Neuropronostication post ACR : quoi de neuf en 2025 ?

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Inserm U1266, institut de psychiatrie et Neurosciences de Paris (IPNP)

Outcomes following admission for out-of-hospital cardiac arrests

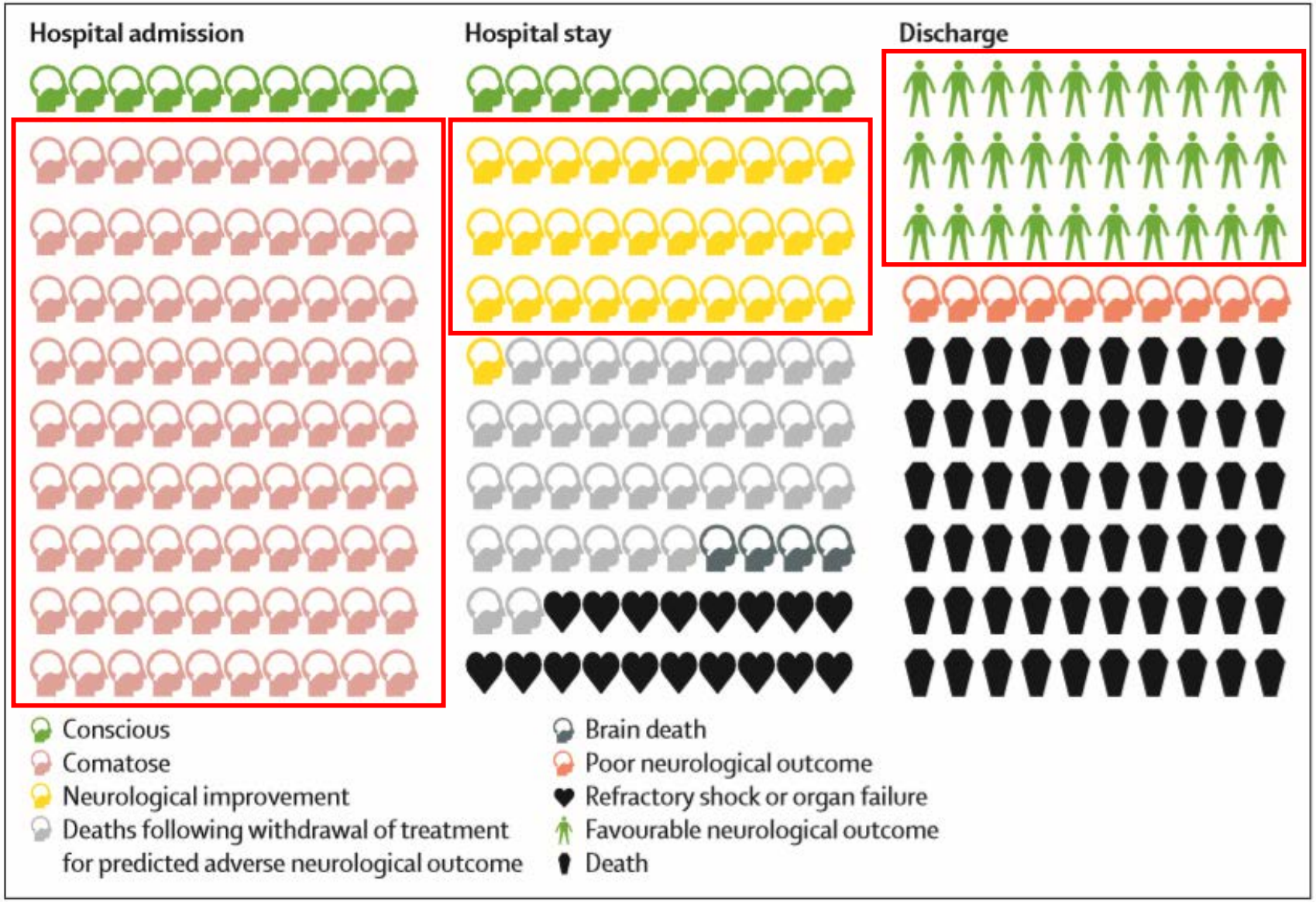
40 000 CA per year

↓

60 % CPR

↓

20 % ROSC



Perkins et al, Brain injury after cardiac arrest, Lancet, 2021

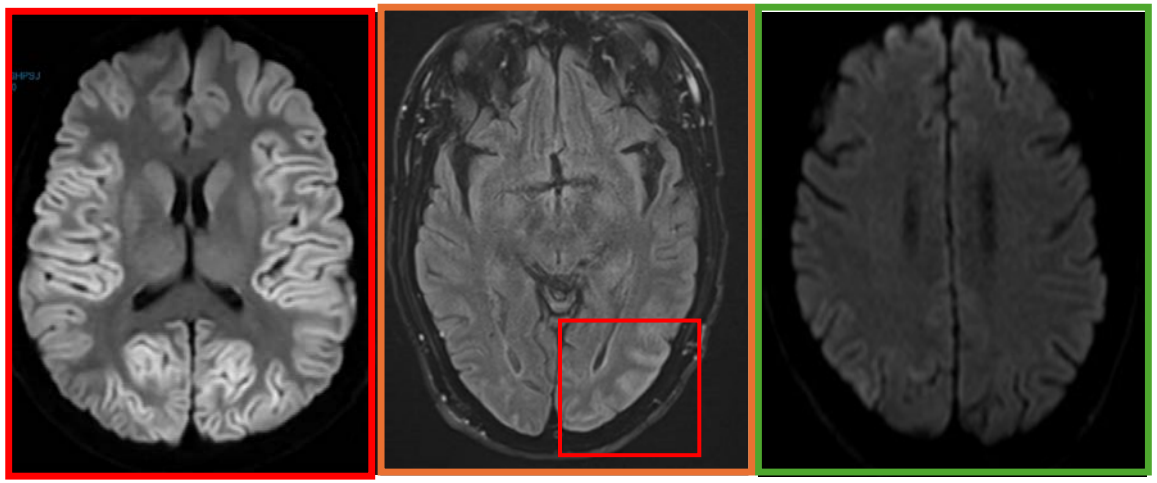
Hypoxic ischemic brain injury

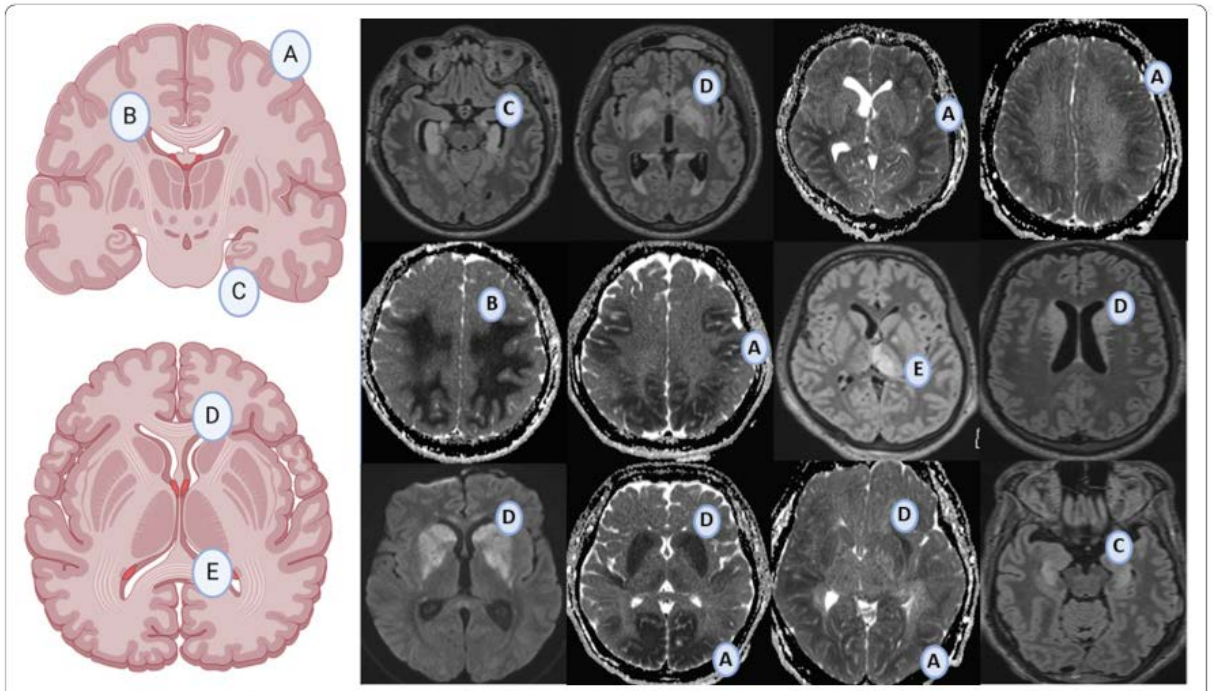
NARRATIVE REVIEW

Clinical heterogeneity and phenotyping of post cardiac arrest brain injury: one size may not fit all

Mypinder S. Sekhon[1,2,3,4*], Fabio Silvio Taccone[5], Markus B. Skrifvars[6], Donald E. Griesdale[7], Jonathan Elmer[8], Lionel Velly[9] and Chiara Robba[10,11]

Homogeneous brain injury ?





