Basıncı



- Sistolik KB düşüşü geç bir bulgu
 - Sistolik KB düşmesi için:
 - Yetişkinlerde %30 kan kaybı
 - Pediatrik %40-45 kan kaybı
- gerekli..
- SKB $\leq$ 90 mm Hg: mortalite %65'e yaklaşır

Hastane-öncesi KB'ını Elerken Dikkatli Ol

Hastane Öncesi
Hipotansiyon

Skeptisizm

Prehospital + AS
Hipotansiyon

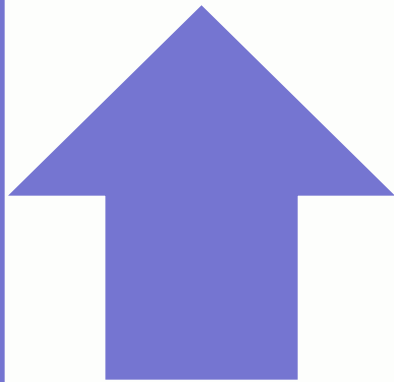
Güçlü Öngörücü

- Mortalite
- Ameliyat İhtiyacı

Hipotansiyon Yeni Tanımı?

Yeni Hipotansiyon : SKB $\leq$ 110

- Fizyolojik değişikliklerin başlangıcı ile ilgili



- Baz Açığı
- GYB Gün Sayısı
- Ventilatör Gün Sayısı
- Komplikasyonlar

- Sadece şoku tanılamak için kullan
- Resüsitasyon uç uç noktası olarak kullanma.

Bilimsel arařtırmalar řokta *mortaliteyi azaltan ideal SKB'nın yařla birlikte arttıđını* iřaret eder.



Yeni SKB

Şokun Erken Tanısı İçin İdeal Nokta?

Yetişkin Travma

60 70 80 90 100 110 120 130

Geriatrik Travma

90 100 110 120 130 140 150 160

Nabız Basıncı



- Daralmış nabız basıncı ciddi kaybını işaret eder
- Kompansatuar katekolamin salınımının sonucu olarak artmış diastolik basıncın sonucu gelişir

100/66 100/74 100/77 100/84

Nabız

- Tek başına özgöl değil
- Yaşa bağımlı
- Etkileyen faktörler:
 - Emosyonel durum
 - Ateş
 - Ağrı
 - İlaçlar
- Nabız & karakter birlikte daha güvenli



- Zamanla *duyarlı?*
olabileceği
düşünülmekte
- Ne zaman
endişelenelim?
80 90 100 **110 > 120**

Soğuk & taşikardik
olan her hasta aksi
ispatlanana kadar
şokta kabul edilir.
(ATLS)

Şok İndeks (SI)



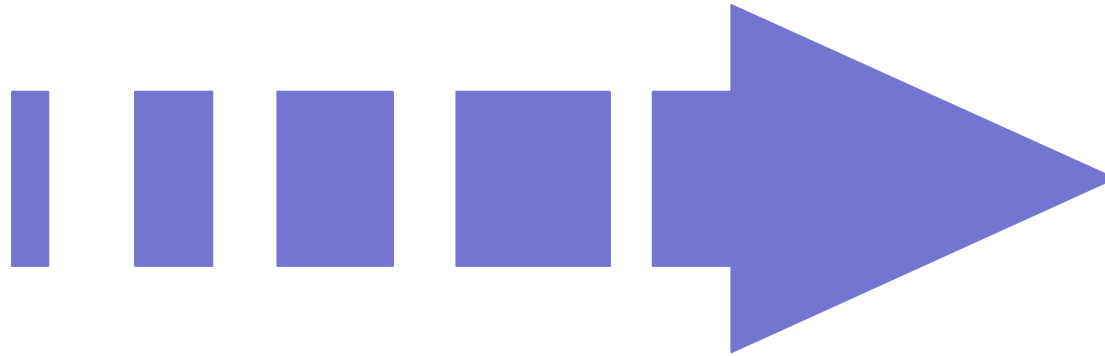
- $SI = KH / SKB$
- Şokta erken eleve olur
- Normal 0.5 - 0.7
- $SI > 0.9$ ise:
 - Normal KH& KB'da akut hipovolemi
 - Yaralanmanın ağırlığı & mortalite için bir marker
 - Bazal SKB'i yüksek hastalarda şokun atlanmasına sebep olur
- Kullanımı
 - Hastane öncesi → triaj
 - Masif transfüzyon riskini öngörmede?

