

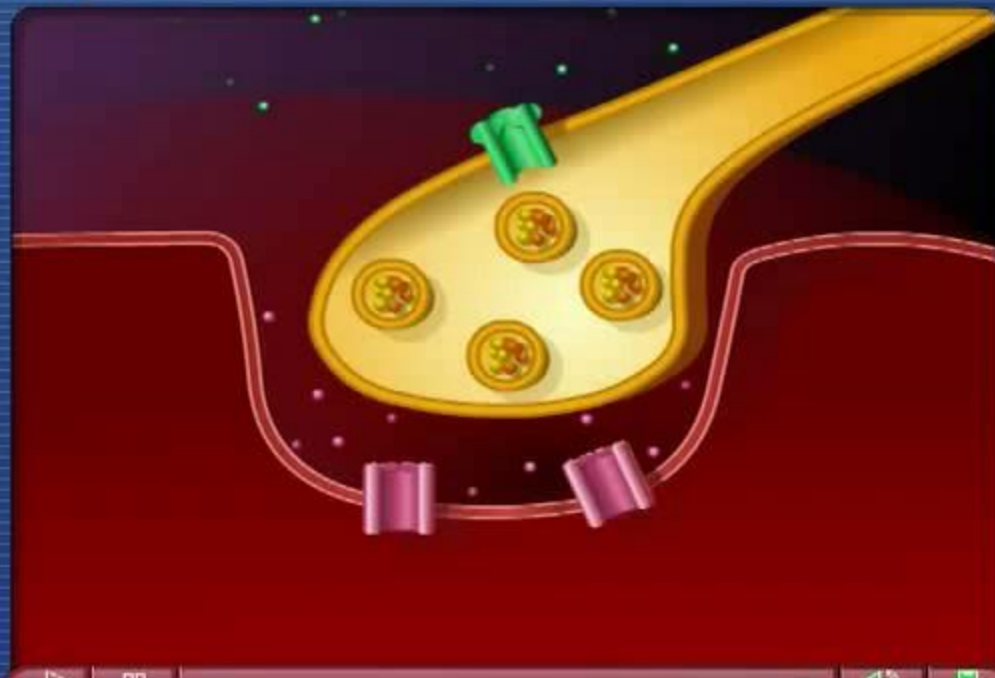
NOROMUSKÜLER

BLOKÖRLER

Nöromusküler blokörler miyonöral kavşakta sinir impulslarının iletimini bloke ederek iskelet kaslarını paralize ederler.



Function of the Neuromuscular Junction



Play



Pause



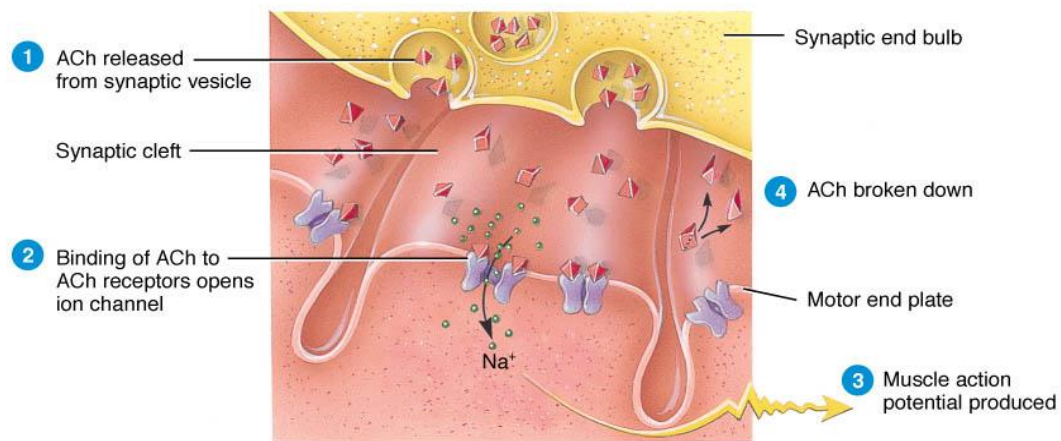
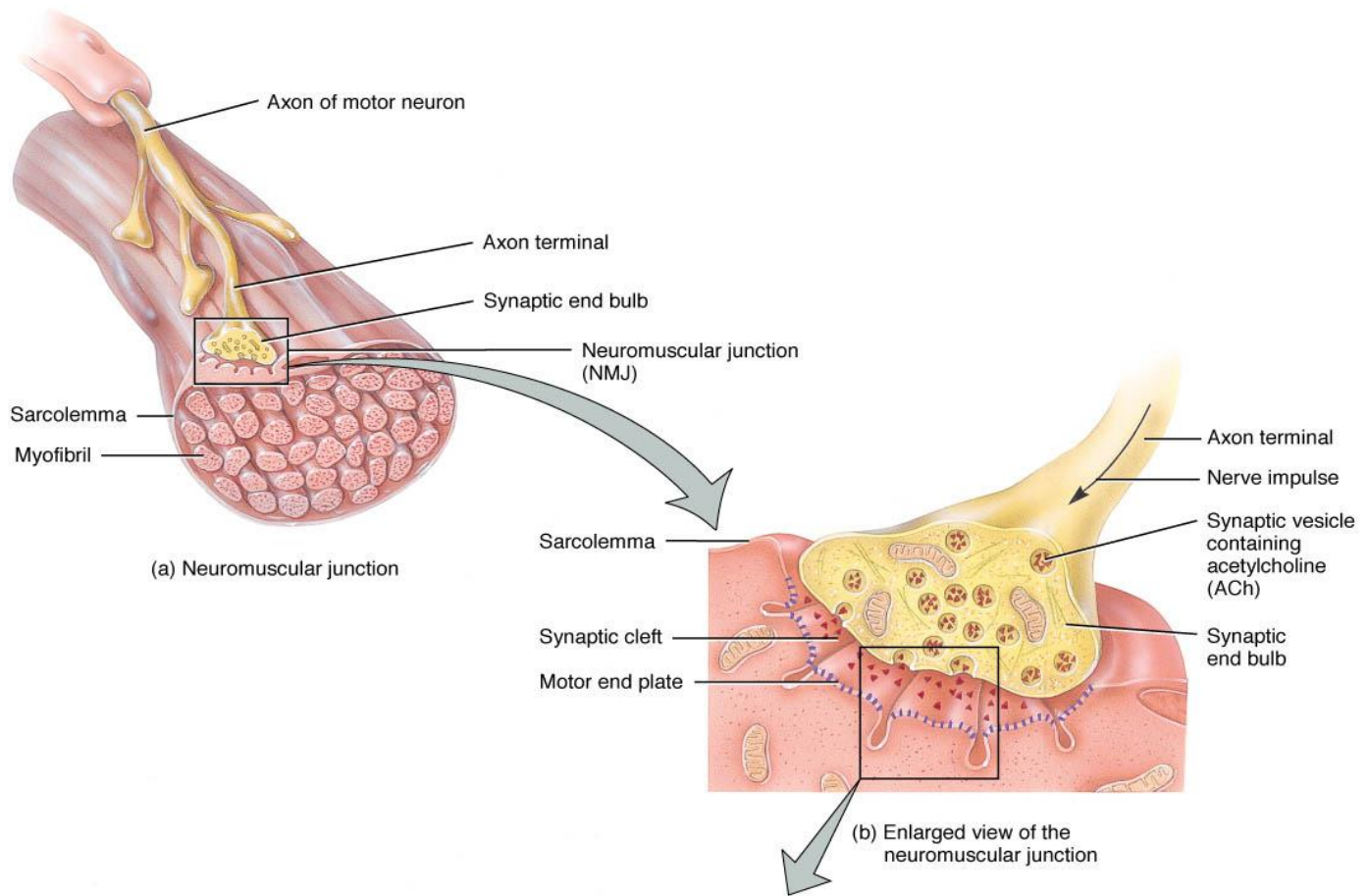
Audio