A. Cortex – grey matter; B. White matter; C.Hippocampi;
D. basal ganglia; E.thalamus

Hypoxic ischemic brain injury range from mild to severe

=> Considerable between-patient heterogeneity in the disease mechanisms and response to therapeutic interventions

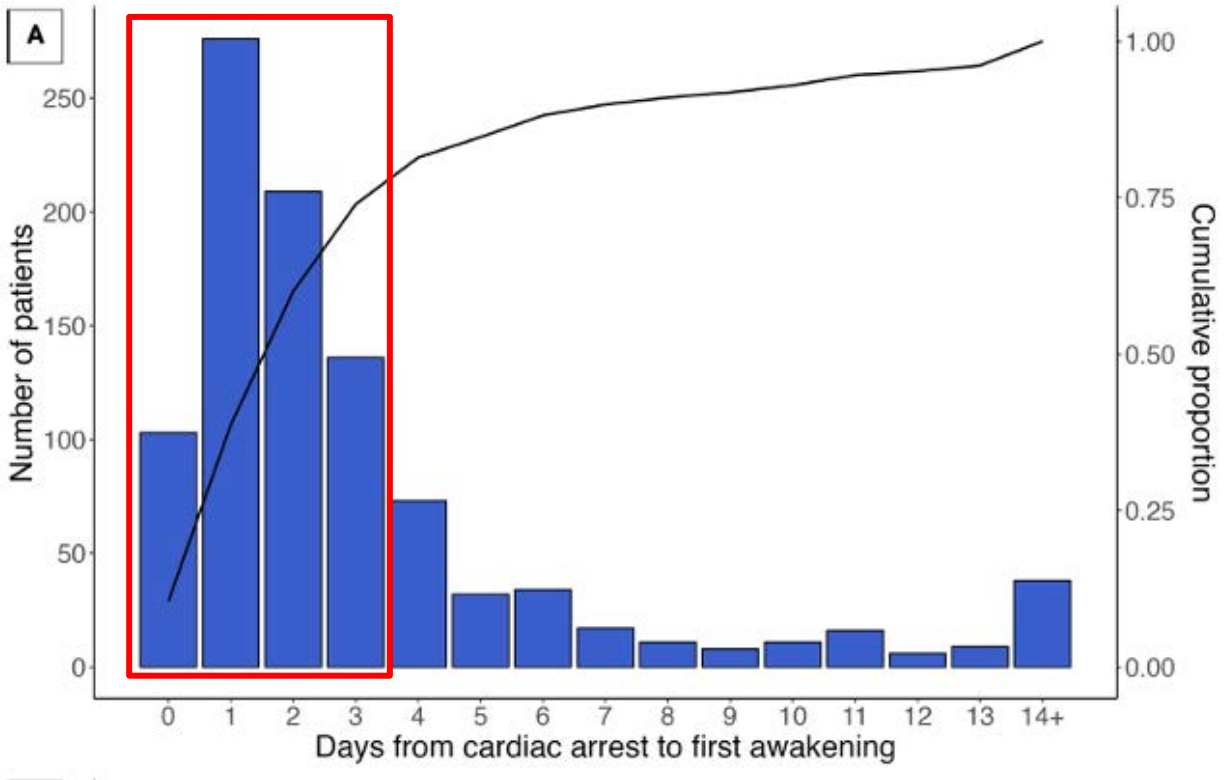
HIBI: time is brain !

Impact of coma duration on functional outcomes at discharge and long-term survival after cardiac arrest

Jonathan Tam[a,b,], Nicholas Case[a], Patrick Coppler[a], Clifton Callaway[a], Laura Faiver[b], Jonathan Elmer[a,b,c], on behalf of the University of Pittsburgh Post-Cardiac Arrest Service*

Resuscitation 2024

N= 979 patients awake during ICU stay



Delayed awakening with good outcome could happen

Risk factors : midazolam, age > 59, acute kidney injury, post resuscitation shock

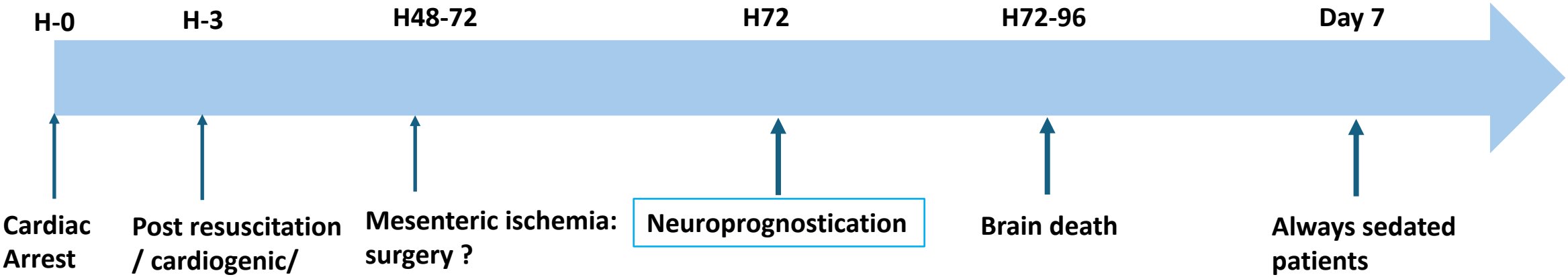
Paul et al ICM 2016
Paul et al Resuscitation 2018

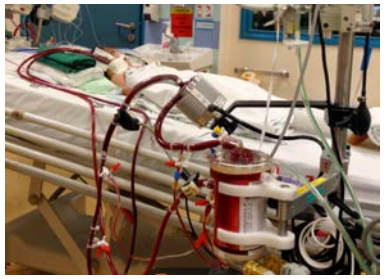
When should we start neuroprognostication ?

- ERC-ESICM guidelines 2025: **« coma ≥72h after CA, without confounding factors »**

⇒ **Avoid early WLST** secondary to *suppose* severe and irreversible hypoxic ischemic brain injury

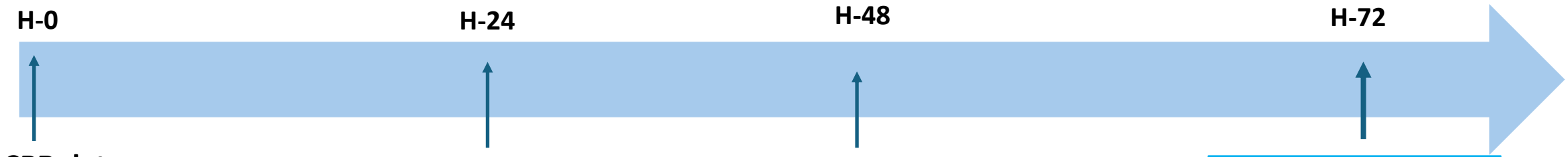
- **Potential complications after CA:**





When should we start neuroprognostication ?

- **Prognostic markers could influence early decisions:**



Could be helpful for withholding therapies but not for withdrawal life sustaining therapies

Not too early
Avoid inappropriate withdrawal

Not too late
avoid futile treatments

Coma or vegetative state at 24 days after CA : awakening is rarely oberved if no confouding factors

Hayamizu, resuscitation 2023

We need robust markers for neuroprognostication!

To predict poor outcome:

High specificity > 95%

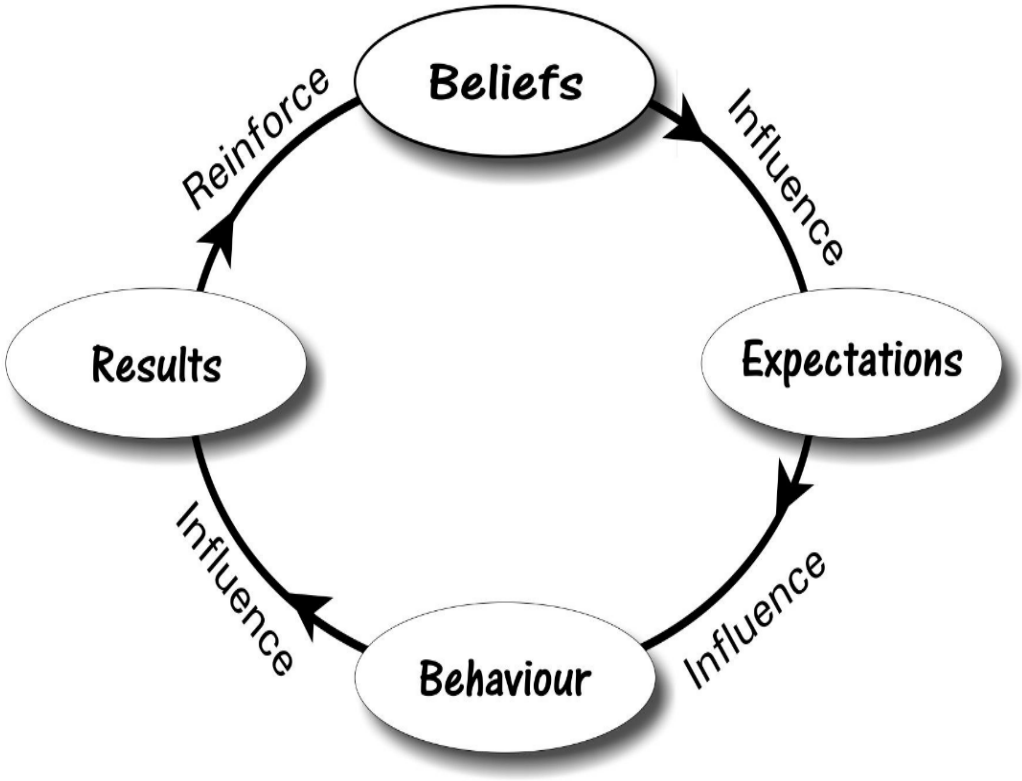
false positive rate < 5%

Good sensitivity

To predict good outcome:

High Predictive positive value (PPV)

Good sensitivity



Self fulfilling prophecy

Neurological prediction after CA: quality assessement

Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review

Claudio Sandroni[1,2], Sonia D'Arrigo[1*], Sofia Cacciola[1], Cornelia W. E. Hoedemaekers[3], Marlijn J. A. Kamps[4], Mauro Oddo[5], Fabio S. Taccone[6], Arianna Di Rocco[7], Frederick J. A. Meijer[8], Erik Westhall[9], Massimo Antonelli[1,2], Jasmeet Soar[10], Jerry P. Nolan[11] and Tobias Cronberg[12]

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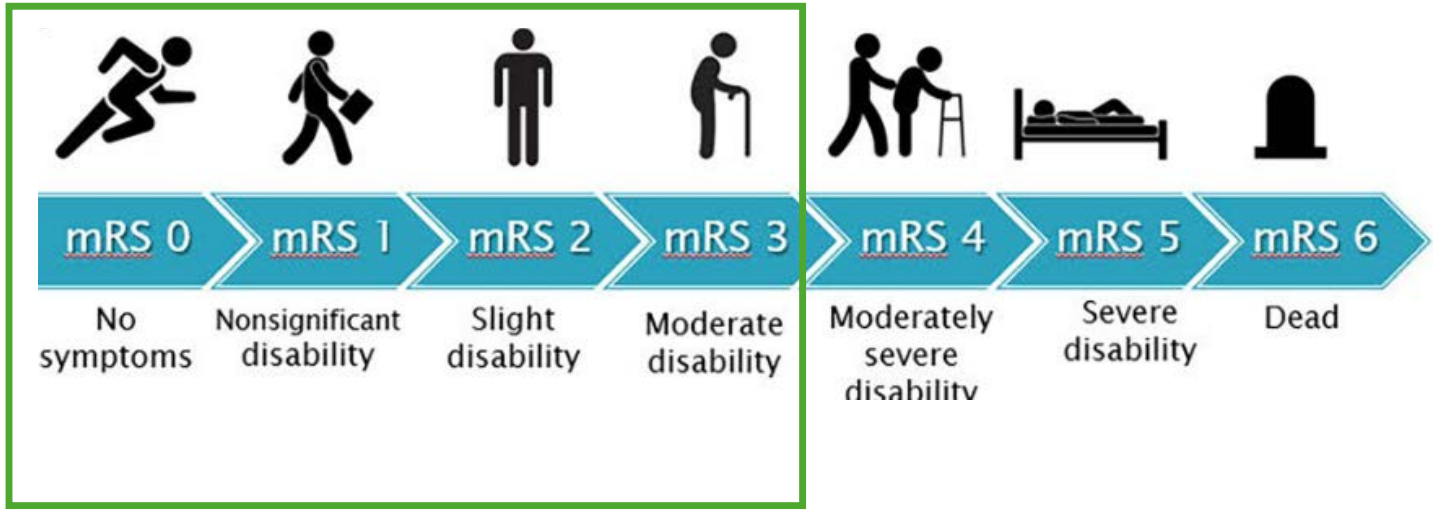
- **Most studies were at moderate or high risk of bias due to:**
- **Assessment on different scales with different thresholds at different time (3 months or more++)**

Cerebral performance category (CPC) score scale.[a]

CPC 1	Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.
CPC 2	Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
CPC 3	Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
CPC 4	Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
CPC 5	Brain death: apnea, areflexia, EEG silence, etc.

[a] From Safar P. Resuscitation after brain ischemia. In: Grenvik A, Safar P, editors. Brain failure and resuscitation. New York: Churchill Livingstone; 1981; p. 155–84.

CPC scale



Modified Rankin scale

Poor outcome prediction in comatose patient after cardiac arrest

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2025 Post-Resuscitation Care ☆

Jerry P. Nolan[a,b,#,], Claudio Sandroni[c,d,#], Alain Cariou[e], Tobias Cronberg[f], Sonia D'Arrigo[b,c], Kirstie Haywood[g], Astrid Hoedemaekers[h], Gisela Lilja[i,j], Nikolaos Nikolaou[k], Theresa Mariero Olasveengen[l], Chiara Robba[m], Markus B. Skrifvars[n], Paul Swindell[o], Jasmeet Soar[p]*

Unconscious patient
Motor score 5 or less at 72 h or later, and confounders excluded*

↓

*At least **TWO** unfavourable signs:*

- No pupillary** and corneal reflexes at 72 h or later
- Bilaterally absent N20 SSEP wave at 24 h or later
- Suppression or burst-suppression on EEG at 24 h or later
- NSE higher than 60µg L^{-1} *** at 48 h and / or 72 h
- Status myoclonus**** within 72 h
- Diffuse and extensive hypoxic-ischaemic injury on brain CT at any time or on MRI after 2 days

↓ YES

Poor neurological outcome very likely

Criteria	Specificity *	Sensitivity
Corneal and PLR absent	> 95%	10-20%
Pupillometry NPI ≤ 2/5	> 95%	10-20%
Absence of N20 SSEP	> 95%	30-60%
Highly malignant EEG	> 95%	10-50%
NSE > 60 µg/L	> 95%	40-80%
Status myoclonus	> 95%	5-40%
CT	> 95%	10-40%
MRI	> 95%	30-90%

*False positive rate < 5%

Nolan et al, ICM/resuscitation 2025

Effects of withdrawal of life-sustaining therapy on long-term neurological outcome after cardiac arrest – A multicentre matched cohort study

Alice Lagebrant[a,b,], Byung Kook Lee[c,d], Chun Song Youn[e], Claudio Sandroni[f,g], Jan Bělohlávek[h,i], Alain Cariou[j], Riccardo Carrai[k], Josef Dankiewicz[a,l], Hans Friberg[a,m], Anders M. Grejs[n,o], Antonello Grippo[k], Christian Hassager[p,q], Janneke Horn[r], Matthias Haenggi[s], Janus C. Jakobsen[t,u], Thomas R. Keeble[v,w], Hans Kirkegaard[o,x], Jesper Kjaergaard[p,q], Michael A. Kuiper[y], Dong Hun Lee[c,d], Helena Levin[a,z], Gisela Lilja[a,aa], Andreas Lundin[ab], Niklas Nielsen[a,ac], Mauro Oddo[ad], Sang Hoon Oh[e], Kyu Nam Park[e], Tommaso Pellis[ae], Chiara Robba[af,ag], Christian Rylander[ah], Seok Jin Ryu[c,d], Manoxj Saxena[ai,aj], Maenia Scarpino[k], Claudia Schrag[ak], Pascal Stammet[al,am], Christian Storm[an], Fabio Silvio Taccone[ao,ap], Matthew Thomas[aq], Susann Ullén[ar], Erik Westhall[a,as], Matt P. Wise[at], Paul Young[au,av,aw,ax], Tobias Cronberg[a,ay], Marion Moseby-Knappe[a,az]*

Patients with :

- **Withdrawal life sustaining therapies - WLST based on neurological criteria during the TTM or TTM2 trials**
- **vs "no WLST"/control patients from the KORHN or ProNeCA studies**

Unconscious patients after 72 h post-arrest

N=1717, including 29 % had WLST due to neurological criteria (median of 143 h)

matched patients with ≥ 2 unfavourable ERC/ESICM criteria.

Deciles of propensity score	Good functional outcome (%)			
	N = 133		*N* = 69	
	WLST	**KORHN**	**WLST**	**ProNeCA**
Outcome in matched cohort	0/133 (0)	0/133 (0)	0/69 (0)	0/69 (0)
Observed outcome in full included cohort[a]	0/303 (0)	0/326 (0)	0/303 (0)	0/87 (0)

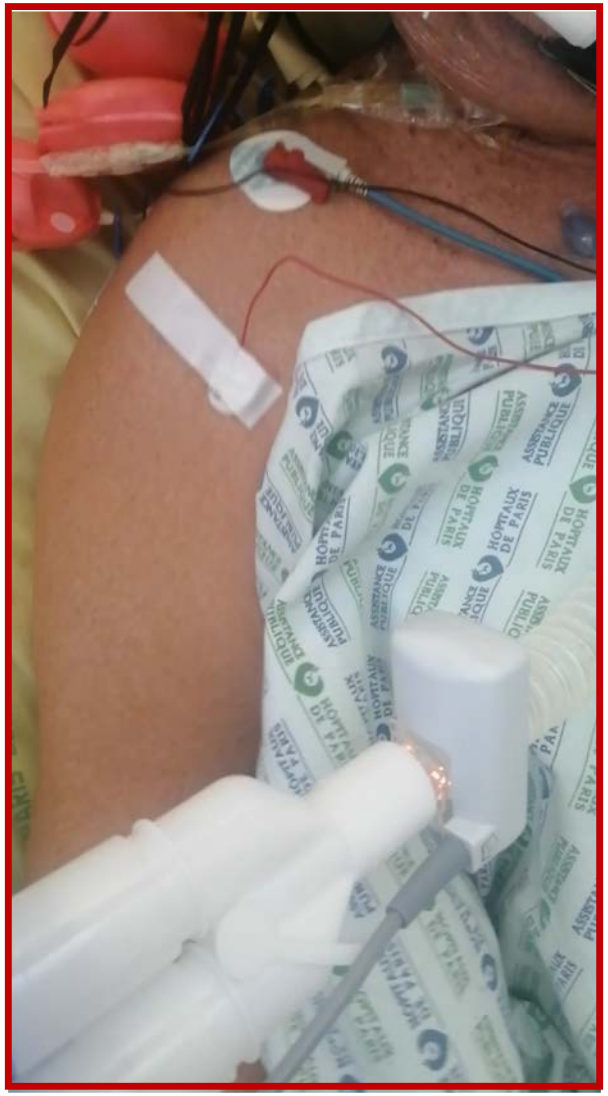
matched patients, irrespective of the number of ERC/ESICM criteria met.