İdrar Çıkışı



Yetişkin	0.5 ml / kg / hour
Çocuk	1.0 ml / kg / hour
Toddler	1.5 ml / kg / hour
Infant	2.0 ml / kg / hour

Hemorajik Şok



Lab Değerleri

Arteryal pH



Asidoz - Serum pH < 7.20

Ağır Fizyolojik Dengesizlikte Devamlı Marker

- Azalmış kardiyak kontraktilite
- Azalmış kardiyak output
- Vazodilatasyon ve azalmış KB
- Azalmış hepatik ve renal kan akımı

Laktat

- Oksijen açığının indirek ölçөгü
- Normal değeri = 1.0 mEq/L
- Değerler > 1.0 şokun büyüklüğünü gösterir
- Laktat Seviyeleri > 5 = ↑ mortalite
- 24 saat içinde laktat kleransı:
 - Sağ kalımı gösterir
- 12 saat içinde laktatın temizlenememesi:
 - Multisistem organ yetmezliğini

Baz Açığı (BA)

- Perfüzyon yetersizliğinin hassas göstergesi
- Normal aralık -3 to +3
- Kan gazı takibi
- BA'nın kabul edilmesi kan kaybı ile ilişkili
- Kötüleşen BA:
 - Devam eden kanama
 - Yetersiz volüm replasmanı

Baz Açığının Sınıflandırılması



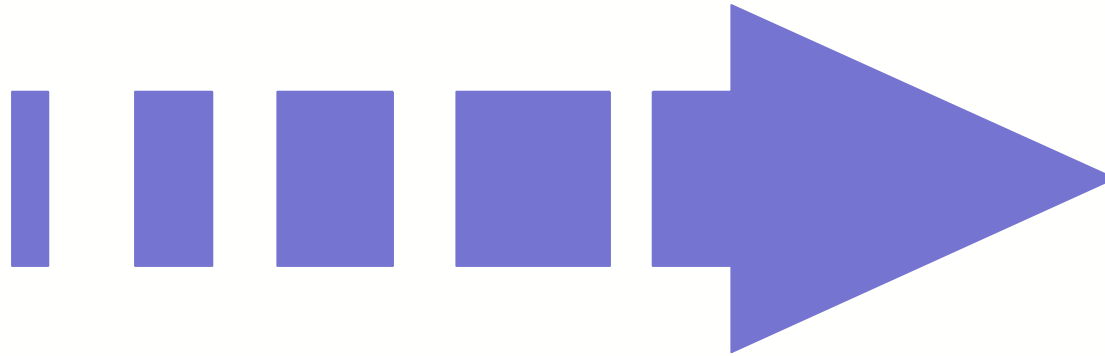
Kategori	Baz Açığı	Mortalite
Hafif	< 5	%11
Orta	6-9	%23
Ağır	10-15	%44
	16-20	%53
	>20	%70

International Normalized Ratio (INR)

- Pıhtılaşma testi (ekstrinsik yolak)
- Protrombin (PT) sonuçlarını tüm dünyada uluslararası kabul görmüş şekilde bildiren metod

