Peripheral and respiratory muscle weakness in ICU: causes and consequences

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Promotor: Prof Dr M Decramer

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Introduction

Muscle weakness in ICU

limbs

impaired rehabilitation

respiratory muscles

delayed weaning

Muscle weakness in ICU

Most frequent cause:

CIP = acute and primary axonal motor and sensory neuropathy *Bolton 1986*

CIM = acute primary myopathy

Zochodne 1986, Lacomis 2000

Incidence:

± 50% in sepsis, MOF, prolonged mechanical ventilation *Stevens, 2007*

Muscle weakness in ICU

Associated with:

Increased ICU stay

Increased hospital stay

Increased mortality

Stevens 2007, Leijten 1995, Garnacho-Montero 2001, Garnacho-Montero 2005, Nanas 2008

Diagnosis:

No universally accepted criteria

Risk factors:

CIP/CIM

De Jonghe, Crit Care Clin 2007

High suspicion

Duration of ICU stay/MV

Persistent SIRS/MOF

Hyperglycemia

Corticosteroids

Neuromuscular blockers

Hypoalbuminemia

Parenteral nutrition

Hyperosmolarity

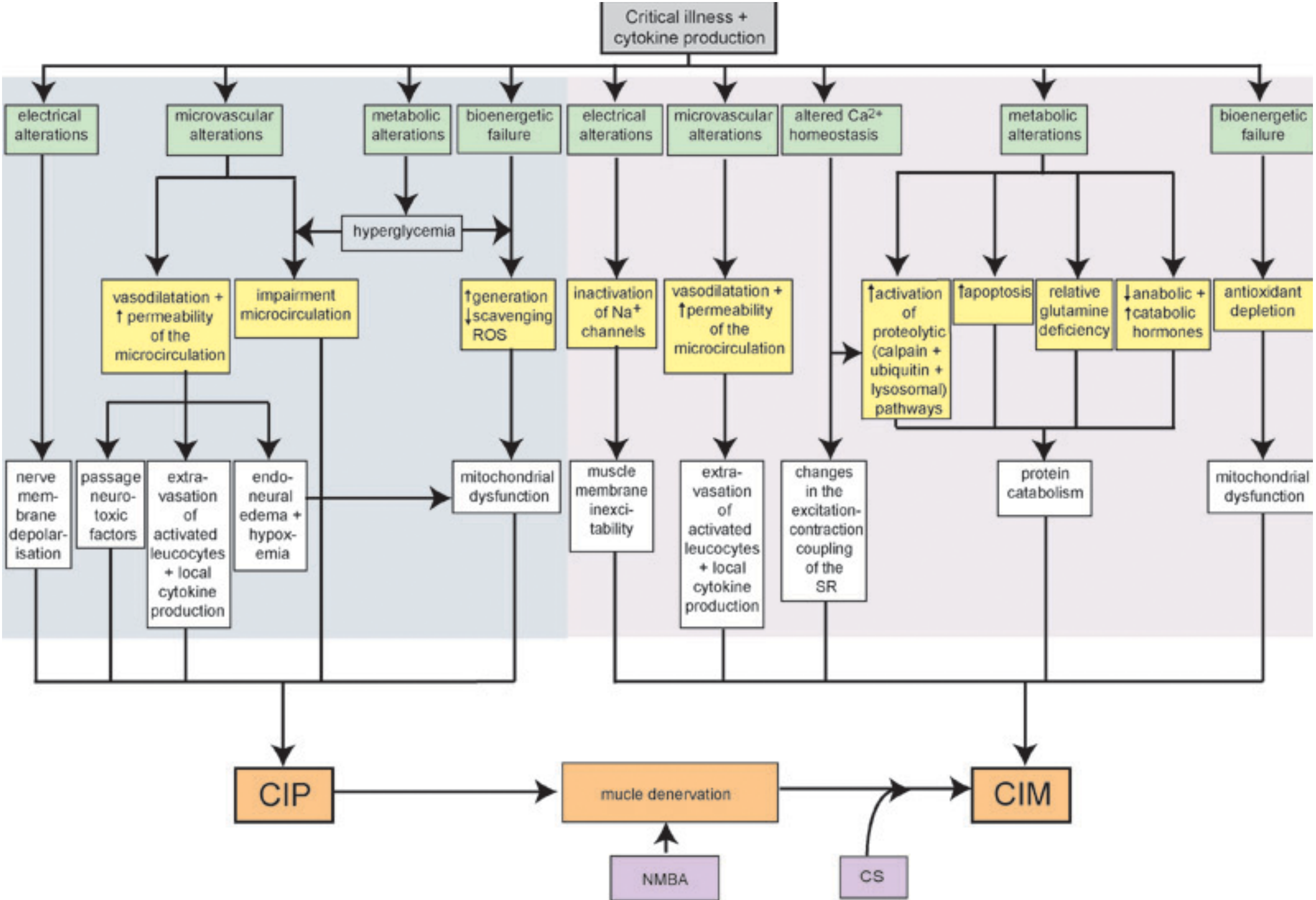
ERR

Low suspicion

Pathophysiology

‘just another organ failure’

Bednarik 2005; Witt 1991; Hund 2001b; Hund 2001a; Tepper 2000; Leijten 1996; Zochodne 1987)



Hermans et al, Cochrane Database of Systematic Reviews -Protocol 2007

Muscle weakness in ICU

Prognosis:

recovery within weeks to months

most severe: incomplete or not occur at all

de Seze, 2000

Prevention/therapy:

reducing risk factors:

agressive sepsis treatment, CS, NMBA

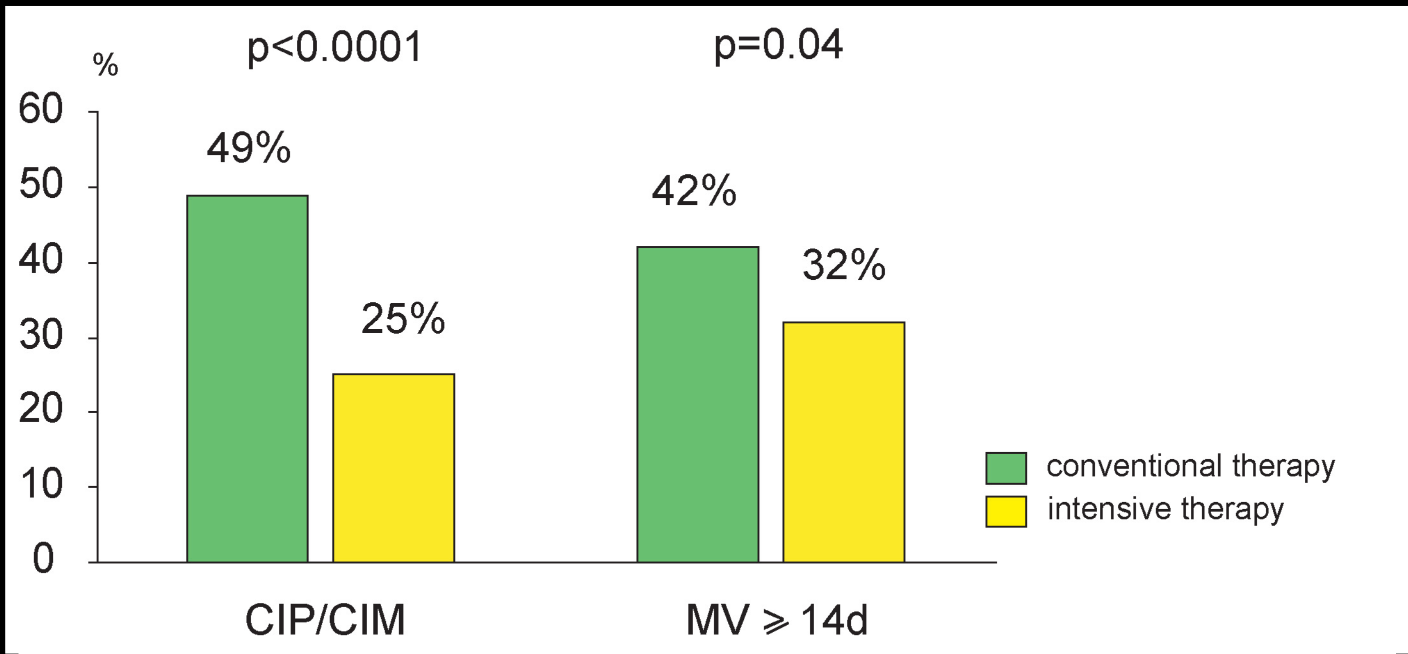
physiotherapy

CIP/CIM

NEUROLOGY

Insulin therapy protects the central and peripheral nervous system of intensive care patients

G. Van den Berghe, MD, PhD; K. Schoonheydt, MD; P. Becx, MD; F. Bruyninckx, MD; and P.J. Wouters, MSc



Muscle weakness in ICU

VIDD: animal experiments:

Controlled mechanical ventilation induces atrophy and weakness of the diaphragm

Mechanisms:

Muscle atrophy

Oxidative stress

Structural injury

Myofiber remodelling

VIDD

Muscle weakness in ICU

VIDD in humans?

