Curarizzazione residua

L. Magnusson, HFR - Fribourg

Sommario

- Curarizzazione residua
- Monitoraggio
- Perché curarizzare?
- Decurarizzazione

1985

Pancuronium, vécuronium e succinylcholine

Nessuna decurarizzazione se:
TOF 4/4 «identico» = TOF > 0,7
Tempo dall'ultima dose somministrata > 4 ore

Néostigmina negli altri casi (+ atropina)
Con estubazione immediata

Utilizzata nel 10 % dei pazienti curarizzati

2018

Rocuronium, atracurium, cisatracurium
e succinylcholina

Nessuna decurarizzazione se:
TOF 4/4 «identico" = TOF > 0,7
Tempo dall'ultima dose somministrata > 4 ore

Néostigmine altrimenti (+ glycopyrrolate)
con estubazione quasi immediata

Sugammadex in alcuni casi

Utilizzata per 30 % - 50 % dei pazienti curarizzati

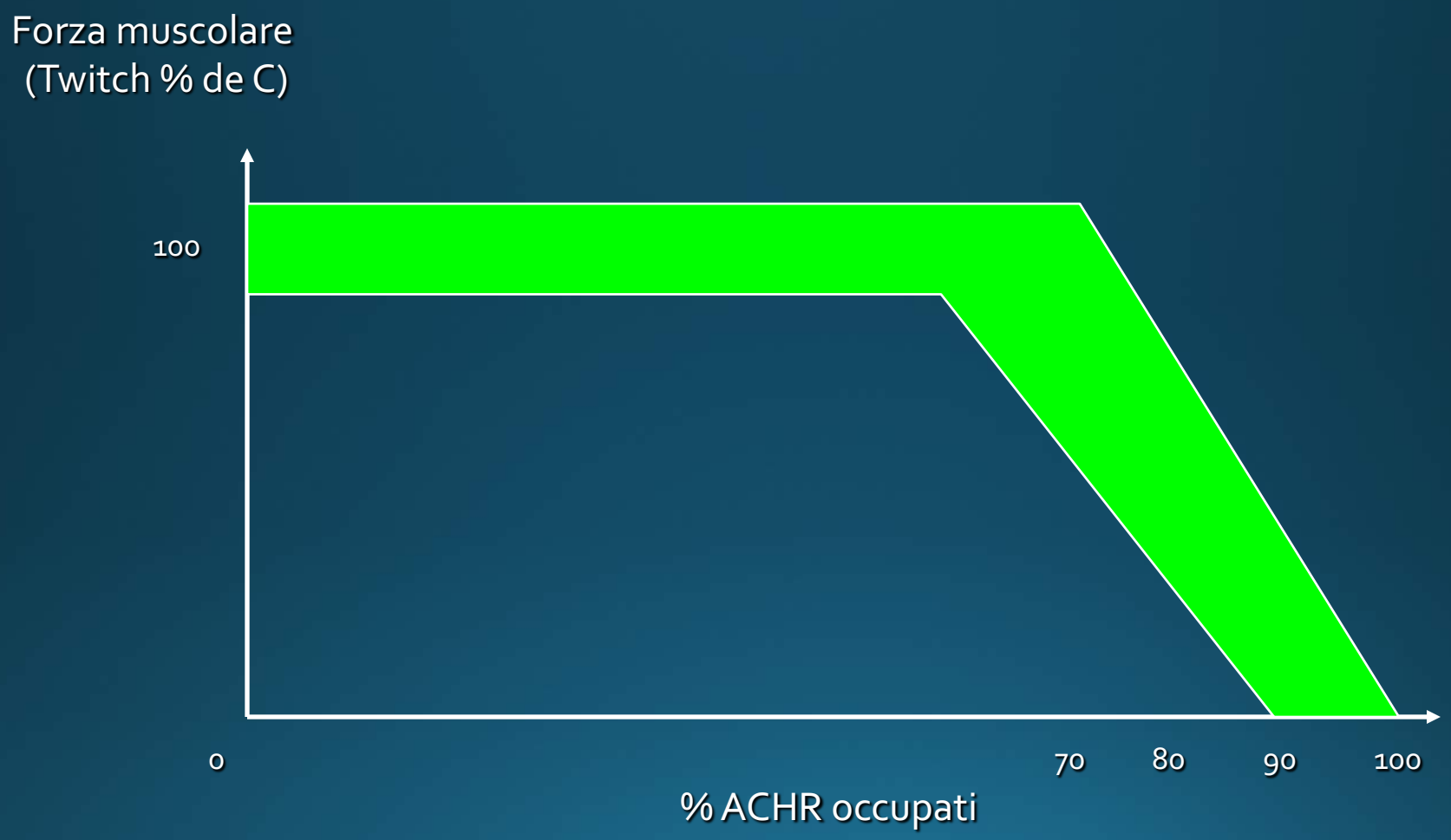
Curararizzazione residua

Presentazione SFAR 2007

Curarizzazione Residua

1. Rumori respiratori
2. Monitoraggio
3. Decurarizzazione

Margine di sicurezza della JNM

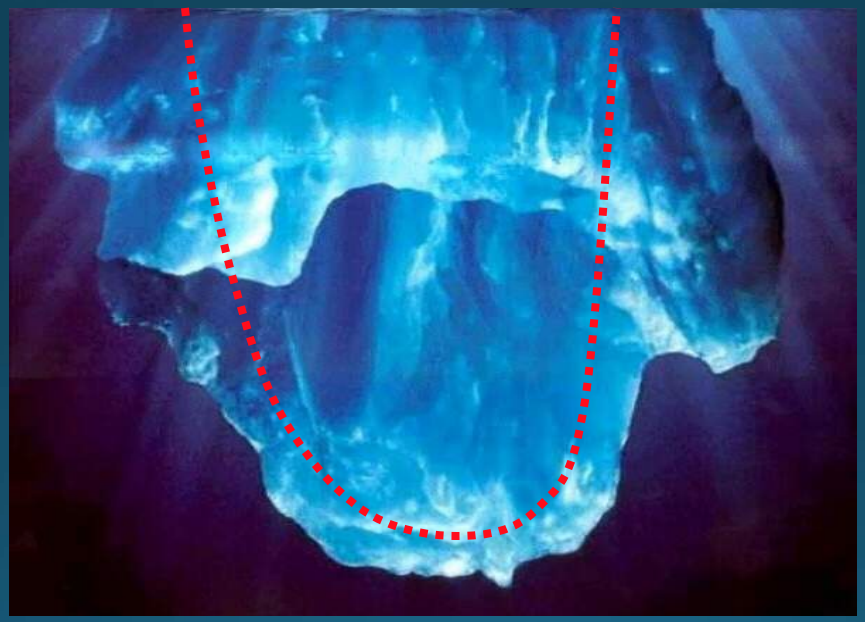


Waud BE, Anesthesiology, 1971

Teoria dell'iceberg

Ciò che riusciamo individuare

Ciò che ignoriamo



Che dire della definizione clinica di curarizzazione residua?
Soglia dei recettori occupati ?