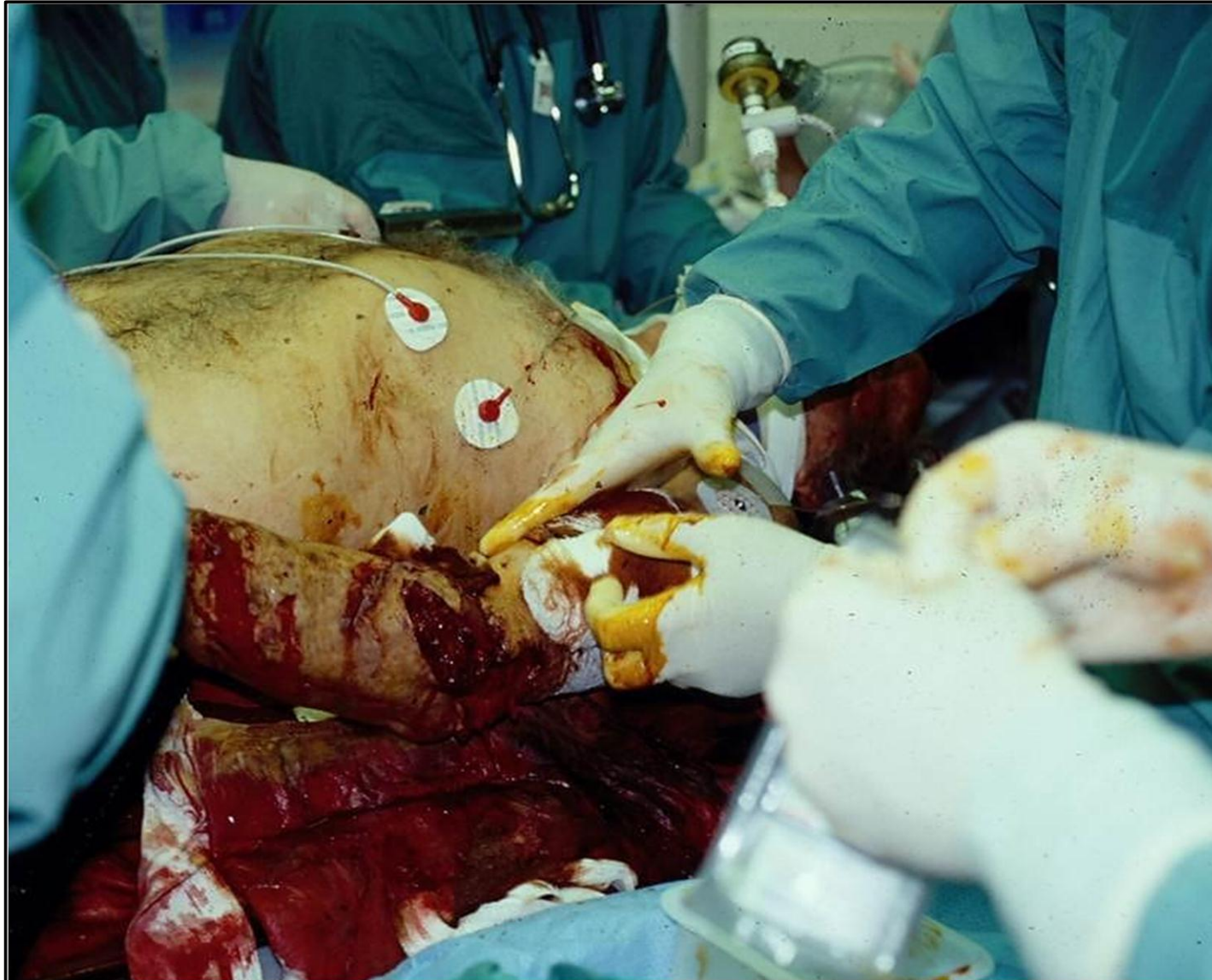
Popülasyon	Değer
Normal	0.8 - 1.2
Antikoagulan Kullanımı	2.0 - 3.0
Travma	> 1.5 = koagulopati

Hemorajik Şok



Tedavi

airway... breathing... circulation...



Kanamayı Durdurmada Mekanik Araçlar

Hemostatik Pansuman

- Araştırmalar hızla ilerlemekte
- Volkanik kaya, çamur, kabuklar
 - Etkiler:
 - Direk kompresyon
 - Pıhtılaşmayı aktive etmek
 - Adhezyon
 - Faydalar:
 - Uygulama hızı (yangın mahallinde)
 - Katlanabilirlik, Z biçiminde bükülebilme



İV Yoldan Kaçın

- Yaralı ekstremiteler
- Olası vasküler yaranın distali
- Diyaframın altında yaralanma varsa femoral yol