Text

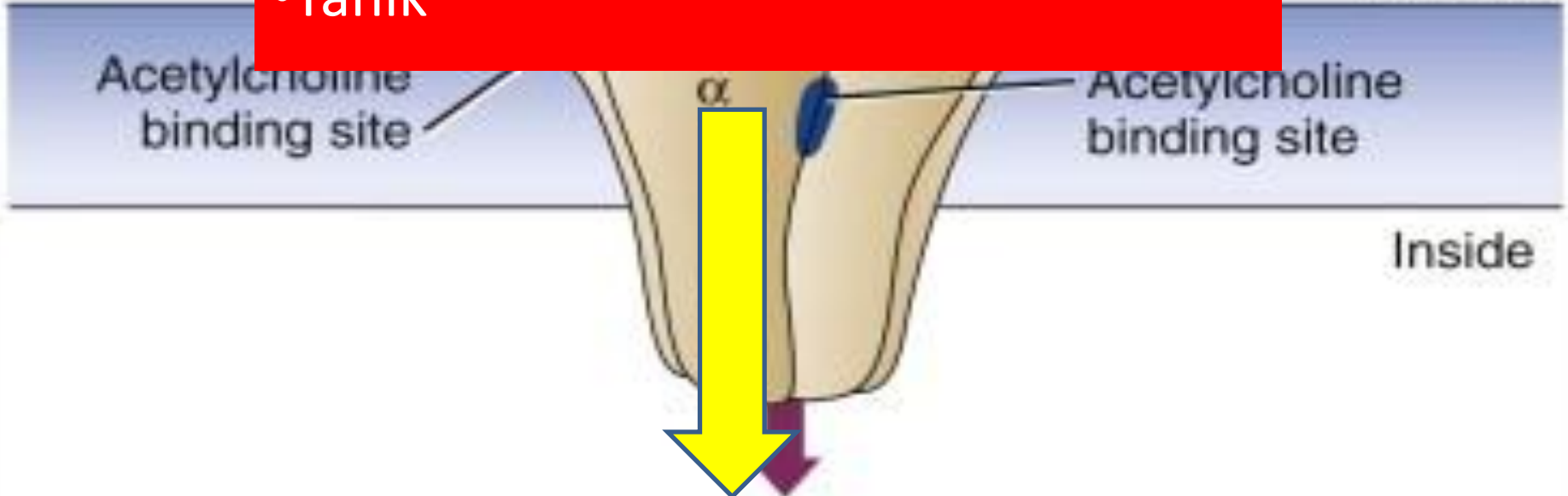
An action potential arrives at the presynaptic terminal causing voltage-gated calcium ion channels to open, increasing the calcium ion permeability of the presynaptic terminal cell membrane.

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(c) Binding of acetylcholine to ACh receptors in the motor end plate

- Strok, guillian barre gibi alt ve üst motor noron hastalıkları
- Sepsis
- Yanık



İMMATÜR NİKOTİNİK
ASETİLKOLİN
RESEPTÖRÜ

- İnfüzörde süksinil koline daha duyarlı hale gelir.

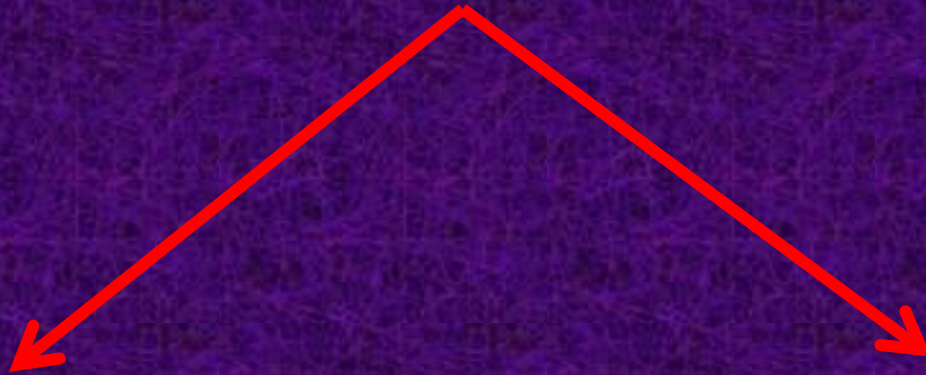
- Yaşlılarda süksinil koline dirençli hale gelirler.

- Süksinilkolinin hiperkalemi gelişme riski artar.

- Matür immatür reseptörler arasında herhangi bir yerde bulunabilir.