Incidenza della Curarizzazione Residua (TOF (AP) >0.9 en SSPI)

- Single-shot iniezione
  - 16%
    - 2 ore dopo una unica dose

Debaene B, Anesthesiology, 2004

- Iniezioni multiple
  - Rocuronium 44%
  - Cis-atracurium 57%

Maybauer DM, Anaesthesia, 2007

Curarizzazione residua

Incidence of residual neuromuscular blockade in a post-anaesthetic care unit

P. C. YIP*, J. A. HANNAM†, A. J. D. CAMERON‡, D. CAMPBELL§

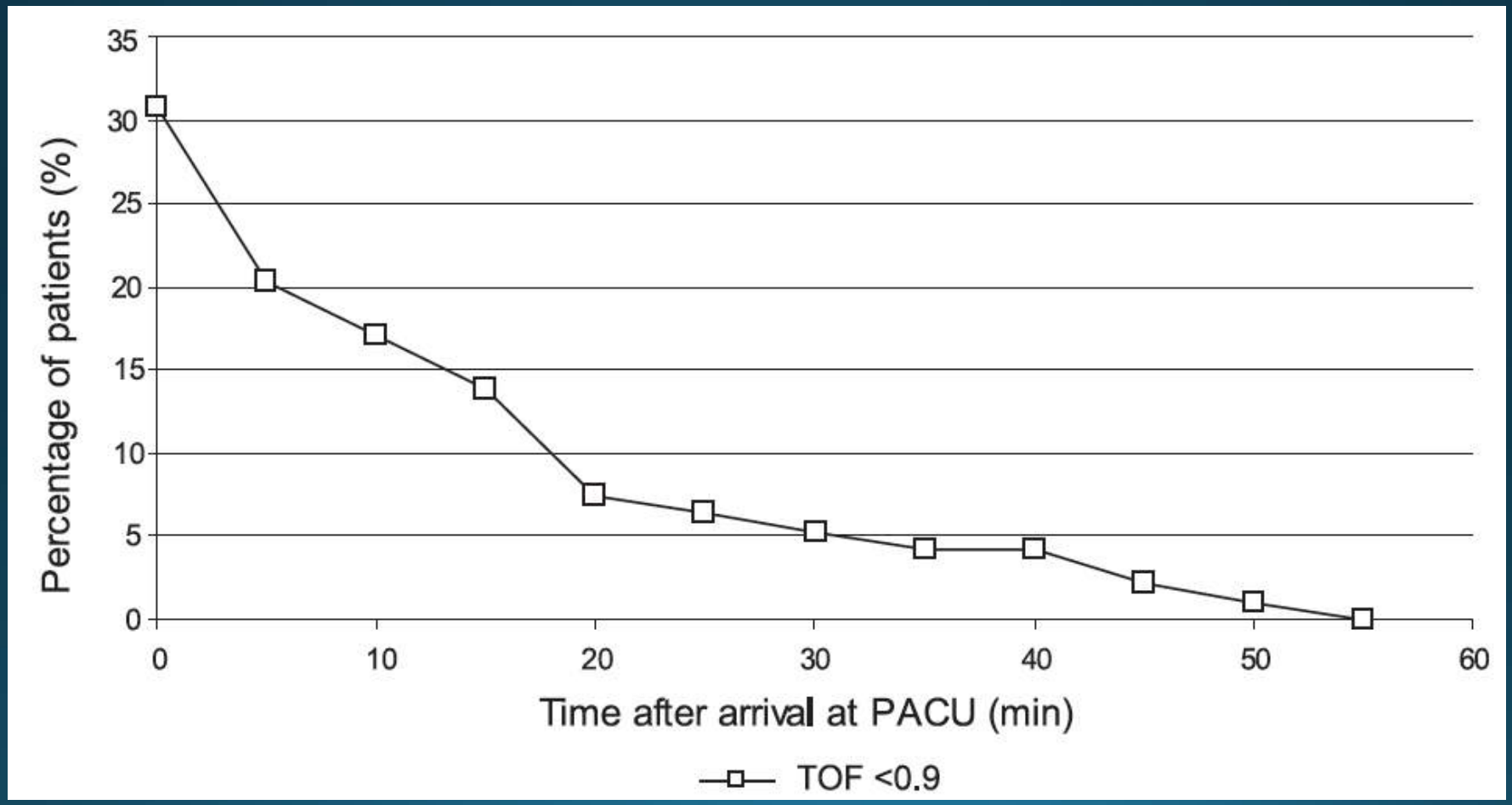
Anaesth Intensive Care 2010; **38:** 91-95

Patient characteristics and anaesthetic variables in patients with and without residual neuromuscular blockade (TOFR <0.9). Data are mean (SD) unless otherwise specified.

	TOFR <0.9 (n=29)	TOFR >0.9 (n=65)	*P* value
Age (y)	60 (16)	57 (16)	0.39
Gender (F/M)	8/21	36/29	0.013
Duration (min) of anaesthesia	97 (66)	141 (74)	0.017
Patients given neostigmine in OR, n (%)	22 (76%)	40 (62%)	0.18
Time (min) from last dose of relaxant to arrival in PACU	81(45)	109(63)	0.016
Mean cumulative dose* ($mg.kg^{-1}.h^{-1}$)	0.46 (0.18)	0.29 (0.14)	0.000032
Requirement for airway support, n (%)	6 (21%)	3 (5%)	0.023

- 31% patients avec TOF < 0,9 (29 / 94 patients)