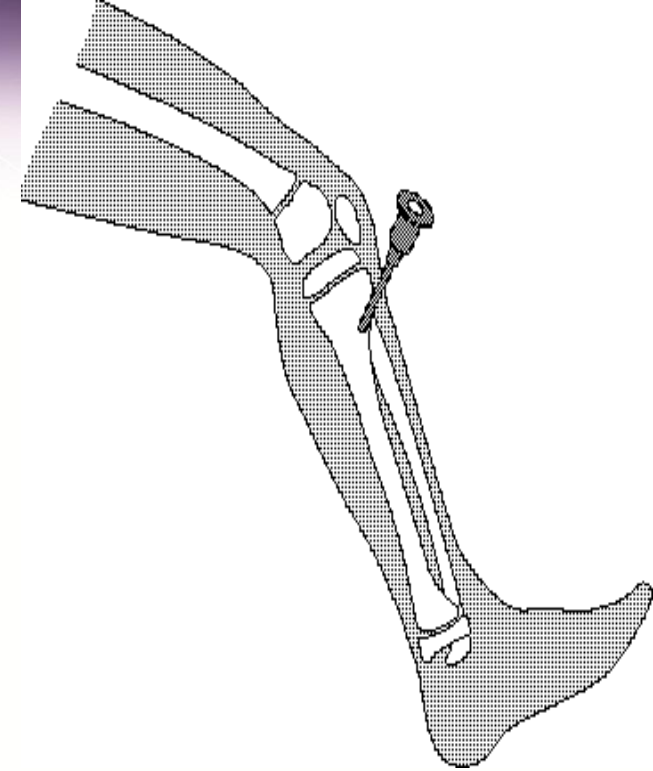


Şokta İV Yol

- **Femoral Ven**
 - 8.5/9.0 French introdüser
 - Yan bağlantılar kapatılır ↑ akış hızı
 - Entübasyon ve göğüs kafesi prosedürlerinin komşuluğunda uzakta
- **Subklavian/İnternal Jug.**
 - Daha yüksek risk (pnömotoraks)
 - Düşük başarı oranı
 - Göğüs kafesi yaralanmalarında, yaralanan tarafa aç.



Intraosseöz Araçlar



- Geçici yol
- Çocuk & yetişkinler
- 1 dakika içinde uygula
- Manuel veya matkapla
- Proks. tibia/humerus/sternum
- Kırık/ yaralanmış bölgelerde uygulama
- Sıvı/kan/ilaçlar için iyi
- Basınç torbası ile 125 mL/dk'ya kadar akım hızı
- Risk: ekstremitas ekstremitas → kompartman sendromu

Sıvı Resüsitasyonu



SIVI YÖNETİMİ DENGESİ

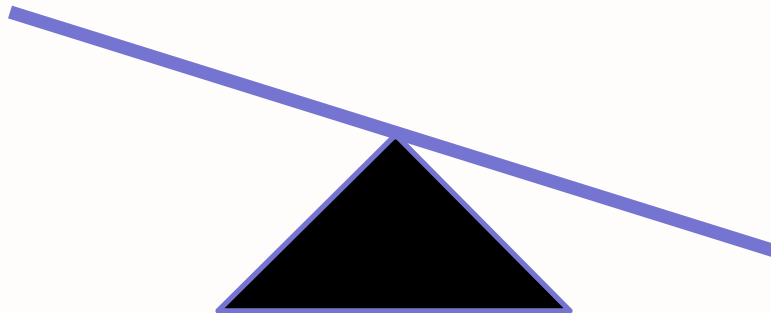


- **Çok az...**

- Süren şok
- Devam eden asidoz
- Koagulopati
- Myokardiyal disfonksiyon
- Renal yetmezlik
- Ölüm

- **Çok fazla...**

- Kanamada artış
- Pıhtı oluşumunun engellenmesi
- Koagülasyon faktörlerinin dilüsyonu
- Kompartman sendromları
- Transfüzyon endişeleri
 - Enflamasyon
 - İmmünosüpresyon
 - Transfüzyona Bağlı Akut Akciğer Hasarı (TRALI)



NS vs. LR



Normal Salin

- Na, Cl
- Dezavantaj:
 - Hiperkloremik asidoz



Laktatlı Ringer

- Na, Cl, K, Ca, Laktat
- Dezavantaj:
 - Immün modülasyon



Kristaloidler (Izotonik Solüsyonlar)