Nöromusküler Blokörler



Depolarizan nöromusküler

blokörler

SÜKSİNİL KOLİN

Nondepolarizan

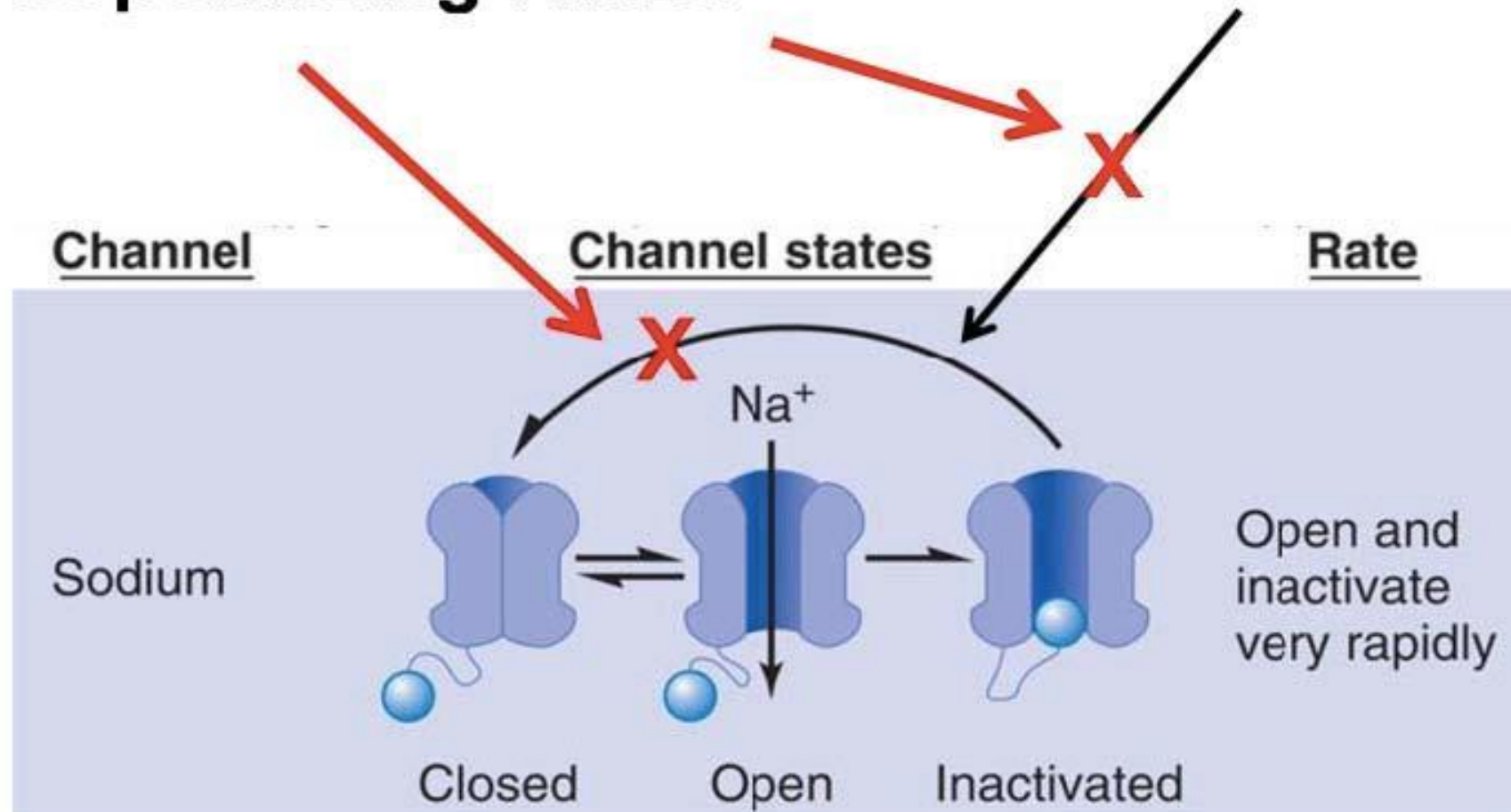
nöromusküler

blokörler

SÜKSİNİL KOLİN

Depolarizing NMBs

Repolarization



Yan etkileri:

- 💣 Sinüs bradikardisi, nodal ritim, ventriküler disritmiler
- 💣 Hiperkalemi
- 💣 Göz içi basınç artışı
- 💣 İntragastrik basınç artışı
- 💣 Kafa içi basınç artışı
- 💣 Masseter kas spazmı
- 💣 Malign hipertermi
- 💣 Rabdomiyoliz

Kontrendikasyonları:

- ☠ Malign hipertermi hikayesi
- ☠ Nöromusküler hastalıklar
- ☠ Müsküler distrofi
- ☠ 72 saatten önce strok
- ☠ Rabdomiyoliz
- ☠ 72 saatten eski yanık
- ☠ EKG'de değişikliğe neden olmuş hiperkalemi



Nondepolarizan Nöromusküler Blokerler:

-  Yarışmalı antagonisttirler.
-  Postsinaptik Ach reseptörünün 2alfa alt birimine bağlanırlar ve iyon kanallarının açılmasını engellerler. Böylece depolarizasyon önlenir.
-  Sinaptik aralıkta ilaç konsantrasyonu arttıkça daha fazla reseptör bağlanarak blok derinleşir.

Nondepolarizan Nöromusküler Blokerler:

A- Steroid Yapılılar

- Pankuronyum (pavulon)
- Vekuronyum (norcuron)
- Rokuronyum (esmeron)
- Pipekuronyum (arduan)

Nondepolarizan Nöromusküler Bloklerler:

B- Benzilizokinoliyum Yapılılar:

- Atrakuryum (Tracrium)
- Sisattrakuryum (Nimbex)
- Mivakuryum (Mivacron)
- Doksakuryum (Nuromax)

Benzylisoquinolium Drugs

Variable	D-Tubocurarine (Curare)	Cisatracurium (Nimbex)	Atracurium (Tracrium)	Doxacurium (Nuromax)	Mivacurium (Mivacron)
Introduced (yr)	1942	1995	1983	1991	1992
ED ₅₀ ^b dose (mg/kg)	0.51	0.05	0.25	0.025–0.03	0.075
Initial dose (mg/kg)	0.1–0.2	0.1–0.2	0.4–0.5	0.025–0.05	0.15–0.25
Duration (min)	80	45–60	25–35	120–150	10–20
Infusion described	...	Yes	Yes	Yes	Yes
Infusion dose (μg/kg/min)	...	2.5–3	4–12	0.3–0.5	9–10
Recovery (min)	80–180	80	40–60	120–180	10–20
% Renal excretion	40–45	Hofmann elimination	5–10 (uses Hofmann elimination)	70	Inactive metabolites
Renal failure	Increased duration	No change	No change	Increased duration	Increased duration
% Biliary excretion	10–40	Hofmann elimination	Minimal (uses Hofmann elimination)	Insufficient data	...
Hepatic failure	Minimal change to mild increased effect	Minimal to no change	Minimal to no change	...	Increased duration
Active metabolites	No	No	No, but can accumulate laudanosine	...	No
Histamine release	Marked	No	Minimal but dose dependent	No	Minimal but dose dependent
hypotension					
Vagal block tachycardia	Minimal	No	No	No	No
Ganglionic blockade	Marked	No	Minimal to none	No	No
hypotension					
Prolonged ICU block	...	Rare	Rare	Insufficient data	Insufficient data

