Quand doit-on commencer à mobiliser les patients...

En sepsis ?

réanimation 2017
PARIS 11-13 JANVIER

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réanimation 2017
PARIS 11-13 JANVIER

Déclaration de liens

mon intervention
ne présente aucun conflit d'intérêt

srlf
SOCIÉTÉ DE RÉANIMATION DE LANGUE FRANÇAISE

International Consensus Definitions for Sepsis and Septic Shock

Sepsis(1)

Bone RC. et al. *CCM*, 1992

SIRS *systemic inflammatory response syndrome*

Sepsis Infection + SIRS

Severe sepsis: sepsis with organ dysfunction

Septic shock persistent arterial hypotension unexplained by other causes.

Sepsis(2)

Levy MM. et al. *ICM*, 2003

SIRS

Sepsis

Severe sepsis
***New criteria**

Septic shock

Sepsis-3

Singer M. et al. *JAMA*, 2016

~~SIRS~~

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection **(~10% mortality)**

~~Severe sepsis~~

Septic shock sepsis with persisting hypotension requiring vasopressors + serum lactate level >2 mmol/L
(>40% Mortality)

Sepsis
↓
Multiple Organ Failure
↓
Death

Is essential

Early recognition and **management** of patients with sepsis or at risk

Early goal-directed therapy
Rivers E. NEJM, 2001,
Simpson SQ et al. *Journal of Critical Care,* 2016

Photo: tasksdonedaily.com

ICUAW

Peripheral nerves → critical illness polyneuropathy (CIP)
Skeletal muscle → critical illness myopathy (CIM)
Both → critical illness polyneuromyopathy (CIPNM)

↑ survival
Sepsis

↑ incidence
ICUAW

"organ failure *per se*"

Puthucheary Z, *J Physiol,* 2010
Stevens RD, *Crit Care Med,* 2009

Could rise the **76%-100%** within **72h** after sepsis onset

Tennila A. Intensive care med, 2000
Tepper M. The Netherlands Journal of Medicine 2000

↑ Mortality

Khan J. Neurology 2006

↑ Long term Dependency

Iwashyna TJ, *Jama,* 2010
Kaukonen KM, *Jama,* 2014

Primary risk factors

Mechanical ventilation

Muscle immobilization

Severe sepsis

Multiple organ dysfunction

Neuro/myotoxic agents

Friedrich O., *Curr Opin Clin Nutr Metab Care,2006*
Hermans G, *Crit Care, 2008*
Visser LH, *Eur J Neurol, 2006*

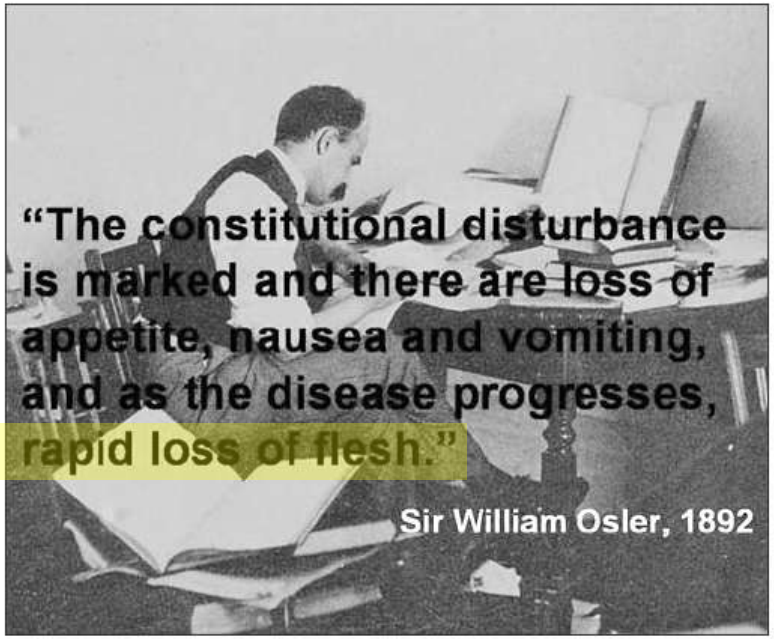


Figure 8: Sir William Osler's comments on the effects of prolonged sepsis on muscle.[29]