Dengeli elektrolit solüsyonları, ECF ile benzer

Kompartmanlar arasında hızla eşitçe yayılır

**17 dakika içinde sadece %25'i
intravasküler boşlukta kalır!**



*Oksijen
taşıımıyorsa
veya
pıhtılaşıımıyorsa!*

*Bana onu
verme!*

Kan Administrasyonu



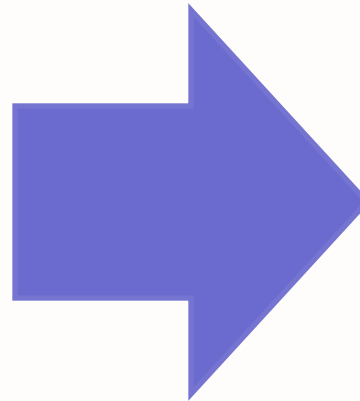
Geleneksel Yönetim		Yeni Kabul Gören Yönetim	
Sıvı	Kan	Sıvı	Kan
2 Litre ver ↓ → Devam et IV yolu geniş açık tutacak kadar	PRBC 5-10 u ↓ Lab sonuçları bekle ↓ Plazma ↓ Platelet	Minimuma indir Erişkinde 1L <40 kg çocukta 20ml/kg kristalloid aşmamak	1:1 or 1:2 (Plazma: RBC) Protokolize ↓ Masif Transfüzyon Protokolü

Masif Transfüzyon Tanımı



Eski Tanım

10 ünite
PRBC
24 saat
içinde



Yeni Tanım

1 saat
içinde >4
ünite
yada 24
saatte
>10 ünite

Hemorajide Kan Progresyonu



Hemen

Acil
Kroslanmamış

O+ Erkekler
O- Kadınlar/
Çocuklar

10 dakika

Tip Spesifik

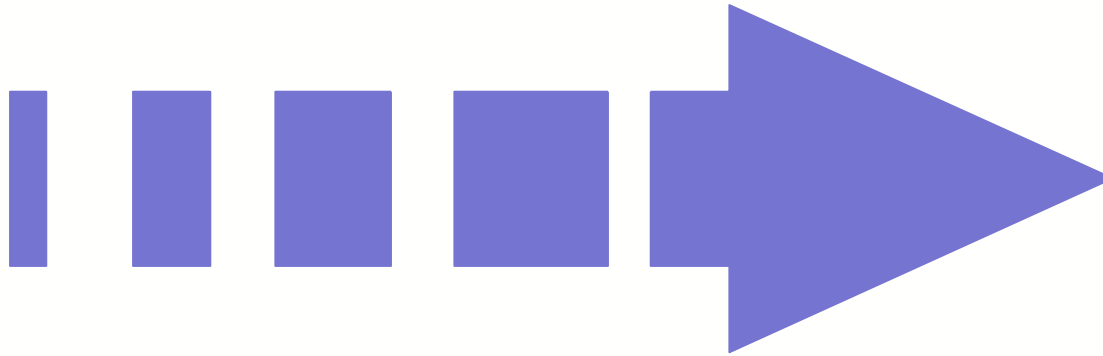
ABO & Rh
Uyumlu

50 dakika

Kroslanmış

ABO & Rh Tip
Antikorlar

Hemorajik Şok



İlaçlar: Bir rolü var mı?

Recombinant Factor VIIa

NovoSeven



- İnatçı kanamalı travma
- Ekstrinsik yolağı aktive eder
- Travmada *off label* kullanım
- Travmada Araştırma Sonuçları:
 - Sayısız anektodal bildiriler
 - 1 RCT yayınlanmış travma:
 - ↓ kan kullanımı
 - ↓ MSOF ↓ ARDS
 - Mortalitede ↓ göstermiş
 - Trombotik olaylarda ↑ yok

Kullanımdan önce düzelt:

- Hipofibrinojenemi:
 - Kriopresipitat ver
- Trombositopeni
 - Platelet ver
- Hipotermi
 - Vucut ısını düzelt.
- Asidoz
 - Bikarbonat tedavisi düşün

Factor VIIa

- Masif Transfüzyon Protokolüne Dahil Et:
 - Çok geç ya da çok erken kullanma
 - 8 - 20 PRBVC aralığında kullan
 - Önerilen doz: 100 mcg/kg
 - Pahalı:
 - $100\text{mcg} \times 70\text{kg} = 7,000\text{mcg} = 7,700\$$
 - Gerekli durumlarda 1-2 saatlik aralar ile tekrar ver

Traneksamik asit (TXA)

- AA Lizin türevi- fibrinolizi inhibe eder
- Ucuz (\$80/dose) ve güvenliliği kanıtlanmış
- **Cochrane review (2007)** 53 RCT's Cardiac/Ortho
 - Sig reduction in bleeding without thrombotic complications
- **CRASH2 trial (2010)** Prospective RCT, > 20,000 pts
 - Stat sig 1.5% reduction in mortality (overall)
 - Subgroup analysis (Severe bleeding & early admin)
 - Reduced bleeding by 30% **IF** given within 1 hour
- **MATTERs trial (2011)** Camp Bastion in Afghanistan
 - Marked improvement in survival in most severely injured compared to those who did not receive it
- Savaş alanında askerlerin otoenjektörler taşınması