- *Critically ill patients have reduced diaphragmatic muscle force*

  Watson 2001, Laghi 2003

- *Diaphragm of organ donors shows atrophy and increased oxidative stress after 18-69u CMV*

  Levine 2008

1. Effect of Intensive Insulin Therapy on Neuromuscular Complications in a Medical ICU

Patients and Methods

- Prospectively planned subanalysis of large RCT comparing CIT versus IIT, in MICU

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Intensive Insulin Therapy in the Medical ICU

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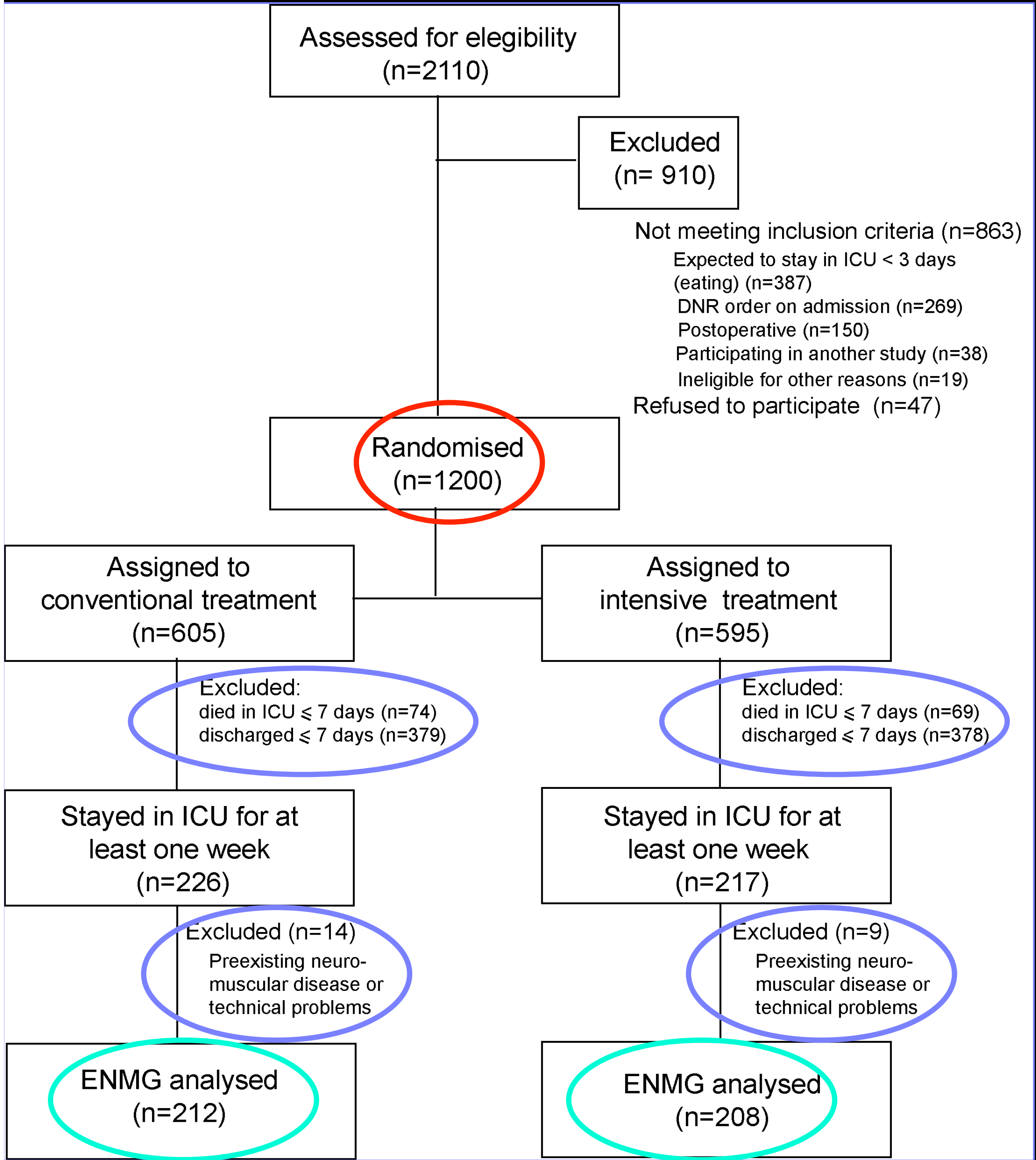
Patients and Methods

- Aim: assess impact of IIT on CIP/CIM and prolonged MV, pt in ICU ≥ 7 days
  - Diagnosis CIP/CIM: EMG/NCS
  - Diagnosis PMV: ≥ 14d

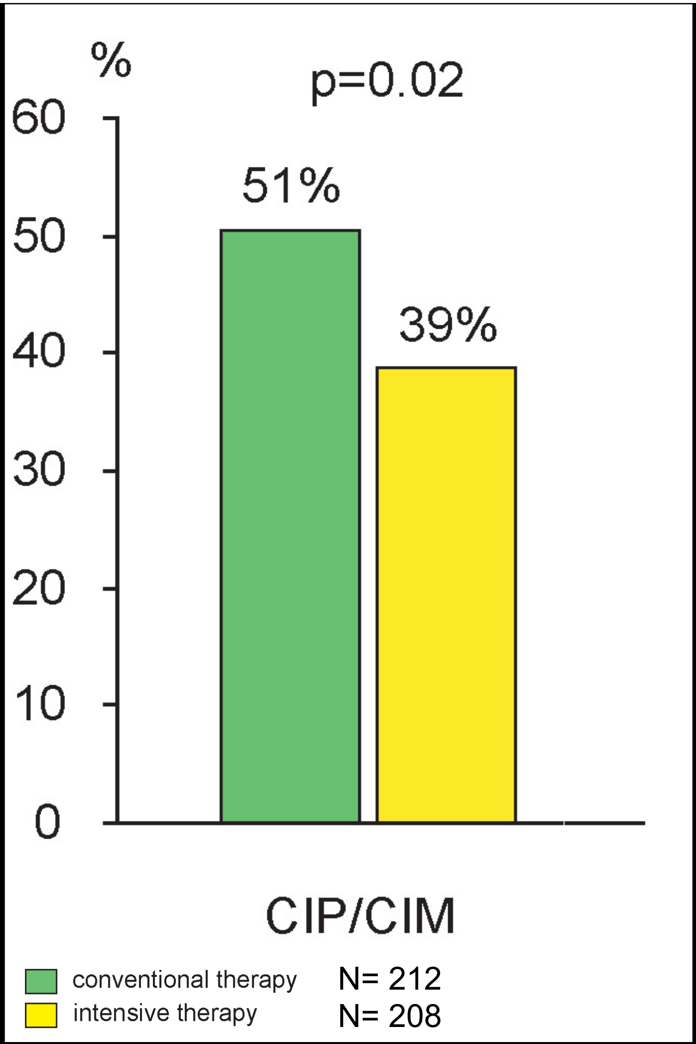


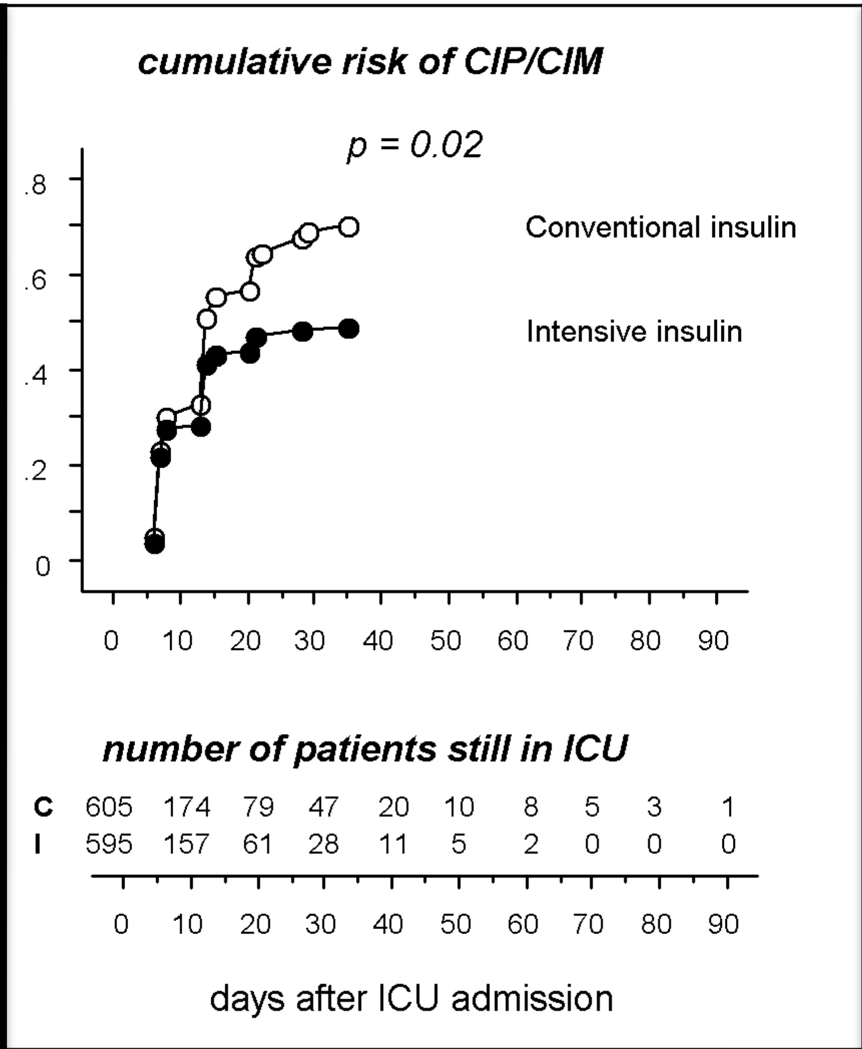
- **Intention-to-treat**
- **Censored**
- **Uncensored**