Yan Etkileri:

💣 Otonomik yan etkiler

💣 Histamin salınımına bağlı taşiflaksi,
bronkokonstrüksiyon

💣 Allerjik reaksiyonlar



Antagonizma:

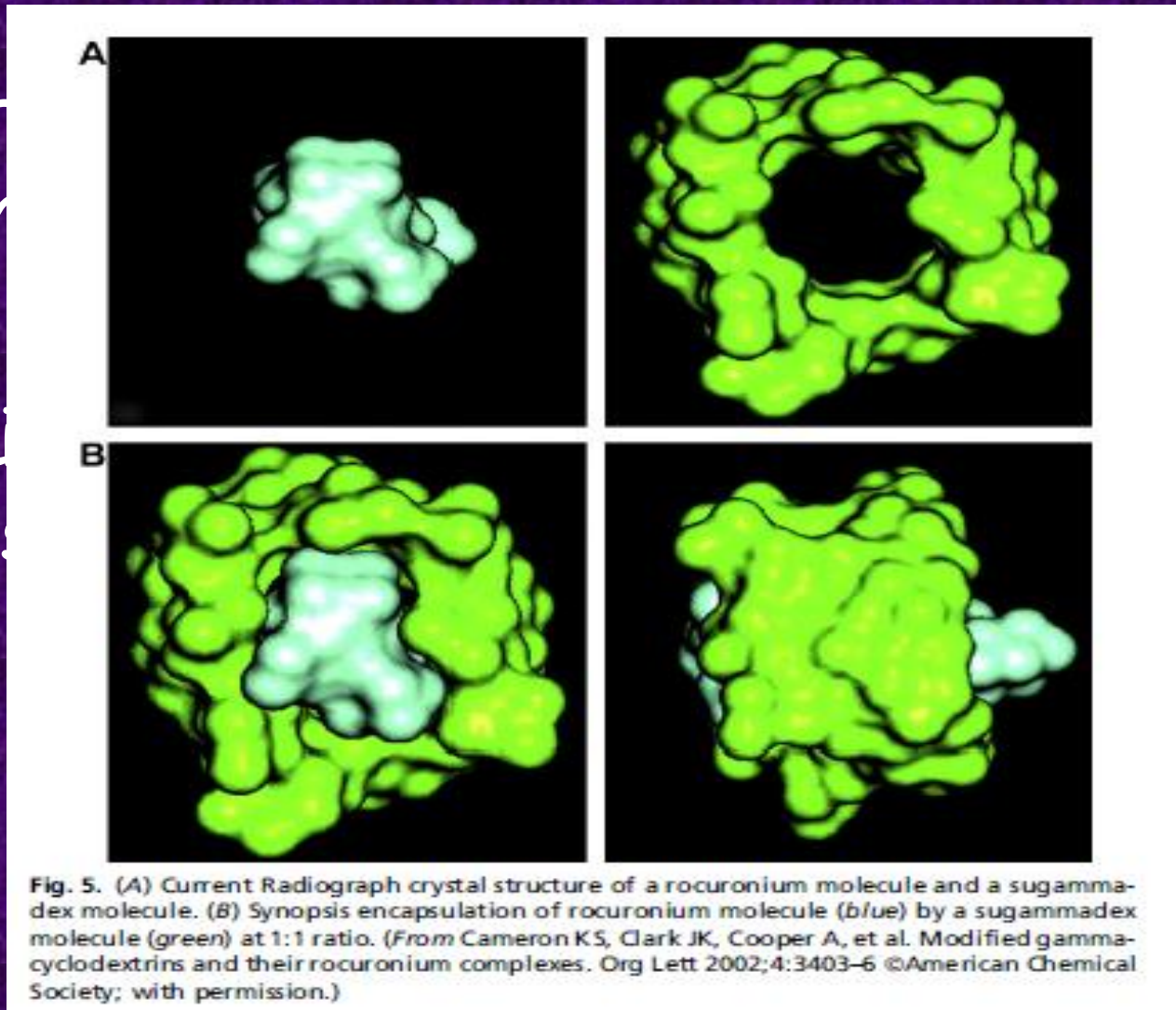
- Süksinilkolin → Nondepolarizan NMBA
- Nondepolarizan NMBA →
1-Antikolinesterazlar
2-Siklodekstrinler

Antikolinesterazlar:

- Neostigmin (atropin dozu neostigminin yarısı kadardır veya 0,035-0,07mg/kg.)
- Pridostigmin
- Edrofonyum

Sugammadex:

- St
- ink
- Gü
- ra



nyumu

ne



☛ Hastaya uygulanacak girişimsel işlemleri kolaylaştırma

☛ Mekanik ventilasyonu kolaylaştırma

☛ Kafa incisi

☛ Kardi

☛ Ter

epileptik
tedavisini kolay

us
talıkların

Hızlı Seri
Entübasyon

Trakeal entübasyonu kolaylaştırmak için indüskiyon ajanının ve NMBA'nın birlikte kullanılmasıdır. Acil entübasyon için tercih edilen bir yöntemdir.

Hızlı Seri Entübasyon

- ✓ İlk tercih eğer herhangi bir kontrendikasyon yoksa Süksinil kolin 1-1,5 mg/kg (Grade 2B)
- ✓ Eğer kontrendikasyon mevcutsa 1mg/kg rokuronyum veya vekuronyum. Beraberinde 16mg/kg IV sugammadeks

Neuromuscular blocking agents (NMBA) for rapid sequence intubation in adults, UpToDate

- Son yıllarda hızlı seri entübasyonda özellikle rokuronyum ve sugammadex kullanımı ile çalışmalar yapılmaktadır.
- 1.2mg/kg rokuronyum ve 3 dk sonra sugammadex uygulamasının 1 mg/kg süksinilkolin ile karşılaştırıldığında, düzelme zamanı süksinilkolinden daha kısa bulunmuştur.
- Bu nedenle entübe edilemez, ventile edilemez durumlarında süksinilkoline tercih edilebileceği bildirilmektedir.