Traneksamik Asit (TXA) Örnek Protokoller



Askeri Protokol

- Yaralanmanın ilk 1-3 saatinde ver.
- 1 ünite kan
- 1 Gm TXA bolus
- 1 Gm TXA infüzyon 8 saate gidecek

Oregon Health & Science University Protokolü

- Masif trasfüzyon protokolü
- Hasta 2 saat içinde >4 ünite aldı
- 1 GmTXA bolus
- 1 Gm TXA infüzyon 8 saate gidecek

Major Bleeding Risk During Anticoagulation with Warfarin, Dabigatran, Apixaban, or Rivaroxaban in Patients with Nonvalvular Atrial Fibrillation

Gboyega Adebeyeje, MD, MS; Gosia Sylwestrzak, MA; John J. Barron, PharmD; Jeff White, PharmD, MS; Alan Rosenberg, MD; Jacob Abarca, PharmD, MS; Geoffrey Crawford, MD, MS; and Rita Redberg, MD, MSc

ABSTRACT

BACKGROUND: The use of non-vitamin K oral anticoagulants (NOACs) has increased steadily following marketing approval; however, their relative safety in nonvalvular atrial fibrillation (NVAf) patients in real-world clinical practice remains unclear.

OBJECTIVE: To compare the risk of major bleeding during anticoagulation therapy between warfarin and NOACs.

METHODS: This retrospective cohort study analyzed administrative claims data on new NVAf users of warfarin, dabigatran, apixaban, or rivaroxaban in routine clinical care from November 2010 to February 2015 in a commercially insured population in the United States. The primary outcome was time to first major bleeding event requiring hospitalization. Patients were followed until discontinuation or switch of anticoagulants, health plan disenrollment, death, or end of study. All patient characteristics were balanced after propensity score inverse probability of treatment (IPT) weighting. Event rates by type of anticoagulant exposure were compared using IPT-weighted Cox proportional hazards models.

What is already known about this subject

- Clinical trial results have demonstrated the efficacy and safety of non-vitamin K oral anticoagulants (NOACs) relative to warfarin for stroke prevention in nonvalvular atrial fibrillation (NVAf) patients.
- Concerns persist regarding the real-world safety of NOACs.

What this study adds

- This study examined major bleeding risk among NVAf patients using NOACs during anticoagulation therapy.
- Relative to warfarin, dabigatran and apixaban were associated with a 33% lower major bleeding risk, while dabigatran and apixaban were associated with a 48% lower risk of major bleeding compared with rivaroxaban.
- Apixaban was associated with a lower risk of major gastrointestinal bleeding than dabigatran.

Efficacy and safety of prothrombin complex concentrate in patients treated with rivaroxaban or apixaban compared to warfarin presenting with major bleeding

Deepa R. J. Arachchillage,^{1,2,3} 
Sharon Alavian,¹ Jessica Griffin,¹
Kamala Gurung,¹ Richard Szydo,¹
Nilanthi Karawitige¹ and Mike Laffan^{1,2}
¹Department of Haematology, Imperial College Healthcare NHS Trust Imperial College London,
²Centre for Haematology, Imperial College London, and ³Department of Haematology, Royal Brompton Hospital, London, UK

Received 12 September 2018; accepted for publication 5 November 2018

Correspondence: Dr. Deepa R. J. Arachchillage, Department of Haematology, Imperial College Healthcare NHS Trust and Imperial College London, Hammersmith Hospital, 4th Floor, Commonwealth Building, Du Cane Road, London W12 0NN, UK.