Bolton CF. *Can. J. Neurol. Sci.* 2010

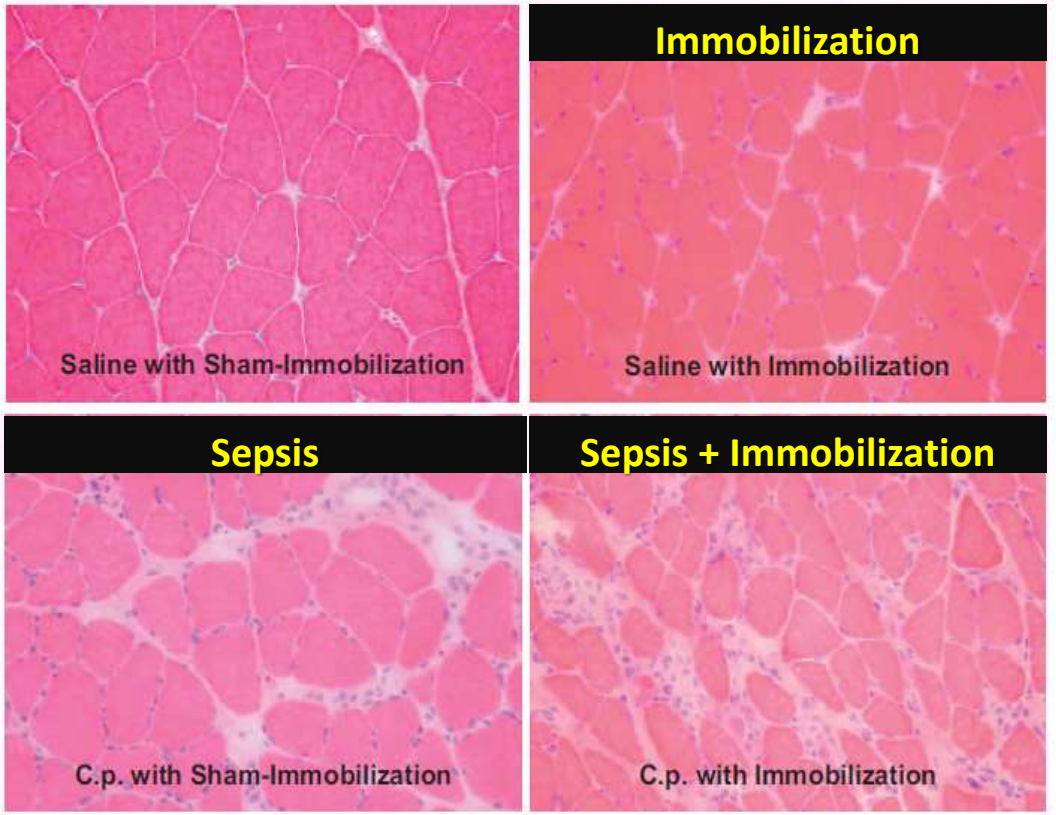
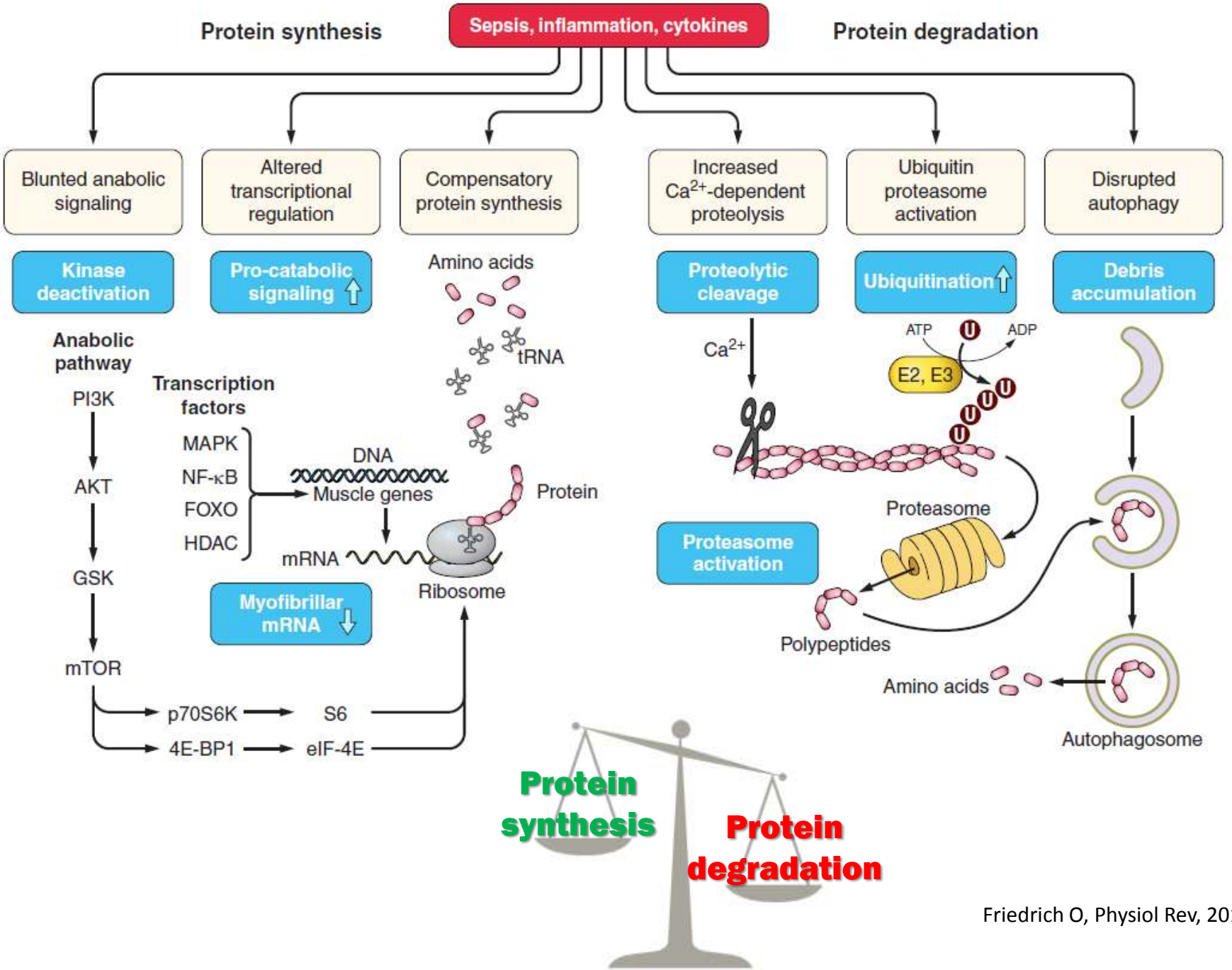
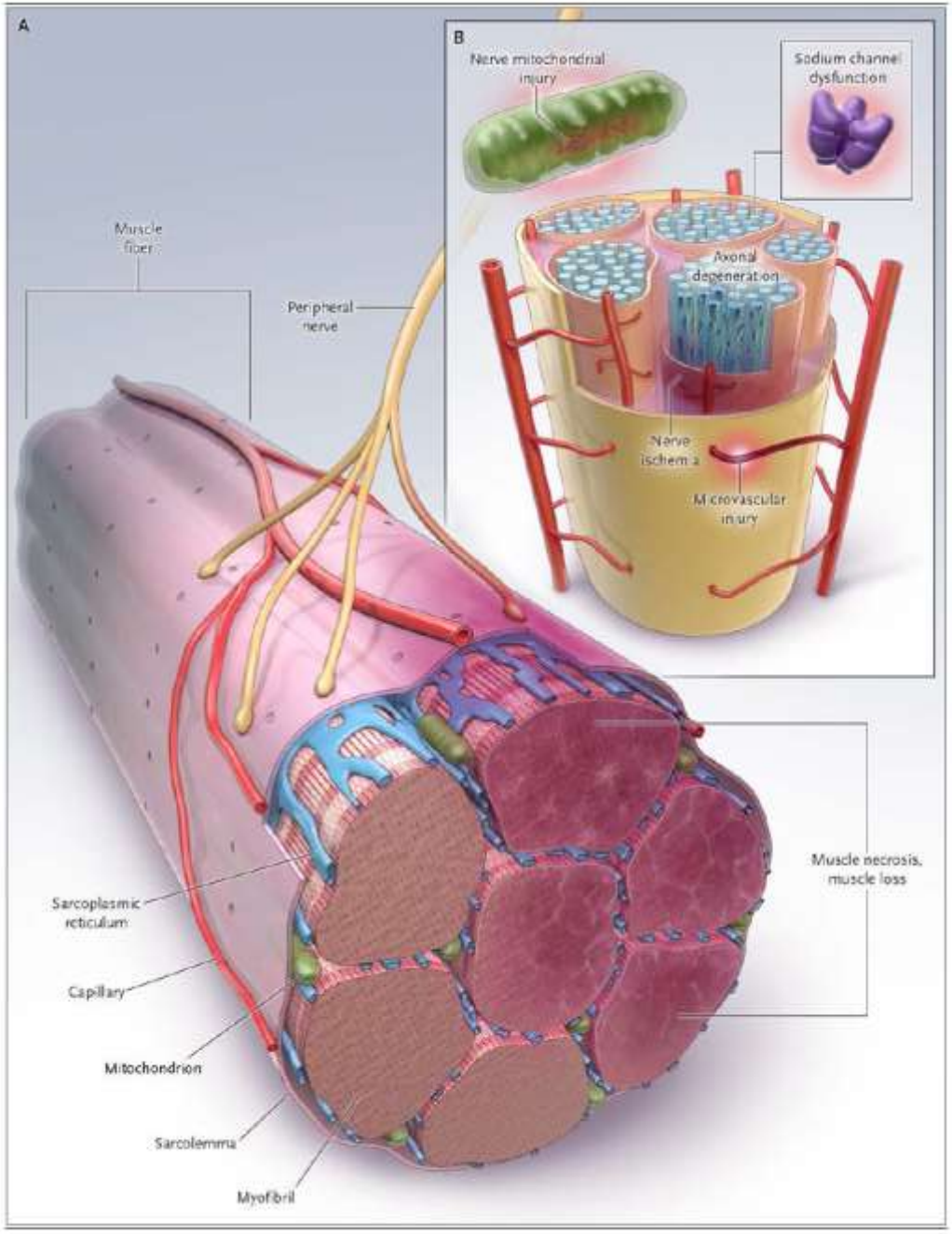


Figure 3. Representative hematoxylin and eosin stains of muscles of the surgical leg (magnification, ×200). Inflammation and immobilization independently increased the number of inflammatory cells in the perimysial and endomysial tissue. The fiber diameters decreased and became inhomogeneous concomitant with an increase in connective tissue. Combination of immobilization with *Corynebacterium parvum* (*C.p.*) resulted in the most severe histopathological changes in the muscle.