Clinical paper

Use of rapid sequence intubation predicts improved survival among patients intubated after out-of-hospital cardiac arrest[☆]

Heemun Kwok^{a,b,*}, Matthew Prekker^{a,c}, Andreas Grabinsky^d, David Carlbom^{a,c}, Thomas D. Rea^{a,e}

^a Department of Medicine, University of Washington School of Medicine, Seattle, WA, United States

^b Division of Emergency Medicine, University of Washington School of Medicine, Seattle, WA, United States

^c Division of Pulmonary and Critical Care Medicine, University of Washington School of Medicine, Seattle, WA, United States

^d Department of Anesthesiology, University of Washington School of Medicine, Seattle, WA, United States

^e King County Emergency Medical Services Division, Seattle King County Department of Public Health, Seattle, WA, United States

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ABSTRACT

Objective: Some observational studies indicate that endotracheal intubation is associated with a worse outcome compared to bag-mask ventilation after out-of-hospital cardiac arrest in emergency medical services (EMS) systems without rapid sequence intubation (RSI). We evaluated the role of RSI in airway management following cardiac arrest.

Methods: We conducted a cohort study of all non-traumatic arrest patients treated by a metropolitan EMS system from 2007 to 2011. Advanced airway management information was obtained from a prospective airway registry and linked to a cardiac arrest registry. We used multivariate logistic regression to estimate the association between attempted intubation status and survival to hospital discharge.

Results: Of 3133 patients, 82% underwent attempted intubation without RSI, 15% underwent attempted RSI, and 3% experienced no intubation attempt. Survival to hospital discharge differed by attempted intubation status: 11% ($n = 291/2576$) for intubation without RSI, 48% ($n = 226/471$) for RSI, and 7.1% ($n = 61/86$) for "no intubation." Compared to the intubation without RSI group, the adjusted odds ratios of survival were 5.6 (95% CI 4.3, 7.2) for the RSI group and 15 (95% CI 9, 27) for the "no intubation" group.

Conclusion: In this population-based cohort of out-of-hospital cardiac arrest, RSI was used in 15% of patients and associated with a better prognosis than intubation attempted without paralytics. Because this subset with a favorable prognosis may not be readily intubated in systems without paralytics, these findings could help to explain the adverse relationship between intubation and survival observed in prior studies.



➔ Hastaya uygulanacak işlemleri kolaylaştırma

➔ M

➔ Ko

➔ Ko

➔ Te
sta
ola



nipotermi

n veya
ktivitesi
stırma

- SCCM 2002 guideline, NMBA'ları derin sedasyon alan, özellikle refraktör hipoksemisi olan efektif akciğer koruyucu ventilasyon sağlamada yetersiz kalındığı durumlarda kullanılmasını önermiştir.

ACC
siset

uat

Daha yüksek 90 günlük sürvi, daha
az ventilatörsüz gün, daha az
organ disfonksiyonsuz gün, azalmış
barotravma

RESEARCH

Open Access

Neuromuscular blocking agents in acute respiratory distress syndrome: a systematic review and meta-analysis of randomized controlled trials

Waleed Alhazzani^{1*}, Mohamed Alshahrani², Roman Jaeschke^{1,3}, Jean Marie Forel⁴, Laurent Papazian⁴, Jonathan Sevransky⁵ and Maureen O Meade^{1,3}

Abstract

Introduction: Randomized trials investigating neuromuscular blocking agents in adult acute respiratory distress syndrome (ARDS) have been inconclusive about effects on mortality, which is very high in this population. Uncertainty also exists about the associated risk of ICU-acquired weakness.

Methods: We conducted a systematic review and meta-analysis. We searched the Cochrane (Central) database, MEDLINE, EMBASE, ACP Journal Club, and clinical trial registries for randomized trials investigating survival effects of neuromuscular blocking agents in adults with ARDS. Two independent reviewers abstracted data and assessed methodologic quality. Primary study investigators provided additional unpublished data.

Results: Three trials (431 patients; 20 centers; all from the same research group in France) met inclusion criteria for this review. All trials assessed 48-hour infusions of cisatracurium besylate. Short-term infusion of cisatracurium besylate was associated with lower hospital mortality (RR, 0.72; 95% CI, 0.58 to 0.91; $P = 0.005$; $I^2 = 0$). This finding was robust on sensitivity analyses. Neuromuscular blockade was also associated with lower risk of barotrauma (RR, 0.43; 95% CI, 0.20 to 0.90; $P = 0.02$; $I^2 = 0$), but had no effect on the duration of mechanical ventilation among survivors (MD, 0.25 days; 95% CI, 5.48 to 5.99; $P = 0.93$; $I^2 = 49\%$), or the risk of ICU-acquired weakness (RR, 1.08; 95% CI, 0.83 to 1.41; $P = 0.57$; $I^2 = 0$). Primary studies lacked ~~protracted measurements of weakness~~.

Conclusions: Short-term infusion of cisatracurium besylate reduces hospital mortality and barotrauma and does not appear to increase ICU-acquired weakness for critically ill adults with ARDS.