E-mail: d.arachchillage@imperial.ac.uk

Summary

This retrospective study investigated the efficacy and safety of prothrombin complex concentrates (PCCs) for management of major bleeding events (MBE) in 344 patients receiving the anticoagulants rivaroxaban, apixaban or warfarin during the period January 2016 to April 2018. Median (range) PCC dose was 2000 units (1000–4500). Intracranial haemorrhage (ICH) was the most common indication (137/344, 39.8%) for PCC use followed by gastrointestinal bleeding (93/344, 27%). ICH patients more frequently received rivaroxaban (62.5%) or apixaban (52.5%) compared to warfarin (34.5%), $P = 0.002$; and visceral bleeding patients received warfarin more frequently (24.2%) than rivaroxaban (5%) or apixaban (10%), $P = 0.003$. Median rivaroxaban and apixaban levels were 230 ng/ml (47–759) and 159 ng/ml (45–255). Median International Normalised Ratio pre- and post-PCC in patients on warfarin were 3.4 (1.9–15.4) and 1.2 (1.0–1.9). Blood products use was the same between groups. Thirty-day mortality and re-bleeding rates in patients with ICH were 35% ($P = 0.50$) and 18% ($P = 0.90$) with no differences between the groups. Thrombosis occurred in 4.1% patients within 30 days with no difference between groups. Two of 91 (2.2%) patients with ICH only (both on warfarin) had ischaemic strokes within 30 days post-PCC. In conclusion, there was no difference in the safety (thrombosis) or efficacy (30-day mortality, re-bleeding) in use of PCC for MBE in patients on warfarin, rivaroxaban or apixaban.

Keywords: prothrombin complex concentrate, warfarin, rivaroxaban, apixaban, major bleeding.

Management of rivaroxaban- or apixaban-associated major bleeding with prothrombin complex concentrates: a cohort study

Ammar Majeed,^{1,4} Anna Ågren,^{1,3} Margareta Holmström,^{1,3} Maria Bruzelius,^{1,3} Roza Chairati,^{3,5,6} Jacob Odeberg,^{1,3,7} Eva-Lotta Hempel,^{1,3} Maria Magnusson,^{6,8,9} Tony Frisk,¹⁰ and Sam Schulman^{11,12}

¹Department of Medicine and ²Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; ³Coagulation Unit, Hematology Center, Karolinska University Hospital, Stockholm, Sweden; ⁴Central Clinical School, Monash University and Alfred Hospital, Melbourne, Australia; ⁵Department of Molecular Medicine and Surgery and ⁶Clinical Chemistry and Blood Coagulation Research, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; ⁷Science of Life Laboratory, School of Biotechnology, Royal Institute of Technology, Stockholm, Sweden; ⁸Division of Pediatrics, Department of Clinical Science Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; ⁹Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden; ¹⁰Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; ¹¹Department of Medicine, McMaster University, Hamilton, ON, Canada; and ¹²Thrombosis and Atherosclerosis Research Institute, Hamilton, ON, Canada

Key Points

- PCCs for the management of major bleeding in patients on rivaroxaban or apixaban is an effective strategy in most cases.
- The thromboembolic complication rate in this setting is low and comparable with that of anticoagulation discontinuation without reversal.

There is uncertainty regarding the effectiveness and occurrence of thromboembolic events in patients treated with prothrombin complex concentrates (PCCs) for the management of major bleeding events (MBEs) on rivaroxaban or apixaban. We investigated the effectiveness of PCCs given for the management of MBEs in patients on rivaroxaban or apixaban. Between 1 January 2014 and 1 October 2016, we prospectively included patients on rivaroxaban or apixaban treated with PCCs for the management of MBEs. The effectiveness of PCCs was assessed by using the International Society of Thrombosis and Hemostasis Scientific and Standardization Subcommittee criteria for the assessment of the effectiveness of major bleeding management. The safety outcomes were thromboembolic events and all-cause mortality within 30 days after treatment with PCCs. A total of 84 patients received PCCs for the reversal of rivaroxaban or apixaban due to a MBE. PCCs were given at a median (interquartile range) dose of 2000 IU (1500–2000 IU). Intracranial hemorrhage (ICH) was the most common site of bleeding requiring reversal ($n = 59$; 70.2%), followed by gastrointestinal bleeding in 13 (15.5%) patients. Management with PCCs was assessed as effective in 58 (69.1%) patients and ineffective in 26 (30.9%) patients. Most patients with ineffective hemostasis with

PCCs had ICH ($n = 16$; 61.5%). Two patients developed an ischemic stroke, occurring 5 and 10 days after treatment with PCC. Twenty-seven (32%) patients died within 30 days after a MBE. The administration of PCCs for the management of MBEs associated with rivaroxaban or apixaban is effective in most cases and is associated with a low risk of thromboembolism. Our findings are limited by the absence of a control group in the study. (*Blood*. 2017;130(15):1706–1712)

