Physiopathologie musculaire de la faiblesse acquise en réanimation

Des observations cliniques à la compréhension mécanistique

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SRLF 2025

No conflict of interest regarding this oral presentation

I declare the following COI:

Fullphysio academy
Asten Santé
SOS Oxygène
Air Liquide medical system

CHEST

Days Spent at Home and Mortality After Critical Illness

A Cluster Analysis Using Nationwide Data

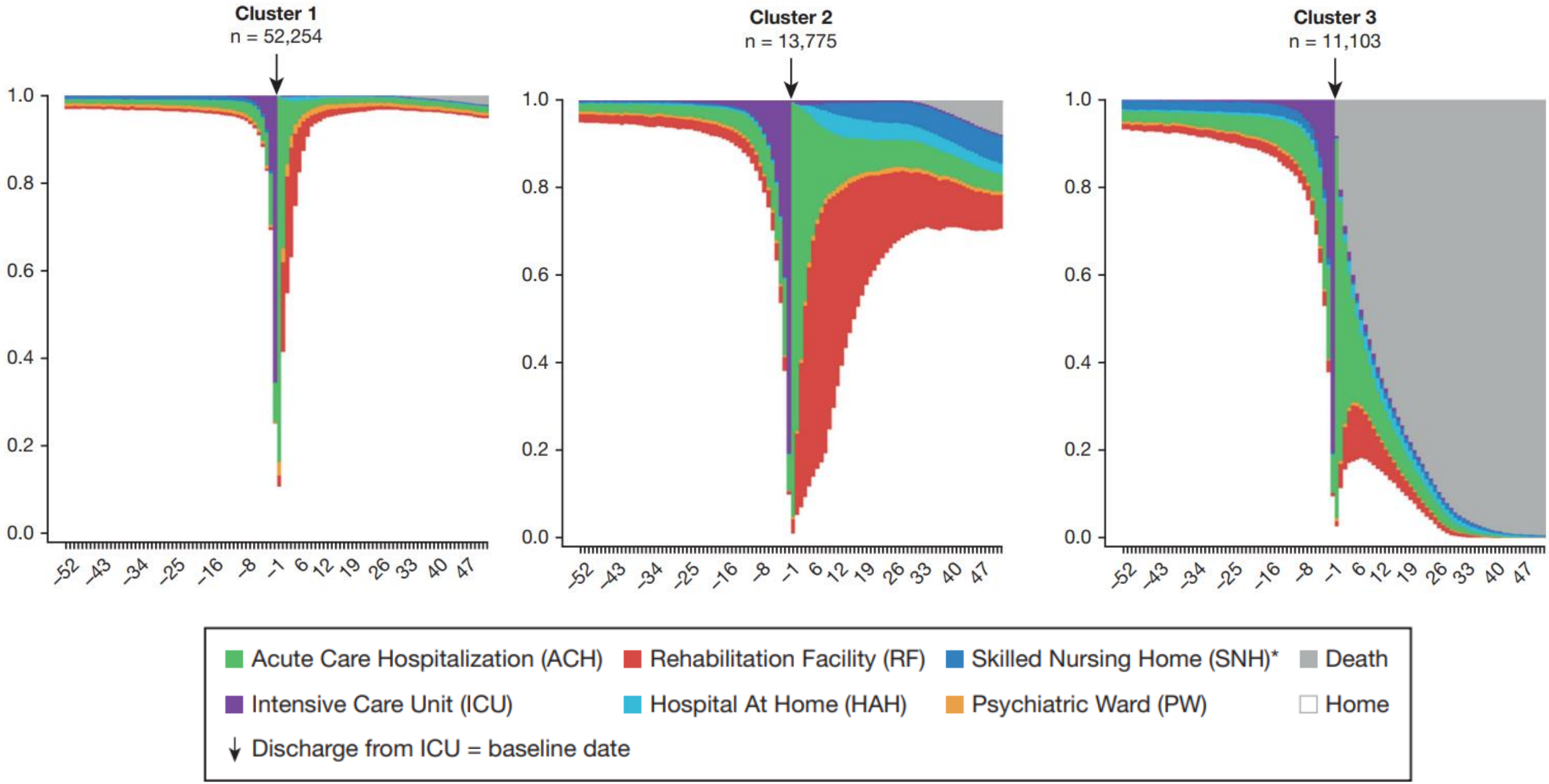
Guillaume L. Martin, MD; Alice Atramont, MD; Marjorie Mazars, MSc; Ayden Tajahmady, MD; Emin Agamaliyev, PhD; Mervyn Singer, MD; Marc Leone, MD; and Matthieu Legrand, MD

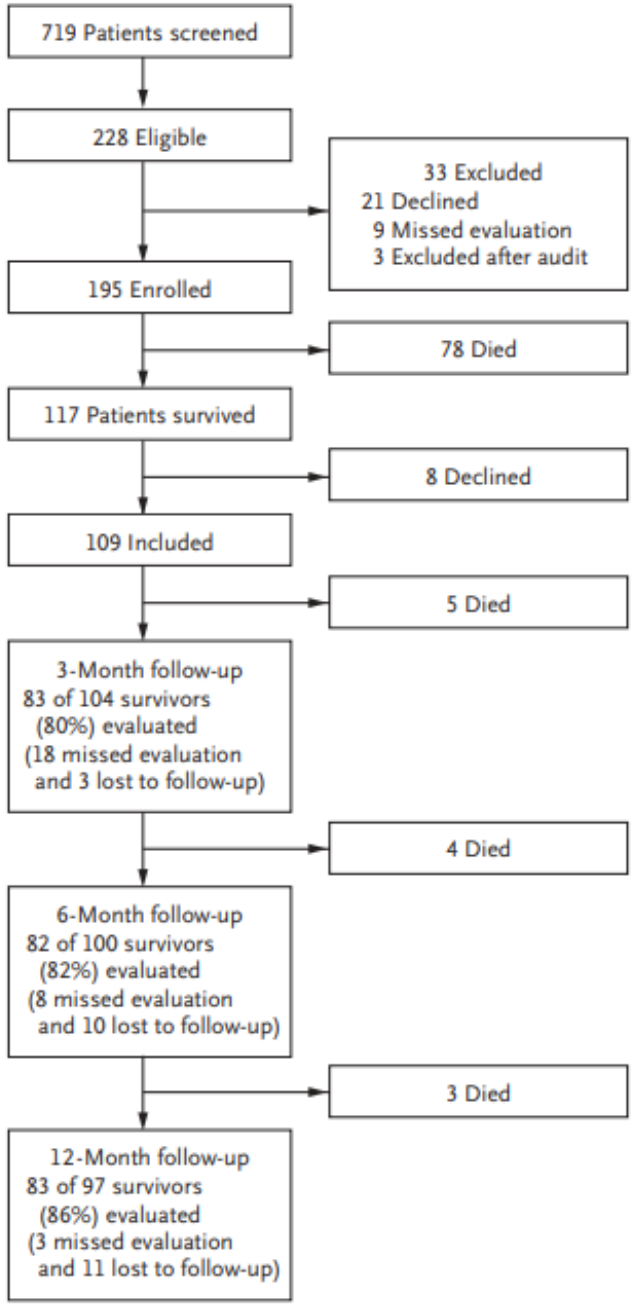
Length of ICU stay in days, median (IQR)	5 (3-10)	...
2-3 d (Quartile 1)	27,387	35.5
4-5 d (Quartile 2)	15,065	19.5
6-10 d (Quartile 3)	16,401	21.3
> 10 d (Quartile 4)	18,279	23.7

96,177 patients admis en réanimation en France en 2018.

40%
Faiblesses musculaires

Martin, Chest, 2022


Cluster 1
n = 52,254
Cluster 2
n = 13,775
Cluster 3
n = 11,103
1.0
0.8
0.6
0.4
0.2
0.0
-52 -43 -34 -25 -16 -8 -1 6 12 19 26 33 40 47
Acute Care Hospitalization (ACH)
Rehabilitation Facility (RF)
Skilled Nursing Home (SNH)*
Death
Intensive Care Unit (ICU)
Hospital At Home (HAH)
Psychiatric Ward (PW)
Home
Discharge from ICU = baseline date



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 20, 2003 VOL. 348 NO. 8

One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

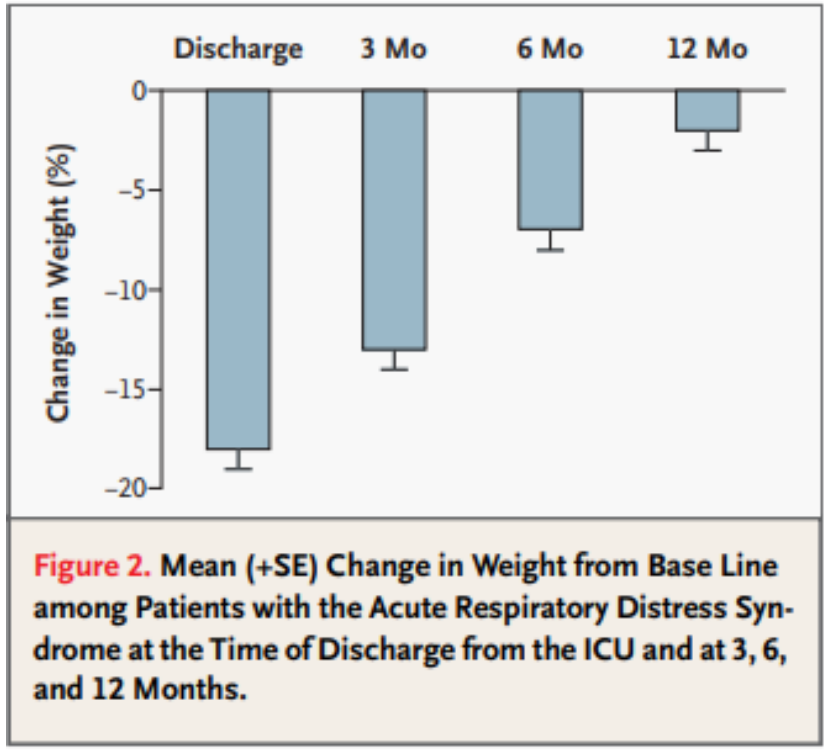


Figure 2. Mean (+SE) Change in Weight from Base Line among Patients with the Acute Respiratory Distress Syndrome at the Time of Discharge from the ICU and at 3, 6, and 12 Months.

Herridge, NEJM, 2003

Table 3. Ability to Exercise and Return to Work and Health-Related Quality of Life among Patients with the Acute Respiratory Distress Syndrome during the First 12 Months after Discharge from the ICU.

Outcome	3 Months	6 Months	12 Months
Distance walked in 6 min			
No. evaluated	80*	78†	81‡
Median — m	281	396	422
Interquartile range — m	55–454	244–500	277–510
Percentage of predicted value§	49	64	66
Returned to work — no./total no. (%)¶	13/83 (16)	26/82 (32)	40/82 (49)‖
Returned to original work — no./total no. (%)	10/13 (77)	23/26 (88)	31/40 (78)
SF-36 score**			
Physical functioning			
Median (normal value)	35 (90)	55 (89)	60 (89)
Interquartile range	15–58	30–75	35–85
Physical role			
Median (normal value)	0 (85)	0 (84)	25 (84)
Interquartile range	0–0	0–50	0–100
Pain			
Median (normal value)	42 (77)	53 (77)	62 (77)
Interquartile range	31–73	37–84	41–100
General health			
Median (normal value)	52 (78)	56 (77)	52 (77)
Interquartile range	35–67	36–74	35–77
Vitality			
Median (normal value)	45 (69)	55 (68)	55 (68)
Interquartile range	30–55	28–63	28–63
Social functioning			
Median (normal value)	38 (88)	63 (88)	63 (88)
Interquartile range	19–69	38–88	38–100
Emotional role			
Median (normal value)	33 (84)	67 (84)	100 (84)
Interquartile range	0–100	0–100	17–100
Mental health			
Median (normal value)	68 (78)	70 (78)	72 (78)
Interquartile range	54–80	54–88	52–88

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One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

Figure 4 Lean Body Mass Loss Over 20 days following surgery and critical illness (20 kg over 20 days = 1 kg lean body mass lost/day).