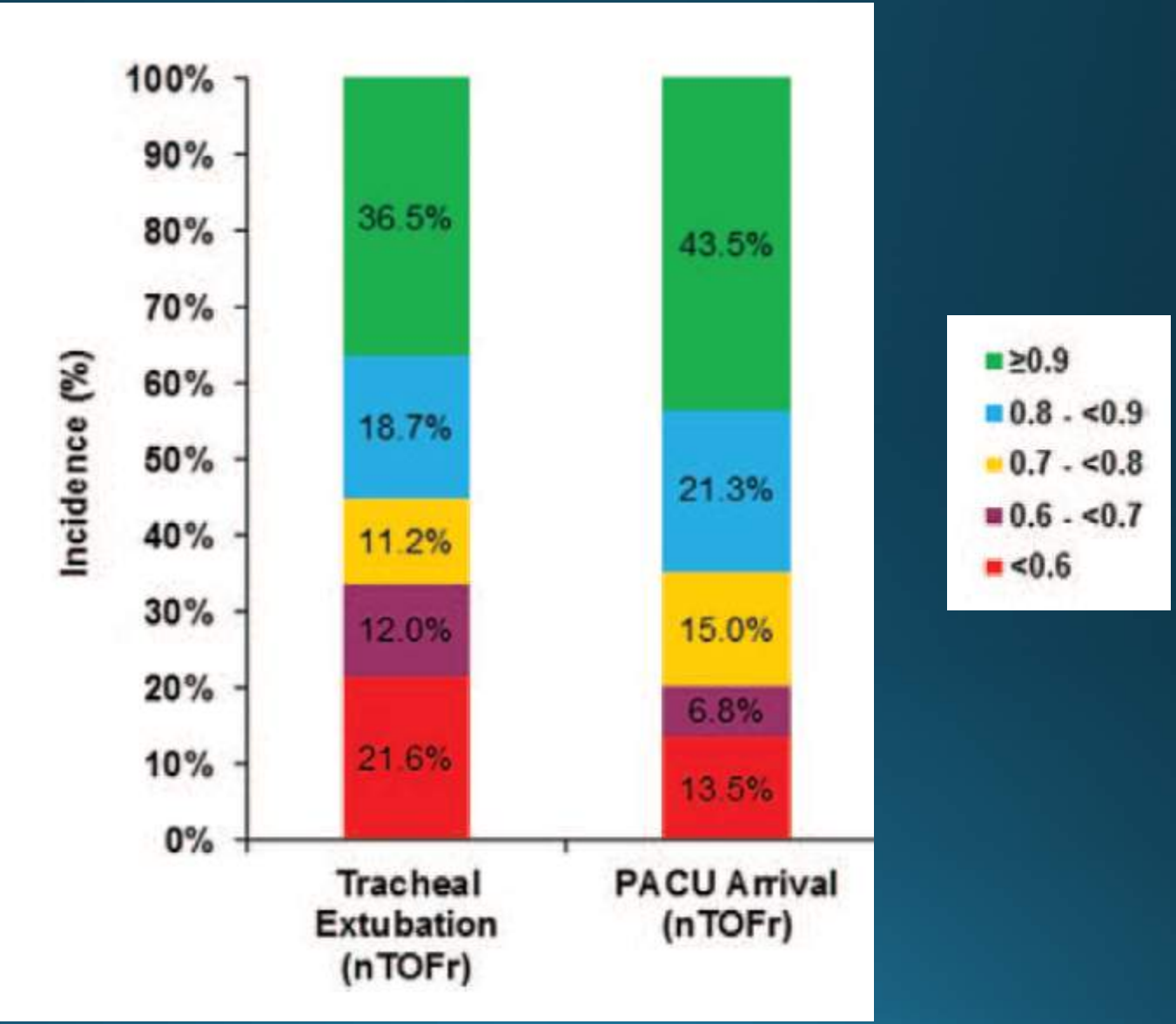
Blocco residuo



The RECITE Study: A Canadian Prospective, Multicenter Study of the Incidence and Severity of Residual Neuromuscular Blockade

(Anesth Analg 2015;121:366–72)

	Extubation	Salle de réveil
Neuromuscular blocking agent, *n* (%)		
Rocuronium	240 (99.6%)	207 (100%)
Cisatracurium	2 (0.8%)	1 (0.5%)
Succinylcholine	15 (6.2%)	6 (2.9%)
Reversal agent use, *n* (%)		
Neostigmine	178 (73.9%)	149 (72.0%)
Peripheral nerve stimulator use, *n* (%)	162 (67.2%)	137 (66.2%)



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Residual neuromuscular blockade in the postanesthesia care unit: observational cross-sectional study of a multicenter cohort

Minerva Anestesiologica 2016 December;82(12):1267-77

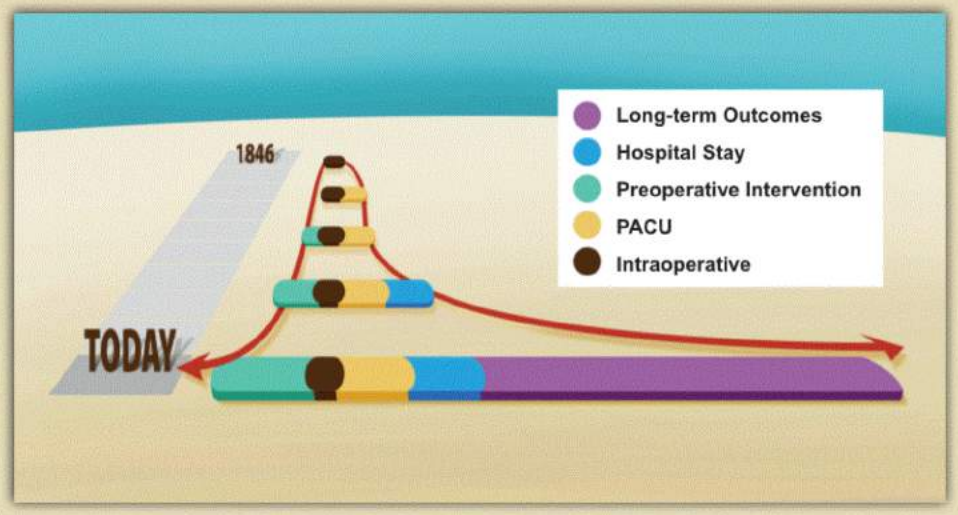
- 190 / 711 pazienti con CR (26,7%)
- 50% con monitoraggio

July 2009
Volume 111, Number 1
ISSN 0003-3022

Anesthesiology

The Journal of the American Society of Anesthesiologists, Inc.
www.anesthesiology.org

The Broadening Horizons of Anesthesia Care



- Sessler: Long-term Consequences of Anesthetic Management, pp. 1–4.

Full Text
OVID

Published for the Society by Wolters Kluwer Health | Lippincott Williams & Wilkins

Conseguenze

- La deglutizione è alterata quando T4/T1 < 0,9
  - Vie aeree non protette
- Effetti residui dei prodotti anestetici agiscono in sinergia sul blocco residuo

In caso del blocco neuromusculare residuo (T4/T1 < 0,9), le complicanze polmonari postoperatorie sono del 17% (vs. 5%)

Sundman E. *Anesthesiology*; 2000,92:765
Berg H. *Acta Anaesth Scand* 1997;41:1095

Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine *versus* sugammadex

Minerva Anestesiologica 2016;82(7):735-42

TABLE II.—*TOFr according to NMBD and reversal agent used.*

TOFr	Cis-none	Cis-neostig	Rocu-none	Rocu-sugamm
<0.7	15 (10.9%)	5 (5.4%)	11 (4.6%)	0 (0.0%)
0.7-0.9	32 (23.2%)	21 (22.8%)	70 (29.4%)	1 (1.2%)
>0.9	91 (65.9%)	66 (71.8%)	157 (66%)	86 (98.8%)

TABLE III.—*Minor CREs according to NMBD and reversal agent used.*

CREs	Cis-none	Cis-neostig	Rocu-none	Rocu-sugamm
Minor CREs	38 (27.5%)	16 (17.4%)	25 (10.5%)	2 (2.3%)
No minor CREs	100 (72.5%)	76 (82.6%)	213 (89.5%)	85 (97.7%)

TABLE IV.—*Major respiratory complications according to NMBD and reversal agent used.*

Complications	Cis-neostig	Cis-none	Rocu-none	Rocu-sugamm
No major compl.	84 (91.3%)	128 (92.8%)	215 (90.3%)	86 (98.9%)
Yes major compl.	8 (8.7%)	10 (7.2%)	23 (9.7%)	1 (1.1%)

TABLE V.—*Respiratory complications according to PORC.*

Complications	no PORC N. (%)	PORC N. (%)
No compl.	366 (80.1%)	91 (19.9%)
Minor compl.	31 (38.3%)	50 (61.7%)
Major compl.	3 (7.1%)	39 (92.9%)