Deciles of propensity score	Good functional outcome (%)			
	N = 298		*N* = 166	
	WLST	**KORHN**	**WLST**	**ProNeCA**
Overall matched cohort	1/298 (0.3)	55/298 (18.5)	0/166 (0)	43/166 (25.9)

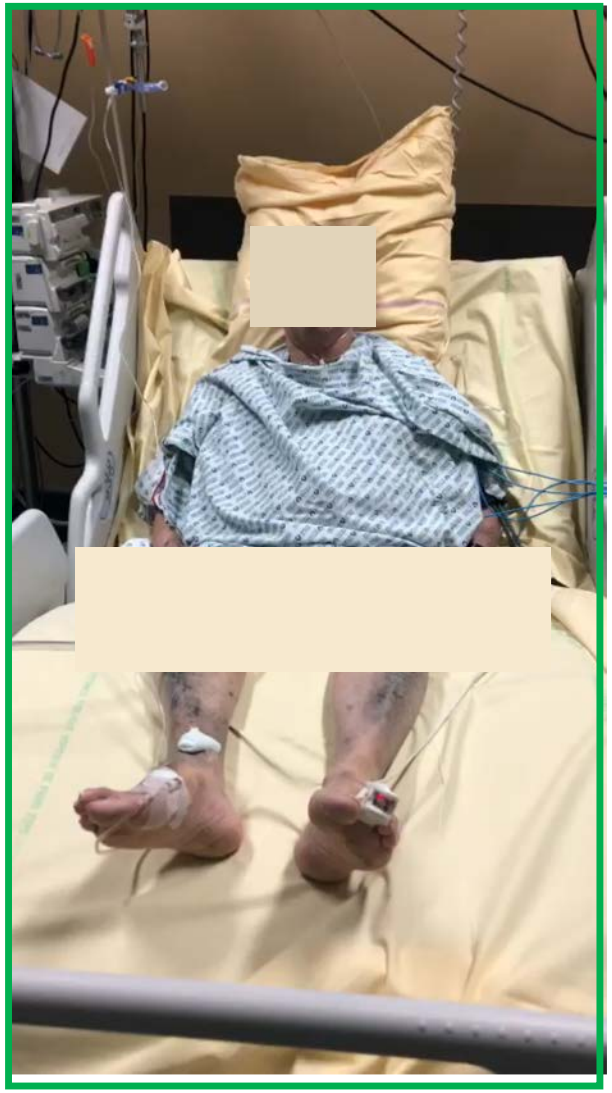
Observe and re-evaluate

Resuscitation 2025

Early localized myoclonus (<72h)
Poor outcome: false positive rate 0-22%



Status myoclonus (<72h): diffuses, mb, continuous, >30 min :
Poor outcome: false positive rate 0 %



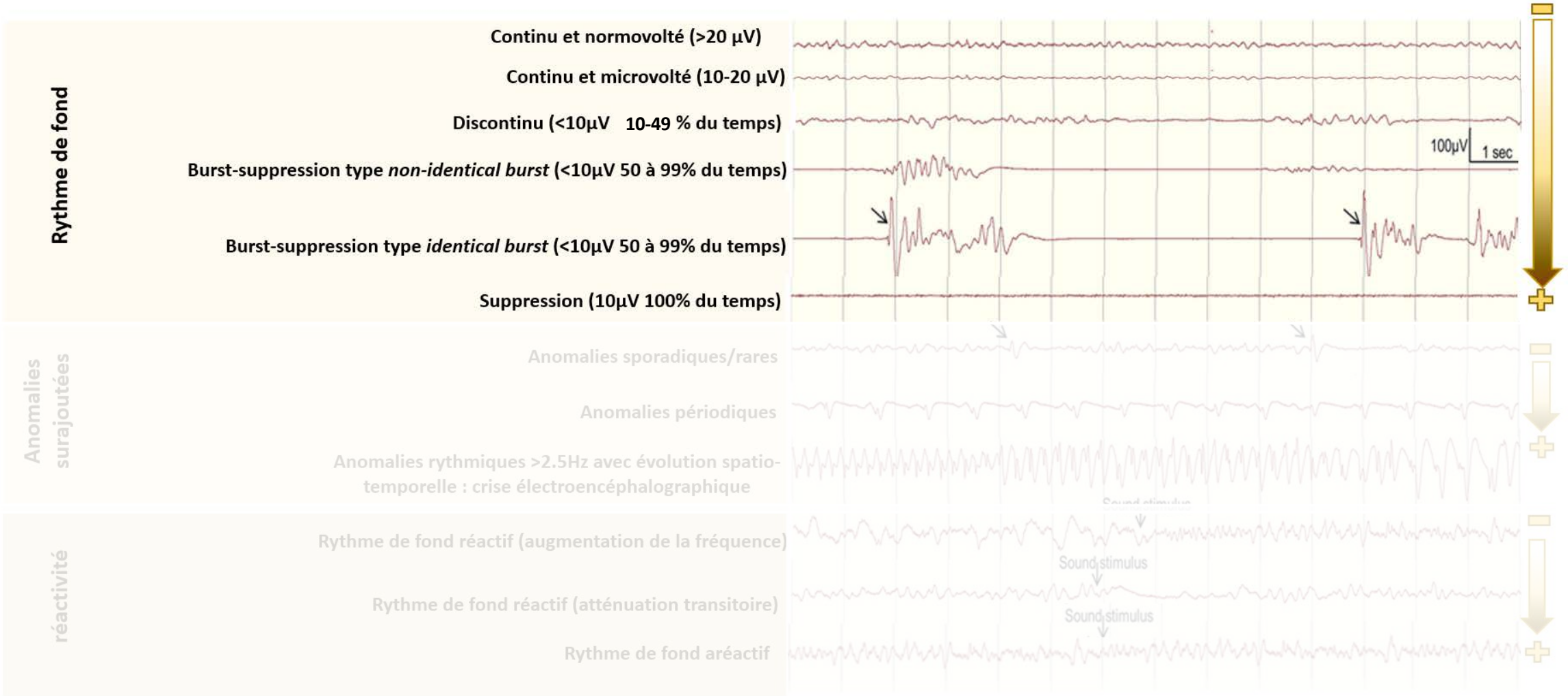
Late myoclonus (>72h) : no prognostic value
=> Lance Adams syndrome => antimyoclonic drugs (keppra, dépakine, nootropyl, fycompa)

Electroencephalogram EEG

Interest and interpretation of the EEG for ICU physicians

Sarah Benghanem[1,2,4,5,*] • Estelle Pruvost-Robieux[2,3,5] • Martine Gavaret[2,3,5]

Medecine intensive réanimation 2023



Benghanem et Rohaut, Traité de réanimation 2025

EEG in comatose patient after cardiac arrest

REVIEW Open Access

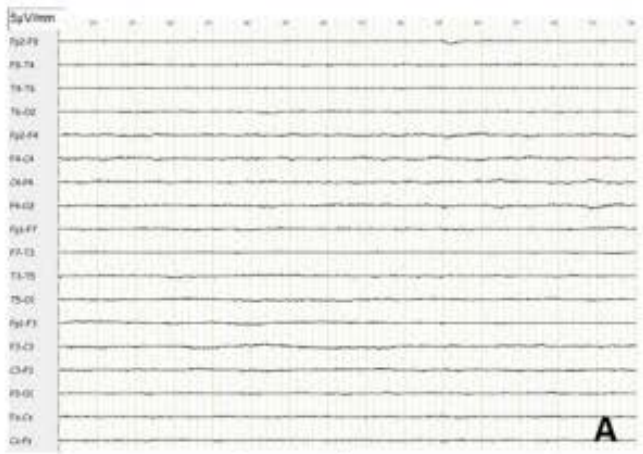
Prognostication after cardiac arrest: how EEG and evoked potentials may improve the challenge

Sarah Benghanem[1,2,5,7*], Estelle Pruvost-Robieux[2,4,7], Eléonore Bouchereau[3,7], Martine Gavaret[2,4,7] and Alain Cariou[1,2,5,6]