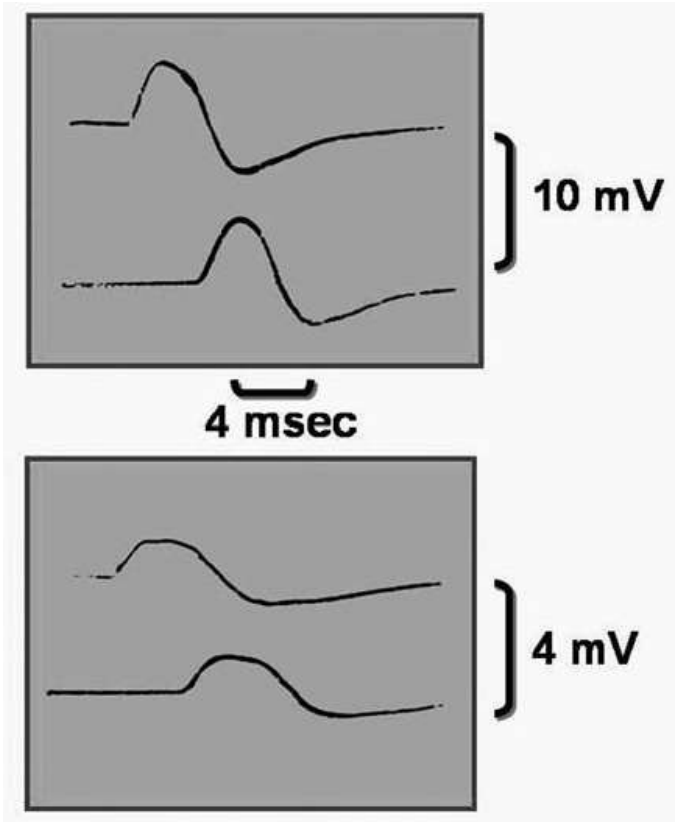
Fink H, *Crit Care Med* 2008



Friedrich O, Physiol Rev, 2015



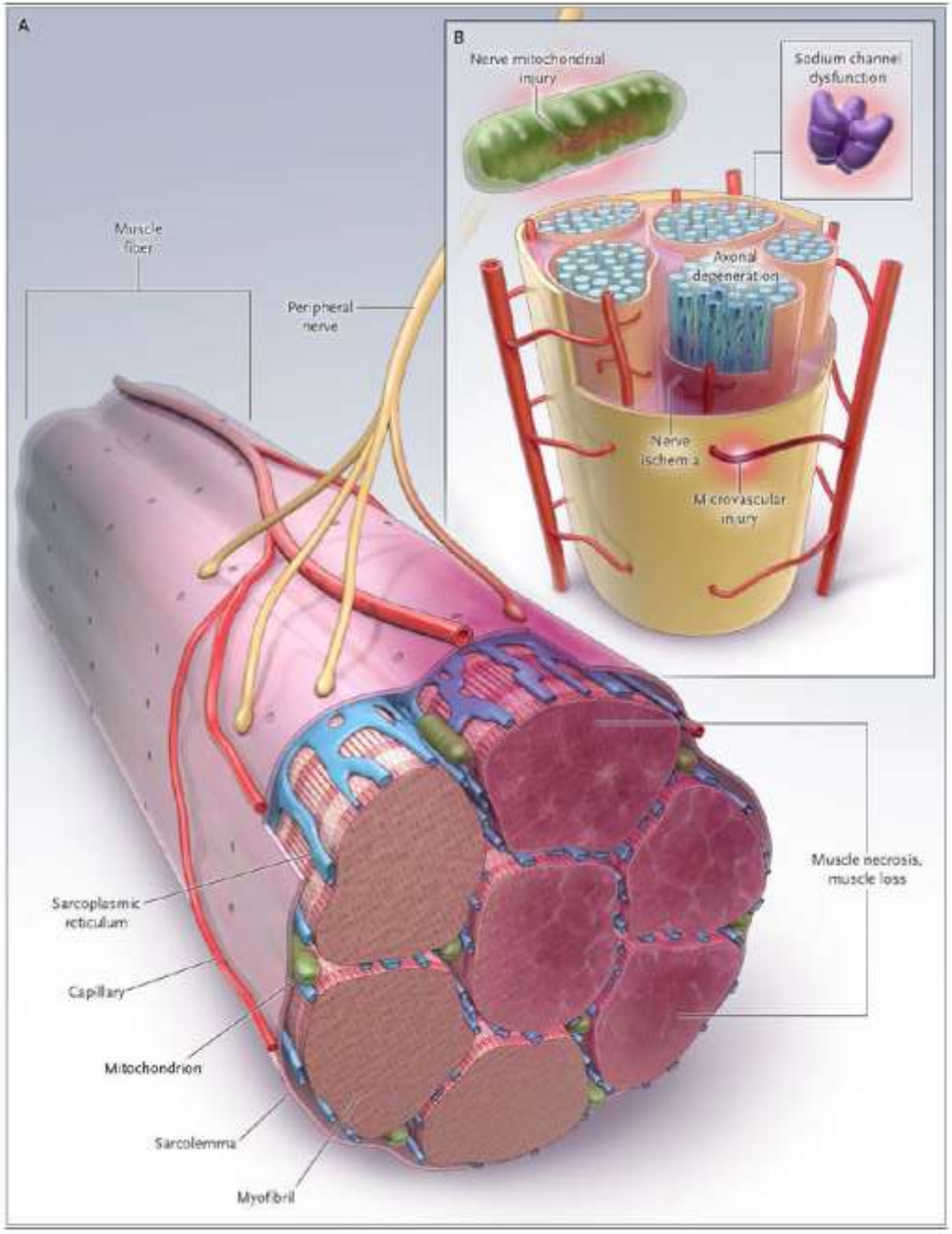
Kress JP, *N Engl J Med* 2014



Bolton CF. *Can. J. Neurol. Sci.* 2010

within **72h** after sepsis onset

Tennila A. Intensive care med, 2000,
Tepper M. The Netherlands Journal of Medicine 2000,
Khan J. Neurology 2006



Kress JP, *N Engl J Med* 2014

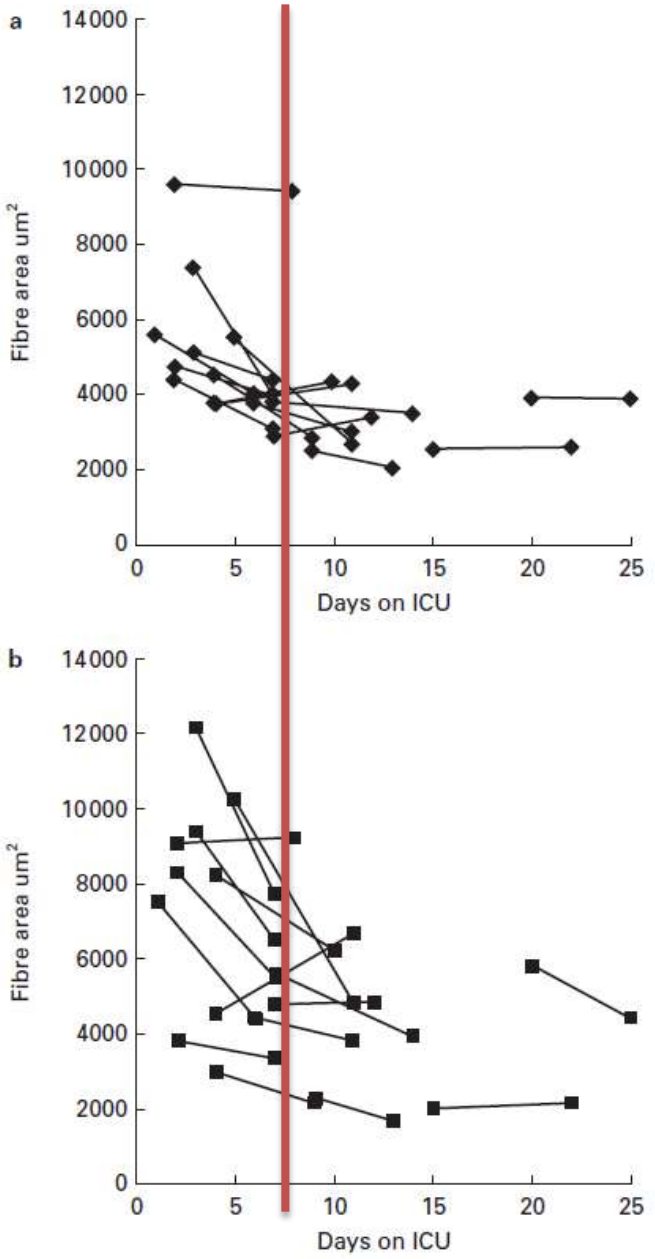


Figure 1. Scatterplot of the changes in the mean areas of **a**, type 1 and **b**, type 2 fibres with time after admission to the intensive care unit (ICU). The lines join data on tissues from each of 15 patients.

Helliwell TR, *Neuropathol Appl Neurobiol. 1998*

Early mobilization must be started EARLY

But…

How early?

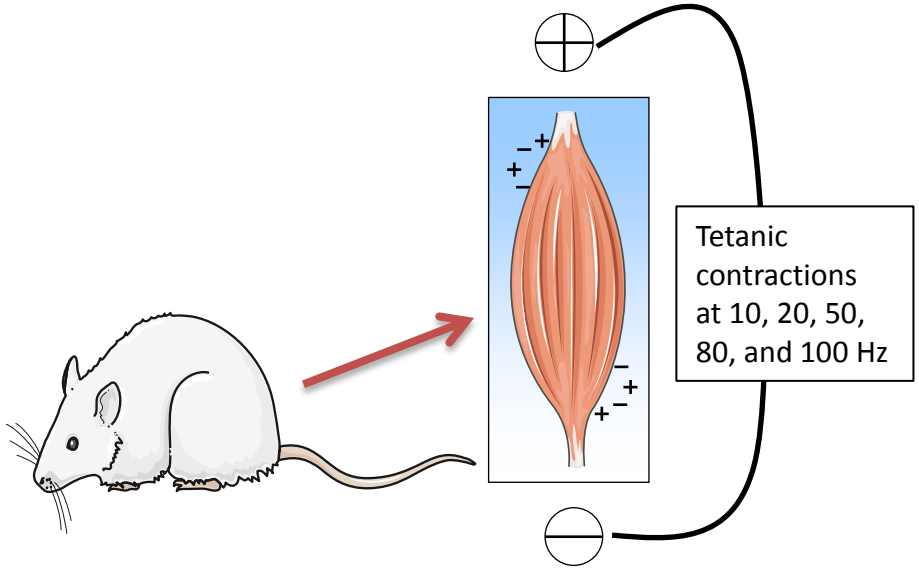
"Primum non nocere"

Sepsis-induced myopathy

Leigh Ann Callahan, MD; Gerald S. Supinski, MD

cle are well described; however, exercise increases cytokines and free-radical generation in muscle (86). In addition, Dumont et al recently showed that reloading muscles induces inflammatory cell infiltration and worsens sarcolemmal injury (87). As a result, it is conceivable that exercising patients with damaged muscles could potentially propagate muscle inflammation and injury, or delay recovery. Such issues should be carefully ex-