Complications pulmonaires postopératoires 1% 22%
PORC

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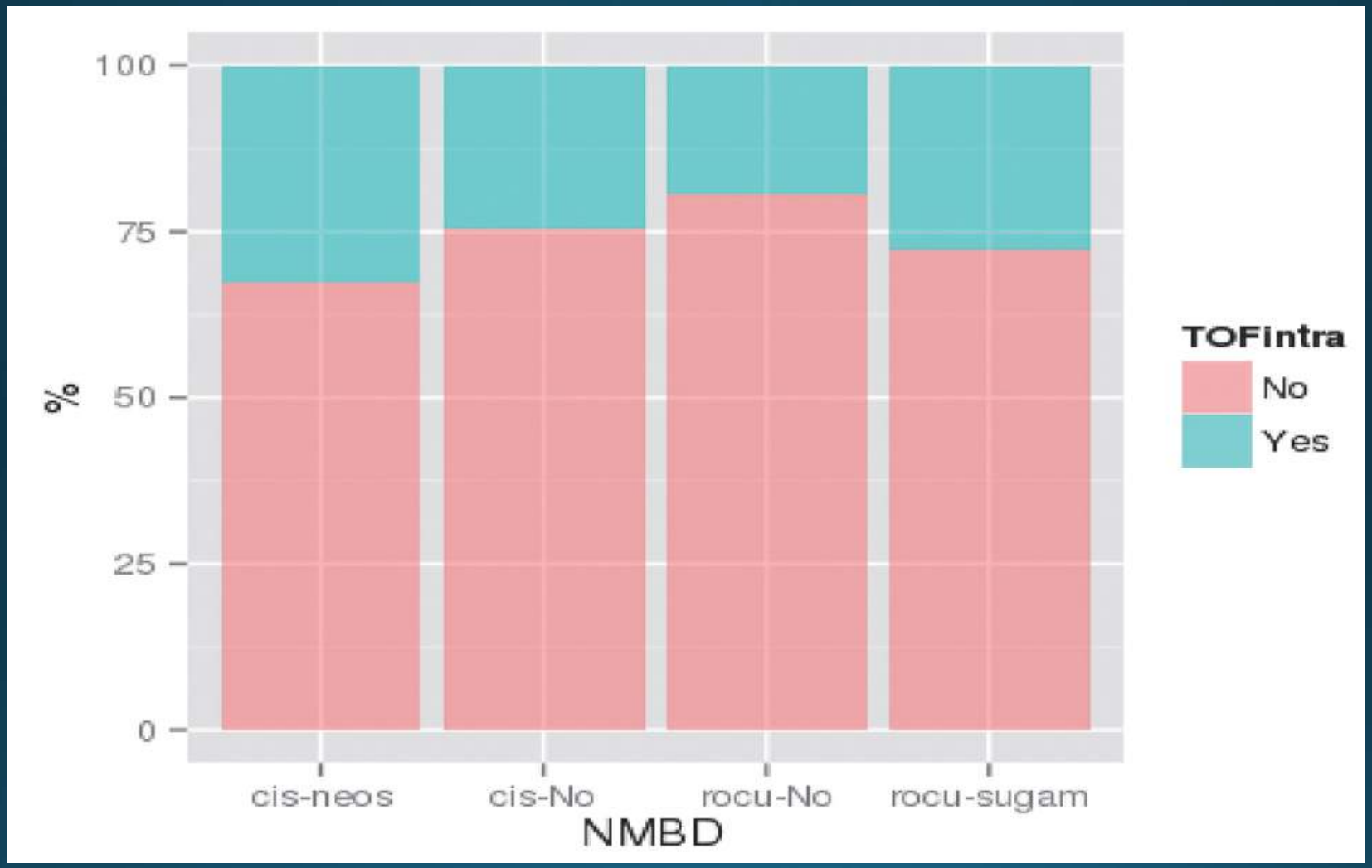

Solo il **30%** dei pazienti hanno un monitoraggio del blocco neuromusculare

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Conseguenze

	Espagne	Suisse
Popolazione	46,56 MIO	8,37 MIO
Chirurgie per anno	4'500'000	800 – 900'000
AG con curari	1'000'000	200'000

Conseguenze

	Espagne	Suisse
Popolazione	46,56 MIO	8,37 MIO
Chirurgie per anno	4'500'000	800 – 900'000
AG con curari	1'000'000	200'000
Curarizzazione residua	300'000	60'000

Conseguenze

	Espagne	Suisse
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Chirurgie per anno	4'500'000	800 – 900'000
AG con curari	1'000'000	200'000
Curarizzazione residua	300'000	60'000
Complicanze polmonari con 30% CR	7'000 + 66'000 = **73'000**	1'400 + 13'200 = **14'600**

Conseguenze

	Espagne	Suisse
Popolazione	46,56 MIO	8,37 MIO
Chirurgie per anno	4'500'000	800 – 900'000
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Curarizzazione residua	300'000	60'000
Complicanze polmonari con 30% CR	7'000 + 66'000 = **73'000**	1'400 + 13'200 = **14'600**
Complicanze polmonari senza CR	10'000	2'000

Conseguenze

	Espagne	Suisse	HFR-Fribourg
Popolazione	46,56 MIO	8,37 MIO	12'000
Chirurgie per anno	4'500'000	800 – 900'000	10'000
AG con curari	1'000'000	200'000	6'000
Curarizzazione residua	300'000	60'000	2'000
Complicanze polmonari con 30% CR	7'000 + 66'000 = **73'000**	1'400 + 13'200 = **14'600**	40 + 440 = **480**
Complicanze polmonari senza CR	10'000	2'000	60

Monitoraggio

Recupero spontaneo

Residual Paralysis in the PACU after a Single Intubating Dose of Nondepolarizing Muscle Relaxant with an Intermediate Duration of Action