Hermans et al, AJRCCM 2007

Results

1. CIP/CIM





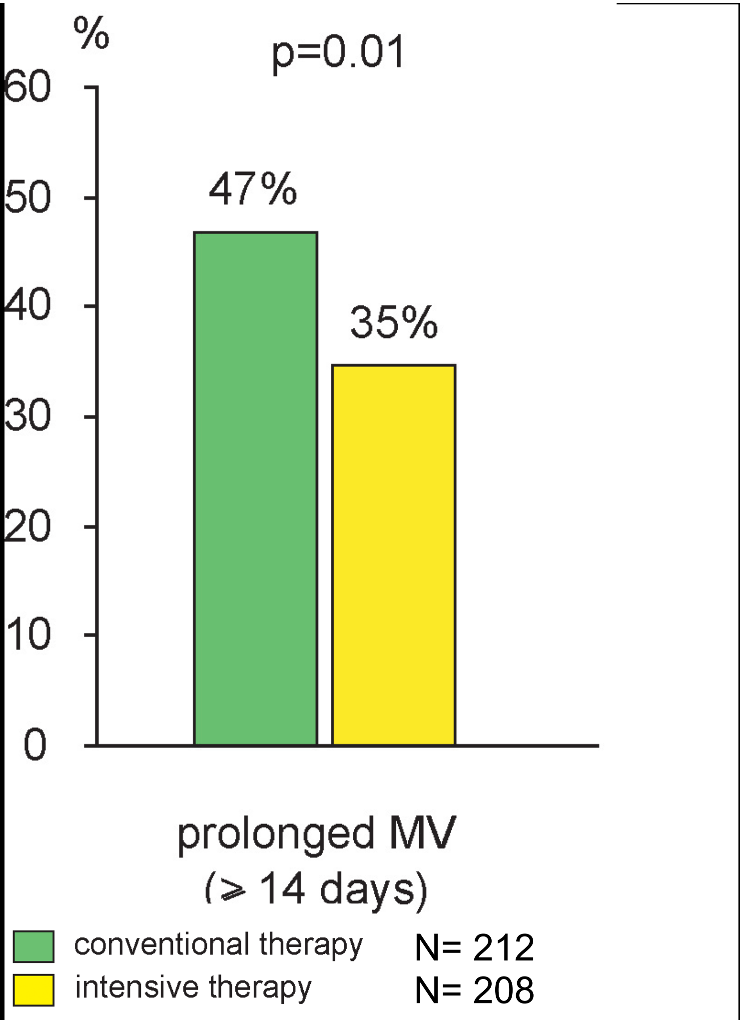
MVLR:

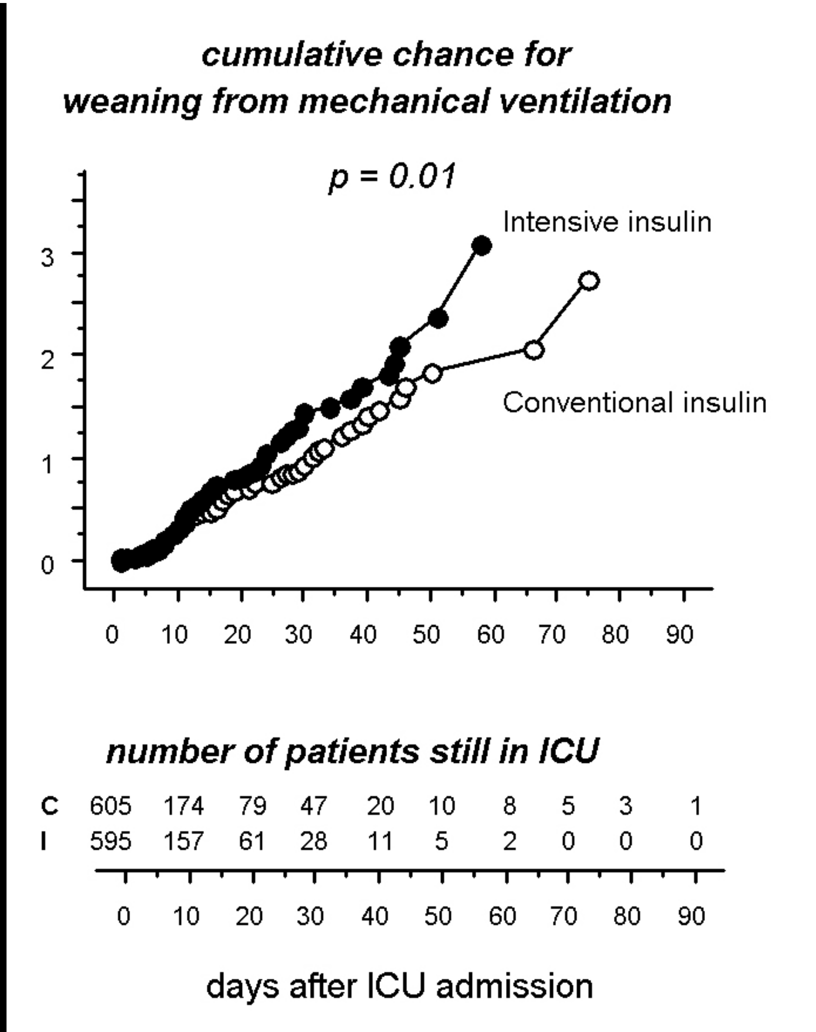
IIT is independent ***protector*** ***(p=0.02)***

Nor glycemia, nor insulin d independently explain benefit

AJRCCM 2007, Hermans et al

2. Prolonged Mechanical Ventilation





MVLR:

IIT is independent ***protector*** ***(p=0.01)***

Beneficial effect of IIT is due to insulin dose

↓ CIP/CIM does not entirely explain beneficial effect on PMV

AJRCCM 2007, Hermans et al

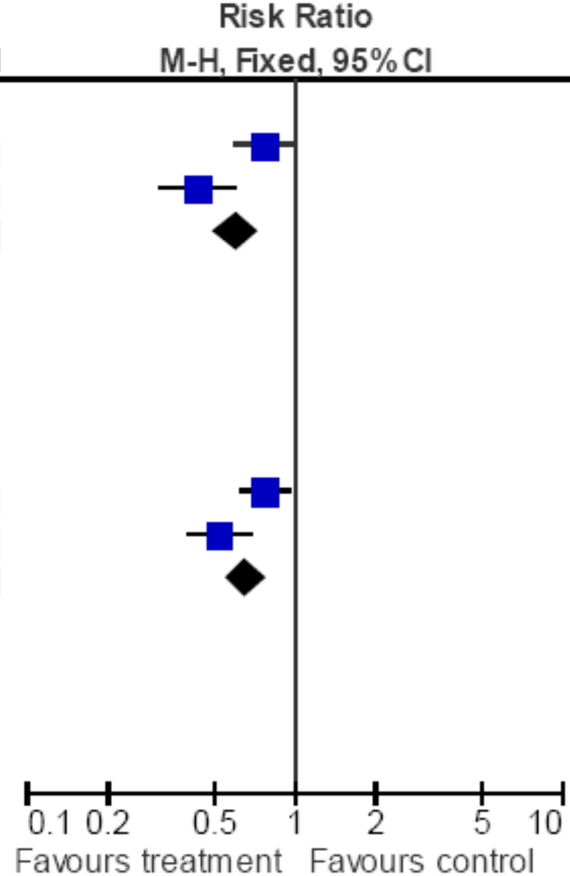
Conclusion

IIT reduces the electrophysiological incidence of CIP/CIM and the need for prolonged mechanical ventilation, also in medical patients, in ICU for at least 7 days.