Herridge, NEJM, 2003

Wischmeyer, Critical Care 2015

Capacités musculaires à 1 an

TABLE 1. Biomechanical Characteristics of ICU Survivors and Age- and Sex-Matched Controls

Characteristic	ICU survivors ($n = 16$)	Controls ($n = 15$)	Differences (95% Confidence Interval)	p
Maximum contraction				
Extension MVC (Nm)	179±66	230±57	51 (6–95)	0.03
Flexion MVC (Nm)	79±22	93±22	14 (–2–30)	0.08
Handgrip strength (Nm)	39±7	50±7	11 (6–16)	0.001
Fast contraction				
Absolute rate of force development (Nm/sec)	868±372	1739±470	871 (561–1181)	0.001
Relative rate of force development (%MVC/sec)	531±257	765±190	234 (66–401)	0.008
Time from force onset to 1/3 MVC (msec)	127±42	101±20	26 (2–56)	0.04
Electromechanical delay (msec)	39±6	35±6	4 (–0.2–8)	0.06
EMG onset (msec)	282±47	277±26	4 (–24–31)	NS
Reaction time (msec)	320±46	312±30	8 (–21–36)	NS
EMG coactivation (% of maximum EMG)	17 (12–35)[a]	18 (14–20)[a]	NA	NS
Agonist EMG motor drive (% of maximum EMG)	81 (54–98)[a]	91 (69–106)[a]	NA	NS
Endurance contraction				
Endurance time (sec)	136±84	226±111	90 (17–160)	0.02
EMG coactivation (% of maximum EMG)	18 (10–38)[a]	14 (9–20)[a]	NA	NS
Agonist EMG motor drive (% of maximum EMG)	28 (26–33)[a]	27 (25–33)[a]	NA	NS

MVC = maximum voluntary contraction; EMG = electromyography; NA = not applicable; NS = not significant.

Data are expressed as means ± SD and 95% confidence interval for differences, except for a non-Gaussian distribution,[a] where data are presented as medians (interquartile range).

Poulsen, CCM, 2013

Capacités aérobiques à 5 ans

ORIGINAL

Aerobic exercise capacity in long-term survivors of critical illness: secondary analysis of the post-EPaNIC follow-up study

Nathalie Van Aerde[1], Philippe Meersseman[2], Yves Debaveye[1,3], Alexander Wilmer[2], Michael P. Casaer[1,3], Jan Gunst[1,3], Joost Wauters[2], Pieter J. Wouters[1,3], Kaatje Goetschalckx[4], Rik Gosselink[5], Greet Van den Berghe[1,3] and Greet Hermans[1,2*]

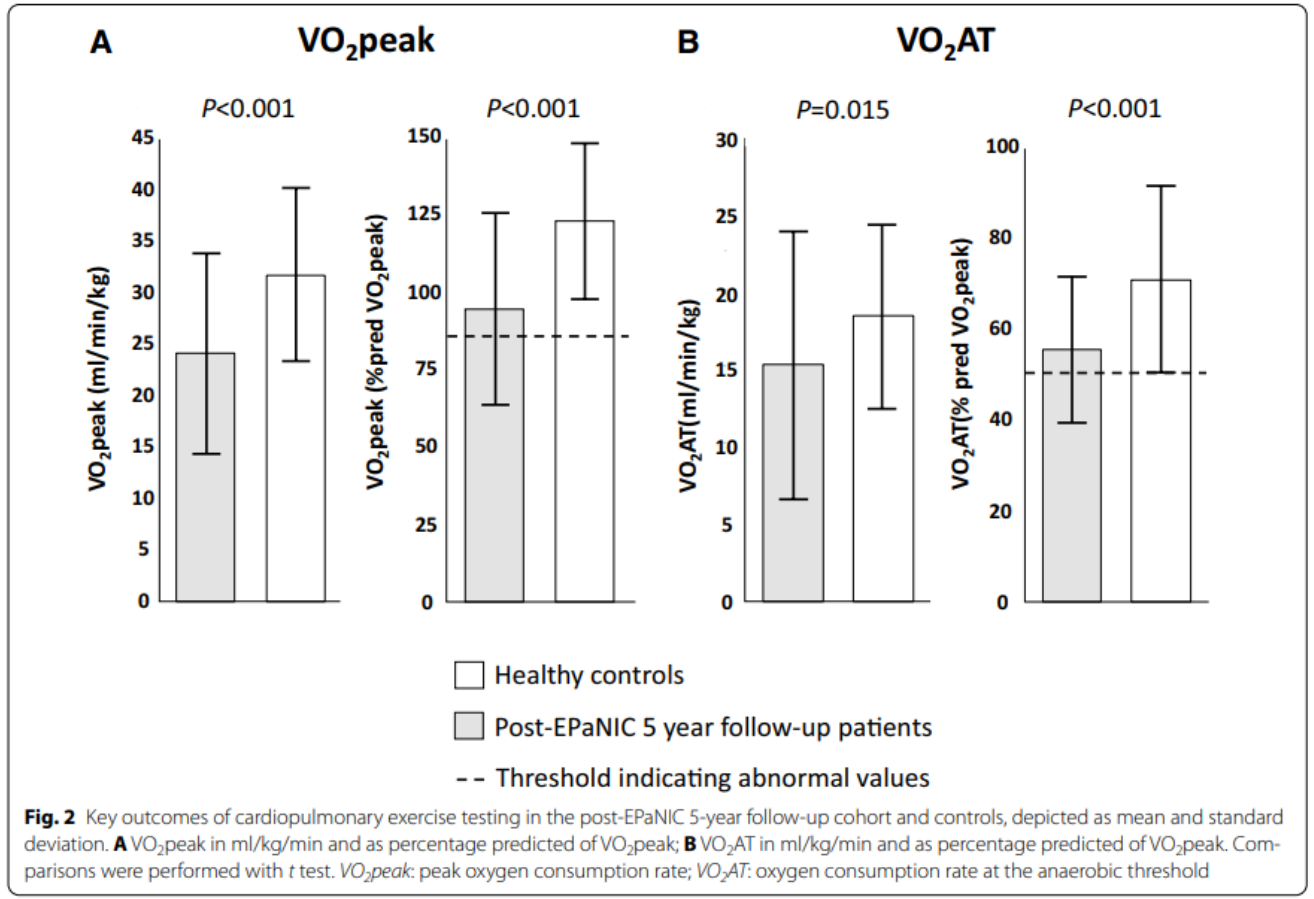
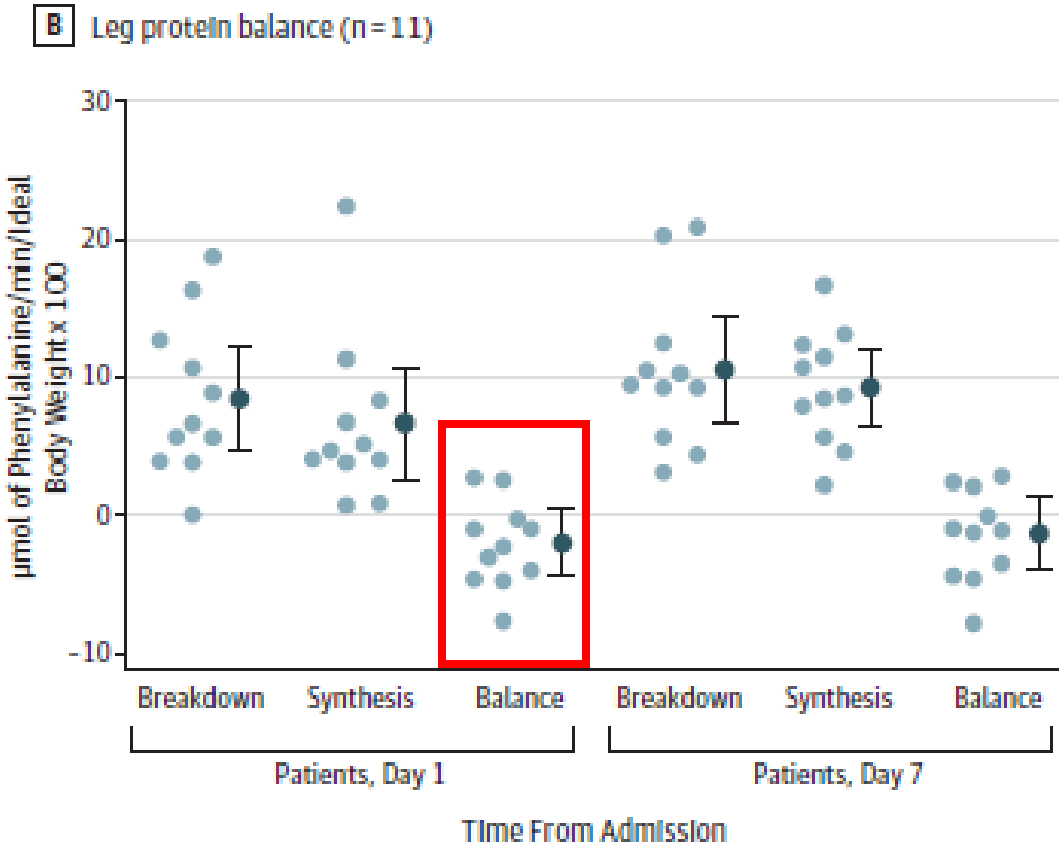
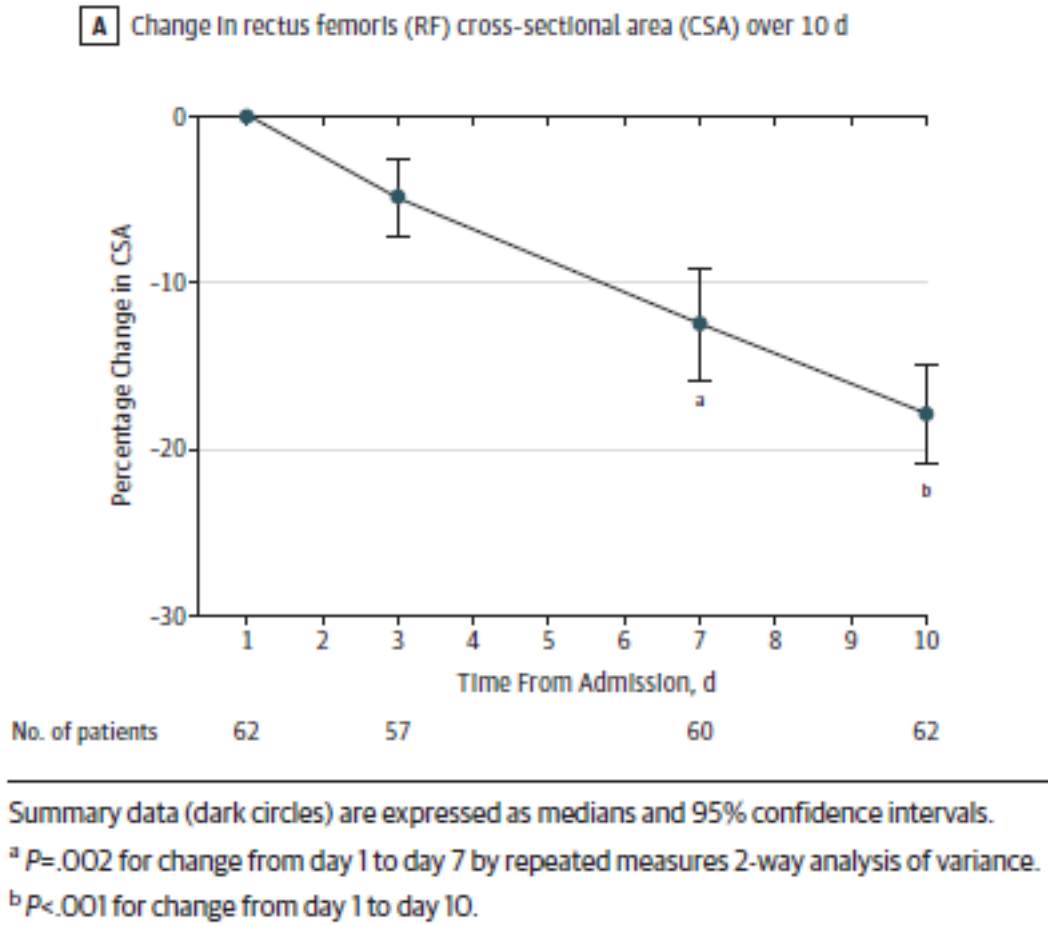