Con NMBA

Anaphylaxis

Risk of insufficient
sedation and memorizing

↗ Lung atelectasis

↗ ICU-acquired
weakness



Corticosteroids
Hyperglycaemia



Pro NMBA

↘ ARDS
mortality

↗ Ventilator free days

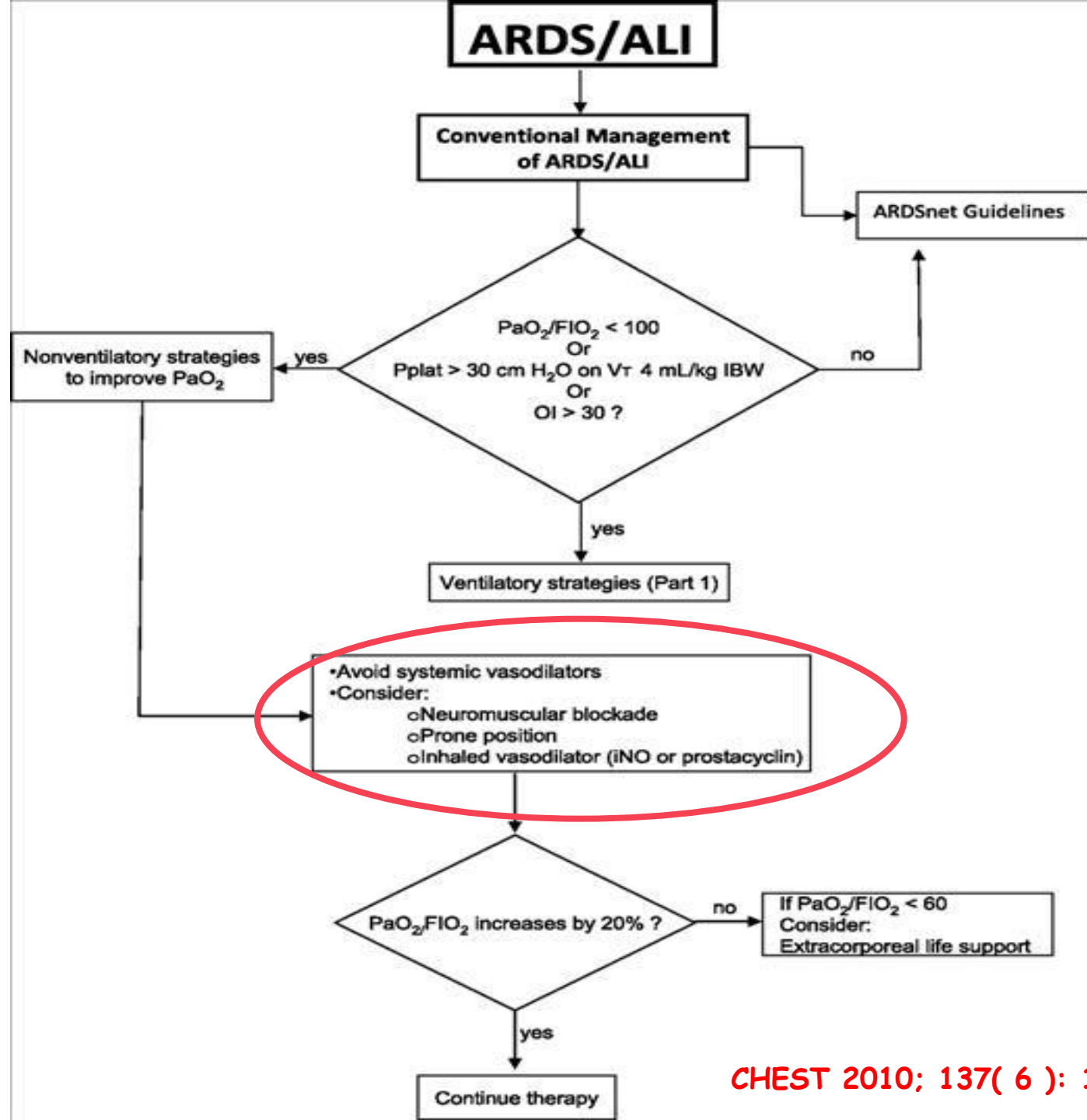
↗ ICU free days

↗ Oxygenation

↘ Barotrauma

↘ Ventilator-induced lung injuries??