1 Intensive Insulin Therapy (IIT) versus Conventional Insulin Therapy (CIT)

1.1 Occurence of CIP/CIM

Study or Subgroup	IIT Events	IIT Total	CIT Events	CIT Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 In total population randomised						
Hermans 2007	81	595	107	605	49.6%	0.77 [0.59, 1.00]
Van den Berghe 2005	46	765	109	783	50.4%	0.43 [0.31, 0.60]
Subtotal (95% CI)		**1360**		**1388**	**100.0%**	**0.60 [0.49, 0.74]**
Total events	127		216			
Heterogeneity: Chi² = 7.20, df = 1 (P = 0.007); I² = 86%						
Test for overall effect: Z = 4.88 (P < 0.00001)						
1.1.2 In screened patients						
Hermans 2007	81	208	107	212	52.1%	0.77 [0.62, 0.96]
Van den Berghe 2005	46	181	109	224	47.9%	0.52 [0.39, 0.69]
Subtotal (95% CI)		**389**		**436**	**100.0%**	**0.65 [0.55, 0.77]**
Total events	127		216			
Heterogeneity: Chi² = 4.68, df = 1 (P = 0.03); I² = 79%						
Test for overall effect: Z = 4.86 (P < 0.00001)						



Hermans et al. Cochrane Cochrane Database of Systematic Reviews 2009

2. Effect of Intensive Insulin Therapy in *routine daily care practice* on Neuromuscular Complications

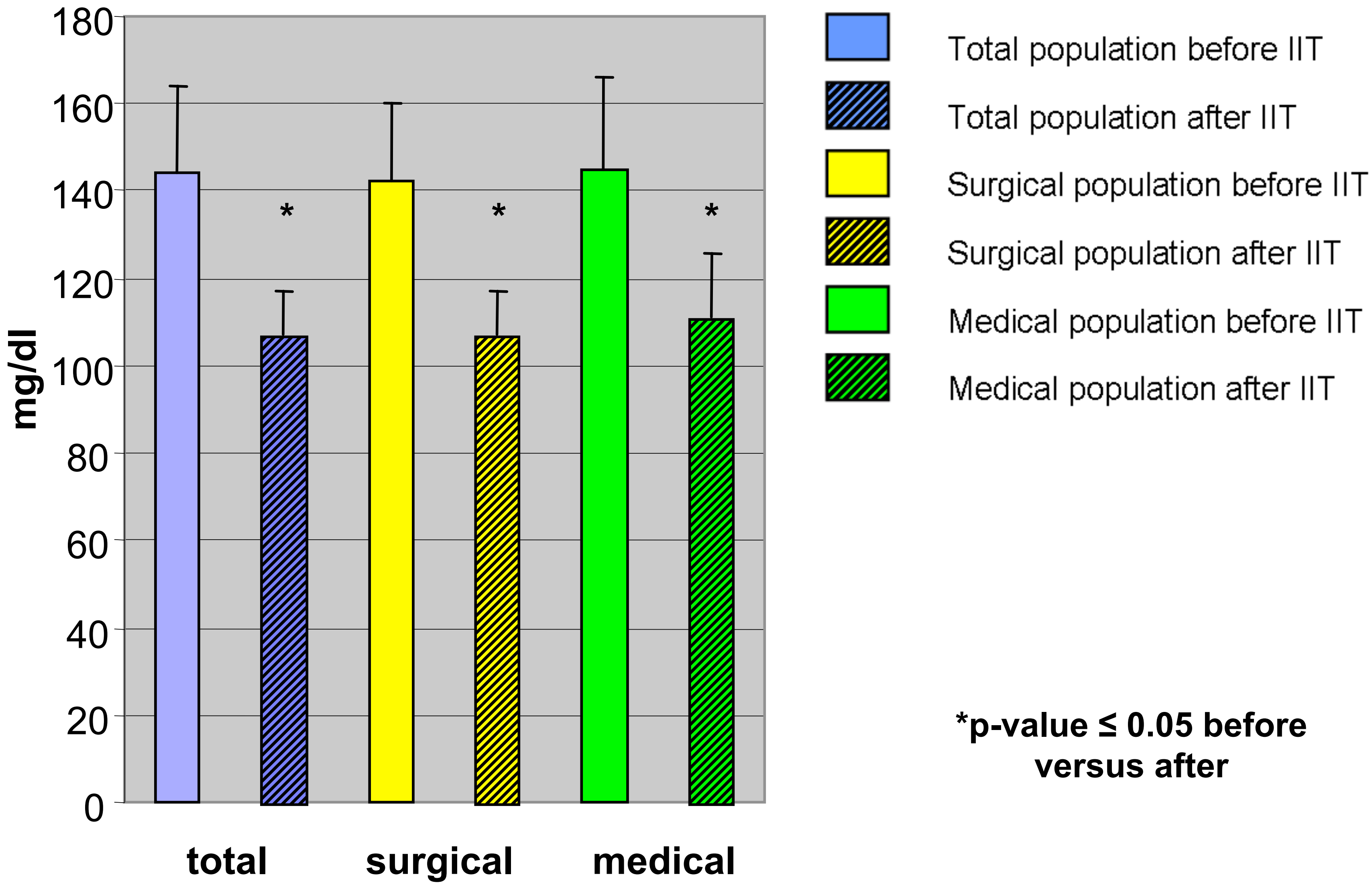
Patients and Methods

- Retrospective analysis of EMG/NCS:
  - performed in MICU and SICU
  - because of weakness/weaning failure
  - from 1998-2006, eliminating RCTs

Results

Glycemic control

Mean glycemia before and after IIT (mean±SD)