Fig. 2 Key outcomes of cardiopulmonary exercise testing in the post-EPaNIC 5-year follow-up cohort and controls, depicted as mean and standard deviation. **A** VO_2peak in ml/kg/min and as percentage predicted of VO_2peak; **B** VO_2AT in ml/kg/min and as percentage predicted of VO_2peak. Comparisons were performed with *t* test. *VO_2peak*: peak oxygen consumption rate; *VO_2AT*: oxygen consumption rate at the anaerobic threshold

Van Aerde, ICM,2021

Une atteinte précoce et rapide…





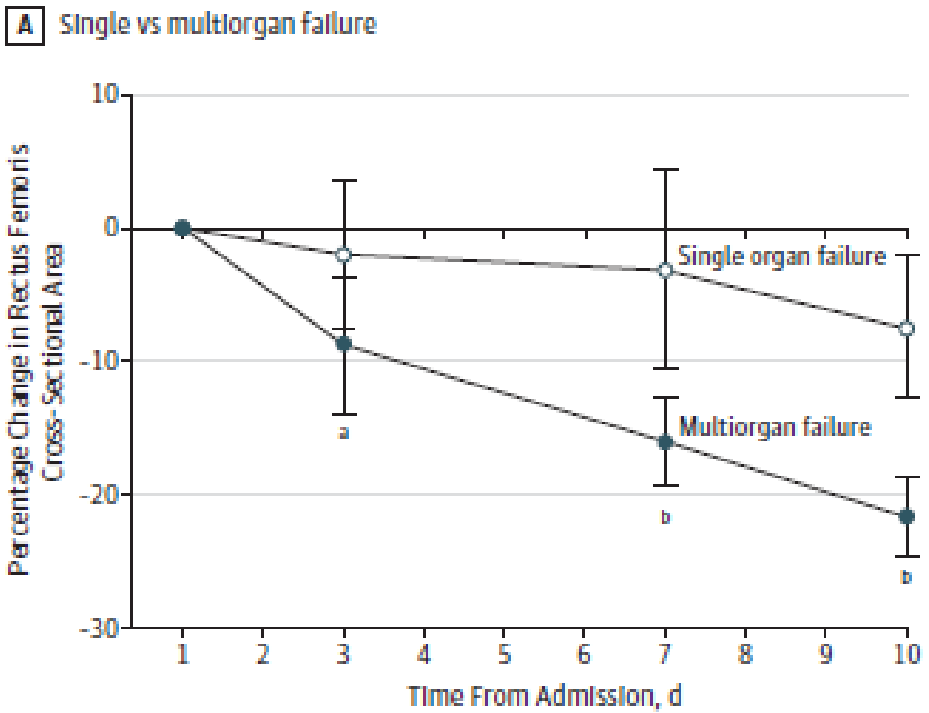
Summary data (dark circles) are expressed as medians and 95% confidence intervals.

[a] P=.002 for change from day 1 to day 7 by repeated measures 2-way analysis of variance.

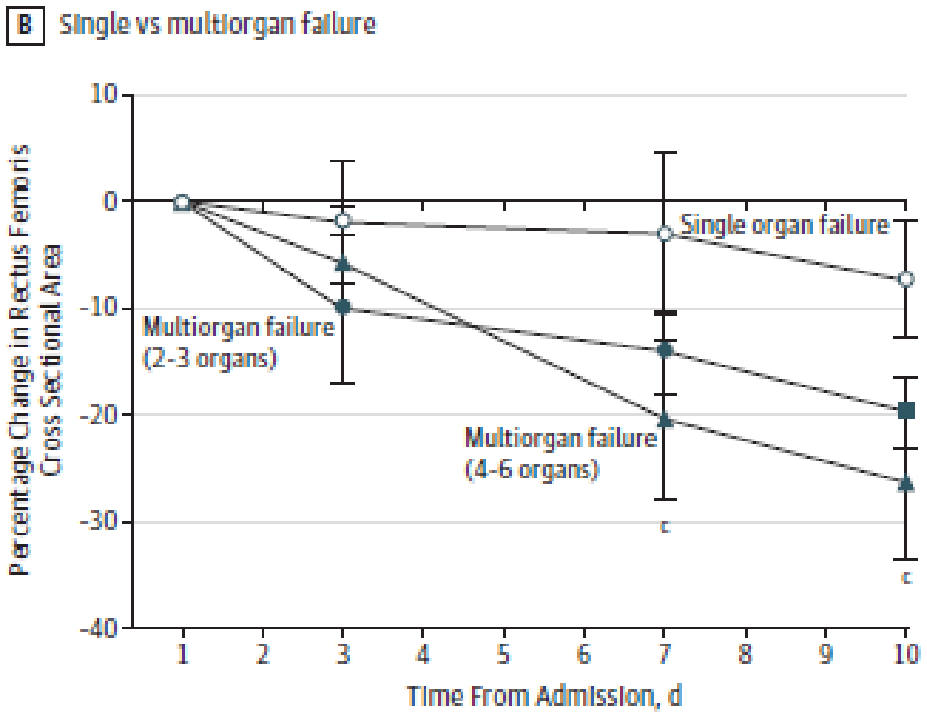
[b] P<.001 for change from day 1 to day 10.

Puthucheary, JAMA, 2013

…majorée par la défaillance multi-organique.



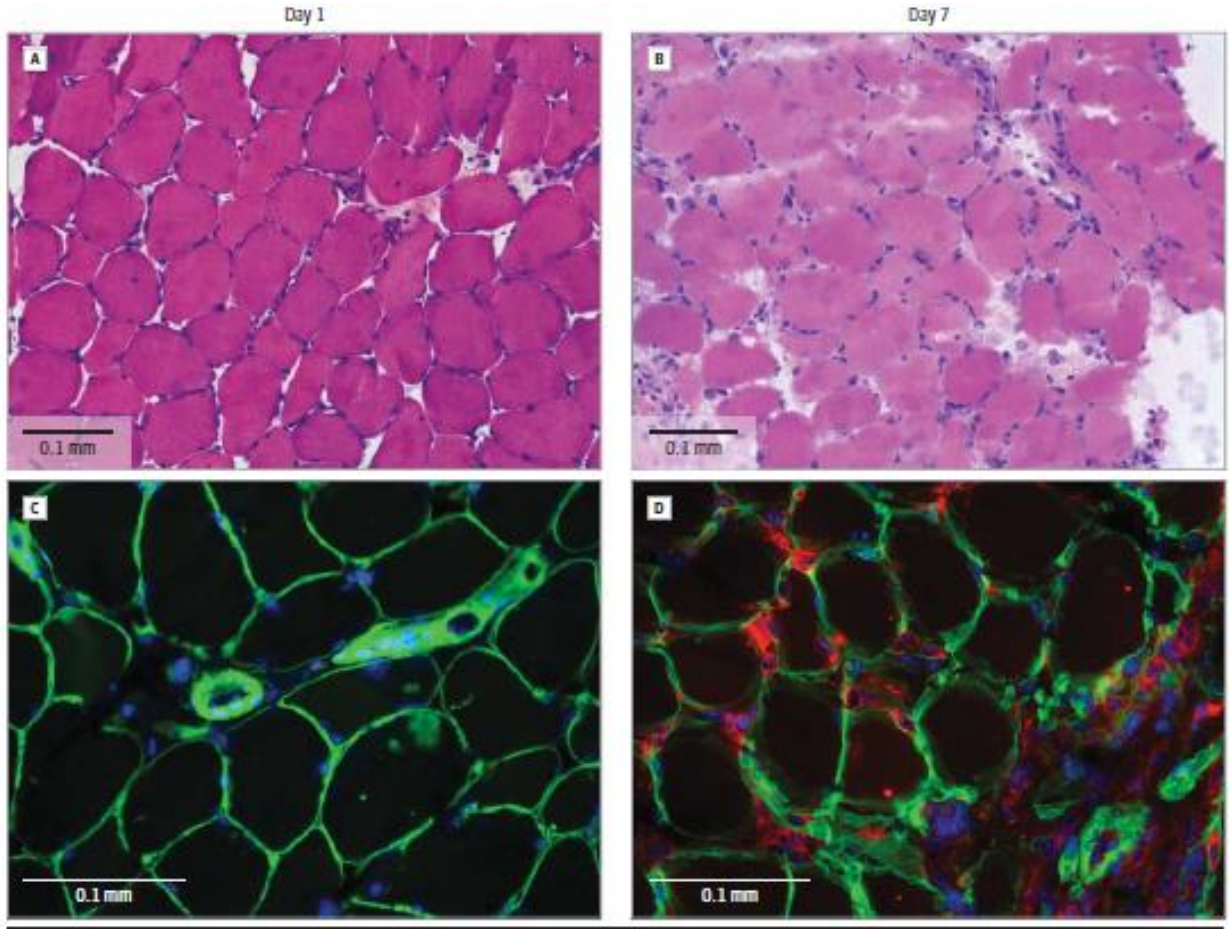
No. of patients				
Single organ failure	15	14	15	15
Multiorgan failure	47	43	45	47



No. of patients				
Single organ failure	15	14	15	15
Multiorgan failure				
2-3 Organs	33	31	32	33
4-6 Organs	14	12	13	14

Puthucheary, JAMA, 2013

Des répercussions musculaires en 7 jours....



- Dès J1:

-Augmentation de la destruction protéinique vs. synthèse protéinique

- Entre J1 et J7:

-Diminution de 10% de la CSA du Droit Fémoral

-Diminution de 20% de la CSA des Fibres Musc

-Diminution de 30% du Ratio Protéine/ADN

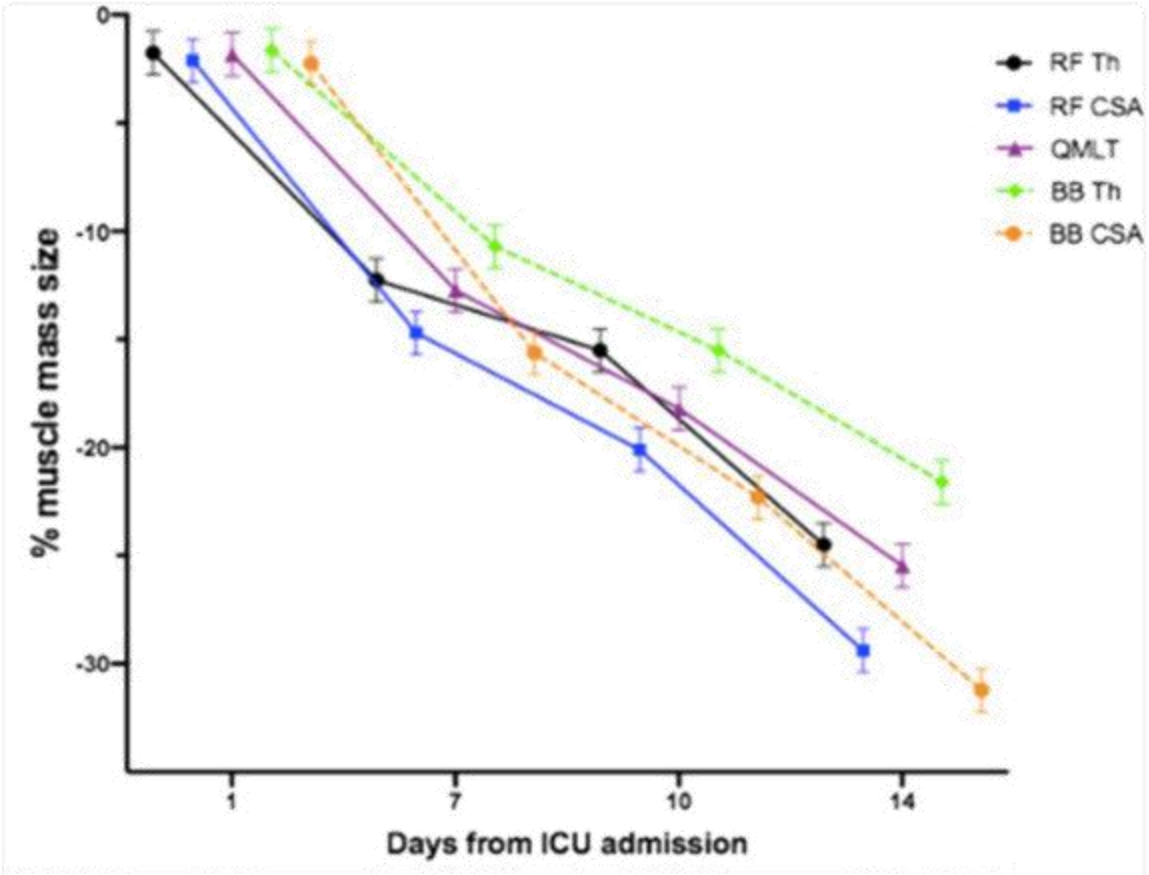
A J10:

- Diminution de 18% de la CSA du Droit Fémoral

Puthucheary, JAMA, 2013

Les patients perdent en moyenne 2% de masse musculaire par jour!