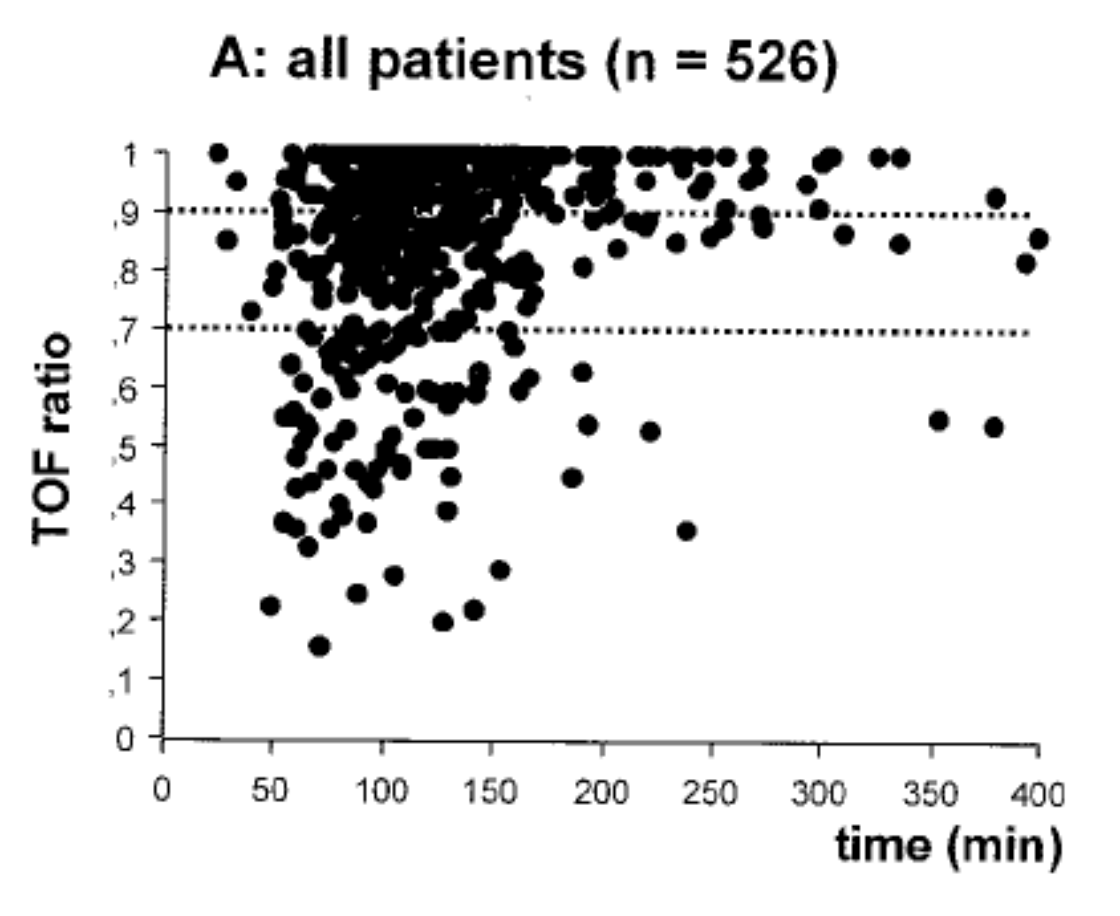
Anesthesiology 2003; 98:1042–8

Recupero spontaneo

- 546 pazienti
- Dose unica
  - vécuronium, rocuronium, atracurium
- Durata 22 – 397 min
- Nessun antagonismo
- Misure:
  - TOF e DBS qualitative
  - TOF con accelerometro
  - Sollevare la testa 5 sec e test dell'abbassa-lingua

Recupero spontaneo

TOF < 0,7: 16% (85)
TOF < 0,9: 45% (237)



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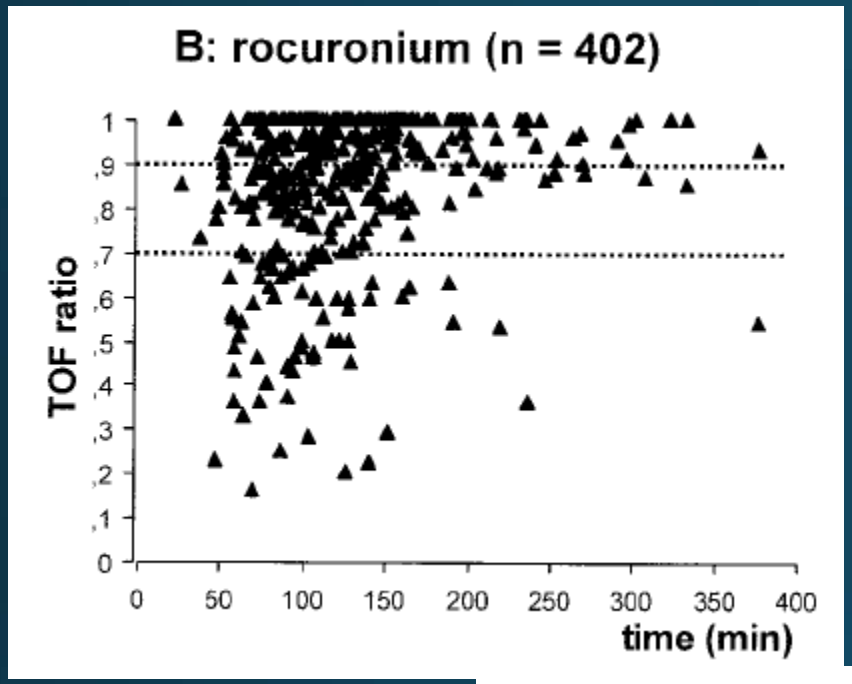
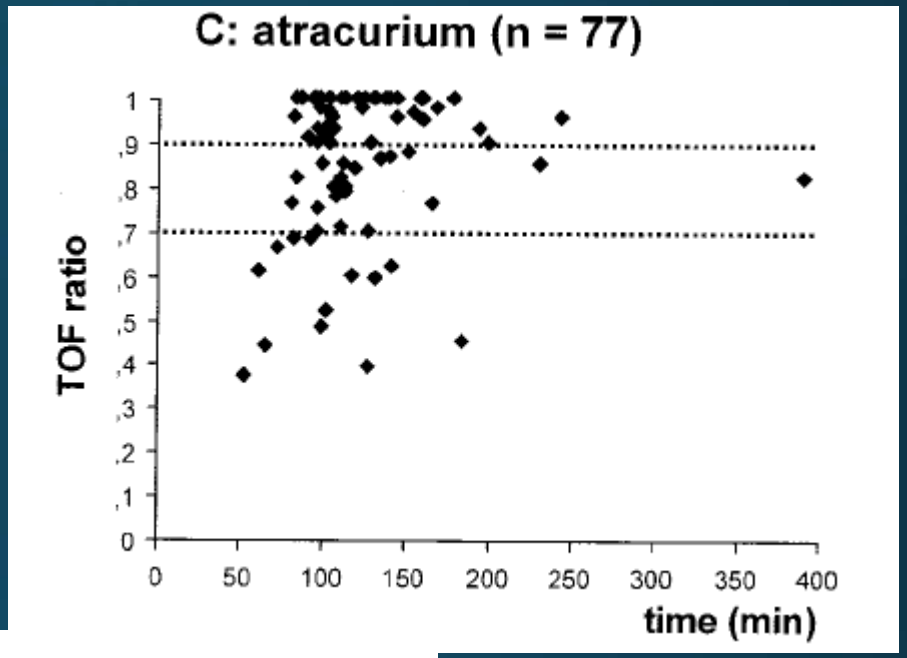

B: rocuronium (n = 402)
TOF ratio
time (min)


C: atracurium (n = 77)
TOF ratio
time (min)

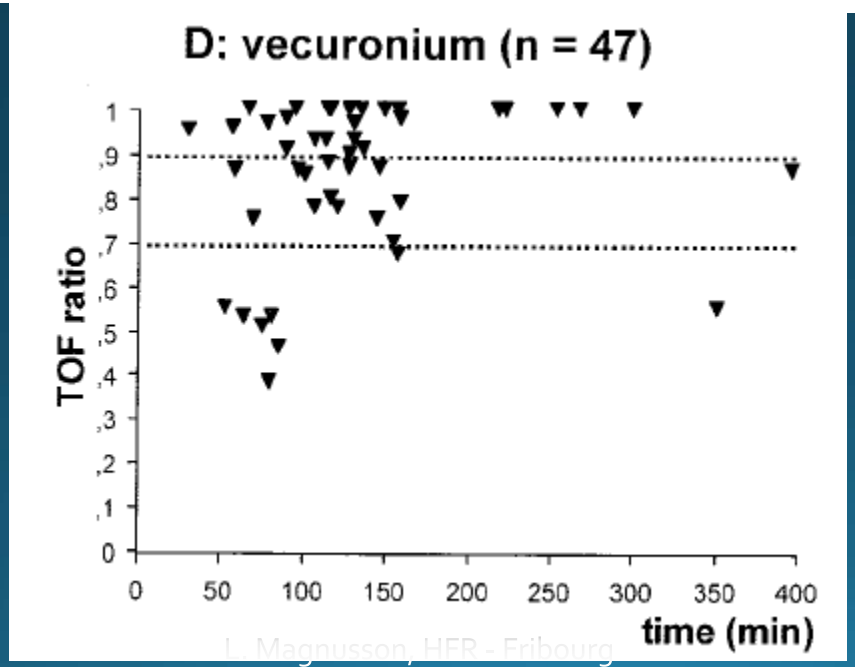

D: vecuronium (n = 47)
TOF ratio
time (min)