In vitro animal model

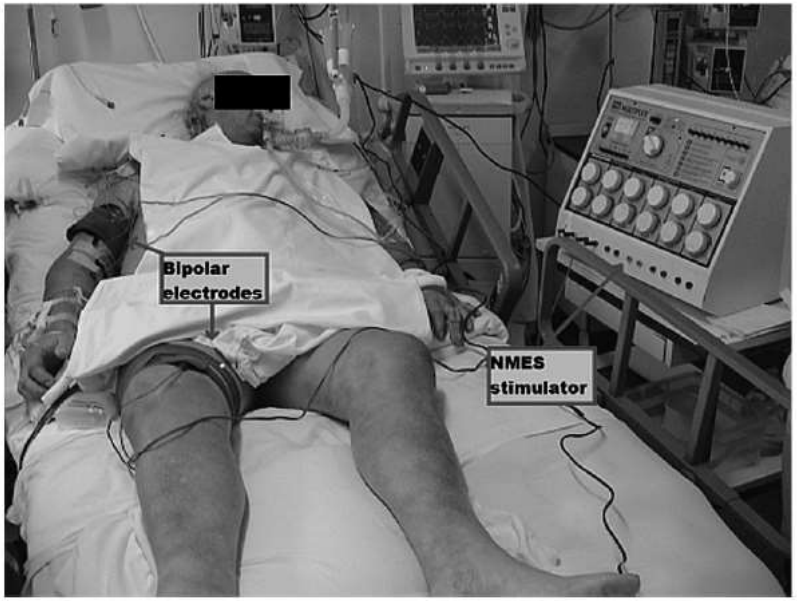


Callahan LA, *Crit Care Med* 2009

Dummond N, *Am J Physiol Regul Integr Comp Physiol*, 2008

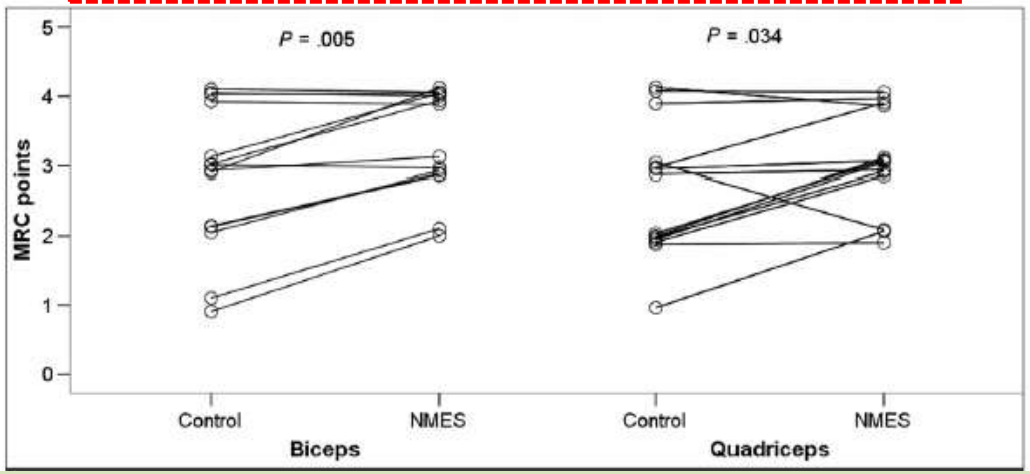
Muscle weakness in septic patients requiring mechanical ventilation: Protective effect of transcutaneous neuromuscular electrical stimulation ☆

Pablo O. Rodriguez MD [a,b,c,*], Mariano Setten PT [a,d], Luis P. Maskin MD [a], Ignacio Bonelli MD [a,b], Silvana Romero Vidomlansky MD [e], Shiry Attie MD [a], Silvana L. Frosiani PT [d], Shigeru Kozima MD [e], Ricardo Valentini MD [a,b]



How Early?

2 days (IQR, 1-2 days) after ICU admission



30 min twice at day, one side:

- ✓ Vastus medialis
- ✓ Brachial biceps

During 13 days (IQR, 7-30).

- ✓ Biceps (P = .005) and quadriceps (P = .034) strengths were significantly higher on the stimulated side
- ✓ Improvement mainly observed in more severe and weaker patients
- ✓ arm circumference decreased only in non stimulated side

Rodriguez PO, *Journal of Critical Care,* 2012

Stefanou et al. Ann. Intensive Care (2016) 6:21
DOI 10.1186/s13613-016-0123-y

Annals of Intensive Care
a SpringerOpen Journal

RESEARCH Open Access

Neuromuscular electrical stimulation acutely mobilizes endothelial progenitor cells in critically ill patients with sepsis

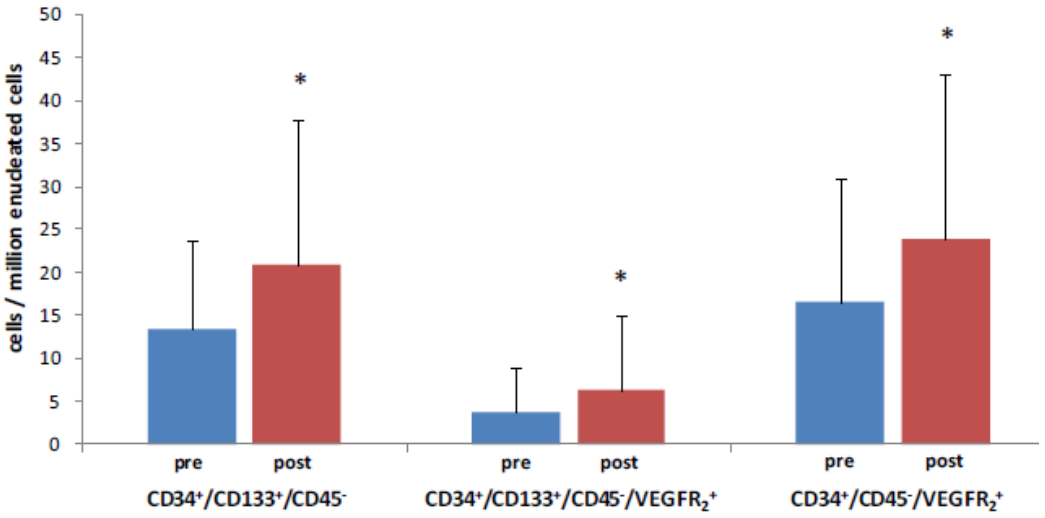
Christos Stefanou[1], Eleftherios Karatzanos[1], Georgios Mitsiou[1], Katerina Psarra[2], Epameinondas Angelopoulos[1], Stavros Dimopoulos[1,3], Vasiliki Gerovasili[1], Efstathios Boviatsis[4], Christina Routsi[1] and Serafeim Nanas[1*]

40 min/day, both lower extremities:

- ✓ vastus lateralis,
- ✓ Vastus medialis
- ✓ peroneus longus

How Early?

Inclusion >72 h of presence of sepsis and MV, but when start (?)



↗HR ↗RR = MAP

↗Creatine phosphokinase

(498 ± 961 to 526 ± 1011 IU/L, p < 0.01)

↗Lactate

(1.1±0.4 to 1.4±0.6 mmol/L, p < 0.01)

Stefanou C. *Ann. Intensive Care, 2016*

Effect of transcutaneous electrical muscle stimulation on muscle volume in patients with septic shock*

Jesper B. Poulsen, MD; Kirsten Møller, MD, PhD; Claus V. Jensen, MD; Sigge Weisdorf, MD; Henrik Kehlet, MD, PhD; Anders Perner, MD, PhD

60 min per day
During 7 days.

How Early?
Within 72 hrs of diagnosis.

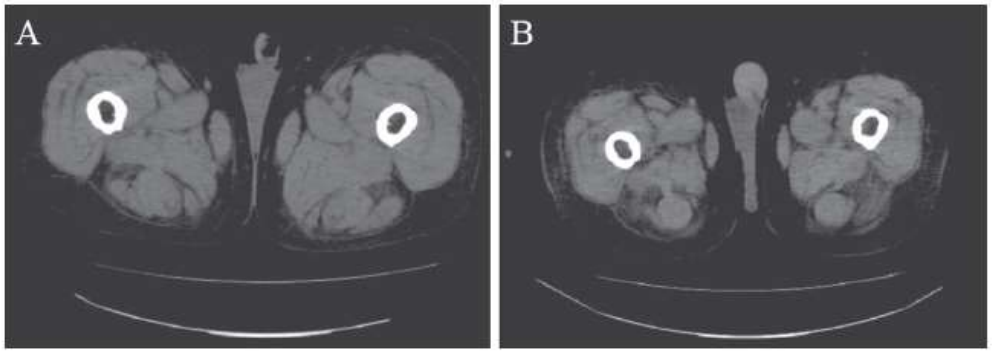


Figure 2. Computed tomographic scans of the thigh in a patient with septic shock at baseline (*A*) and 7 days later (*B*) showing the changes in muscle volume.