150g de viande/Jour



% RF th	-1.75	-12.25	-15.5	-24.5
% RF CSA	-2.10	-14.7	-20.1	-29.4
% QMLT	-1.82	-12.74	-18.2	-25.48
% BB Th	-1.64	-10.7	-15.5	-21.6
% BB CSA	-2.23	-15.61	-22.30	-31.22

Fazzini, Crit care, 2023

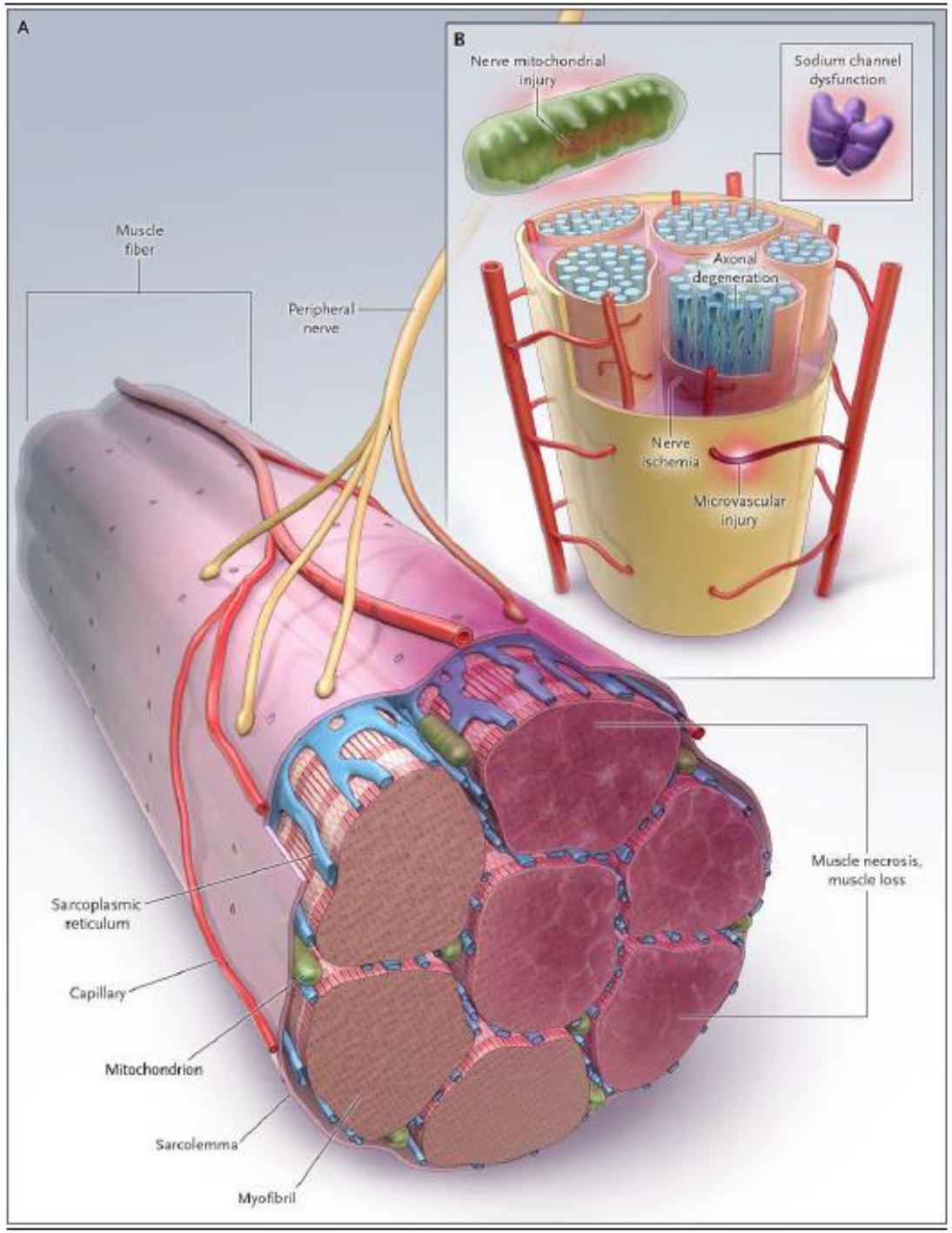


Table 3. Clinical Risk Factors and Pathophysiological Features of Critical Illness Polyneuropathy and Critical Illness Myopathy.

Variable	Reference
Clinical risk factors of both critical illness polyneuropathy and critical illness myopathy	
Female sex	De Jonghe et al.[11]
Sepsis	Garnacho-Montero et al.[28]
Catabolic state	Trojaborg et al.,[15] Garnacho-Montero et al.[28]
Multiorgan system failure	De Jonghe et al.[11]
Systemic inflammatory response syndrome	Jaber et al.,[33] Levine et al.[34]
Long duration of mechanical ventilation	De Jonghe et al.[11]
Immobility	Levine et al.,[32] Papazian et al.,[39] Iwashyna et al.[41]
Hyperglycemia	Van den Berghe et al.[13]
Glucocorticoids	De Jonghe et al.[11]
Neuromuscular blocking agents	MacFarlane and Rosenthal,[3] Leatherman et al.[12]
Pathophysiological processes	
Critical illness polyneuropathy	
Motor nerves affected more than sensory nerves	Bolton et al.[4]
Secondary denervation muscle injury (myopathy)	Bolton et al.[4]
Proposed mechanisms	
Nerve ischemia	Bolton[20]
Nerve microvascular injury	Bolton,[20] Fenzi et al.[21]
Nerve mitochondrial injury	Van den Berghe et al.[22]
Sodium channelopathy	Rich and Pinter[26]
Critical illness myopathy	
Primary myopathy — selective myosin loss, muscle necrosis (e.g., ubiquitin–proteasome proteolysis)	Derde et al.[8]
Mitochondrial dysfunction	Carré et al.[29]
Oxidative stress	Reid and Moylan[30]
Sodium channelopathy	Rich and Pinter[26]

Neuromyopathie de réanimation

Faiblesses musculaires acquises en réanimation

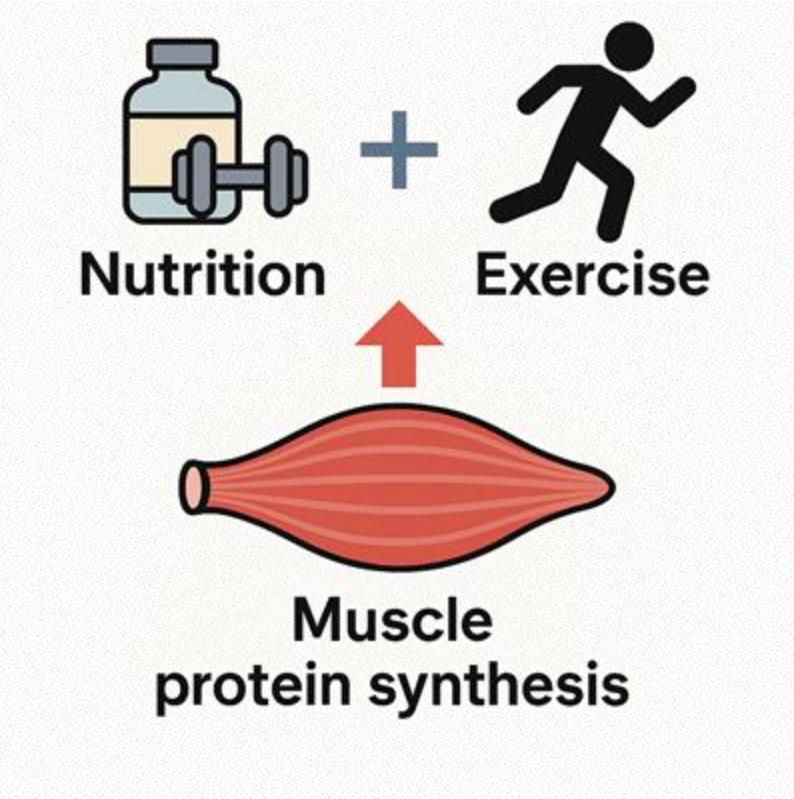
ICU acquired weakness

Critical illness weakness

Kress, NEJM, 2014

Contexte

Healthy



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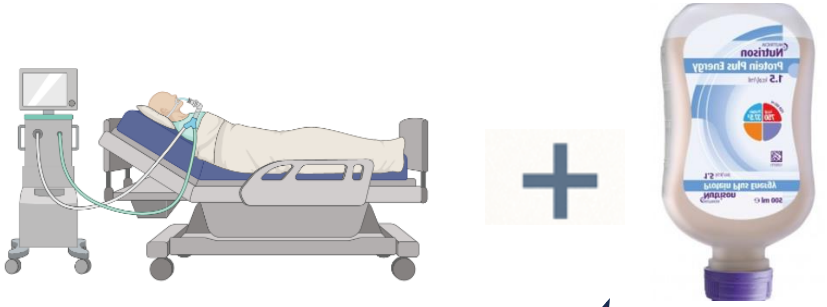
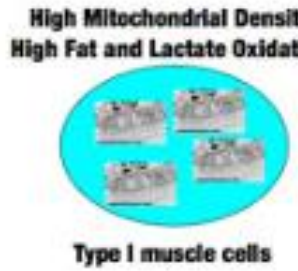
ICU