Table 2. Relationship Between Measured Train-of-Four Ratio Threshold (0.7 or 0.9) and Clinical Weakness

		Measured TOF Ratio		Measured TOF Ratio	
		<0.7 (n = 85)	>0.7 (n = 441)	<0.9 (n = 237)	>0.9 (n = 289)
TOF fade detected (n = 526)	Yes	23 (27)	6 (1)	27 (12)	2 (<1)
	No	62 (73)	435 (99)	210 (88)	287 (99)
DBS fade detected (n = 526)	Yes	30 (35)	6 (1)	35 (15)	1 (<1)
	No	55 (65)	435 (99)	202 (85)	288 (99)
		Measured TOF Ratio		Measured TOF Ratio	
		<0.7 (n = 51)	>0.7 (n = 280)	<0.9 (n = 146)	>0.9 (n = 185)
Head lift test (n = 331)	Failure	10 (20)	41 (15)	27 (18)	24 (13)
	Success	41 (80)	239 (85)	119 (82)	161 (87)
		Measured TOF Ratio		Measured TOF Ratio	
		<0.7 (n = 46)	>0.7 (n = 262)	<0.9 (n = 139)	>0.9 (n = 169)
Tongue depressor test (n = 308)	Failure	10 (22)	25 (10)	19 (14)	16 (10)
	Success	36 (78)	237 (90)	120 (86)	153 (90)

		Sensitivity % (CI)	
	n	TOF < 0.7	TOF < 0.9
Head lift	331	19 (15–23)	11 (9–14)
Tongue depressor	308	21 (17–26)	13 (10–17)
TOF	526	27 (23–31)	11 (9–13)
DBS	526	35 (33–38)	14 (11–16)

Anesthesiology 2003; 98:1042–8

L. Magnusson, HFR - Fribourg

NMT
Recherche supramax.
MAC
%
N2O
Td4%
Total
ET
FI
35 mA
DIA
Réglage moniteur
Procédures
Données et pages
Tendances
Imprimer courbes

ml/cmH20
CO2
Adulte
SYS 80 180
DIA
NMT
Td4%
96
Total
4
10 s
MAC
%
N2O
ET
FI
Réglage alarmes
Réglage moniteur
Procédures
Données et pages
Tendances
Imprimer courbes

Curarizzazione obbligata

- Per le intubazioni
- Per le chirurgie più rischiose:
  - ORL, chir cardiaca, neurochir…

Curarizzazione desiderata o comfort

- Ortopedia
- Laparotomia
- Laparoscopia
- …

Laparotomia

- Diminuzione della pressione dei divaricatori ⇨
  - Riduzione dei dolori postop
- Diminuzione del tono muscolare alla chiusura ⇨
  - riduzione del rilascio delle suture ed eventrazione
  - Riduzione delle infezioni della parete
- Atmosfera più tranquilla

Deep neuromuscular block to optimize surgical space conditions during laparoscopic surgery: a systematic review and meta-analysis

British Journal of Anaesthesia, 118 (6): 834–42 (2017)

Spazio chirurgico

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Dubois 2014	4.58	0.67	50	3.78	1.27	50	12.5%	0.80 [0.40, 1.20]
Kim 2016	4.6	0.67	30	3.84	0.52	31	16.9%	0.76 [0.46, 1.06]
Koo 2016	4.13	1.13	32	3.16	1.02	32	8.6%	0.97 [0.44, 1.50]
Madsen 2015	5	0.00001	7	4.29	0.49	7	14.0%	0.71 [0.35, 1.07]
Martini 2013	4.7	0.4	12	4	0.4	12	16.0%	0.70 [0.38, 1.02]
Staehr-Rye 2014	3.92	0.86	25	3.91	0.67	23	11.2%	0.01 [−0.42, 0.44]
Torensma 2016	4.8	0.36	50	4.2	0.76	50	20.9%	0.60 [0.37, 0.83]
Total (95% CI)			206			205	100.0%	0.65 [0.47, 0.83]

Heterogeneity: Tau^2=0.03; Chi^2=11.19, df=6 (P=0.08); I^2=46%
Test for overall effect: Z=7.04 (P<0.00001)

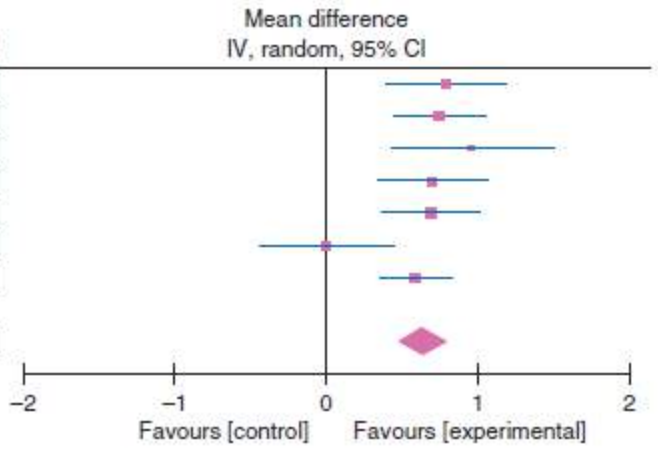


Fig 3 Surgical space conditions are improved by the use of deep neuromuscular block (NMB). Forest plot of studies comparing surgical space conditions during laparoscopic procedures with deep NMB *vs* moderate, shallow, or no NMB. The effect size is calculated as the mean difference in surgical rating score (range 1–5) and corresponding 95% confidence intervals (95% CI).