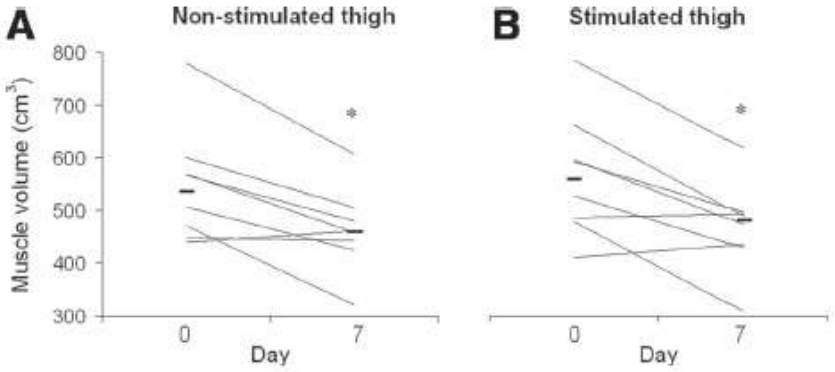


Figure 3. Quadriceps muscle volume in individual patients (bars represent medians) from start of intervention at day 0 to day 7 in the nonstimulated (*A*) and stimulated leg (*B*). *$p < .05$ vs. the same group at baseline. No significant differences were observed between groups.

Loss of muscle mass was unaffected by TEMS

Poulsen JB, *Critical Care Med,* 2014

Feasibility of neuromuscular electrical stimulation in critically ill patients☆,☆☆

Johan Segers, PT, MSc [a], Greet Hermans, MD, PhD [b], Frans Bruyninckx, MD, PhD [c], Geert Meyfroidt, MD, PhD [d], Daniel Langer, PT, PhD [a], Rik Gosselink, PT, PhD [a,*]

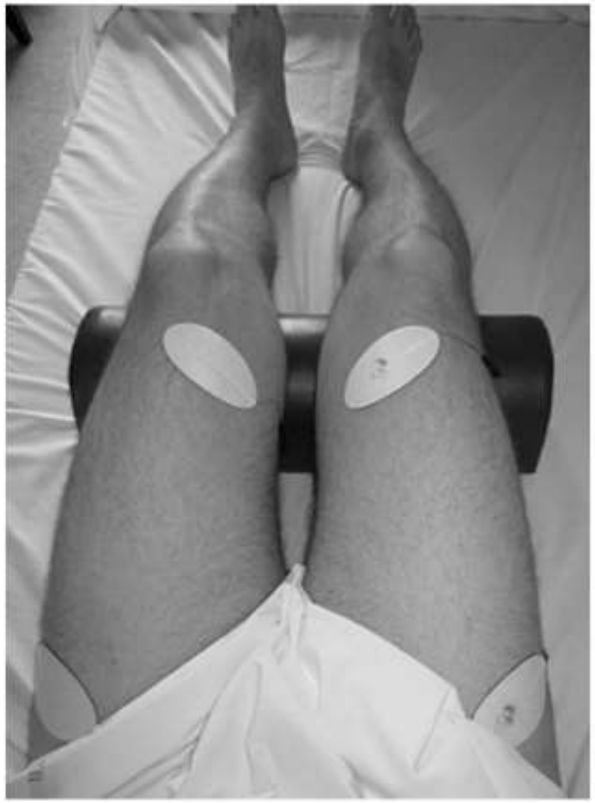
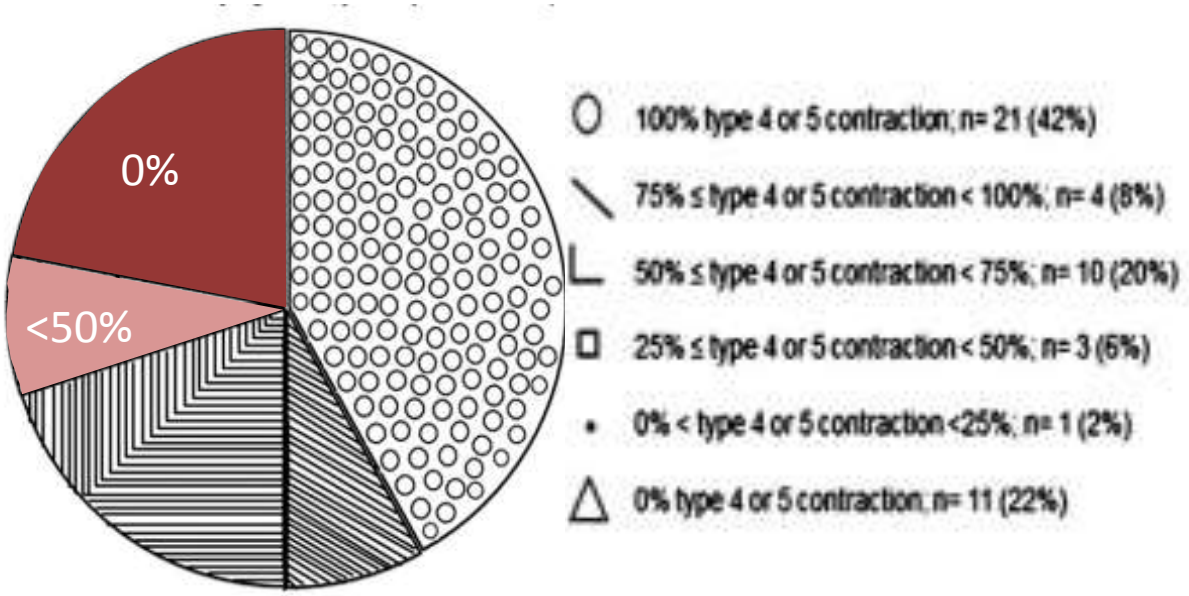


Fig. 1. Placing of electrodes.



Impaired quadriceps contraction

✓Lower limb edema (p<.001)

✓**Sepsis (P = .008),**

✓Admission to the medical ICU (P = .041)

✓Treatment with vasopressors (P = .011)

Segers J. *Journal of Critical Care*, 2016

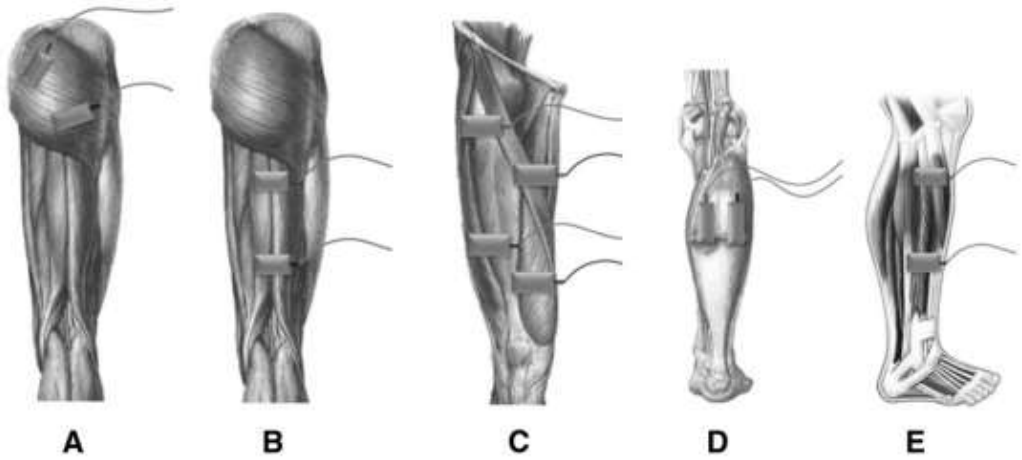
Safety and feasibility of a neuromuscular electrical stimulation chronaxie-based protocol in critical ill patients: A prospective observational study