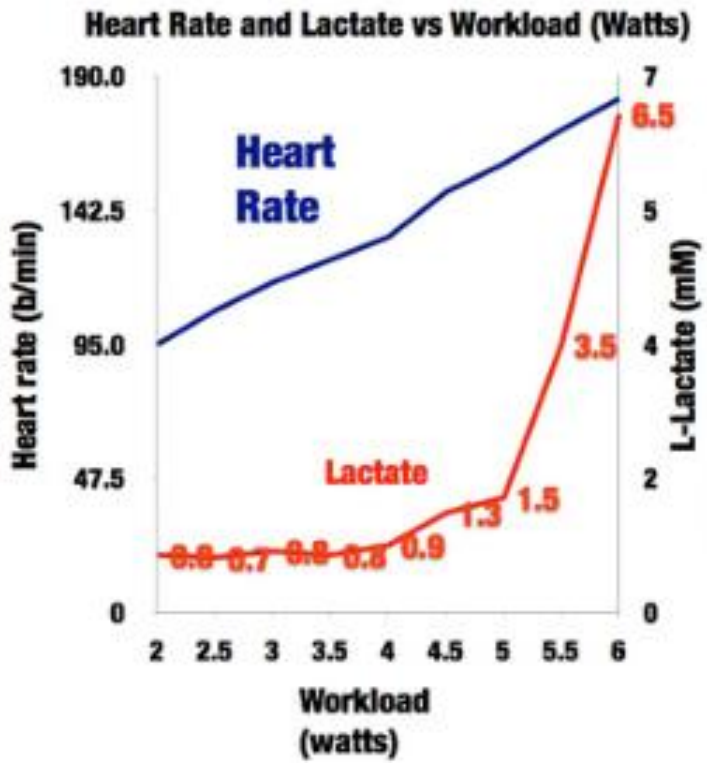


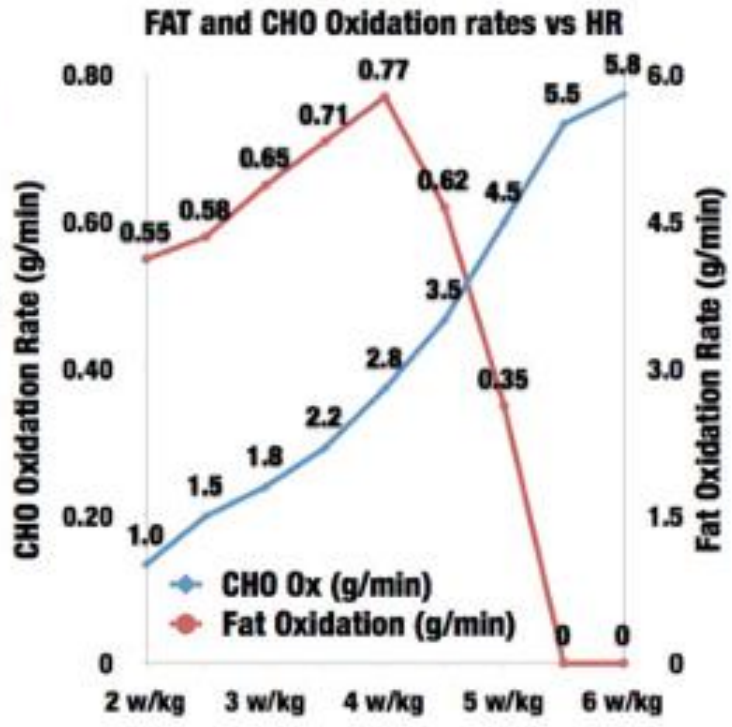
Verrou lipidique et Résistance anabolique



Exercise Physiology Testing

World Class Athlete





Wischmeyer, Crit care, 2015

Chute des réserves de glycogène

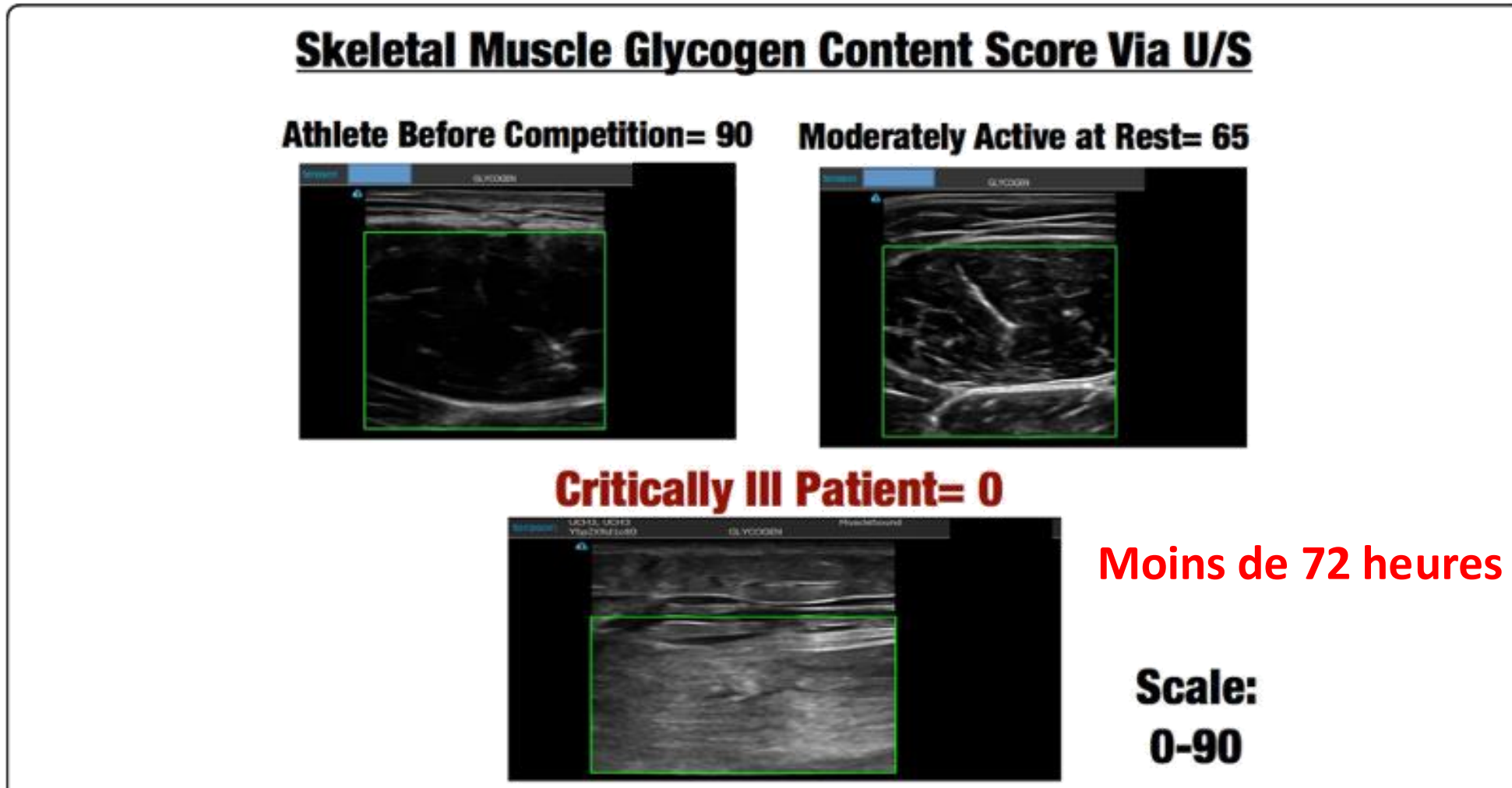
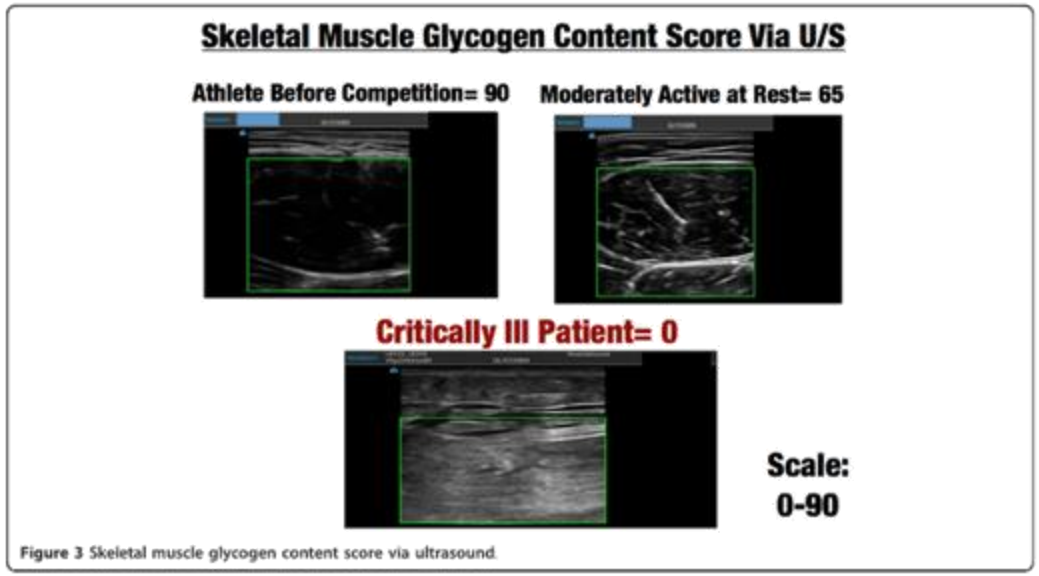


Figure 3 Skeletal muscle glycogen content score via ultrasound.

Chute des réserves de glycogène



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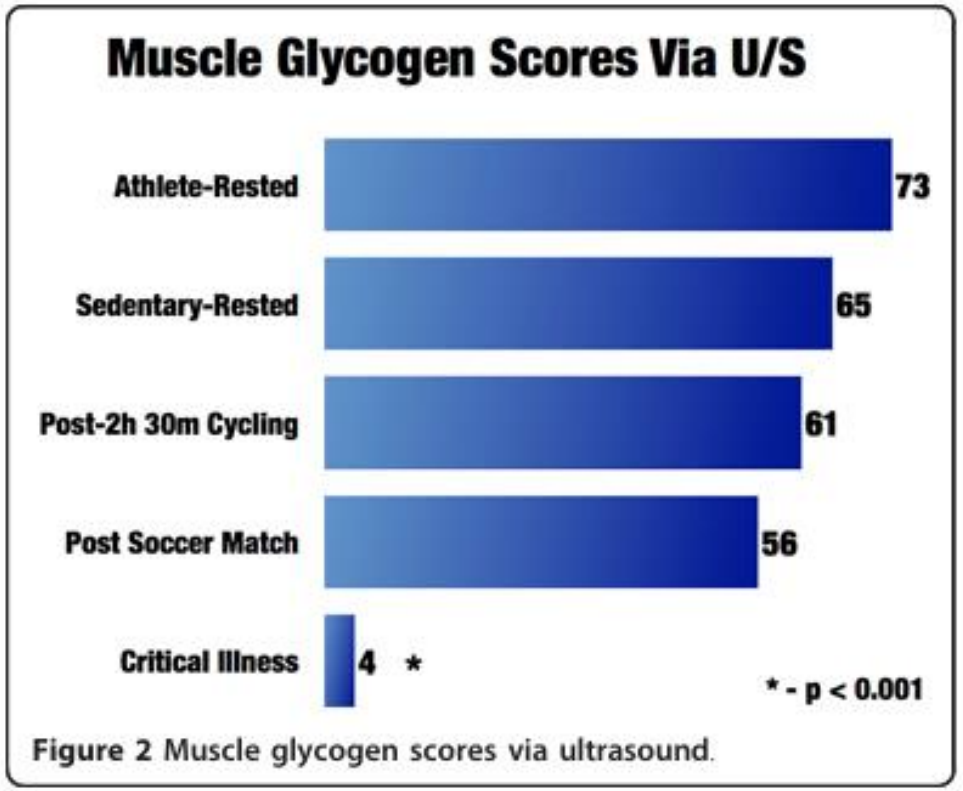


Figure 2 Muscle glycogen scores via ultrasound.