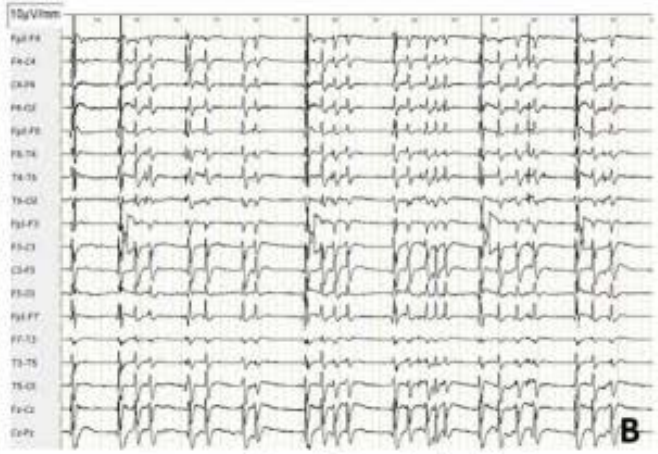
Annals of intensive care 2022

Highly malignant > 24h
Specificity 95-100 %
False positive rate 0-5%

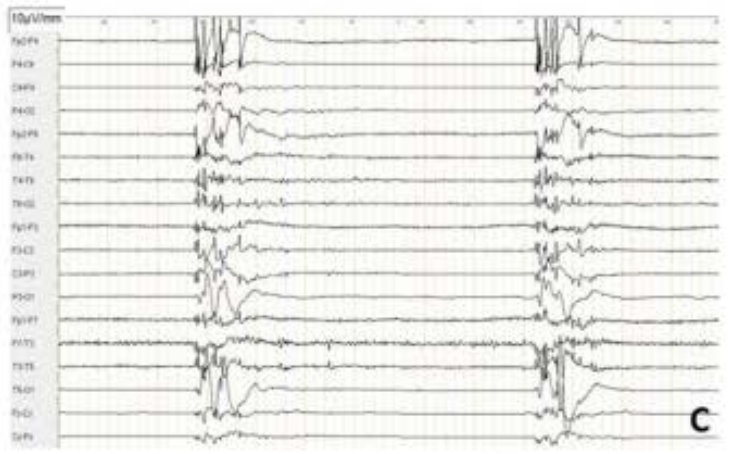
Highly malignant patterns: poor outcome prediction



Suppression

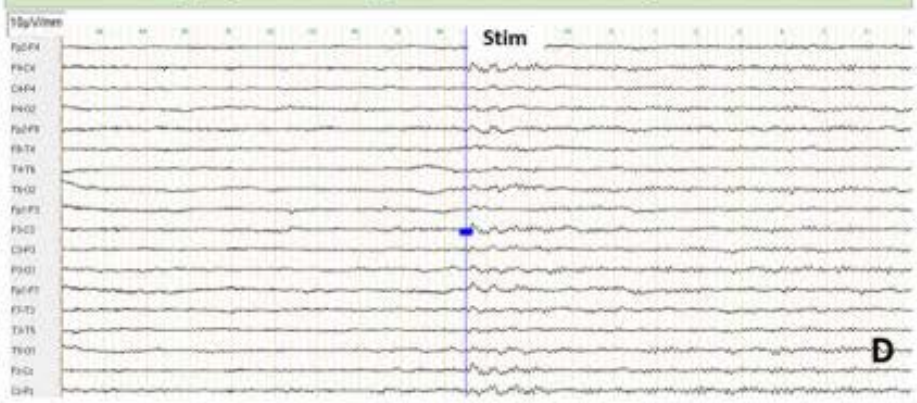


Suppression with periodic discharges



Burst Suppression

Benign pattern: good outcome prediction



Continuous and reactive background

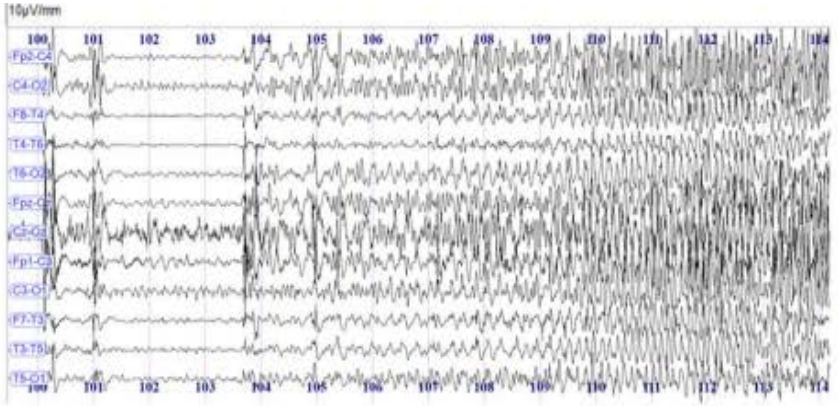
Benign EEG < 72h
PPV 70-94%

Hirsch et al, J Clin neurophysiol 2021
Westhall et al, Neurology 2016

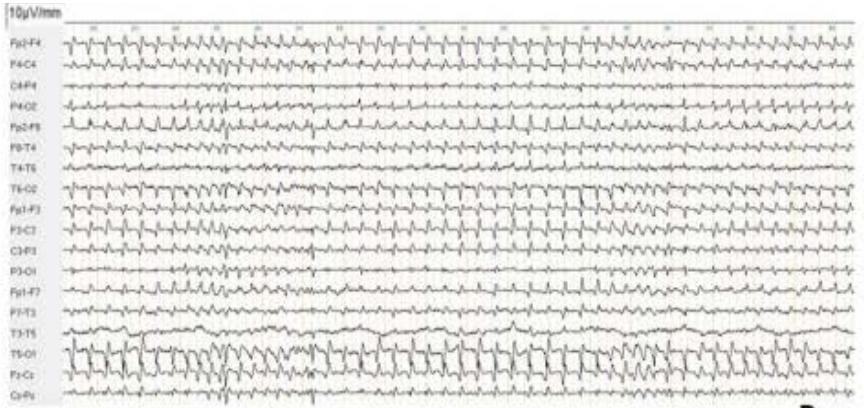
Malignant EEG after cardiac arrest

Malignant EEG: catch-all category

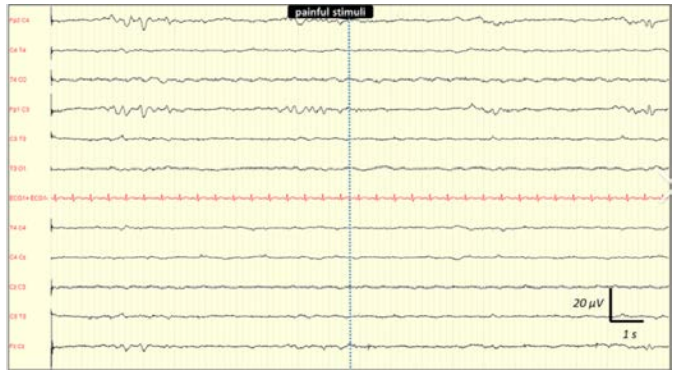
Different EEG patterns with different pathophysiological mecanisms of brain injury



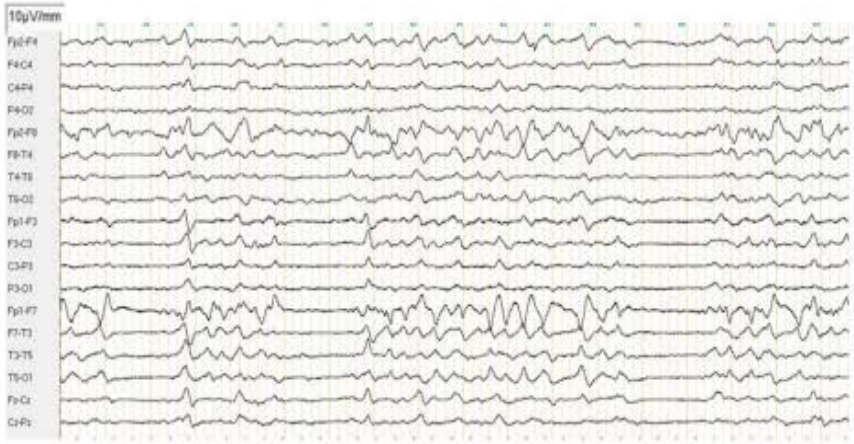
Electroencephalographic seizure A



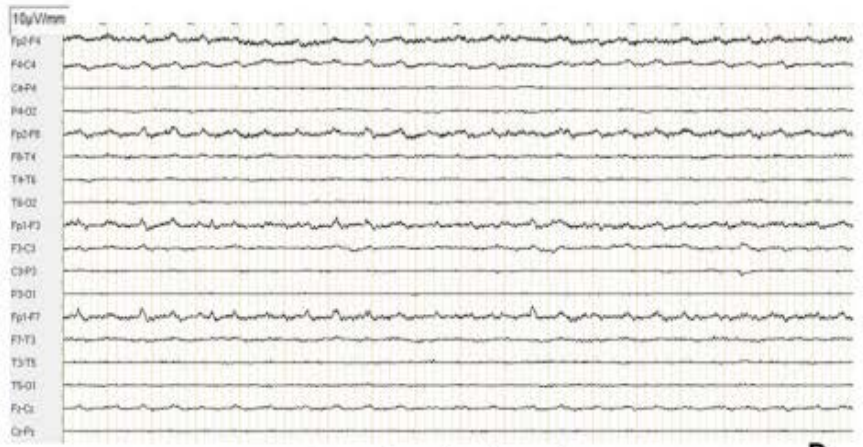
Periodic discharges i.e., epileptiform features B