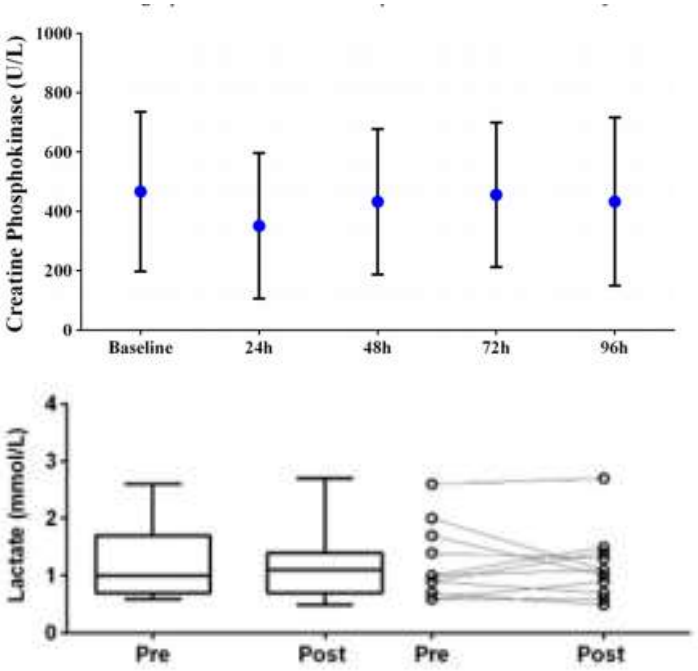
Paulo Eugênio Silva, PT, MSc [a,f,*], Nicolas Babault, PhD [b], João Batista Mazullo, PT, MSc [c], Tamires Pereira de Oliveira, PT [c], Bárbara Letícia Lemos, PT [c], Vitor Oliveira Carvalho, PT, PhD [d], Joao Luiz Quagliotti Durigan, PT, PhD [e]

It's necessary to assess neuromuscular excitability to apply effective electrical stimuli

*When **excitability is decreased** it is necessary to adjust **larger pulse widths***

Chronaxie assessments were performed in all muscles at every session

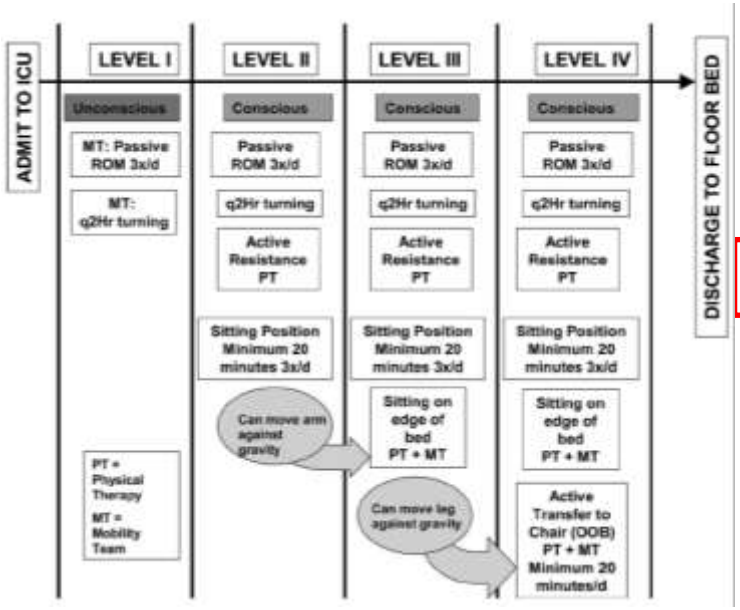




Silva PE, *Journal of Critical Care*, 2017

Early intensive care unit mobility therapy in the treatment of acute respiratory failure*

Peter E. Morris, MD; Amanda Goad, RN; Clifton Thompson, RN; Karen Taylor, MPT; Bethany Harry, MPT; Leah Passmore, MS; Amelia Ross, RN, MSN; Laura Anderson; Shirley Baker; Mary Sanchez; Lauretta Penley; April Howard, RN; Luz Dixon, RN; Susan Leach, RN; Ronald Small, MBA; R. Duncan Hite, MD; Edward Haponik, MD



How Early?

Within 48 hrs of MV start.

- ✓ was feasible and safe
- ✓ = costs
- ✓ ↓ ICU and hospital LOS

±30 % sepsis

Table 1. Enrollment population baseline parameters

Parameter	Usual Care (n = 165)	Protocol (n = 165)	p
Diagnoses (no. and %)			.915
Acute lung injury: out-patient pneumonia	33 (20.1%)	32 (19.8%)	
Acute lung injury: severe sepsis (nonpneumonia)	23 (14.0%)	26 (16.0%)	
Acute lung injury: aspiration pneumonia	32 (19.5%)	27 (16.7%)	
Acute lung injury: pancreatitis	2 (1.2%)	4 (2.5%)	
Acute lung injury: other	10 (6.1%)	6 (3.7%)	
Coma	20 (12.2%)	25 (15.4%)	
Post-op	4 (2.4%)	7 (4.3%)	
Congestive heart failure	10 (6.1%)	12 (7.4%)	
Cardiac arrest[a]	6 (3.7%)	3 (1.9%)	
Acute on chronic lung dz: asthma	4 (2.4%)	4 (2.5%)	
Acute on chronic lung dz: chronic obstructive pulmonary disease	18 (11.0%)	14 (8.6%)	
Acute on chronic lung dz: nonasthma/non-chronic obstructive pulmonary disease	2 (1.2%)	2 (1.2%)	
Age in yrs (mean ± SD)	55.4 ± 16.8	54.0 ± 16.8	.782
Gender-male (no. and %)	88 (53.3%)	93 (56.4%)	.581
Body mass index (mean ± SD)	27.7 ± 7.1	29.0 ± 6.8	.376
Acute Physiology and Chronic Health Evaluation II	21.6 ± 8.0	23.5 ± 8.8	.092
Activity of daily living	96.5 ± 9.8	95.3 ± 12.6	.243
Charlson index	3.16 ± 2.23	2.87 ± 2.31	.249
Patients on vasopressors (no. and %)	60 (36.4%)	53 (32.1%)	.815
Patients with previous home O_2 (no. and %)	9 (5.5%)	13 (7.9%)	.378
Patients with previous chronic renal failure (no. and %)	9 (5.5%)	9 (5.5%)	1.00

Morris PE, Crit Care Med, 2008

Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

William D Schweickert, Mark C Pohlman, Anne S Pohlman, Celerina Nigos, Amy J Pawlik, Cheryl L Esbrook, Linda Spears, Megan Miller, Mietka Franczyk, Deanna Deprizio, Gregory A Schmidt, Amy Bowman, Rhonda Barr, Kathryn E McCallister, Jesse B Hall, John P Kress

86 and 82% sepsis

How Early?

Median of 1.5 days (range, 1.0 –2.1 days) after intubation.

- ✓ Safe and well tolerated,
- ✓ Better functional outcomes at hospital discharge
- ✓ Shorter duration of delirium, and MV

Patients with **sepsis** associated with poorer outcomes, in both study arms

	Intervention (n=49)	Control (n=55)
Age (years)	57·7 (36·3–69·1)	54·4 (46·5–66·4)
Female	29 (59%)	23 (42%)
Black race	30 (61%)	31 (56%)
Barthel Index score	100 (85–100)	100 (90–100)
Body-mass index (kg/m²)	27·4 (25·1–32·4)	28·0 (23·5–34·1)
APACHE II score	20·0 (15·8–24·0)	19·0 (13·3–23·0)
Sepsis	42 (86%)	45 (82%)
Diabetes	18 (37%)	18 (33%)
Primary diagnosis on admission to intensive care		
Acute lung injury	27 (55%)	31 (56%)
COPD exacerbation	4 (8%)	6 (11%)
Acute exacerbation of asthma	5 (10%)	4 (7%)
Sepsis	7 (14%)	9 (16%)
Haemorrhage	1 (2%)	2 (4%)
Malignancy	2 (4%)	1 (2%)
Other	3 (6%)	2 (4%)

Data are number of patients (%) or median (IQR). APACHE II=Acute Physiology and Chronic Health Evaluation II. COPD=chronic obstructive pulmonary disease. Barthel Index scale 0–100, APACHE II scale 0–71.

Table 1: **Baseline characteristics of the study population**

Schweickert WM, .*Lancet* 2009

Hickmann et al. Ann. Intensive Care (2016) 6:80
DOI 10.1186/s13613-016-0184-y

Annals of Intensive Care

RESEARCH Open Access

Teamwork enables high level of early mobilization in critically ill patients

Cheryl Elizabeth Hickmann, Diego Castanares-Zapatero, Emilie Bialais, Jonathan Dugernier, Antoine Tordeur, Lise Colmant, Xavier Wittebole, Giuseppe Tirone, Jean Roeseler and Pierre-François Laterre*

34% interventions in patients with severe sepsis/septic shock.