Review Article

Novel reversal agents and laboratory evaluation for direct-acting oral anticoagulants (DOAC): An update

Shagun B Shah, Akhilesh Pahade, Rajiv Chawla

Department of Anaesthesia, Rajiv Gandhi Cancer Institute and Research Centre, Sector-5, Rohini, New Delhi, India

ABSTRACT

Novel oral anticoagulants (NOACs) are no longer “novel” but their reversal agents definitely are. Although NOACs enjoy high clinical efficacy, monitoring and reversal of their effect is a challenge which this review attempts to surmount. Ideally, for NOAC activity measurement, specific anti-Factor IIa levels and anti-Factor Xa levels should be monitored (chromogenic assays), but such tests are not readily available. Modifications of the existing coagulation tests catering to this unmet need for quantification of DOAC activity have been reviewed. The available United States Food and Drug Administration (FDA) approved reversal agents, idarucizumab for dabigatrin and andexanet alfa for anti-Xa direct acting oral anticoagulants have given promising results but are prohibitively priced. Medline, Embase, and Scopus databases were thoroughly searched for clinical trials on laboratory investigations and specific as well as non-specific reversal-agents for DOACs.

Key words: Andexanet alfa, idarucizumab, oral anticoagulants, PRT064445, reversal, treatment outcome

How can we reverse bleeding in patients on direct oral anticoagulants?

Mark Crowther¹, Adam Cuker²

¹McMaster University, Hamilton, Ontario, Canada

²University of Pennsylvania, Philadelphia, PA, United States

Abstract

The direct oral anticoagulants (DOACs), or non-vitamin K antagonist oral anticoagulants (NOACs), including dabigatran, which inhibits thrombin, as well as rivaroxaban, apixaban, edoxaban, and betrixaban, which inhibit coagulation factor Xa, are associated with similar or lower risk of bleeding compared with warfarin. The need for reversal of their anticoagulant effect may occur in patients with life-threatening bleeding or those requiring urgent surgery. Currently, the only specific reversal agent for dabigatran, idarucizumab, is widely available, while andexanet alfa, which reverses factor Xa inhibitors, was approved in the United States in May 2018. Ciraparantag, which has been designed to reverse all DOACs and other anticoagulants, is being investigated in clinical trials. In the absence of licensed reversal agents for the oral factor Xa inhibitors, prothrombin complex concentrates are suggested in patients with life-threatening bleeding. Vitamin K and fresh frozen plasma should not be used to reverse DOACs. This review presents the current evidence regarding bleeding risk on DOACs and the reversal strategies to provide guidance on the management of patients treated with DOACs, who experience serious bleeding.

Key words: bleeding, non-vitamin K antagonist oral anticoagulants, reversal agents

Kardiol Pol 2019; 77, 1: 3–11

SUMMARY

Reversal strategies in patients receiving DOACs depend on the anticoagulant involved, the location and severity of the bleeding, and/or the urgency of the invasive procedure. The available specific reversal agent for dabigatran, idarucizumab, is used infrequently for the reversal of DOACs, without increasing the underlying risk of thrombosis. Andexanet alfa to reverse FXa inhibitors has been approved by the FDA recently. Evidence supporting non-specific reversal therapies including PCC, aPCC, or recombinant factor VIIa is still limited in terms of clinical outcome data. Administration of PCC or aPCC may be considered in addition to supportive measures for patients with severe or life-threatening bleeding.

Most importantly, the best way to treat a bleed related to a DOAC is to prevent it by using the right drug at the right dose in the right patient and by withdrawing anticoagulation in patients without an indication for such therapy.

This review was based on a lecture at the 4th McMaster International Review Course in Internal Medicine in Krakow, Poland, on 12th May 2018.

Address for correspondence:

Dr. Shagun B Shah,
H. No: 174-175, Ground
Floor, Pocket -17, Sector-24,
Rohini, Delhi -110 085, India.
E-mail: drshagun_2010@
rediffmail.com

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.ija_734_18

Quick response code



Özet

- Koagülopatiyi erken sapta
- Travmada sıvı tedavi ilk seçeneği SF/RL
- Masif Transfüzyon Protokolünü uygula
- Küçük volüm resusitasyon teknikleri
- Traneksamik asit and Faktör VIIa'yı düşün
- Asidoz ve hipotermiyi durdur
- KANAMAYI DURDUR!