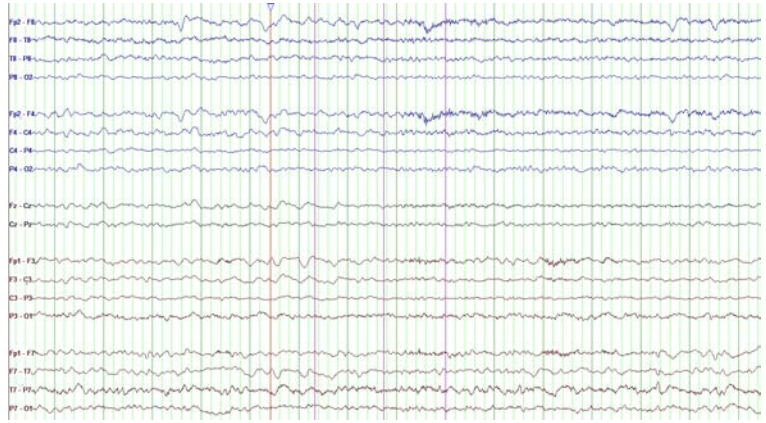
Unreactive EEG



Discontinuous background C



Low voltage background D



Antero-posterior gradient reversion

False positive rate 0-30%: « Grey zone »

Westhall et al, Neurology 2016
Benghanem et al, Neurology 2025

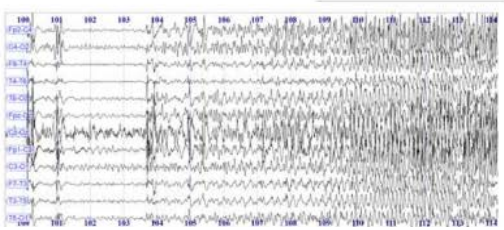
Electrographic seizures

Epileptiform Electrographic Patterns After Cardiac Arrest
Give Up or Treat?

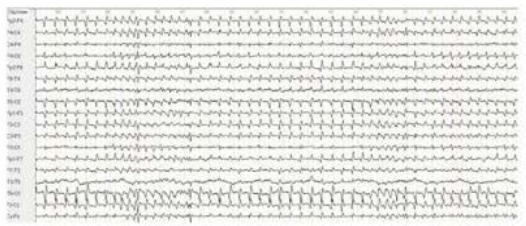
Andrea O. Rossetti, MD, FAES; Sarah Benghanem, MD, PhD

JAMA Neurology 2024

Seizures



Generalized periodic discharges



EEG epileptiform features / rythmic-periodic patterns

Assess other markers of hypoxic-ischemic brain injury

At least 2 markers of unfavorable outcome:

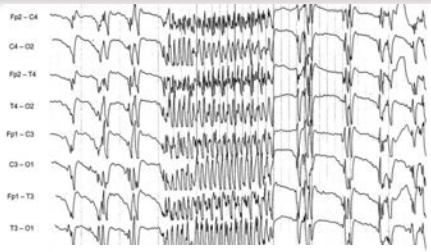
- Highly malignant EEG (suppression, burst suppression) at > 24h
- Bilaterally absent N20 SSEP
- Serum NSE > 60µg/L at 48-72h
- Sustained myoclonus within 72h
- Pupillary and corneal reflexes abolition at >72h
- Diffuse anoxic injury on CT/MRI

Yes

No

85%

ASM probably futile



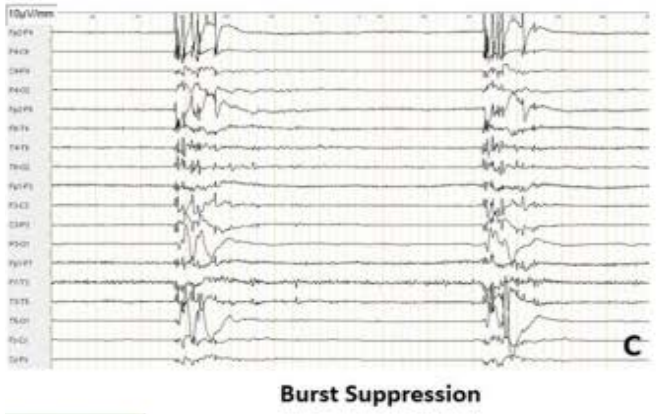
Unfavorable SE

Admiraal, et al Neurology 2025

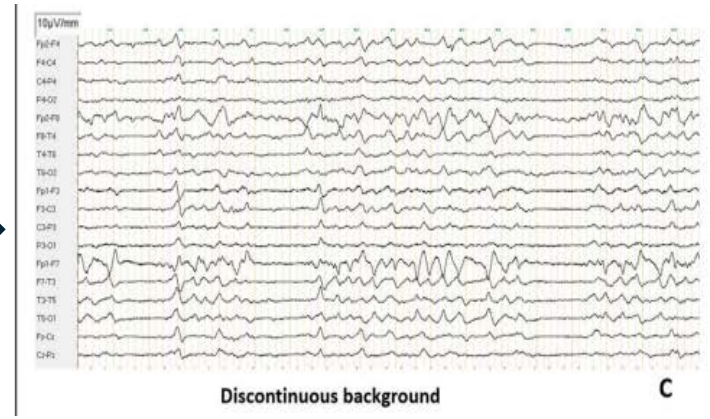
- **Timing of assessment:**

EEG> 24h after CA => early EEG recordings (at 12-24h) may have a higher prognostic value than later recordings (>48-72h), irrespective of sedation protocols

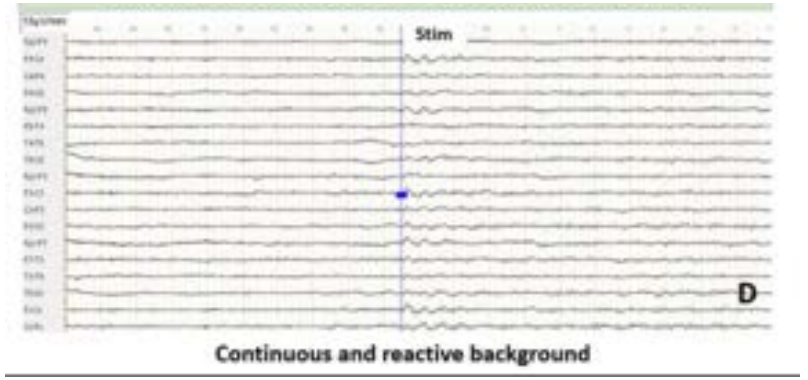
12 - 24 - 36h – highly malignant



48-72h - malignant



Late EEG - benign



- **Sedative drugs:**

Sedation at low-moderate doses, administered for TTM (<3mg/kg/h propofol) does not significantly impair the EEG prognostic accuracy

Benghanem et al., PMID: 31211949, Rossetti et al., PMID: 27017468; Cloostermans et al., PMID: 22824933, Oddo et al. PMID: 24463859; Drohan et al, PMID: 29197598; Ruijter et al., PMID: 31163372; Hofmeijer et al, PMID: 26070341; Spaletti et al PMID: 27291880; Sivaraju et al PMID: 25940963; Ruijter et al PMID: 31155751; Rossetti et al PMID: 27017468, Ruijter et al PMID: 31163372; Turella et al, PMID: 38172300

SYSTEMATIC REVIEW

Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review

Claudio Sandroni[1,2], Sonia D'Arrigo[1*], Sofia Cacciola[1], Cornelia W. E. Hoedemaekers[3], Marlijn J. A. Kamps[4], Mauro Oddo[5], Fabio S. Taccone[6], Arianna Di Rocco[7], Frederick J. A. Meijer[8], Erik Westhall[9], Massimo Antonelli[1,2], Jasmeet Soar[10], Jerry P. Nolan[11] and Tobias Cronberg[12]

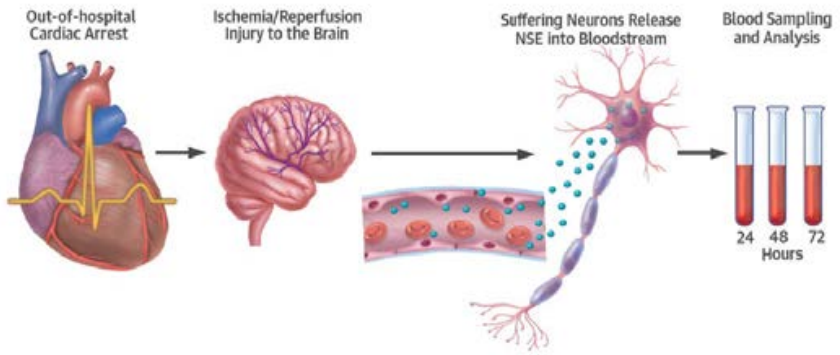


Table 14 Biomarkers. Neuron-specific enolase (NSE)