How Early?
at 19 hours (IQR 15-23hours)

Table 2 Characteristics of mobilized and non-mobilized patients

	ICU patient-days	EM performed				No EM performed
		Sitting in chair			In bed PTS+	
		All sitting in chair	PTS+	PTS-		
Total	709	527	337	190	83	99
Invasive mechanical ventilation (MV)	327	223 (68 %)	142 (43 %)	81 (25 %)	40 (12 %)	64 (20 %)
Severe sepsis/sepsis shock	241	166 (69 %)	102 (42 %)	64 (27 %)	28 (12 %)	47 (20 %)
Vasoactive drugs (VAD)	211	149 (71 %)	99 (47 %)	50 (24 %)	25 (12 %)	37 (18 %)
Renal replacement therapy (RRT)	115	76 (66 %)	59 (51 %)	17 (15 %)	11 (10 %)	28 (24 %)
Sedatives (SD)	260	193 (74 %)	122 (47 %)	71 (27 %)	22 (8 %)	45 (17 %)
MV + VAD	158	104 (66 %)	72 (46 %)	32 (20 %)	21 (13 %)	33 (21 %)
MV + VAD + RRT	77	46 (60 %)	38 (49 %)	8 (10 %)	8 (10 %)	23 (30 %)
MV + without SD	122	77 (63 %)	49 (40 %)	28 (23 %)	22 (18 %)	23 (19 %)
RASS −1 to +1	576	454 (79 %)	284 (49 %)	170 (30 %)	58 (10 %)	64 (11 %)
RASS >+1	25	21 (84 %)	18 (72 %)	3 (12 %)	1 (0.4 %)	3 (12 %)
RASS <−1	108	50 (46 %)	33 (31 %)	17 (16 %)	22 (20 %)	36 (33 %)

Values expressed as number (percentage)

MV mechanical ventilation, *VAD* vasoactive drugs, *RRT* renal replacement therapy, *SD* sedatives drug, *RASS* Richmond agitation-sedation scale, *PTS+* physical therapy session carried out, *PTS−* no physical therapy session carried out, *EM* early mobilization

Hickmann CE, Ann. Intensive Care, 2016

Hickmann et al. Ann. Intensive Care (2016) 6:80
DOI 10.1186/s13613-016-0184-y

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Supplemental Digital Content3: Multivariate analyses for risk factors associated with mortality.

ICU mortality

	AOR (95% CI) *Adjusted on 15 covariables*	*p*-value	AOR (95% CI) *Adjusted on 4 covariables*	*p*-value
Early Mobilization	**0.06 (0.01-0.42)**	**0.004***	**0.06 (0.01-0.29)**	**0.001***
ICU length of stay	1.10 (1.04-1.17)	0.001*	1.08 (1.03-1.12)	0.001*
Male	1.78 (0.27-11.63)	0.55		
Age (years)	1.09 (1.01-1.17)	0.04*	1.07 (1.02-1.13)	0.01*
Tracheotomy	0.67 (0.05-8.47)	0.76		
Berlin classification	1.95 (0.78-4.90)	0.15	2.26 (1.01-5.03)	0.04*
Surgery#	1.54 (0.50-4.69)	0.45		
Cirrhosis	2.81 (0.35-22.77)	0.33		
BPCO	0.24 (0.01-5.07)	0.36		
Cancer	1.32 (0.21-8.18)	0.77		
Neurologic	1.24 (0.06-26.49)	0.89		
APACHE II score	1.06 (0.91-1.23)	0.49		
SOFA score	1.24 (0.92-1.69)	0.16	1.38 (1.14-1.67)	0.001*
Sedatives drug use	1.04 (0.07-15.33)	0.98		
Vasoactive drug use	1.99 (0.15-26.70)	0.60		
Renal replacement therapy	0.24 (0.04-1.40)	0.11		

AOR: Adjusted Odd-Ratio; #surgery: elective or urgent surgery; *denotes p-value <0.05

Hickmann CE, Ann. Intensive Care, 2016

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Potential effect of physiotherapeutic treatment on mortality rate in patients with severe sepsis and septic shock: A retrospective cohort analysis☆,☆☆

Maik Sossdorf, PhD [a,b,*], Gordon P. Otto, MD, MSc [a,b], Katja Menge, MD [b], Ralf A. Claus, PhD [a,b], Wolfgang Lösche, MD [a,b], Björn Kabisch, PhD [b,c], Matthias Kohl, PhD [d], Ulrich C. Smolenski, MD [e], Peter Schlattmann, MD, MSc [f], Konrad Reinhart, MD [a,b], Johannes Winning, MD [b]

index relative numbers of PT intervention (RNPTI)
(Interventions/day):

Limb exercises
Mobilization
Positioning
Breathing exercises

How Early?
at 4 days (IQR 2–7 days) after ICU admission
The first prescription of PT treatment was at day 1

Table 3
Multivariate Cox proportional-hazards regression analyses for modeling prediction on the ICU mortality rate (n = 701)*

Predictor variable	Regression coefficient (B)	HR (two-sided 95% CI)[a]	*P* Values
Age	0.020	1.020 (1.006-1.035)	.006
SOFA score	0.144	1.155 (1.062-1.257)	.001
APACHE II score at admission	0.014	1.014 (1.000-1.028)	.046
Sedation index[b]	0.593	1.810 (1.494-2.194)	<.001
RNPTI index	−0.018	0.982 (0.974-0.990)	<.001
Renal replacement therapy	0.002	1.002 (0.996-1.007)	.524
Cancer	0.456	1.578 (1.119-2.225)	.009
Heart failure	0.229	1.257 (0.889-1.779)	.196
Liver failure	0.145	1.156 (0.715-1.867)	.554
Gastric/duodenal ulcer	0.341	1.407 (0.881-2.246)	.153
Digestive tract disorders	−0.118	0.888 (0.629-1.255)	.502
Blood vessel disorders	0.612	1.844 (1.260-2.697)	.002
Locomotor system disorders	−0.106	0.899 (0.501-1.614)	.721

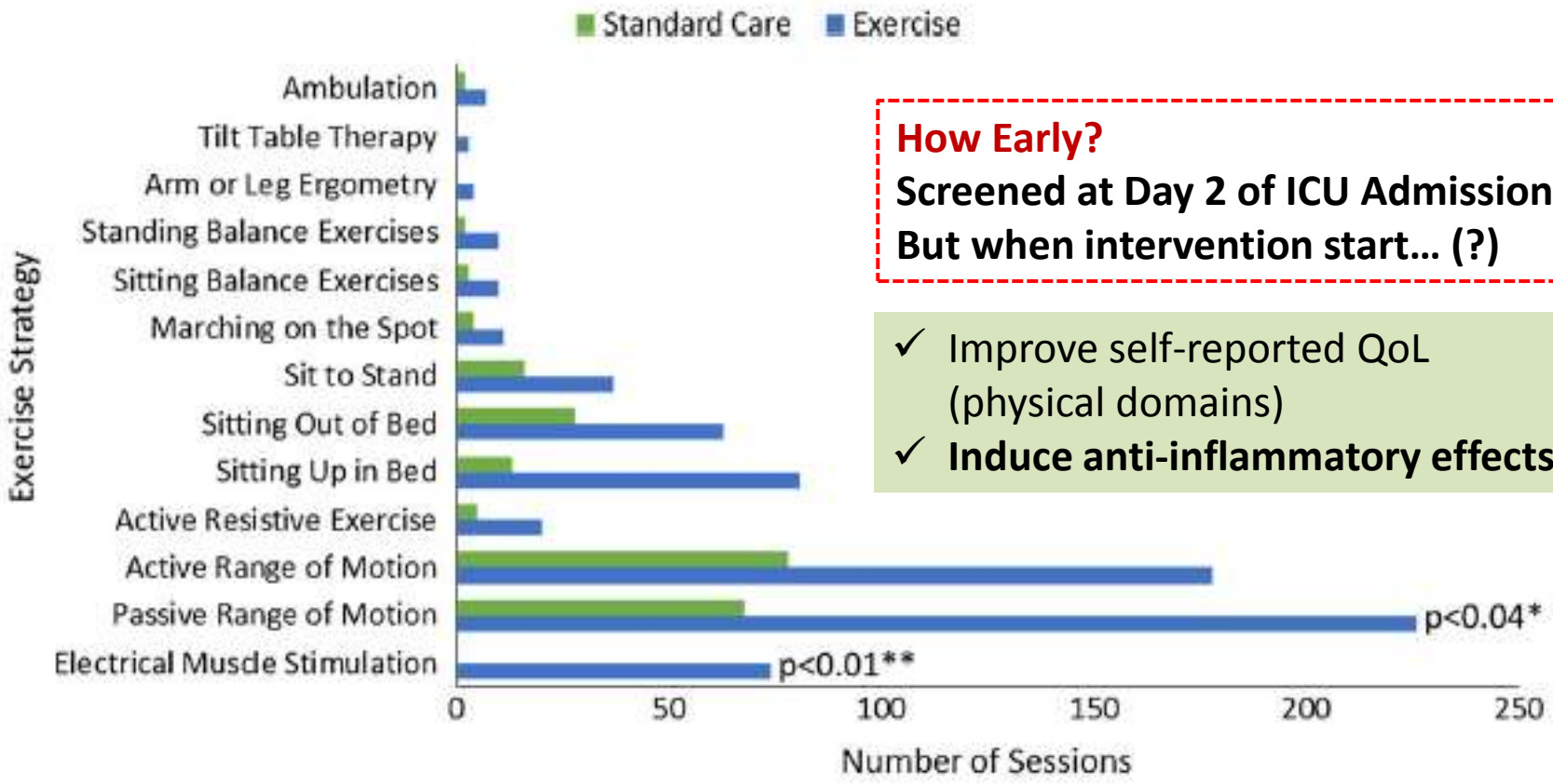
Sossdorf M. J Crit Care 2013

Intensive Care Med
DOI 10.1007/s00134-015-3763-8

ORIGINAL

Geetha Kayambu
Robert Boots
Jennifer Paratz

Early physical rehabilitation in intensive care patients with sepsis syndromes: a pilot randomised controlled trial



How Early?