Early use of NMBA in severe ARDS

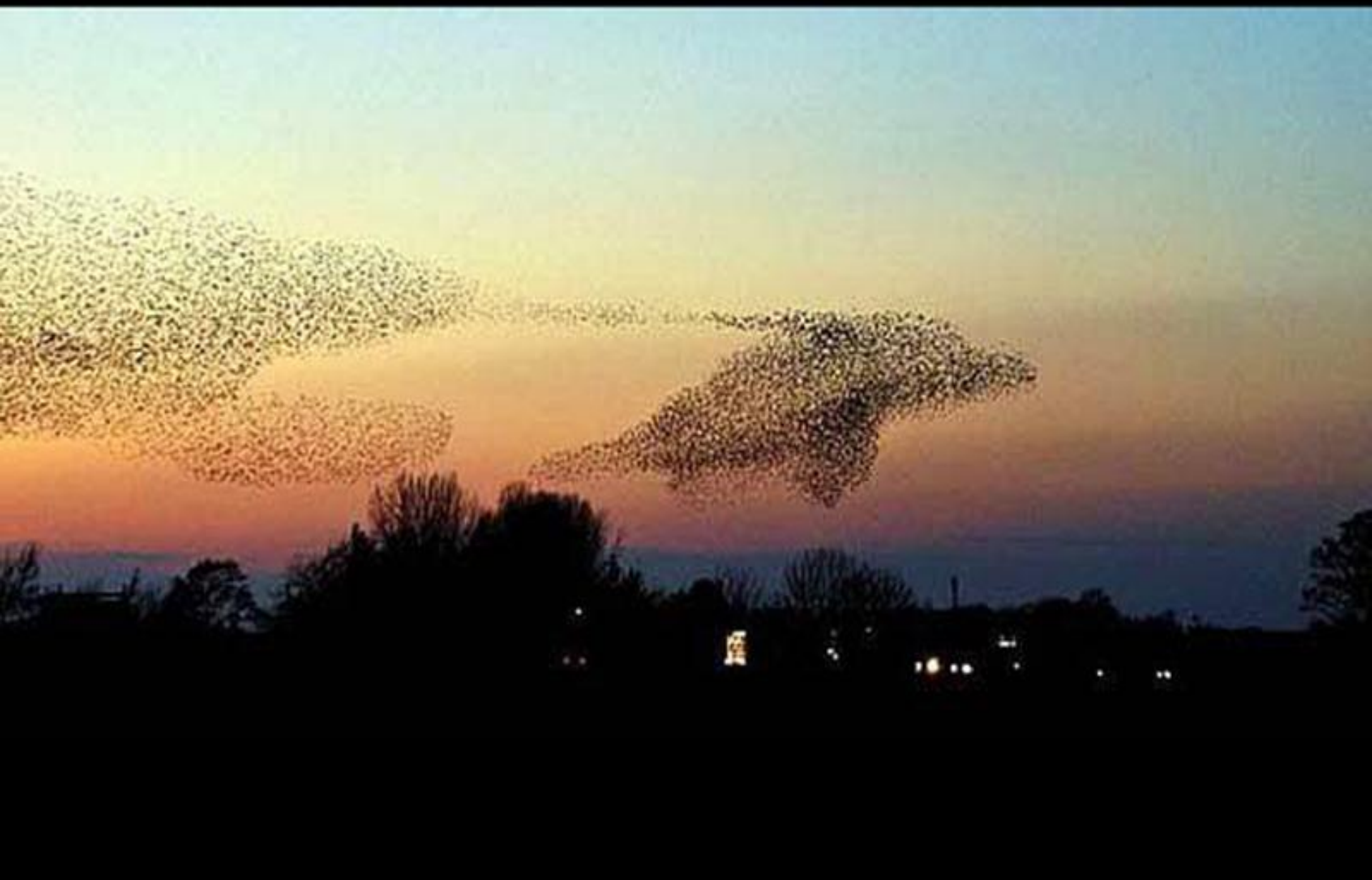


Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock

ARDS olmayan septik hastalarda mümkünse nöromusküler bloke edici ajanlardan (NMBAs) kaçınılmalıdır. NBMA'nın sürdürülmesi gerekirse, ya intermittant bolus ya da sürekli infüzyon yapılmalı ve blokaj derinliği monitorize edilmelidir. (grade 1C)

$\text{PaO}_2/\text{FiO}_2 < 150$ mmHg ve erken sepsisin indüklediği ARDS hastalarında kısa süreli (3 saat) NBMA kullanılmalıdır. (Grade 2C)

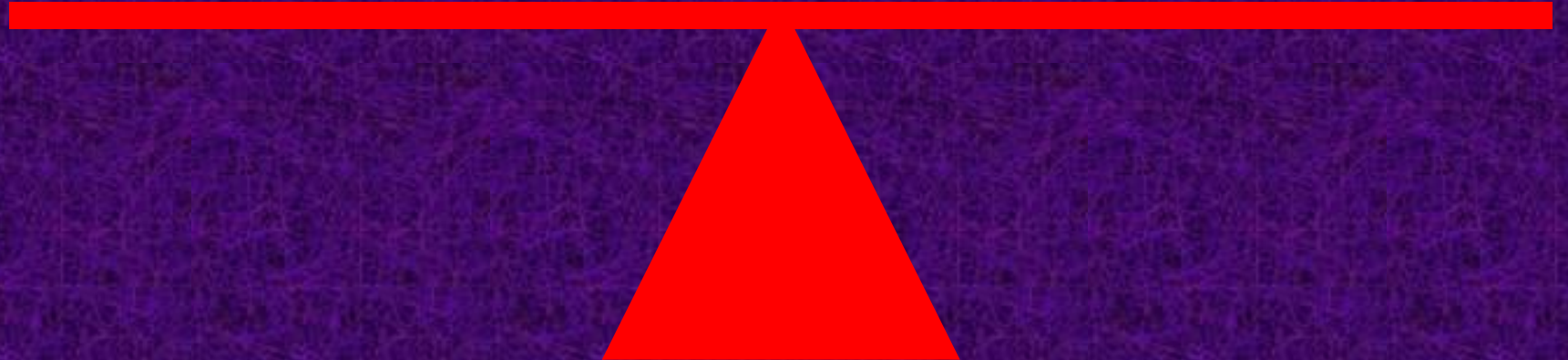
Derek C. Angus, MD, ¹and Maria R. Pinsky, MD, PhD¹⁸;
Gordon D. Rubenfeld, MD¹⁹; Steven M. Opresko, MB BS, PhD²⁰; and J. Beale, MB BS²¹;
Jean-Louis Vincent, MD, PhD²²; Rui M. Moreno, MD, PhD²³; and the Surviving Sepsis Campaign
Guidelines Committee including the Pediatric Subgroup*



- ☛ Hastaya uygulanacak işlemleri kolaylaştırma
- ☛ Mekanik ventilasyonu kolaylaştırma
- ☛ Kafa içi basınç artışı
- ☛ Kardiyak arrest sonrası terapötik hipotermi
- ☛ Tetanoz, noroleptik malign sendrom veya status epileptikus gibi artmış kas aktivitesi olan hastalıkların tedavisini kolaylaştırma

ICU'da kalma süresinde artma
Pnomonide artış
Bitkisel hayat veya ağır
özürlülük durumunda artış
Norolojik muayenede
maskelenme

Öksürük nöbet gibi ICP'yi artıran
durumları kontrol altına alır.
Ventilatör ile senkronizasyonu
sağlar.
Daha düşük mortalite oranı



- Nondepolarizan NMBA sadece geleneksel tedaviye cevap vermeyen refrakter intrakranial hipertansiyon için kullanılır.



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Trauma

Clinical practice guidelines in severe traumatic brain injury in Taiwan

Kuo-Hsing Liao, MD^a, Cheng-Kuei Chang, MD, PhD^b, Hong-Chang Chang, MD^c,
Kun-Chuan Chang, MD^d, Chieh-Feng Chen, MD^{e,x}, Tzu-Yung Chen, MD^f,
Chi-Wen Chou, MD^g, Wen-Yu Chung, MD^h, Yung-Hsiao Chiang, MD, PhD^{i,t,x},
Kuo-Sheng Hong, MD, PhD^{a,t}, Sheng-Huang Hsiao, MD, PhD^j, Yu-Hone Hsu, MD^k,
Hsu-Lin Huang, MD, PhD^l, Sheng-Chien Huang, MD^m, Ching-Chang Hung, MDⁿ,
Sui-Sum Kung, MD^o, Ken N. Kuo, MD, PhD^p, Kun-Hsing Li, MD^l, Jia-Wei Lin, MD, PhD^{a,t},
Tzu-Gan Lin, MD^q, Chien-Min Lin, MD^{a,t}, Chuan-Fa Su, MD^r, Ming-Ta Tsai, MD, PhD^s,
Shin-Han Tsai, MD, PhD^{a,t,y}, Yu-Chih Wang, MD^u, Ta-Yu Yang, MD^v,
Kuo-Fan Yu, MD^w, Wen-Ta Chiu, MD, PhD^{a,t,x,*}

Set up ICP Monitor



B Raise the bed head by 30 degrees to keep CVP at 8-12mmHg; rule out (be sure of the absence of) hyponatremia and fever when CPP > 60mmHg