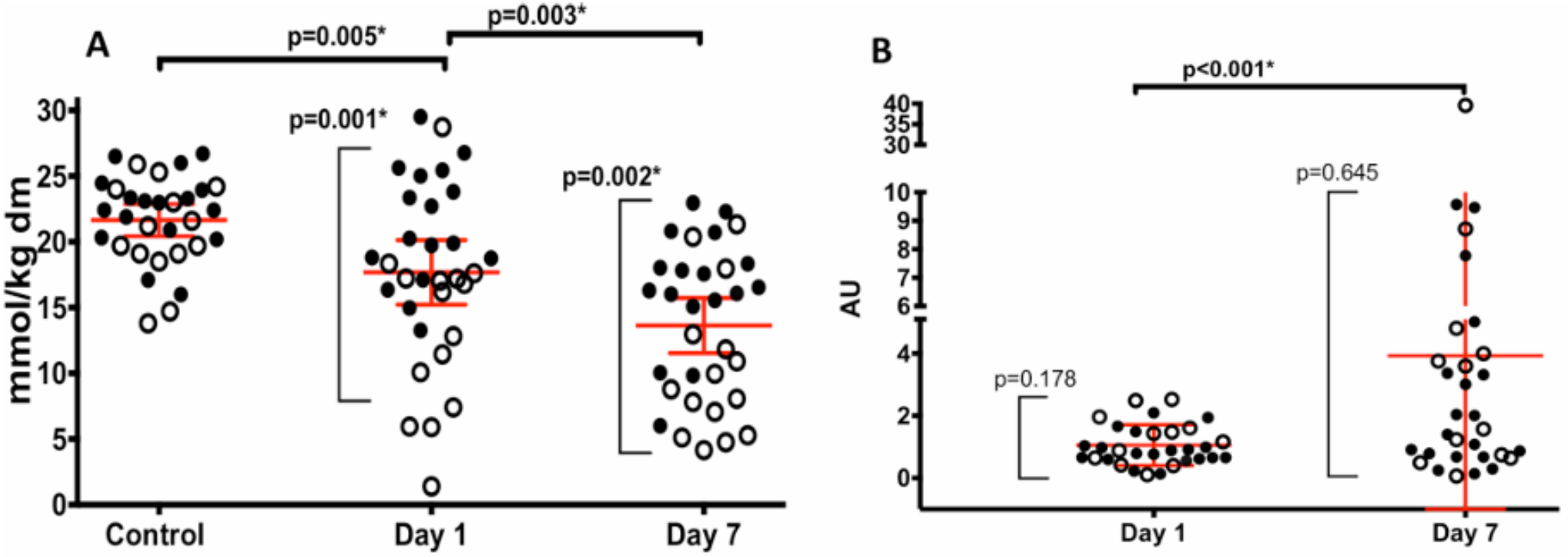
+ Insulinorésistance

↓ ATP

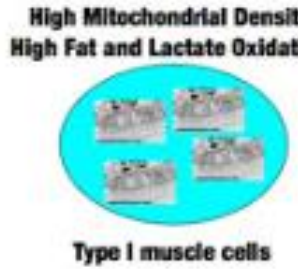
↑ AMPK → baisse de la synthèse protéique (mTORC1)

Wischmeyer, Crit care, 2015

ATP et AMPK



Puthucheary ZA, et al. Thorax 2018



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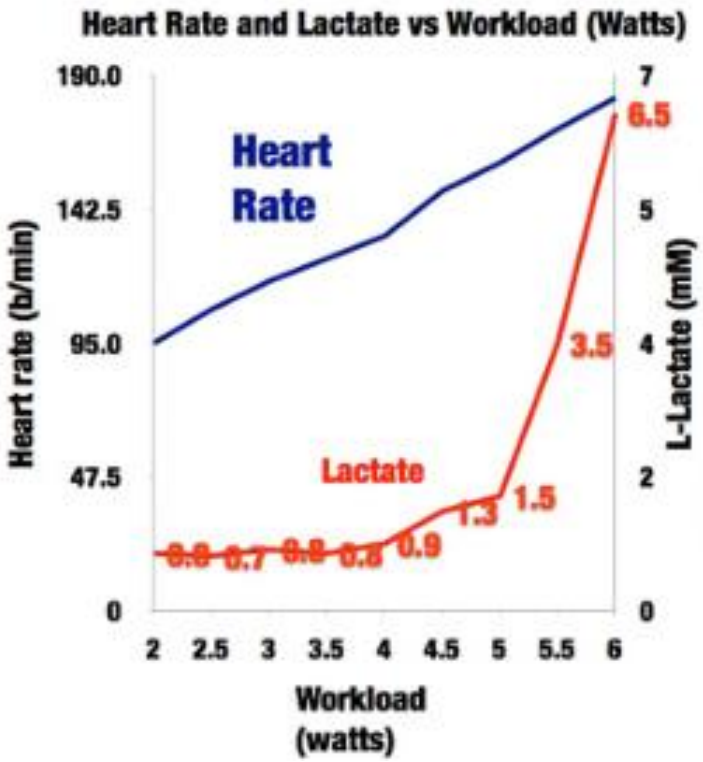
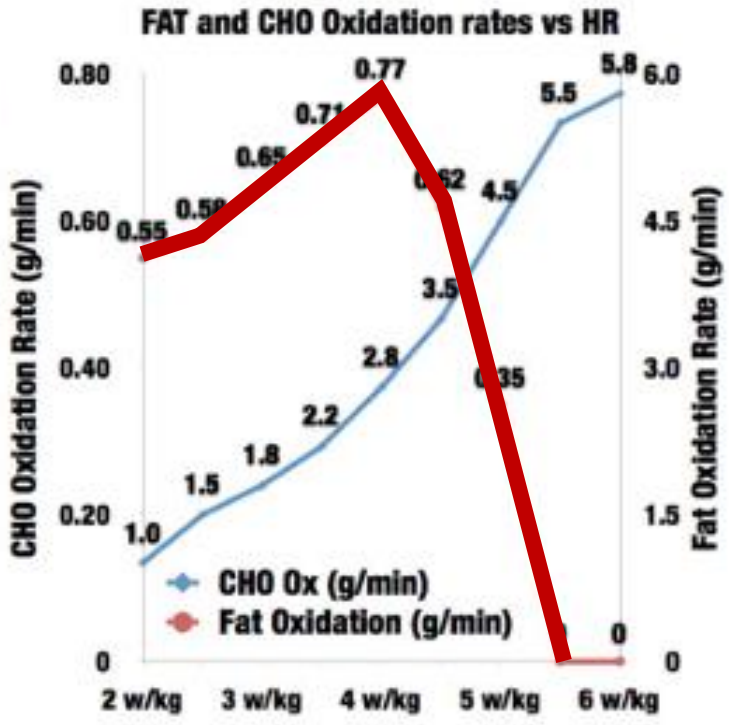
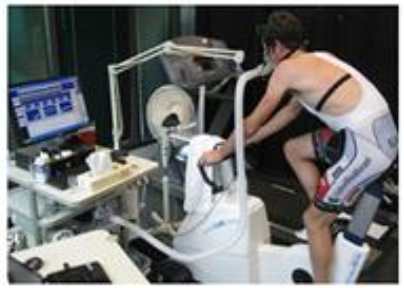


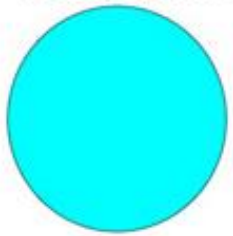


Wischmeyer, Crit care, 2015

Post-Burn Patient Testing

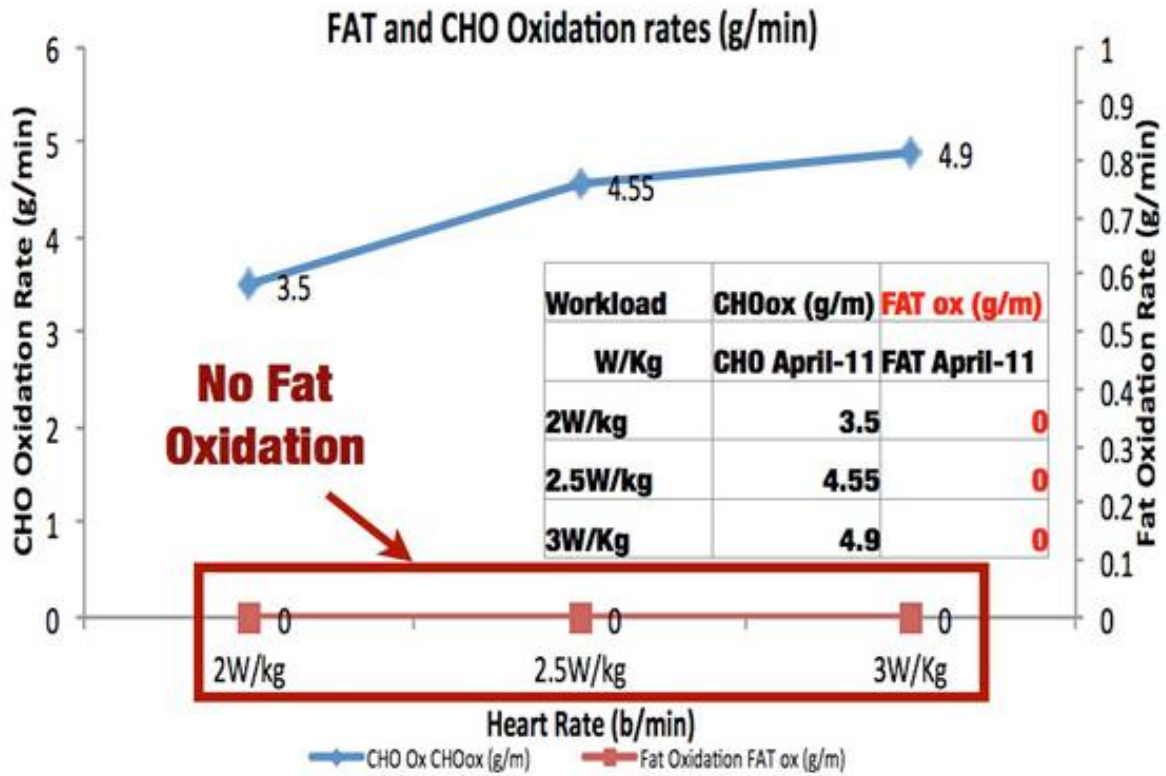


No Mitochondrial Fxn
No Fat Oxidation



Type I muscle cells

EXERCISE TESTING RESULTS



Workload	CHOox (g/m)	FAT ox (g/m)
W/Kg	CHO April-11	FAT April-11
2W/kg	3.5	0
2.5W/kg	4.55	0
3W/Kg	4.9	0

Wischmeyer, Crit care, 2015

Le verrou lipidique

63 patients intubés et ventilés>48h

Biopsies du VL
Prélèvements sanguins au **J1** et J**7**

Étapes	**Résultats**
Baisse d'enzymes de β-oxydation	–25 % à –40 % sur 7 jours
Diminution de PGC-1α et ADNmt	–27 % & –1 859 copies
Augmentation phosphocholine	+847 UA
ATP musculaire ↓	–4,8 mmol·kg-1

Conséquences

Les AG ne rentrent plus efficacement dans la mitochondrie.

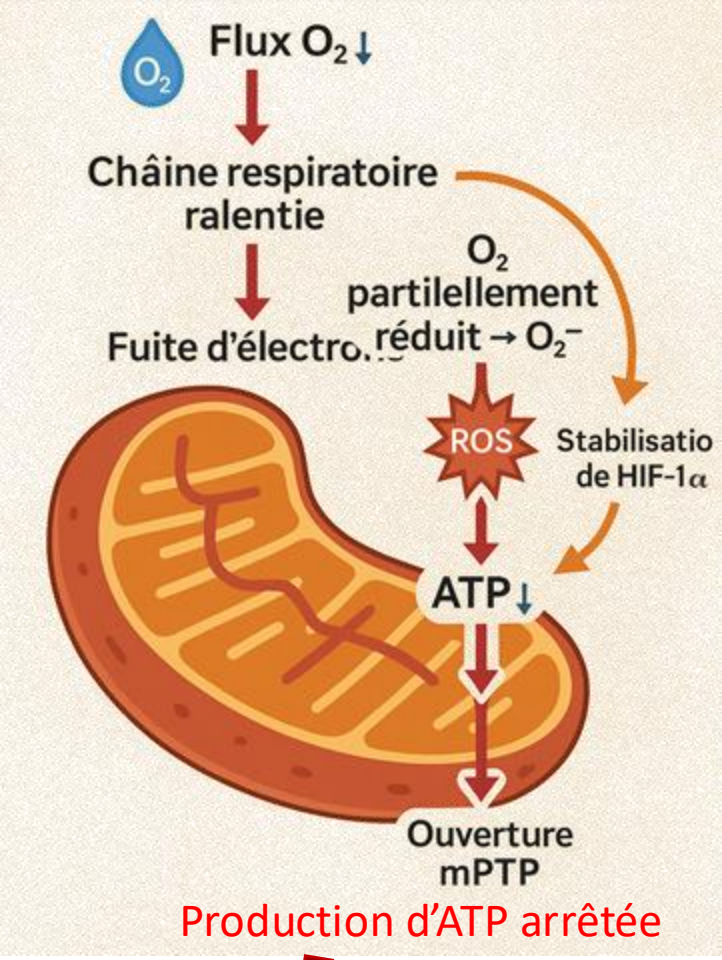
Moins de mitochondries = moins de capacité à produire de l'ATP.

Stockage/accumulation de lipides non oxydés.

Moins d'énergie pour la synthèse protéique.