Author, year	Sample size, *n*	Threshold value, µg/L	Timing	Timing outcome	TP	FP	FN	TN	Sensitivity % [95% CI]	FPR % [95% CI]
48 h										
Chung-Esaki, 2018 [92]	68	33	48 h	6 mo	23	1	27	17	46 [31.8–60.7]	5.6 [0.1–27.3]
Helwig, 2017 [38]	100	34	48 ± 12 h	1 mo	27	0	34	39	44.3 [31.5–57.6]	0 [0–7.4]
Duez, 2018 [37]	115	45.12	48 h	6 mo	11	0	25	79	30.6 [16.3–48.1]	0 [0–3.7]
Vondrakova, 2017 [47]	153	51.1	48 h	1 mo	14	0	43	96	24.6 [14.1–37.8]	0 [0–3.1]
Lee, 2013 [102]	224	52.7	48 h	HD	50	0	33	141	60.2 [48.9–70.8]	0 [0–2.1]
You, 2019 [48]	34	54.6	48 h	6 mo	13	0	3	18	81.3 [54.4–96]	0 [0–15.3]
Pfeifer, 2014 [42]	139	66.1	48 h	1 mo	46	0	87	6	34.6 [26.6–43.3]	0 [0–39.3]
Nakstad, 2020 [105]	229	87	48 h	6 mo	39	0	69	121	36.1 [27.1–45.9]	0 [0–2.4]
Stammet, 2015 [44]	686	120	48 h	6 mo	91	0	247	348	26.9 [22.3–32]	0 [0–0.9]

NSE: > 60µg/L at 48h et/ou 72h :

best compromise between high specificity and good sensitivity

Neuron-specific-enolase

Neuron-specific enolase and S-100b in prolonged targeted temperature management after cardiac arrest: A randomised study☆

Christophe Henri Valdemar Duez[a,b,*], Anders Morten Grejs[a,b], Anni Nørgaard Jeppesen[a,b], Anne Dilani Schrøder[c], Eldar Søreide[d,e], Jørgen Feldbæk Nielsen[f], Hans Kirkegaard[b]

Resuscitation 2018

Absolute blood levels and kinetics of neurofilament light (NFL) chains for neurological prognosis in comatose patients after cardiac arrest

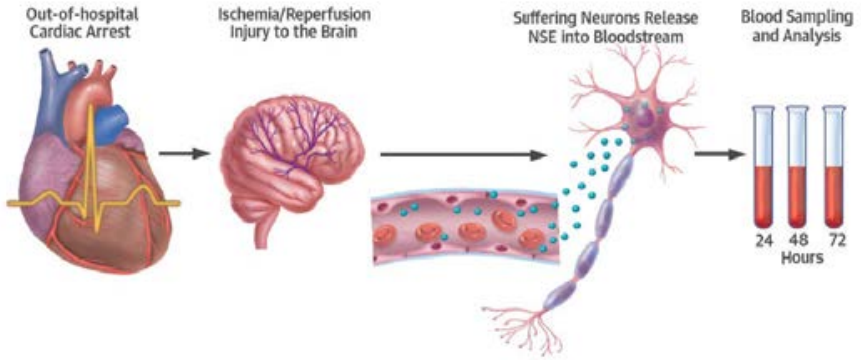
Timothée Ayasse[1], Maxime Touron[1], Marie-Céline Blanc[2], Estelle Pruvost-Robieux[3,4,5], Jean-Baptiste Lascarrou[6], Clara Vigneron[1], Jean-Paul Mira[1,4], Frédéric Pène[1,4], Alain Cariou[1,4,7,8] and Sarah Benghanem[1,4,5,8*]

Annals of intensive care 2025

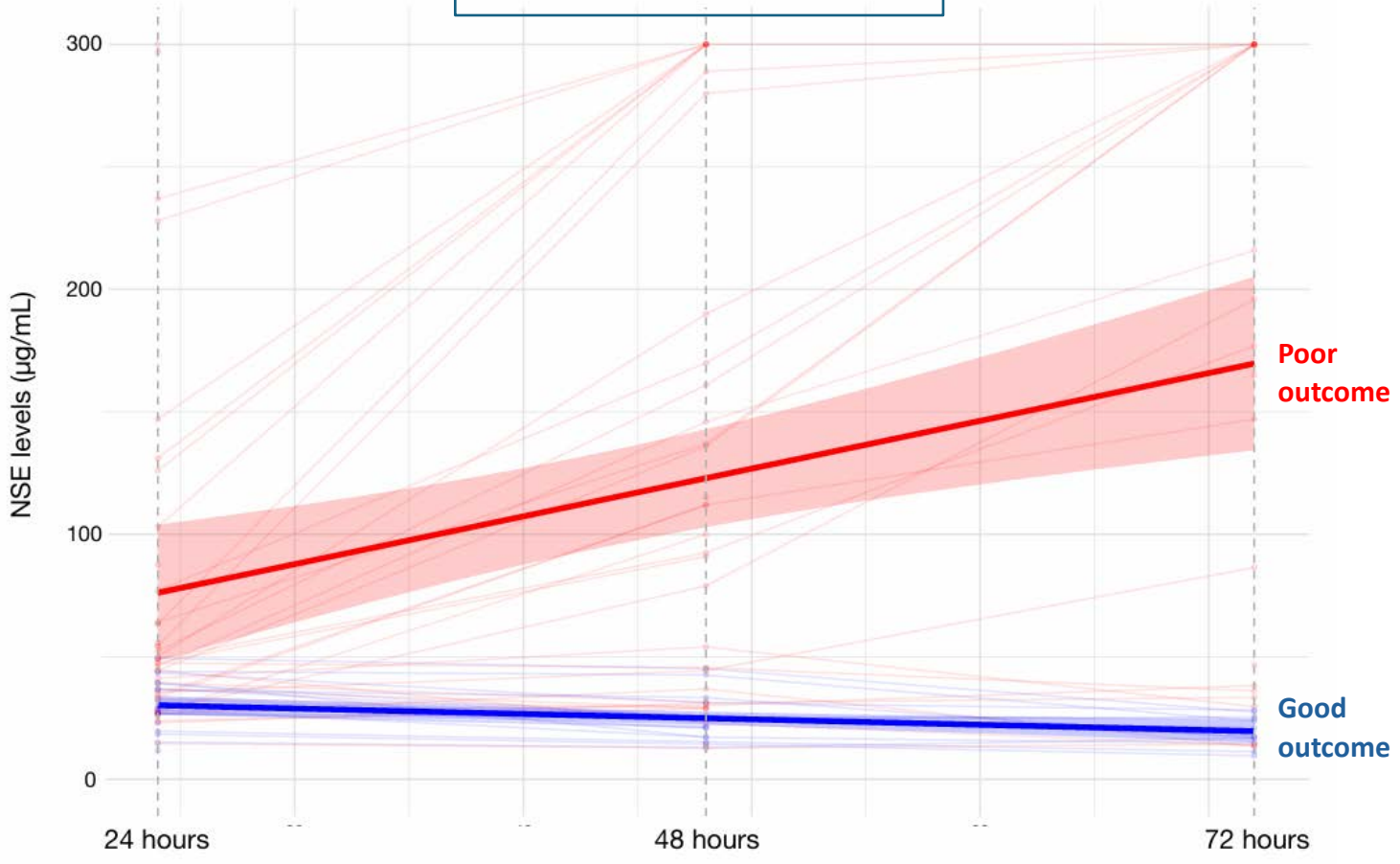
Personalized neuron-specific enolase level based on EEG pattern for prediction of poor outcome after cardiac arrest

Juliette Pelle[1,2], Estelle Pruvost-Robieux[2,3,4], Florence Dumas[2,5], Antonin Ginguay[6], Julien Charpentier[1], Clara Vigneron[1,2], Frédéric Pène[1,2], Jean Paul Mira[1,2], Alain Cariou[1,2] and Sarah Benghanem[1,2,4*]

Annals of intensive care 2025



Kinetics of NSE levels



Poor outcome prediction

Unconscious patient
Motor score 5 or less at 72 h or later,
and confounders excluded*

*At least **TWO** unfavourable signs:*

- No pupillary** and corneal reflexes at 72 h or later
- Bilaterally absent N20 SSEP wave at 24 h or later
- Suppression or burst-suppression on EEG at 24 h or later
- NSE higher than 60µg L^{-1} *** at 48 h and / or 72 h
- Status myoclonus**** within 72 h
- Diffuse and extensive hypoxic-ischaemic injury on brain CT at any time or on MRI after 2 days

YES

Poor neurological outcome very likely

Does the guidelines algorithm really performant?