Durata della chirurgia

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Blobner 2015	69	10.2	25	69	13.8	15	9.8%	0.00 [−8.05, 8.05]
Kim 2016	197.2	59	30	213.6	77.4	31	0.5%	−16.40 [−50.87, 18.07]
Koo 2016	39.3	9	32	46.8	15.7	32	16.2%	−7.50 [−13.77, −1.23]
Madsen 2015	65	46.5	49	70	26.5	50	2.8%	−5.00 [−19.95, 9.95]
Martini 2013	144	35	12	141	50	12	0.5%	3.00 [−31.53, 37.53]
Staehr-Rye 2014	39	5.2	25	39.25	6.7	23	54.6%	−0.25 [−3.66, 3.16]
Torensma 2016	43	13.5	50	41	22.75	50	11.8%	2.00 [−5.33, 9.33]
Yoo 2015	111	21	34	115	32	32	3.7%	−4.00 [−17.14, 9.14]
Total (95% CI)			257			245	100.0%	−1.47 [−4.00, 1.05]

Heterogeneity: Tau^2=0.00: Chi^2=6.17, df=7 (P=0.52): I^2=0%
Test for overall effect: Z=1.15 (P=0.25)

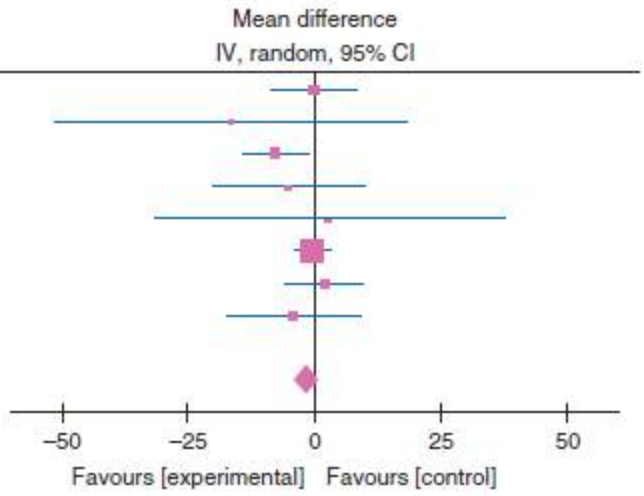


Fig 4 The duration of surgery is not significantly decreased by the use of deep NMB. Forest plot of studies comparing the duration of surgery during laparoscopic procedures with deep *vs* moderate or no NMB. The effect size is calculated as the mean difference in duration of surgery in minutes and corresponding 95% confidence intervals (95% CI).

Dolori postoperatori

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Kim 2016	2.3	0.6	30	2.9	0.3	31	66.2%	−0.60 [−0.84, −0.36]
Koo 2016	6	1.5	32	6	1.75	32	5.9%	0.00 [−0.80, 0.80]
Martini 2013	2.1	2.2	12	2.6	1.6	12	1.6%	−0.50 [−2.04, 1.04]
Torensma 2016	3.9	1.44	50	4.4	1.26	50	13.5%	−0.50 [−1.03, 0.03]
Yoo 2015	2.62	0.7	34	2.97	1.42	32	12.7%	−0.35 [−0.90, 0.20]
Total (95% CI)			158			157	100.0%	−0.52 [−0.71, −0.32]

Heterogeneity: Tau^2=0.00: Chi^2=2.44, df=4 (P=0.66): I^2=0%

Test for overall effect: Z=5.21 (P<0.00001)

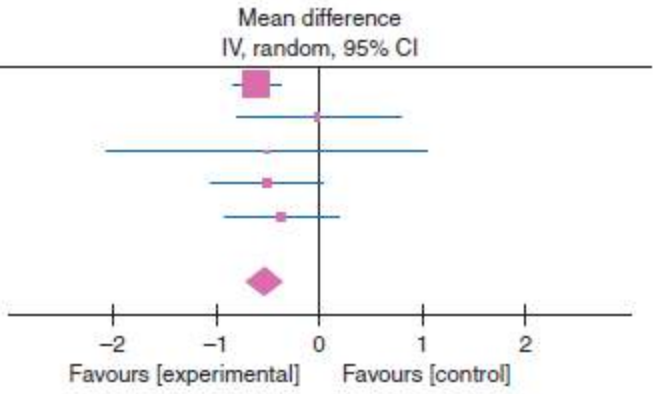


Fig 5 Postoperative pain in the postanaesthesia care unit is reduced by the use of deep neuromuscular block (NMB). Forest plot of studies comparing postoperative pain 1 h after laparoscopic procedures with deep NMB *vs* moderate NMB. The effect size is calculated as the mean difference in NRS (range 0–10) and corresponding 95% confidence intervals (95% CI).

Deep neuromuscular blockade and low insufflation pressure during laparoscopic hysterectomy

Dan Med J 64/5 | May 2017

Events during laparoscopy in the deep and standard neuromuscular block groups.

	Deep, n (%) (N = 55)	Standard, n (%) (N = 55)	ARR (95% CI)	p-value[a]
Sudden abdominal contraction	0	12 (21.8)	0.22 (0.11-0.34)	< 0.001
Insufflator alarm	0	10 (18.2)	0.18 (0.07-0.30)	0.001
Increased abdominal wall tension	0	8 (14.5)	0.14 (0.05-0.26)	0.006

ARR = absolute risk reduction; CI = confidence interval.

Surgical conditions while suturing the fascia. The values are number of patients.

Ratings***	Deep NMB group	Standard NMB group
1: excellent	40	23
2: good	2	17
3: acceptable	0	1
4: poor	0	0

NMB = neuromuscular block.