Puthucheary ZA, et al. Thorax 2018

Stress mitochondrial

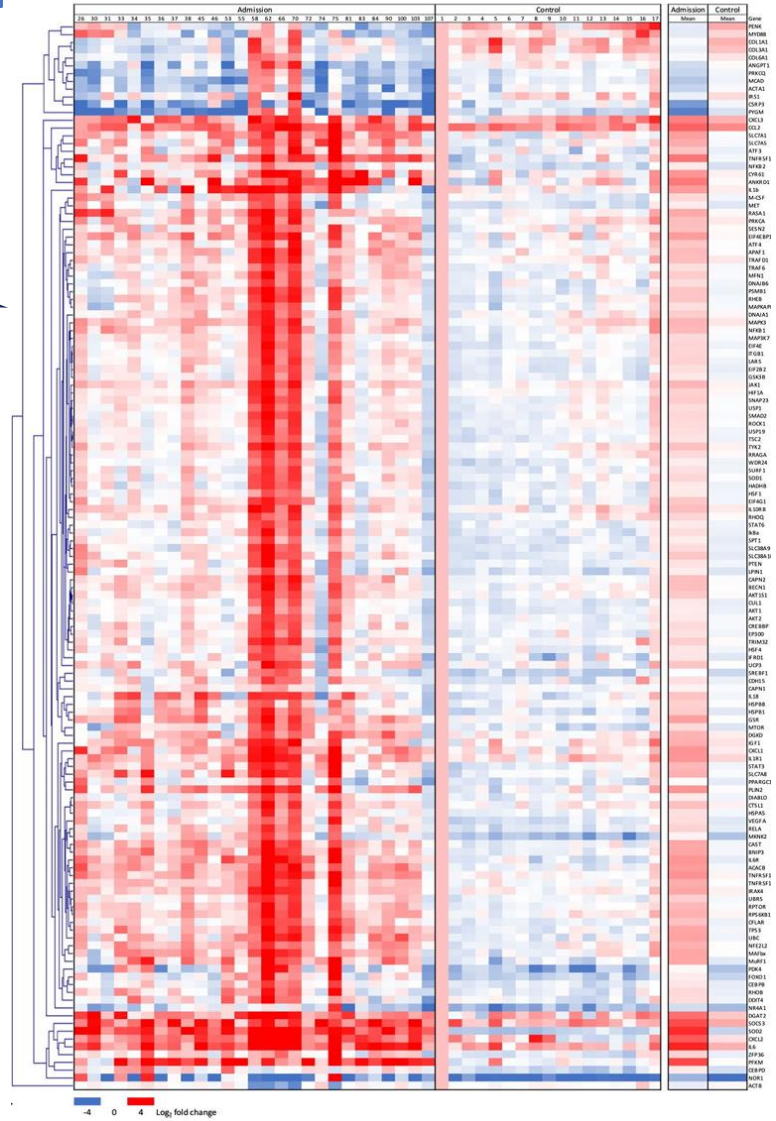


Signal d'alerte cytoplasmique

Activation AMPK

Résistance anabolique

Digestion myofibrille



Jameson, Crit Care, 2023

Résistance anabolique

POPULATION

15 ICU patients
10 healthy controls

METHOD

Double-tracer study
(IV + duodenal)
Biopsies of vastus lateralis

RESULTS

Absorption of AAs

Whole-body protein balance

Muscle incorporation **–60%**

Pic plasmatique de phénylalanine exogène plus lent mais quantité totale absorbée égale

Incorporation de phénylalanine dans la myofibrille :
Sains : 0,017 ± 0,009 MPE
ICU : 0,007 ± 0,007 MPE

Chapple, Am J Respir Crit Care Med, 2022

Cascade de la faiblesse musculaire en réanimation

Inflammation systémique (IL-6, TNF, sepsis)

↓

Lésion endothéliale → hypoperfusion & oédème

↓

Ischémie nerveuse + canaux Na dysfonctionnels → dénervation

↓

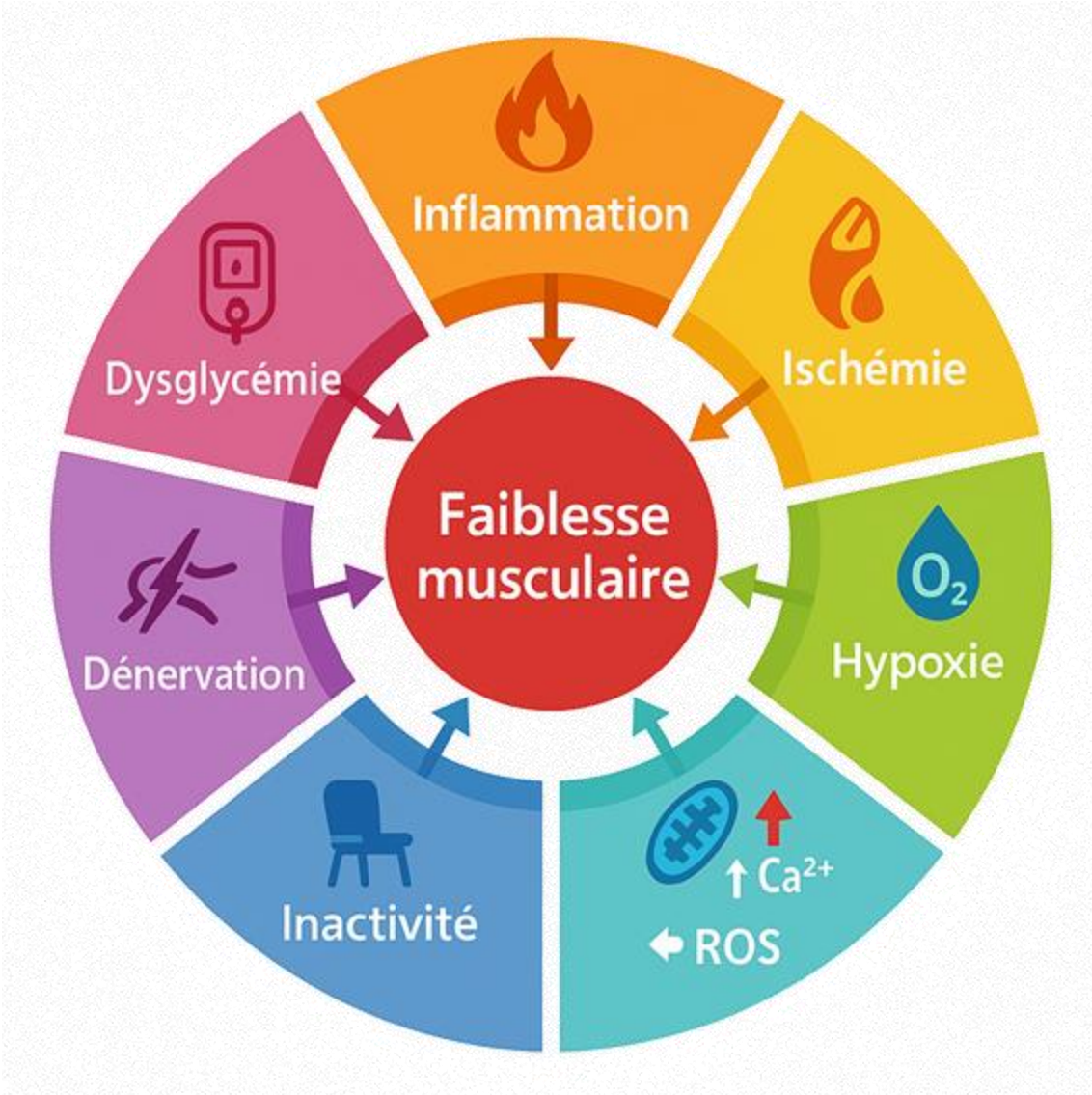
Muscle inactif hypoxique

↓

Crise mitochondriale + ↓ATP ↑Ca ↑ROS

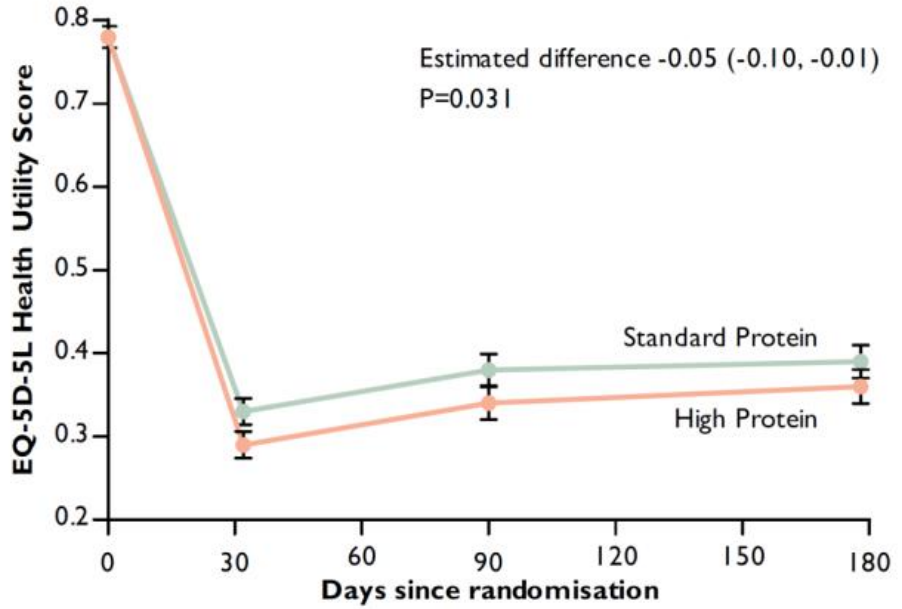
↓

Destruction des myofibrilles → Faiblesse musculaire



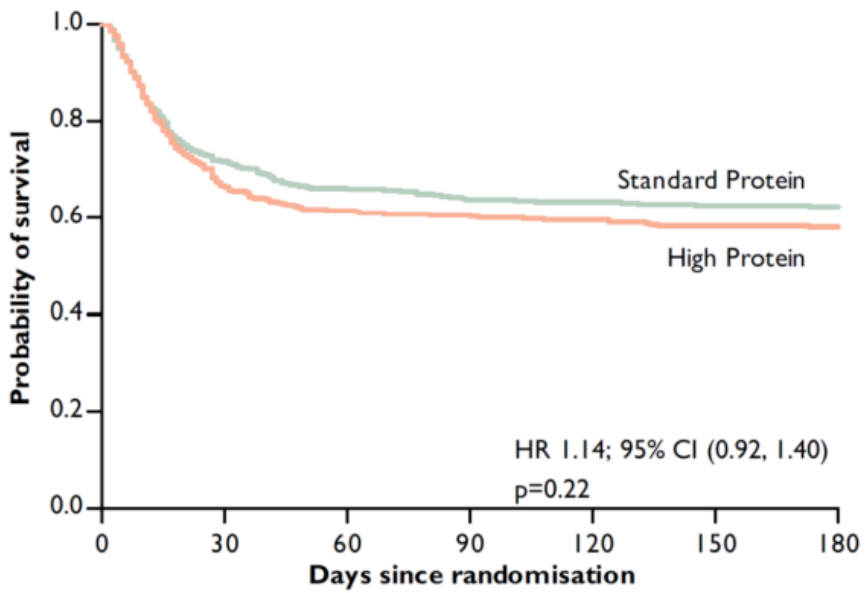
Générée par IA

Intérêt d'une supplémentation protéinique?



No. of observations			
Standard Protein (N=430)	407	396	394
High Protein (N=419)	398	386	393

The secondary endpoint overall survival over 180 days.