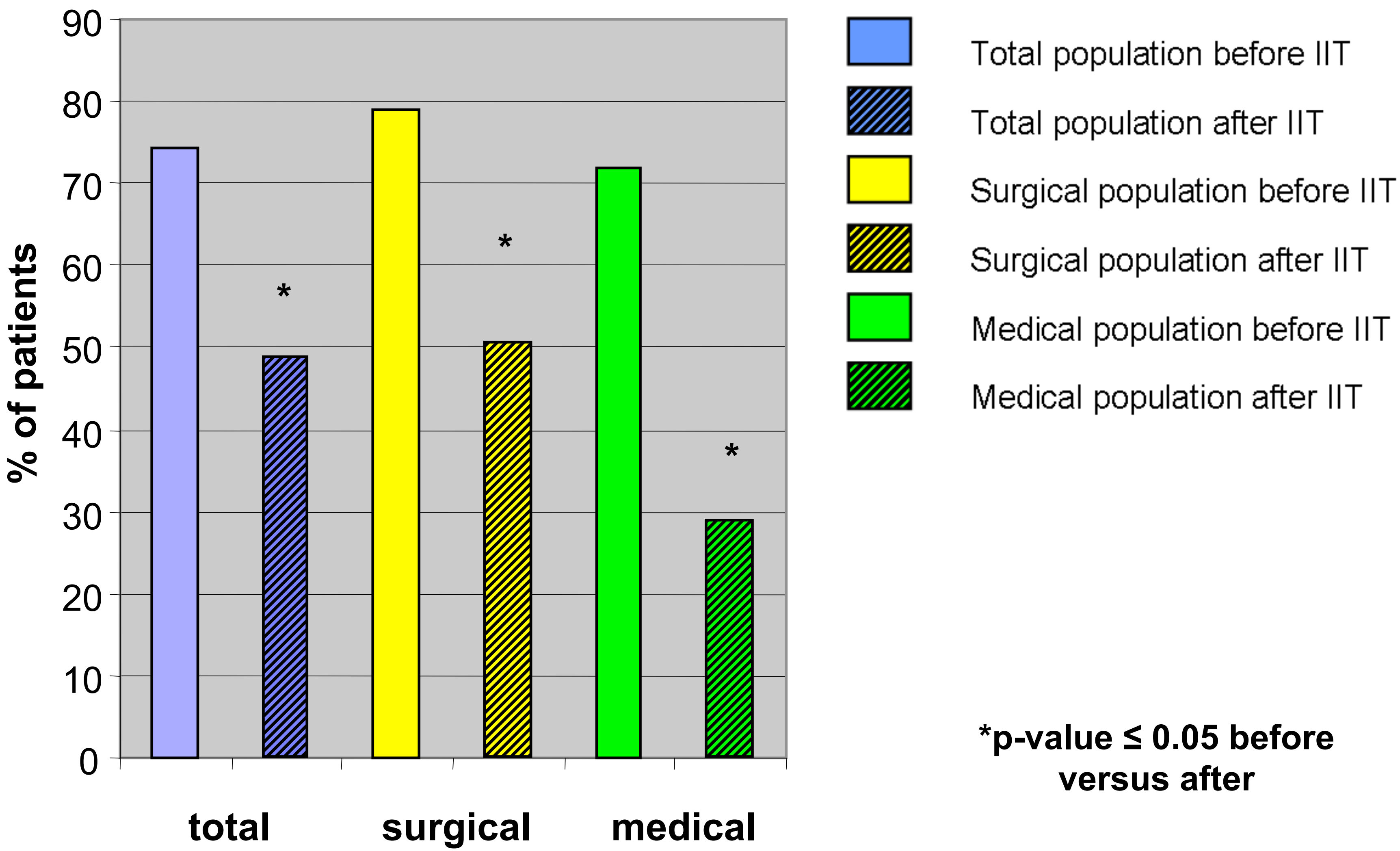


***p-value ≤ 0.05 before versus after**

Hermans et al, Crit Care 2009

Electrophysiological data

Spontaneous electrical activity before and after IIT

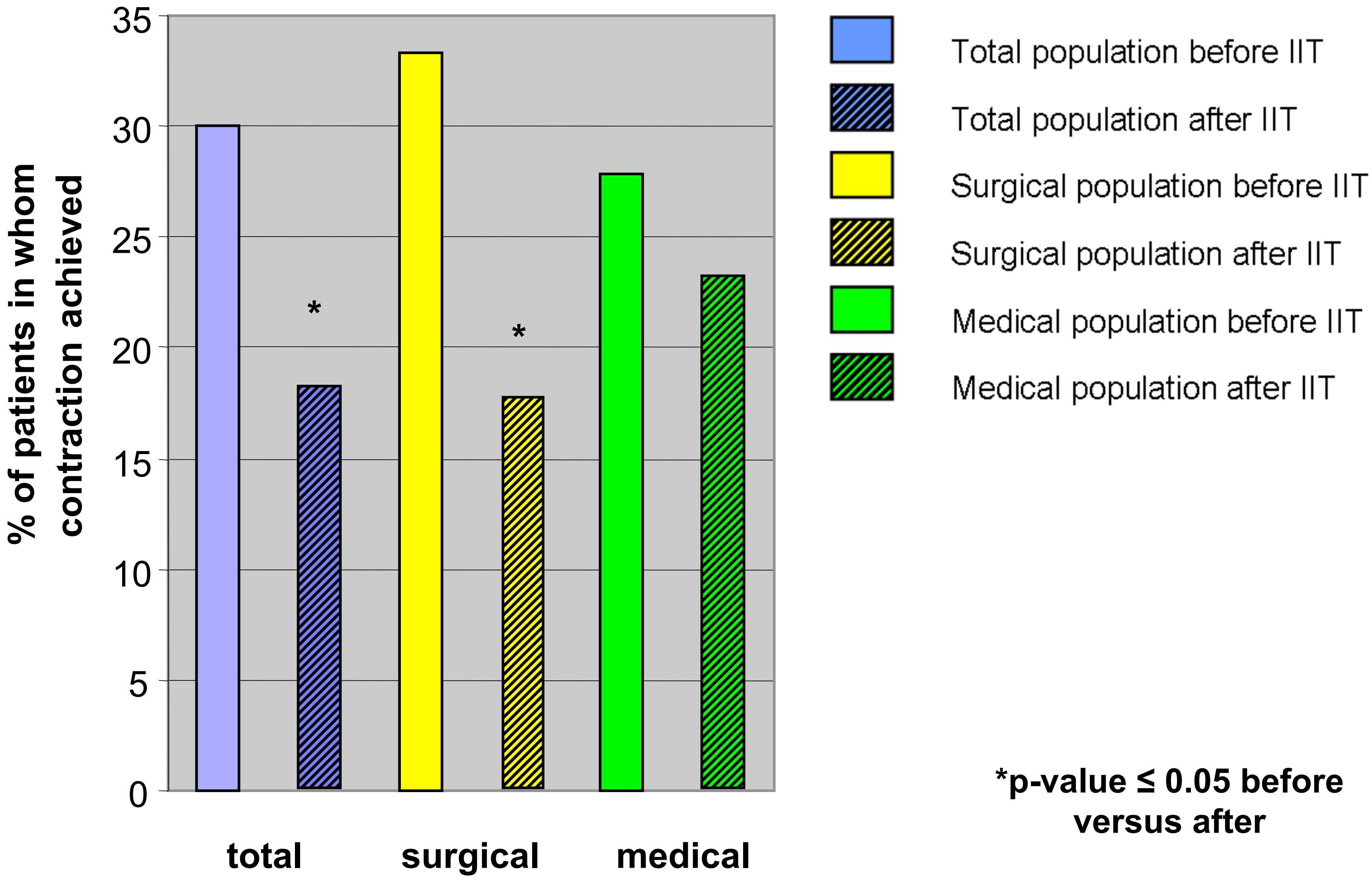


***p-value ≤ 0.05 before versus after**

MVLR: ***IIT*** = independent ***protector (p<0.0001)***

Hermans et al, Crit Care 2009

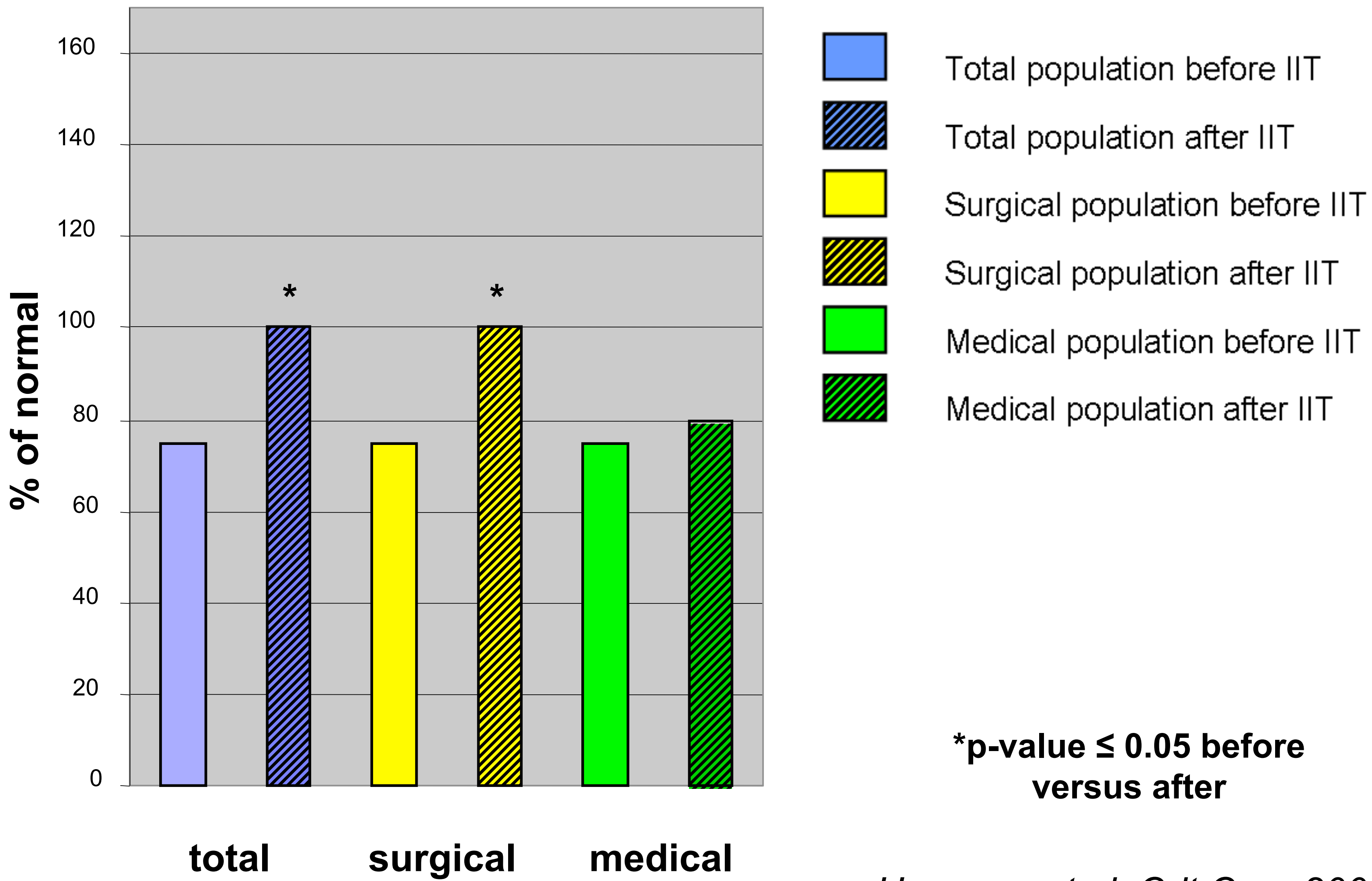
Myopathic pattern present on EMG before and after IIT