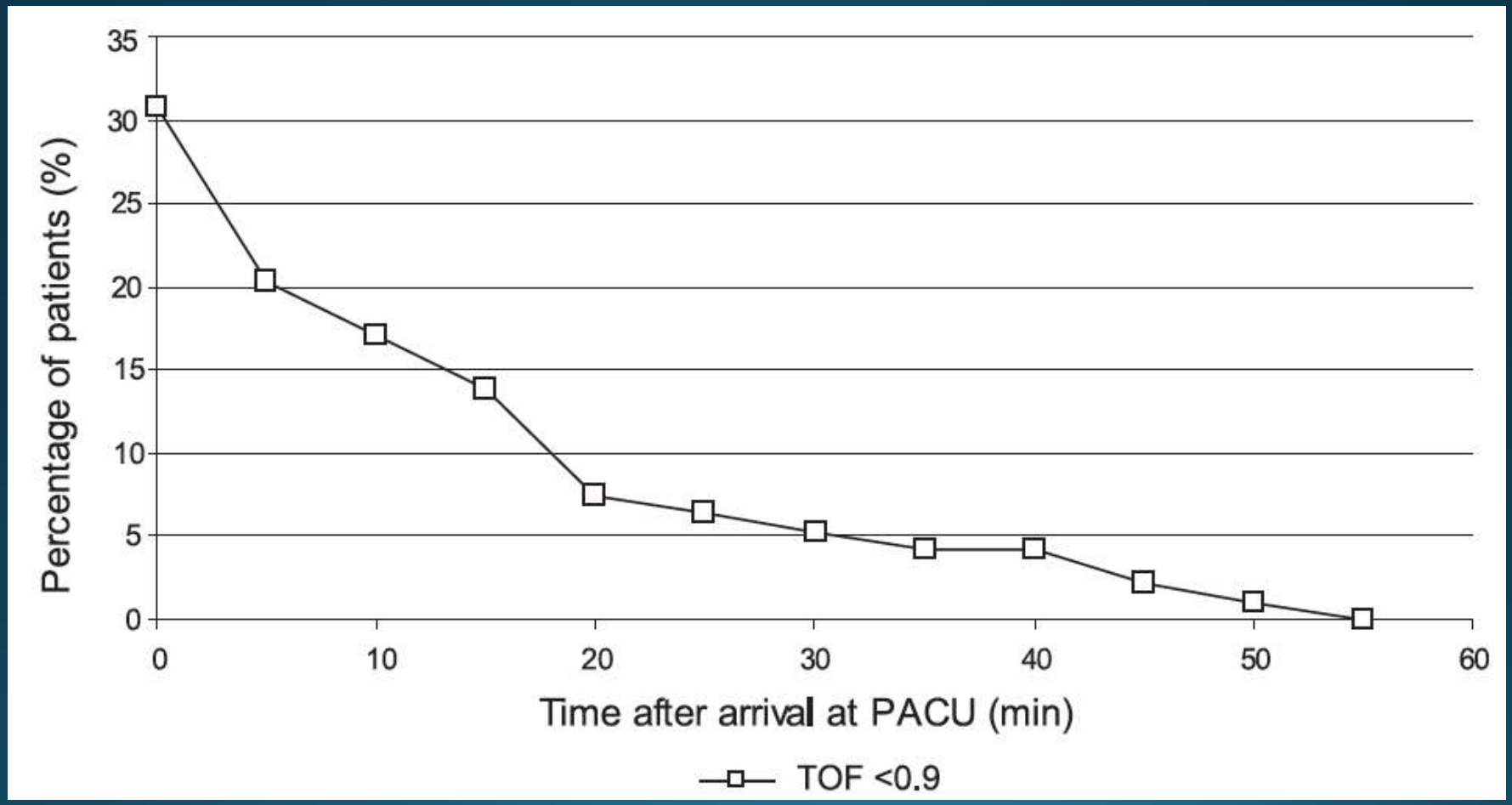
Riassunto

- Rilassamento muscolare ottimale:
  - TOF 0 – 1
  - Laparotomia, toracotomia, ORL
- Curarisation musculaire maximale:
  - TOF = 0 et CPT < 5
  - Laparoscopie, risque vital
- Bolus répétés ou perfusion continue de rocuronium

Antagonismo

- Recupero spontaneo (monitoraggio obbligatorio)
- Néostigmina
- Sugammadex

Néostigmina vs sugammadex



Néostigmina vs sugammadex

Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: results of a randomised, controlled trial

Manfred Blobner, Lars I. Eriksson, Jens Scholz, Johann Motsch, Giorgio Della Rocca and Martine E. Prins

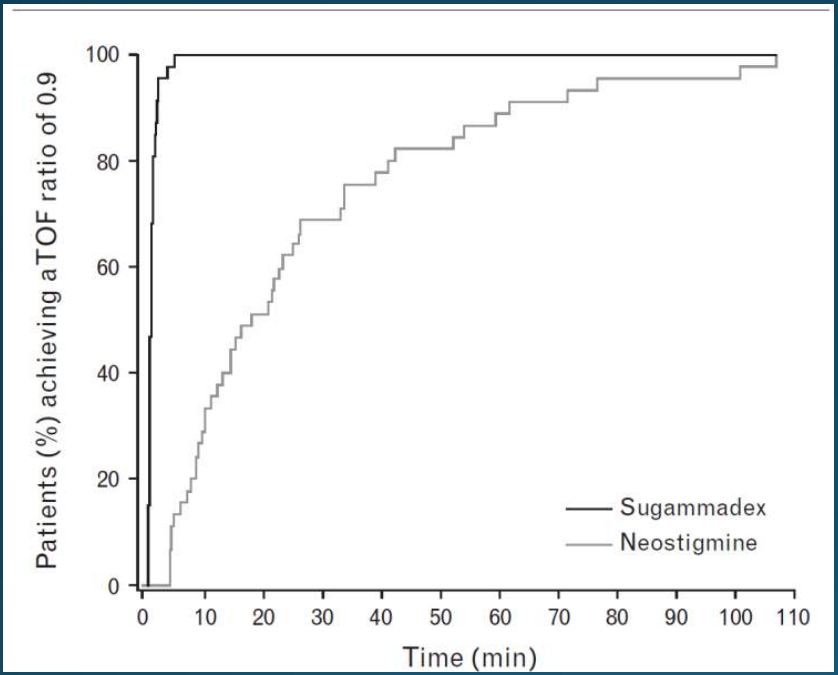
Eur J Anaesthesiol 2010;27:874–881

	Sugammadex (N = 48)	Neostigmine (N = 48)	P[a]
Recovery of T_4/T_1 ratio to 0.9			
n	47[b]	45[b]	
Geometric mean (min)	1.5	18.6	<0.0001
95% CI[c]	1.3–1.6	14.2–24.4	
Median (min)	1.4	18.5	
Range (min)	0.9–5.4	3.7–106.9	
Recovery of T_4/T_1 ratio to 0.8			
n	47[b]	48	
Geometric mean (min)	1.2	10.8	<0.0001
95% CI[c]	1.1–1.3	8.5–13.7	
Median (min)	1.2	9.8	
Range (min)	0.9–3.4	2.7–67.9	
Recovery of T_4/T_1 ratio to 0.7			
n	47[b]	48	
Geometric mean (min)	1.1	7.2	<0.0001
95% CI[c]	1.0–1.2	5.8–8.9	
Median (min)	1.0	6.2	
Range (min)	0.7–2.7	2.4–41.1	

Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: results of a randomised, controlled trial

Manfred Blobner, Lars I. Eriksson, Jens Scholz, Johann Motsch, Giorgio Della Rocca and Martine E. Prins

Eur J Anaesthesiol 2010;27:874–881



- Con sugammadex 98% dei pazienti recuperano un TOF > 0,9 in meno di 5 minuti rispetto all' 11% con néostigmina
- Per ottenere 98% occorrono **101 minuti**

- Fine intervento
- TOF 4/4, 20%
- Néostigmina 50 mcg/kg

- Après 6 minutes: photo

L. Magnusson, HFR - Fribourg

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Sugammadex 100 mg

Monitoring systématique

- TOF = 0, conto post-tetanico > 1: sugammadex 4 mg/kg
- TOF 2-3/4: sugammadex 2 mg/kg
- TOF 4/4: néostigmina ET monitorare sino a TOF > 90%

- Dopo néostigmina o sugammadex
- Monitoraggio sino a TOF > 90%

Estubazione solamente sino a TOF > 90%

- Se limite massimo raggiunto o impazienza : Sugammadex 1 mg / kg

Rischi aumentati di CPP

- Ogni anestesia generale con curarizzazione nei:
  - Pazienti obesi con morbidita'
  - Pazienti con SAOS
  - Pazienti con malattia della giunzione neuro-muscolare
- **Tutti i pazienti ASA 3-4 e/o età > 60 anni**
- **Chirurgia addominale o toracica**

Strategia se rischi aumentati

Estubazione solo con TOF = 100%

Considerazioni economiche

- Diminuzione tempo occupazione della sala
- Diminuzione CPP
- Diminuzione ammissione non prevista in cure intense
- Diminuzione mortalità
- Diminuzione rischio di reintubazione
- Diminuzione durata soggiorno in sala risveglio

Ciò può esser ottenuto con un monitoraggio quantitativo sistematico

Considerazioni economiche

- Diminuzione del tempo di occupazione della sala
- **Diminuzione CPP**
- **Diminuzione ammissione non pevista in cure intense**
- Diminuzione mortalità
- Diminuzione rischio di reintubazione
- **Diminuzione durata soggiorno in sala risveglio**

Ciò può esser ottenuto con un monitoraggio quantitativo sistematico

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