ICP > 20 mmHg



B CSF drainage (with ventricular drain), 3-5cc each time



B Use sedatives and analgesics, and neuromuscular blockers agents when necessary



B Light hyperventilation to keep PaCO₂ 30-35mmHg



B Mannitol 0.25 – 1 g/kg/intravenous injection

→ Cranial CT-brain: edema or hemorrhage



Craniotomy or decompressive craniectomy



Second Tier Therapy

Kuo-Hsing Liao

(Barbiturate coma, hyperventilation (PaCO₂ 25-30mmHg) hypertonic saline, hypothermia, therapeutic hypertension, hyperventilation (PaCO₂ <30mmHg), decompressive craniectomy)



- ☛ Hastaya uygulanacak girişimsel işlemleri kolaylaştırma
- ☛ Mekanik ventilasyonu kolaylaştırma
- ☛ Kafa içi basınç artışı
- ☛ Kardiyak arrest sonrası terapötik hipotermi
- ☛ Tetanoz, noroleptik malign sendrom veya status epileptikus gibi artmış kas aktivitesi olan hastalıkların tedavisini kolaylaştırma



Clinical Paper, Clinical

Contin

M



Hipotermide ilaçların
farmakodinami ve
farmakokinetik özelliklerini
değiştirdiğinden doz belirsiz.

Neu
Lactic ac
Shock

...romuscular blockade, ... without sustained neuro- ... muscular blockade was associated ... was a trend toward improved functional ... (adjusted 28%; $p=0.07$). Sustained neuromuscular blockade was associated with improved lactate clearance (adjusted $p=0.01$).
Conclusions: We found that early neuromuscular blockade for a 24-h period is associated with an increased probability of survival. Secondly, we found that early, sustained neuromuscular blockade is associated with improved lactate clearance.

A

16-26.



- ☛ Hastaya uygulanacak işlemleri kolaylaştırma
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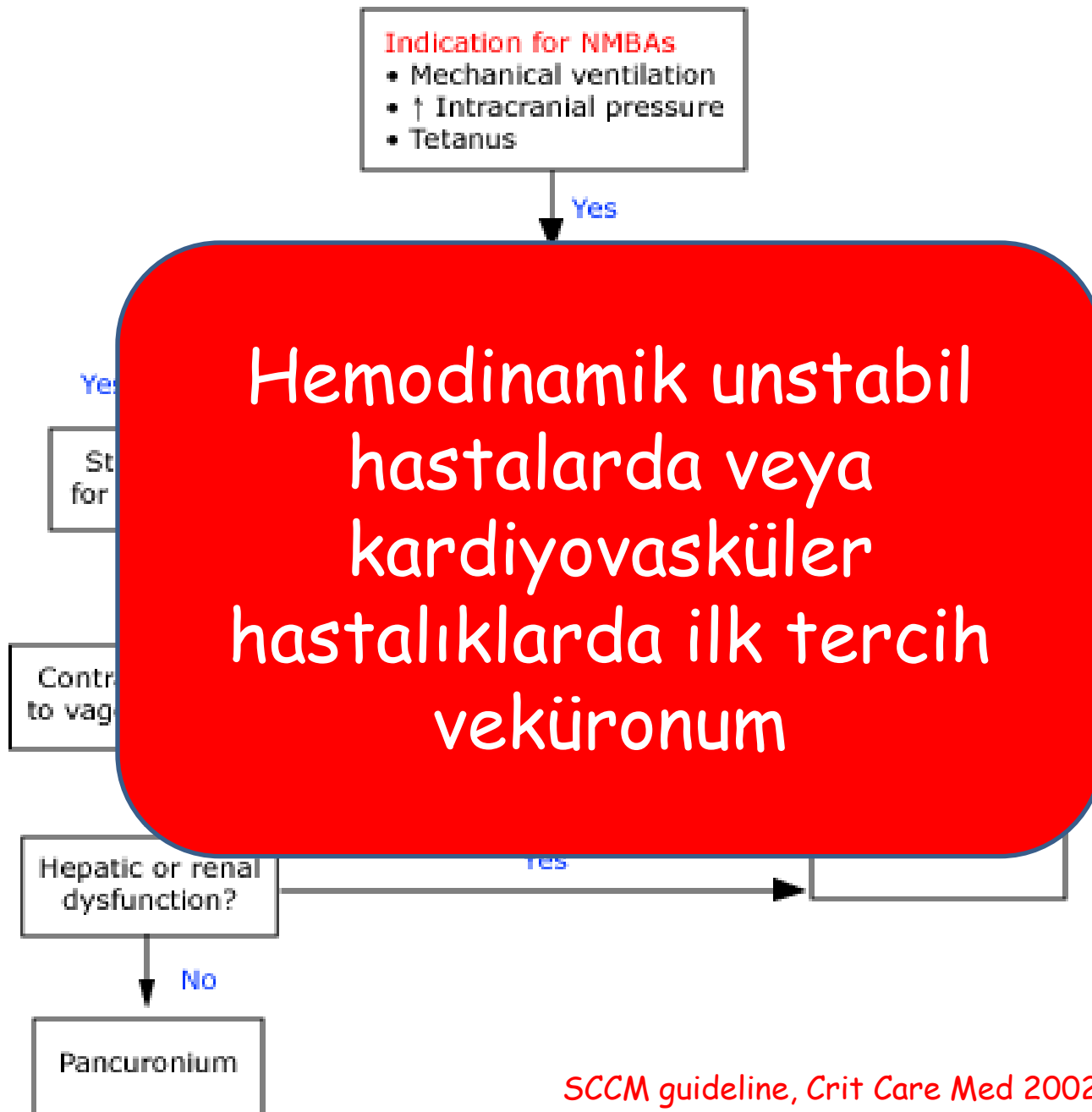


Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient

Michael J. Murray, MD, PhD, FCCM; Jay Cowen, MD; Heidi DeBlock, MD; Brian Erstad, PharmD, FCCM; Anthony W. Gray, Jr, MD, FCCM; Ann N. Tescher, RN; William T. McGee, MD, MHA; Richard C. Prielipp, MD, FCCM; Greg Susla, PharmD, FCCM; Judith Jacobi, PharmD, FCCM, BCPS; Stanley A. Nasraway, Jr, MD, FCCM; Philip D. Lumb, MB, BS, FCCM. Developed through the Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), in collaboration with the American Society of Health-System Pharmacists (ASHP), and in alliance with the American College of Chest Physicians; and approved by the Board of Regents of ACCM and the Council of SCCM and the ASHP Board of Directors

GRADE C

SCCM guideline, Crit Care Med 2002;30;1





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