*p-value ≤ 0.05 before versus after

Hermans et al, Crit Care 2009

SNAPs UL before and after IIT



***p-value ≤ 0.05 before versus after**

Hermans et al, Crit Care 2009

Prolonged mechanical ventilation

Risk for prolonged mechanical ventilation

Glycemic control, IIT	**0.40 (0.22-0.72)**	**0.002**
ICU type, medical	0.35 (0.18-0.67)	0.002
On admission blood glucose	0.99 (0.99-1.002)	0.4
Gender, female	0.74 (0.48-1.12)	0.2
N of d treatment with norepinephrine, per d added	1.16 (1.11-1.22)	<0.0001
Cumulative dose hydrocortisone equivalent, per mg added	1.00 (1.00-1.00)	0.9
Treatment with aminoglycosides, yes	1.72 (1.003-2.96)	0.05
N of d treatment with NMBAs (≥1 bolus or drip), per day added	1.15 (1.04-1.27)	0.007
Number of days treatment with dialysis, per day added	1.09 (1.03-1.15)	0.004
Bactaemia, yes	2.11 (1.26-3.55)	0.005
…	…	…

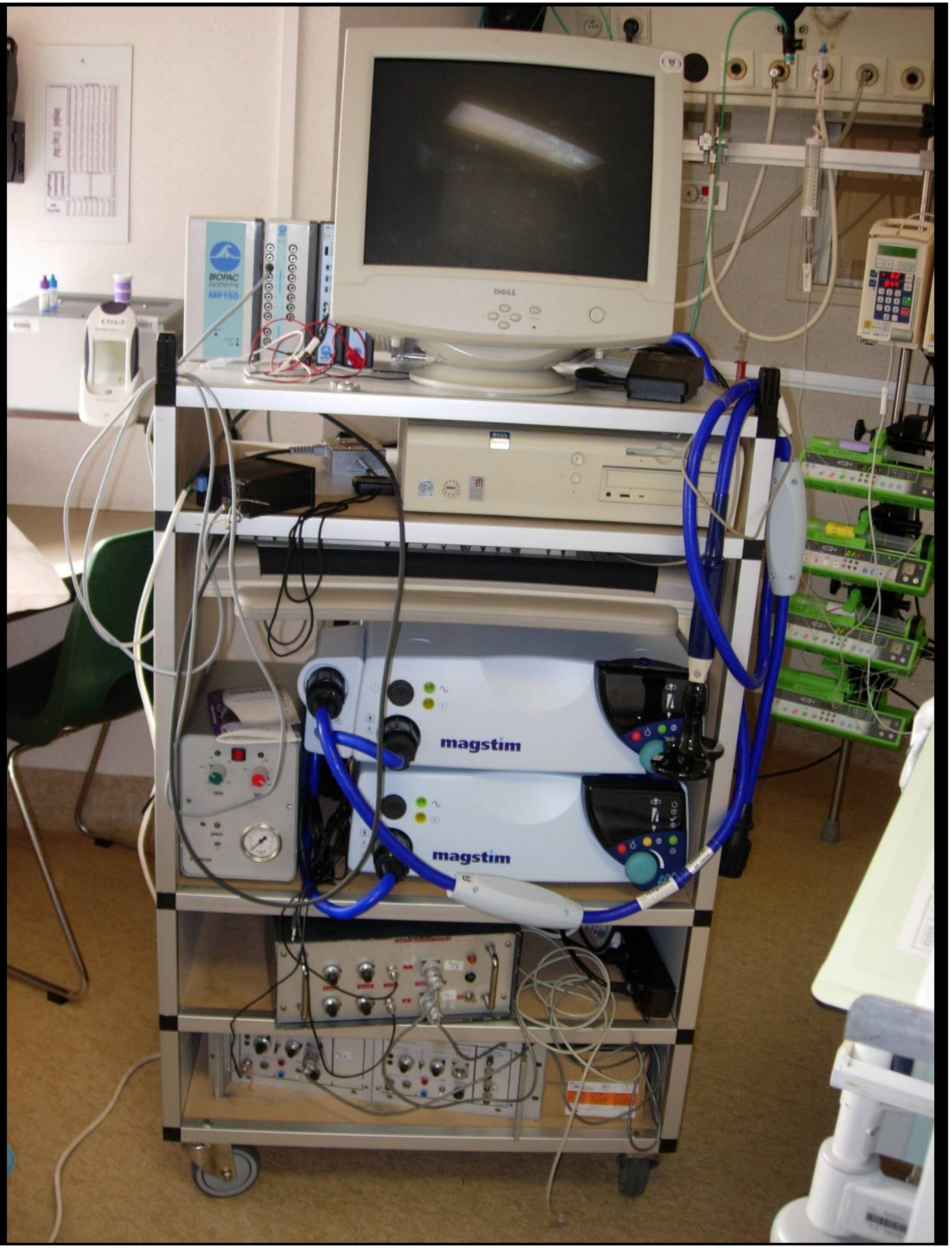
Conclusion

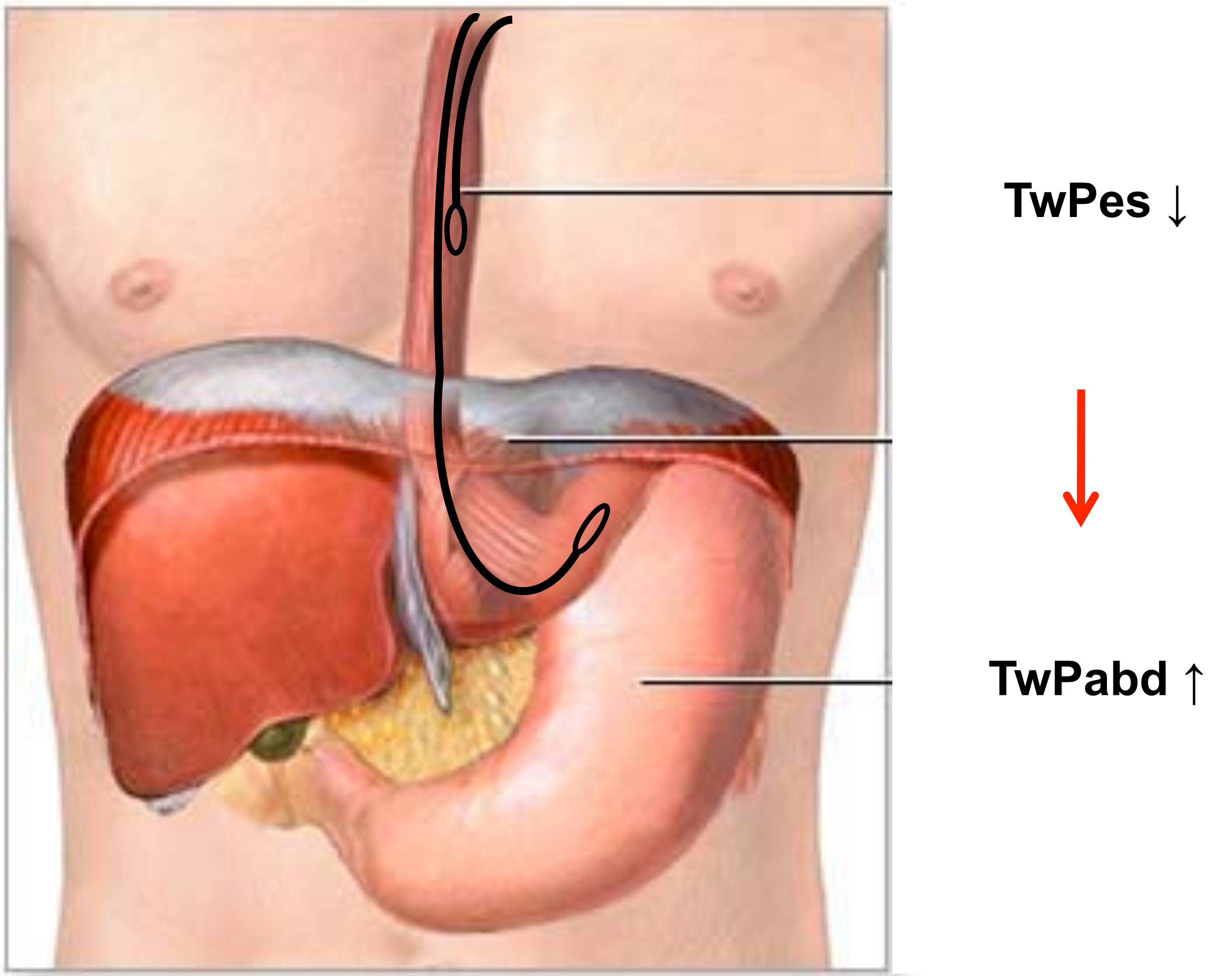
IIT reduces the electrophysiological incidence of CIP/CIM and the need for prolonged mechanical ventilation, also in routine daily practice.