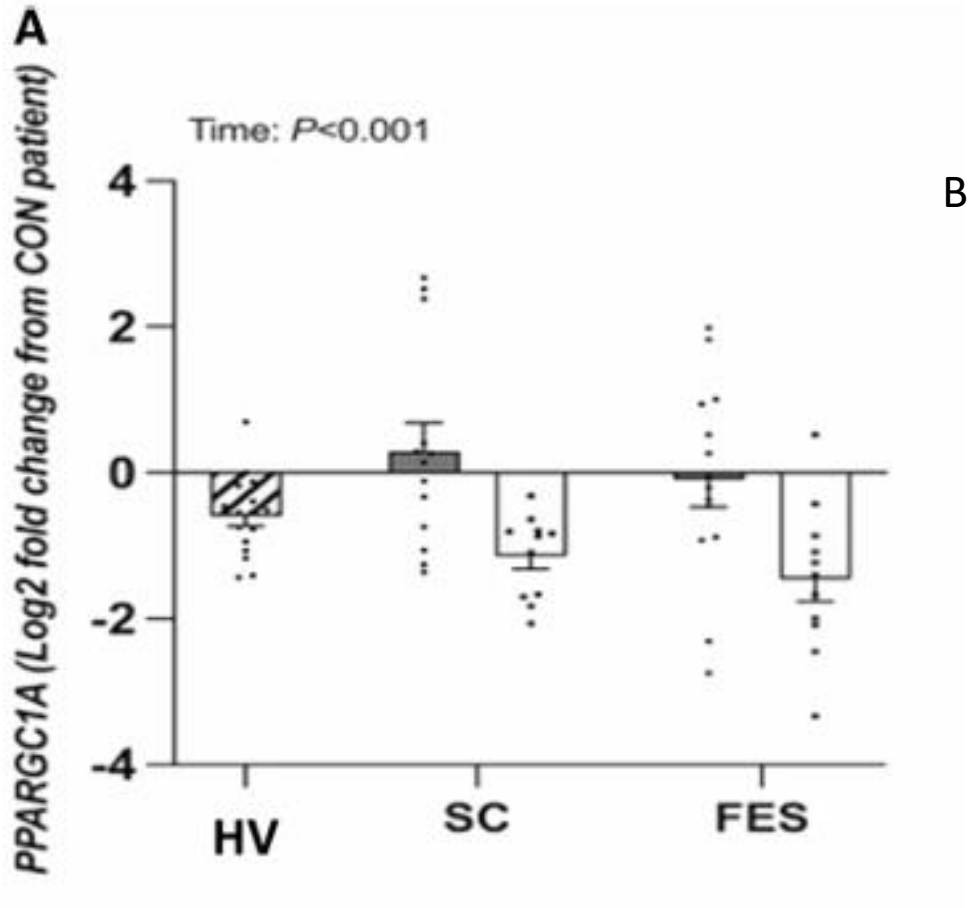


No. at risk							
Standard Protein	465	316	280	262	254	251	250
High Protein	470	286	256	247	241	235	233

Résultats similaires pour l'étude EFFORT Protein (Heyland, Lancet, 2023)

Bels, Lancet, 2024

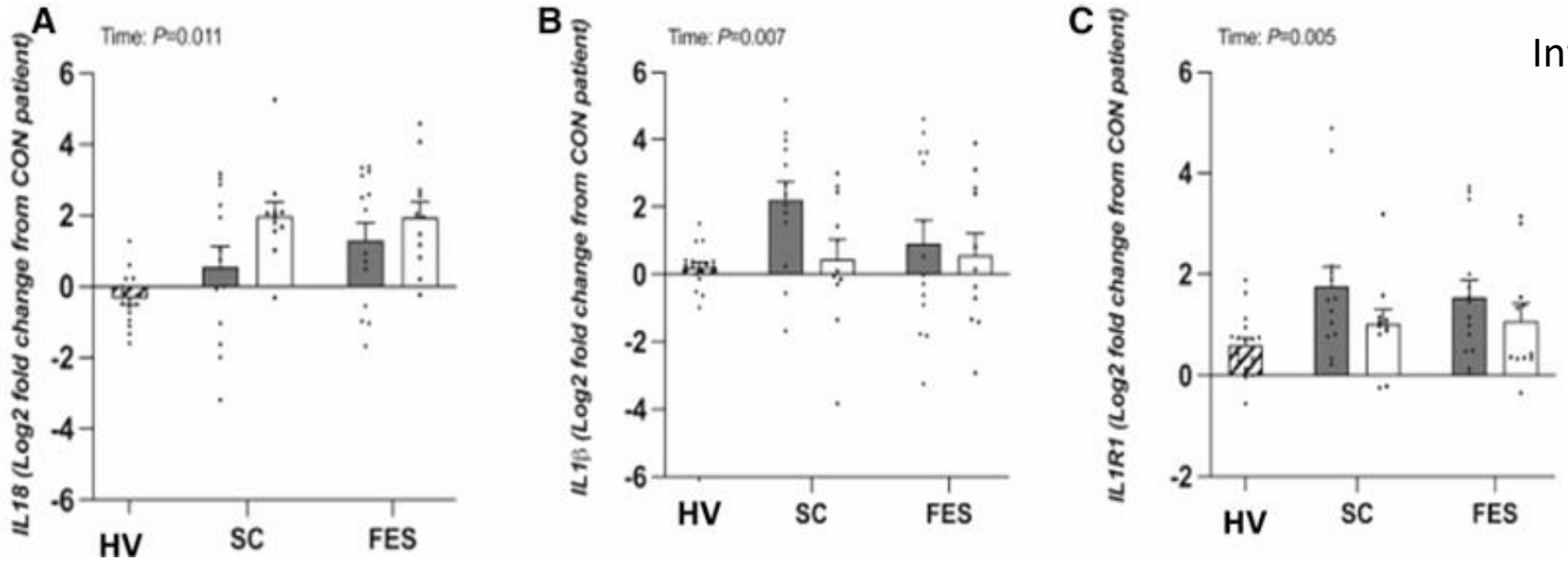
Intérêt d'une activité musculaire précoce?



Biogénèse mitochondriale

Jameson, Crit Care, 2023

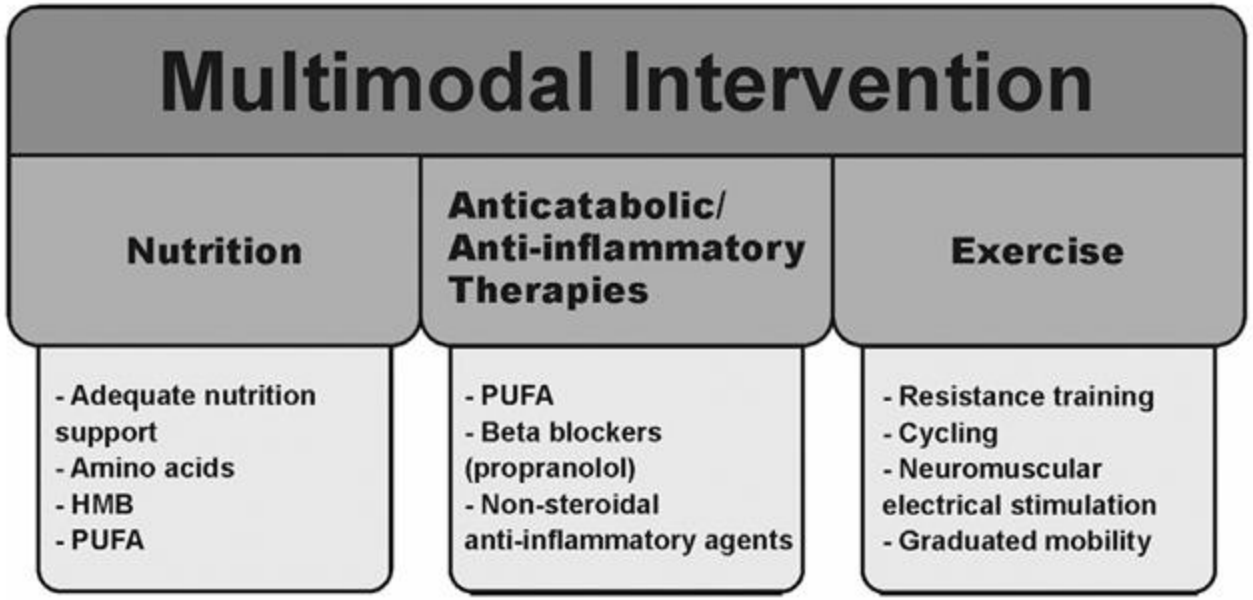
Intérêt d'une activité musculaire précoce?



Inflammation musculaire

Jameson, Crit Care, 2023

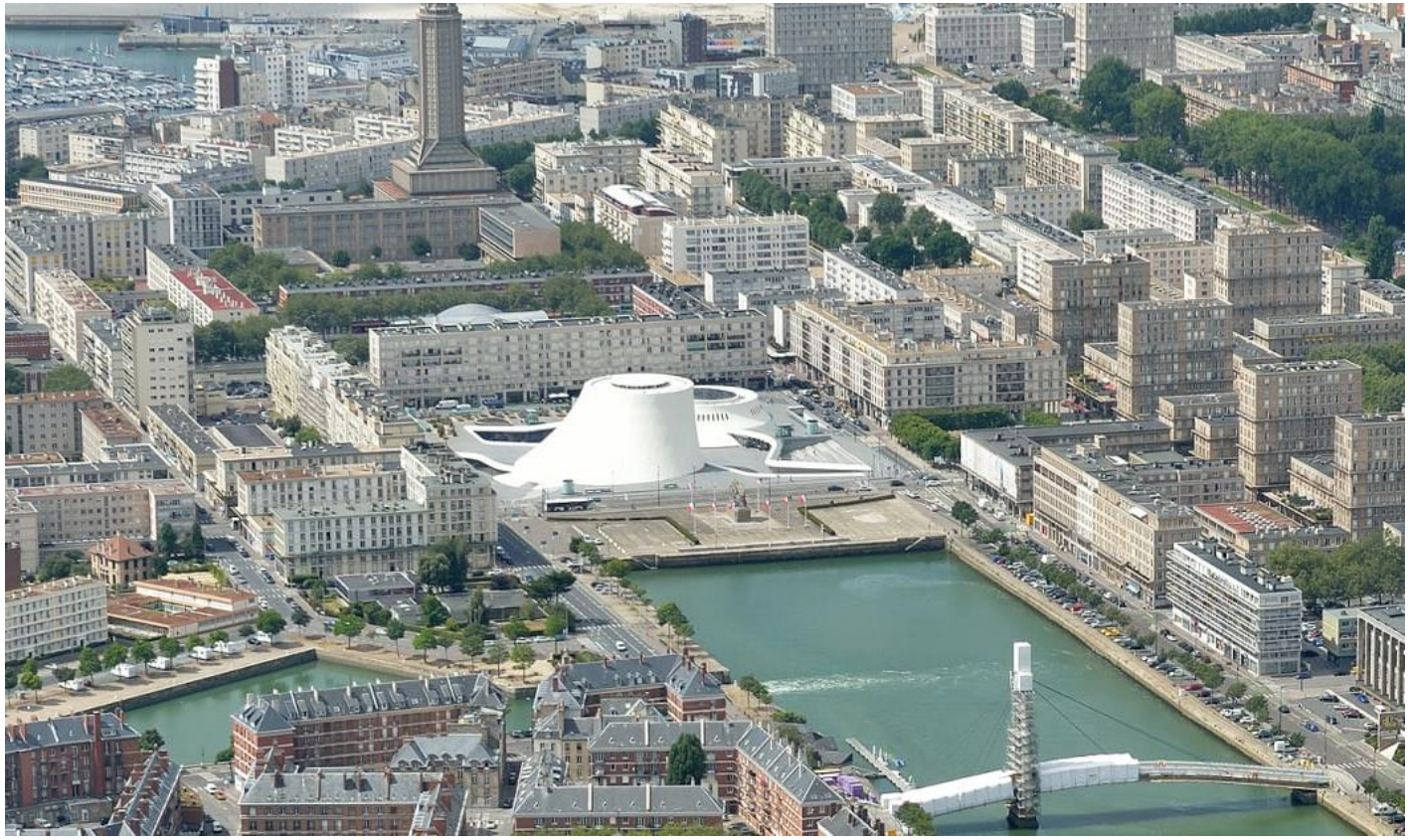
Besoin accru de stimulus?



Legend: PUFA: Polyunsaturated fatty acids (eicosapentaenoic acid, n-3, fish oil); HMB: β-Hydroxy β-methylbutyric acid. Multimodal interventions can include treatments from all domains. While we have focused on protein and amino acids in the proposed intervention, the potential use of n-3 fatty acids to attenuate inflammation while also promoting anabolism in other clinical scenarios could be investigated.

Fig. 1. Multimodal approach to optimize recovery from critical illness.

Heyland, Clin Nutr, 2015



Merci de votre attention

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