Screened at Day 2 of ICU Admission

But when intervention start… (?)

- ✓ Improve self-reported QoL (physical domains)
- ✓ **Induce anti-inflammatory effects.**

Kayambu G, Intensiv Care Med 2015

Jeu 12 Janvier

SKR

13:40 - 15:10 | Communications libres en kinésithérapie
Session orale

Salle Asie 1

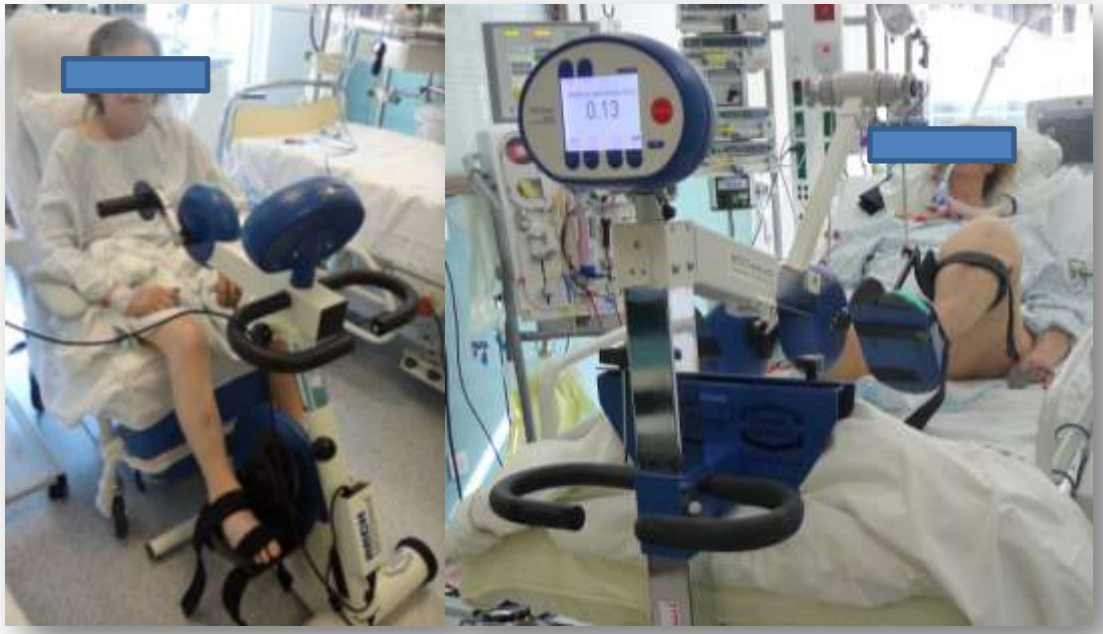
14:10
O81

Physical therapy during the early course of sepsis is safe and preserves skeletal muscle mass

Cheryl Hickmann *(Bruxelles)*

21 ICU patients with **septic shock** (within the first 2-days)

How Early?
Starting at Day 1±1



Standard practice:
Reduced sedation,
Adjusted nutritional intake
Manual mobilization (5/7days)
Bed to chair transfer *asap*

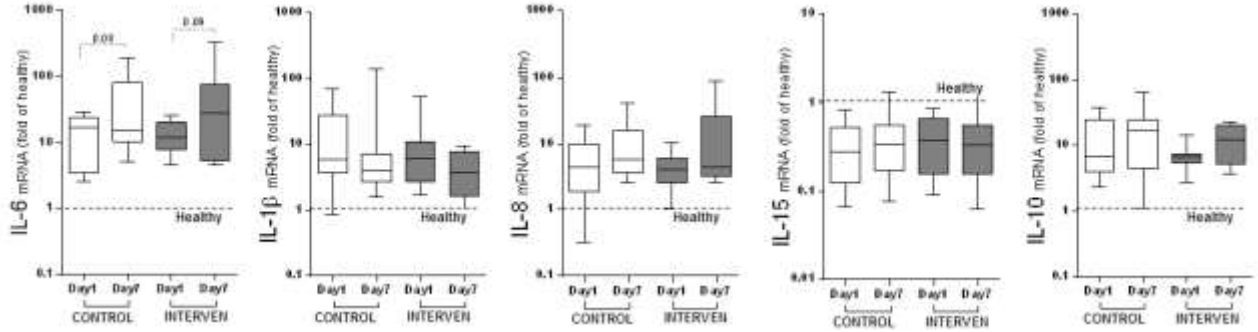
Intervention: 2 x 30min/day (7/7days)

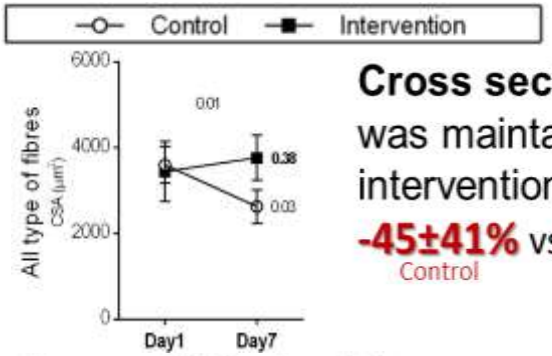
Skeletal muscle biopsies at Day1 and Day7

Hickmann CE, *In preparation*

Results:

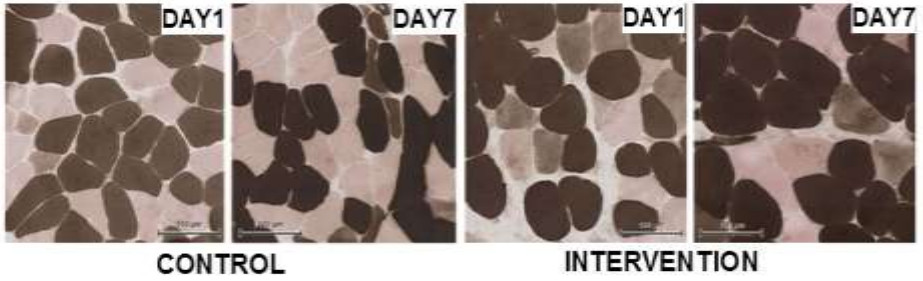
Inflammation was <u>not enhanced</u> by early exercise



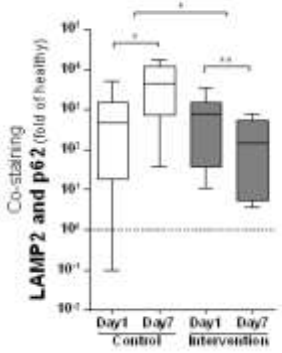


Cross sectional area was maintained in the intervention group

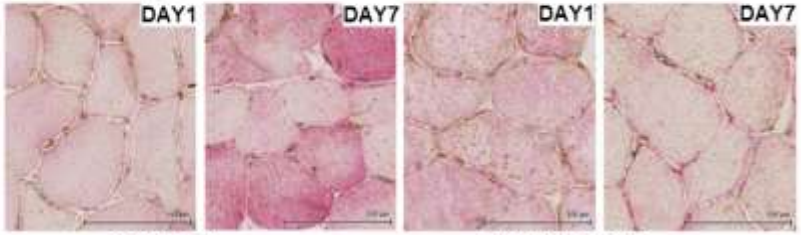
-45±41% vs **12±19%**, p=0.003
Control Intervention



Immunohistochemistry



LAMP-2/p62



co-localization of LAMP-2/p62 was <u>reduced</u> in the intervention group

Hickmann CE, *In preparation*

Conclusion

- ❑ **Important to start mobilization asap**
- ❑ **If NEMS is used, more research is needed to find the optimal parameters (personalized).**
- ❑ **Few data in this specific population, but promising in favor to start during the first days.**

Kayambu *et al. BMC Anesthesiology* 2011, **11**:21
http://www.biomedcentral.com/1471-2253/11/21

BMC Anesthesiology

STUDY PROTOCOL Open Access

Early rehabilitation in sepsis: a prospective randomised controlled trial investigating functional and physiological outcomes *The i-PERFORM Trial* (Protocol Article)

Geetha Kayambu[1*†], Robert J Boots[1,2] and Jennifer D Paratz[1]

Merci beaucoup