3. Measuring diaphragmatic force in ICU

Methodology

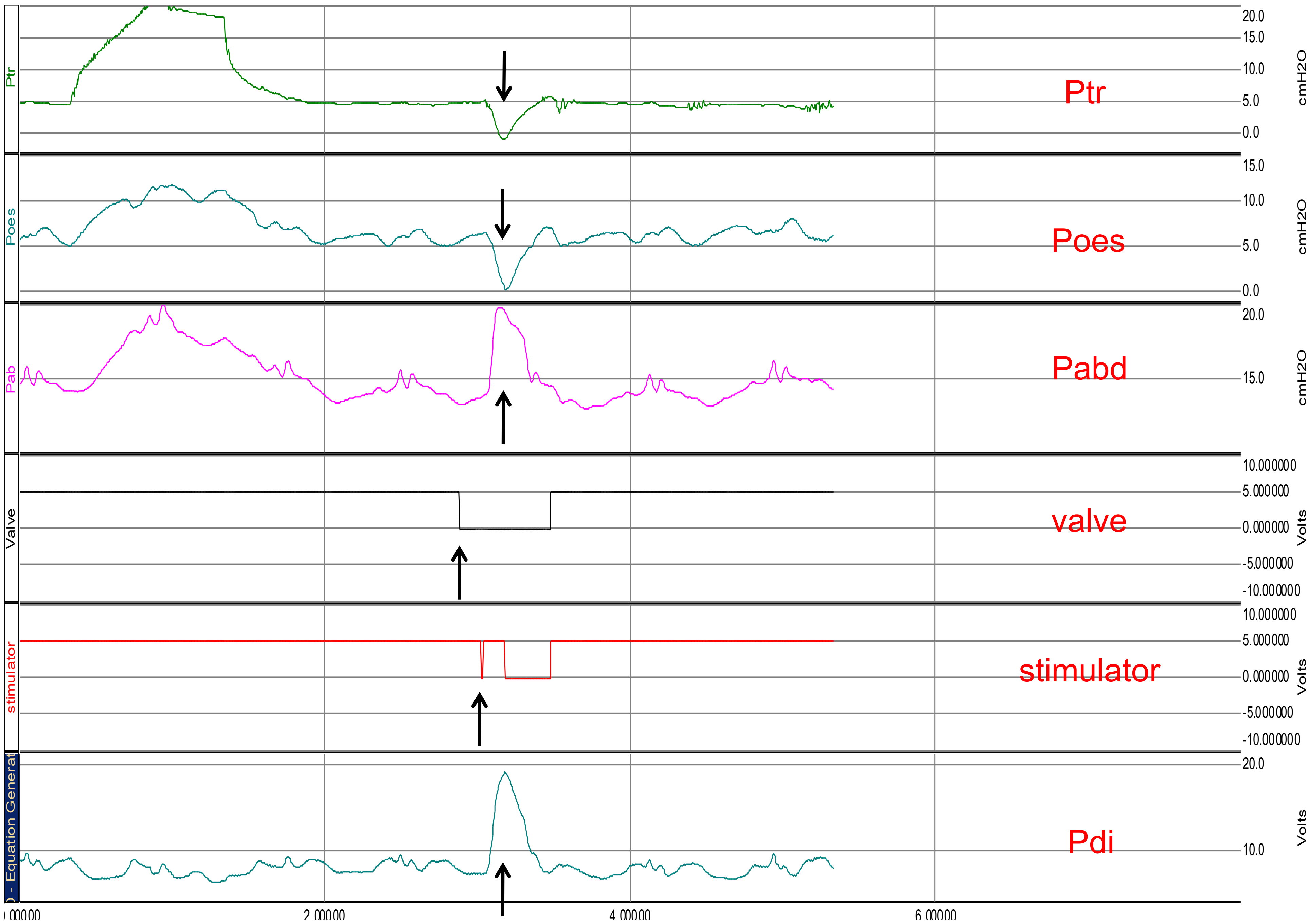
BAMPS


BIOPAC
Systems
MP150
DELL
magstim
magstim



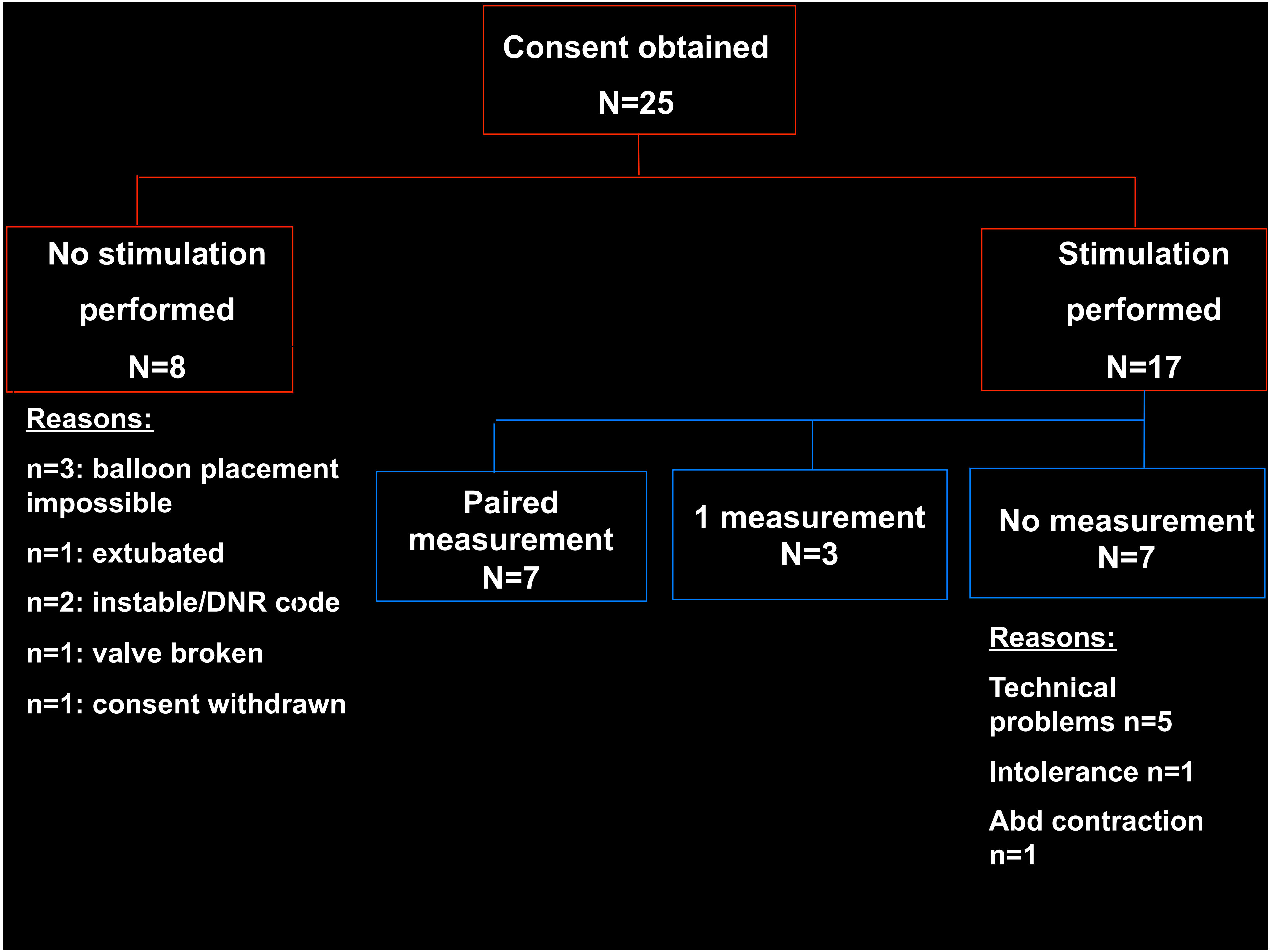
TwPdi =TwPabd-TwPes

!


Ptr
Poes
Pabd
valve
stimulator
Pdi
cmH2O
Volts
20.0
15.0
10.0
5.0
0.0
10.000000
5.000000
0.000000
-5.000000
-10.000000
Valve
stimulator
Equation Generat
0.00000
2.00000
4.00000
6.00000

Results

1. Patients


Consent obtained
N=25
No stimulation performed
N=8
Reasons:
n=3: balloon placement impossible
n=1: extubated
n=2: instable/DNR code
n=1: valve broken
n=1: consent withdrawn
Stimulation performed
N=17
Paired measurement
N=7
1 measurement
N=3
No measurement
N=7
Reasons:
Technical problems n=5
Intolerance n=1
Abd contraction n=1

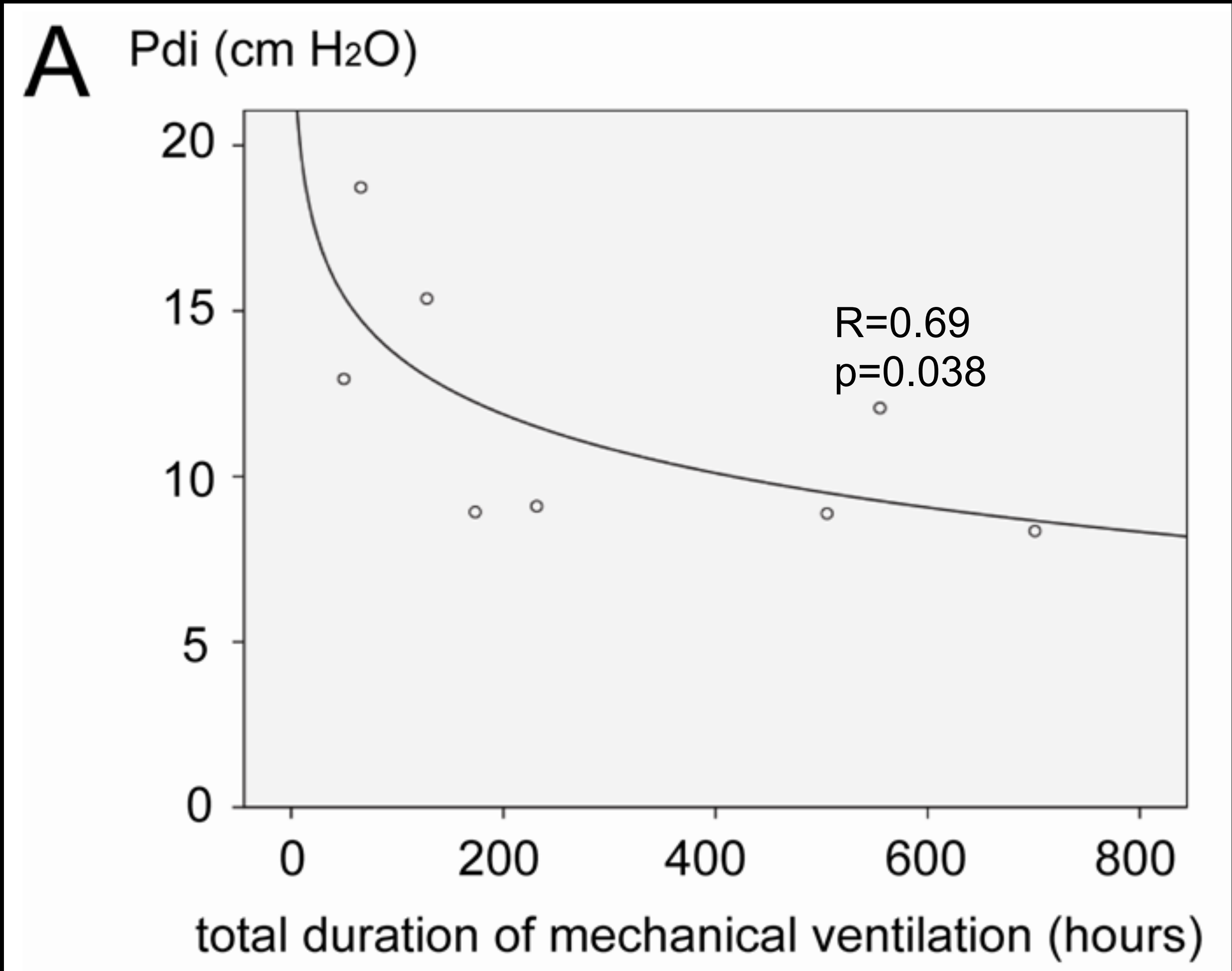
2. Reproducibility

Between-occasion coefficient of variation

Patient	Mean value Pdi	Number of measurements	Time span	Coefficient of variation
Patient 1	12.2	2	24h	1.9 %
Patient 4	11.7	2	24h	15.5 %
Patient 5	8.7	2	48h	6.5 %
Patient 6	15.6	2	48h	2.0 %
Patient 7	9.5	2	120h	16.6 %
Patient 9	10.0	2	24h	16.3 %
Patient 10	20.5	4	24h	9.3 %
mean	**12.6**	**2.3**		**9.7 %**

3. Relationship between TwPdi and duration of mechanical ventilation

Duration of mechanical ventilation



Conclusion

1. *Similar reproducibility of BAMPS Pdi on ICU as in healthy volunteers*
2. *Logarythmic decline of TwPdi with increasing duration of MV*

3. Future perspectives

1. Mechanistic approach:

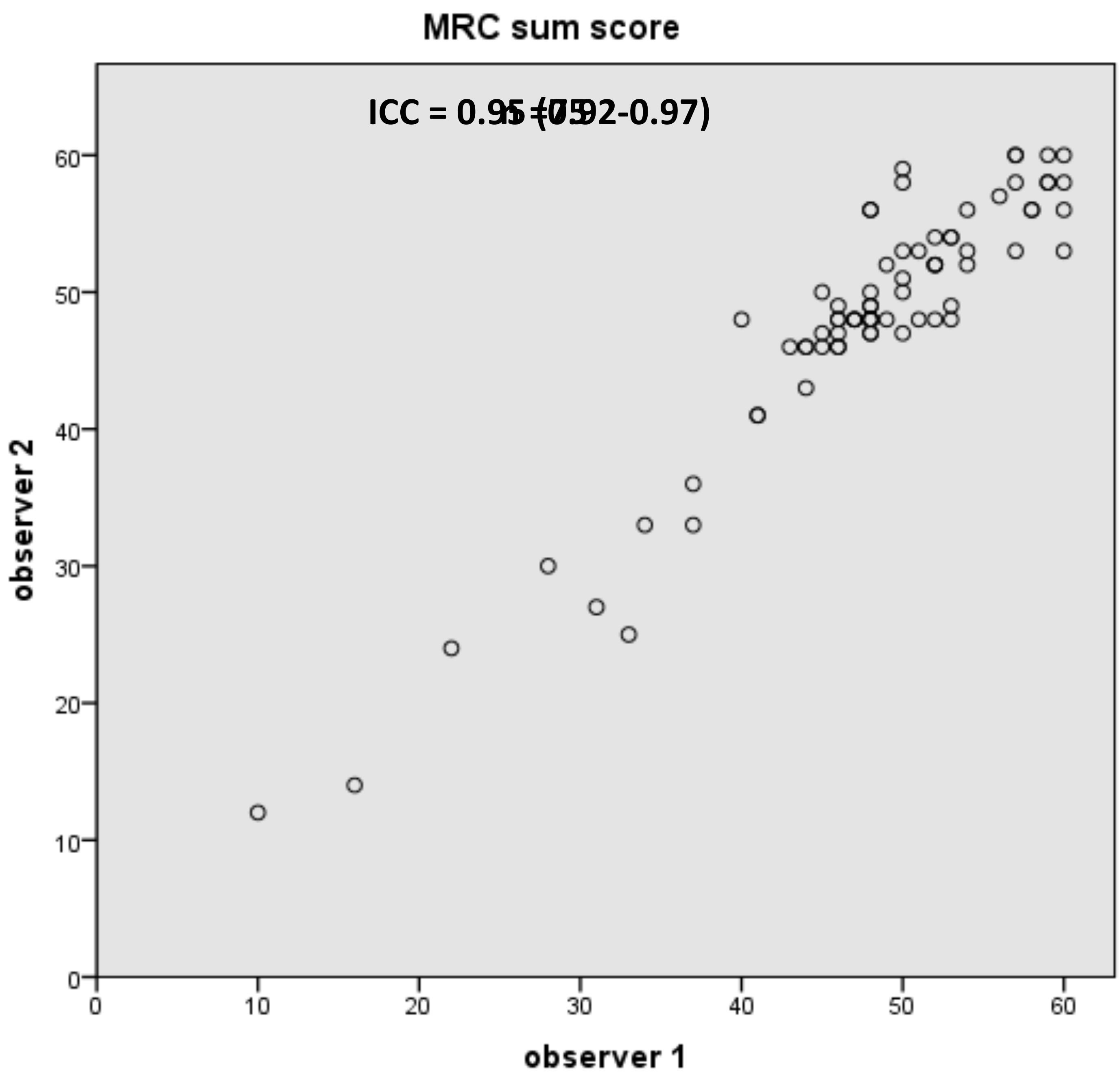
    200 muscle biopsies: effects IIT

2. New potential intervention:

    EPaNIC

3. Diagnostic approach:

    Clinical evaluation muscle force in ICU


MRC sum score
ICC = 0.95 (0.92-0.97)
n = 75
observer 2
observer 1
0
10
20
30
40
50
60

Thank you:

Promotors:

G Van den Berghe

M Decramer

G Gayan-Ramirez

Thank you:

Electrophysiologist:

F Bruyninckx

Neurologists:

P Van Damme
M Schrooten
W Robberecht

ICU teams:

Nurses

Trainees

Residents

Staff members

Study nurses:

P Wouters

and team

Physiotherapists:

B Clerckx

T Vanhullebusch

C Robbeets

R Gosselink

ICU Lab:

I Vanhorebeek
S Derde