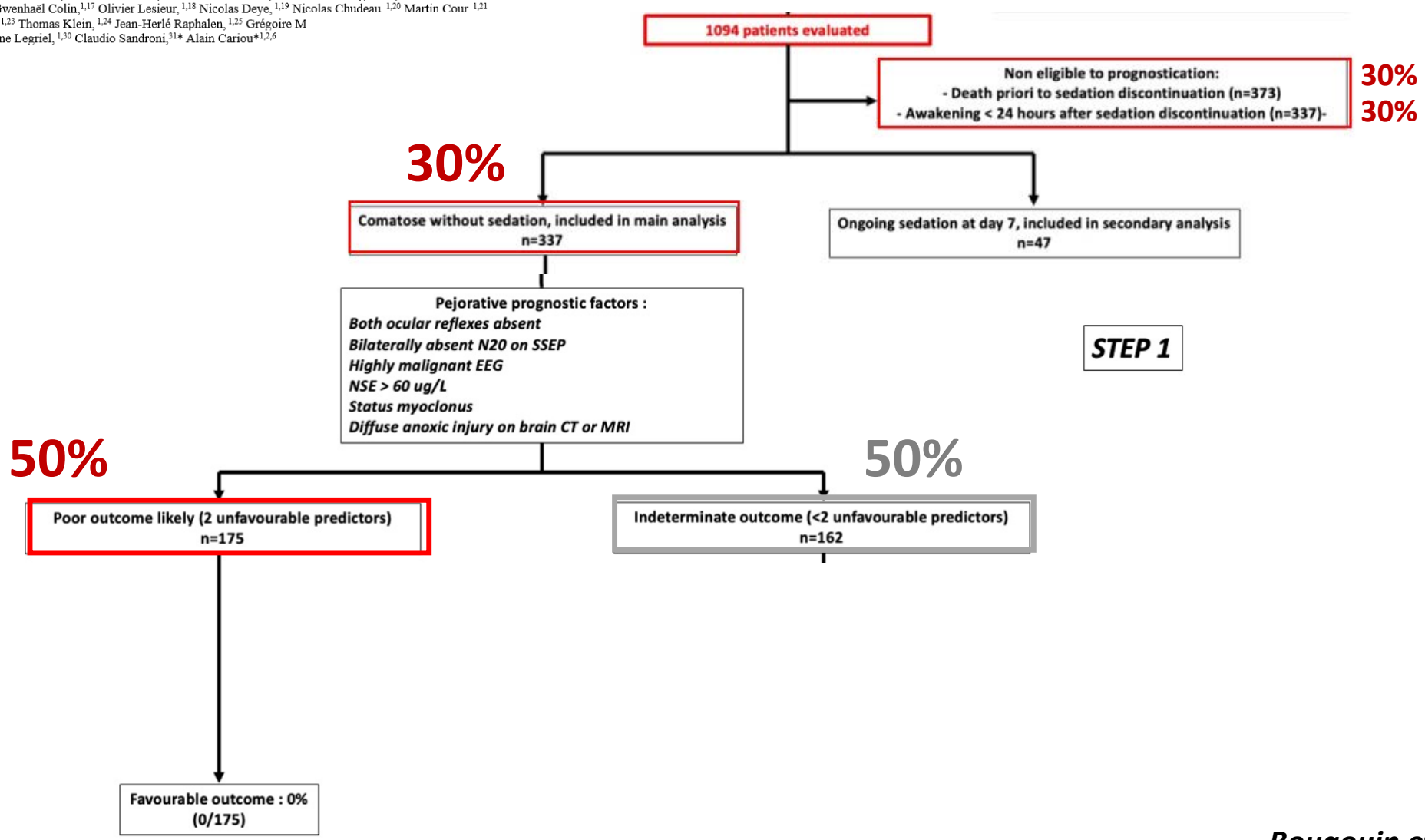
How many patients remain in the grey zone despite this algorithm ?

Nolan et al, ERC-ESICM post resuscitation care, ICM/Resuscitation 2021

Performance of neuroprognostication algorithm

Performance of neuroprognostication indicators after cardiac arrest: insights from a prospective multicenter cohort

Wulfran Bougouin,[1,2,3] Jean-Baptiste Lascarrou,[1,2,4] Jonathan Chelly,[1,5] Sarah Benghanem,[1,6] Guillaume Geri,[1,7] Julien Maizel,[1,8] Nicolas Fage,[1,9] Ghada Sboui,[1,10] Nicolas Pichon,[1,11] Cédric Daubin,[1,12] Bertrand Sauneuf,[1,13] Nicolas Mongardon,[1,14] Fabio Taccone,[1,15] Bertrand Hermann,[1,16] Gwenhaël Colin,[1,17] Olivier Lesieur,[1,18] Nicolas Deye,[1,19] Nicolas Chudeau,[1,20] Martin Cour,[1,21] Jeremy Bourenne,[1,22] Kada Klouche,[1,23] Thomas Klein,[1,24] Jean-Herlé Raphalen,[1,25] Grégoire M Bruel,[1,28] Sophie Jacquier,[1,29] Stéphane Legriel,[1,30] Claudio Sandroni,[31]* Alain Cariou*[1,2,6]
*These authors contributed equally



Bougouin et al, resuscitation 2024
Lagebrant et al, resuscitation 2025

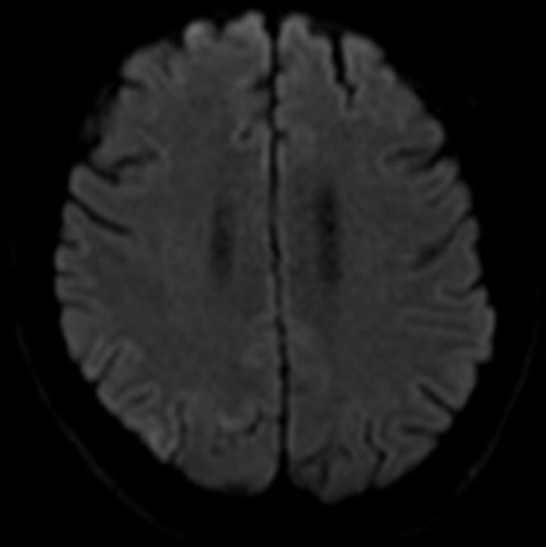
How can we improve the challenge of neuroprognostication ?

1. Assess markers of good outcome

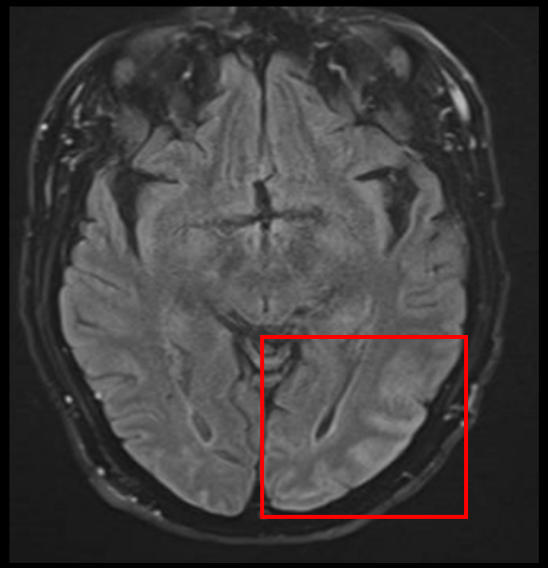
2. identify new prognostic markers

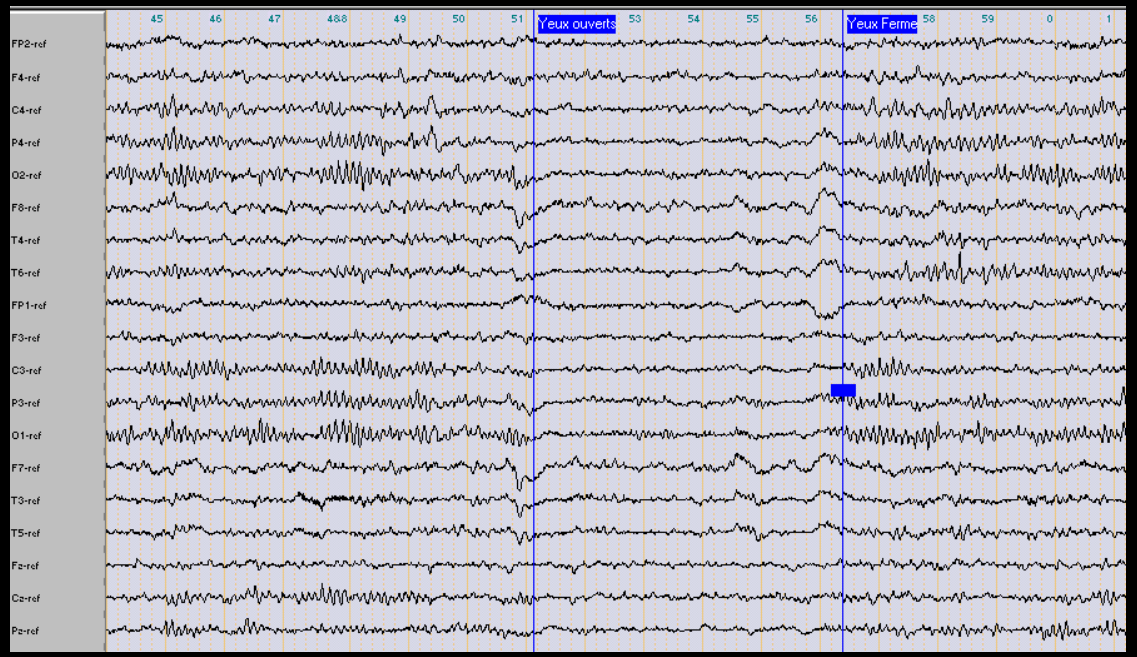
Good outcome prediction ?

Normal diffusion



Focal injury (asymetric cortical or only basal ganglia)





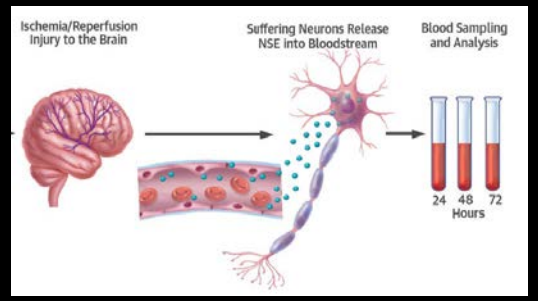
Normal or « sub normal » diffusion MRI < Day 7

Benign EEG < 72h (continuous, normovoltage, reactive)

Low NSE level :

- **< 17 µg/L**
- **<40-45 µg/L**

Decreasing NSE



=> good outcome likely

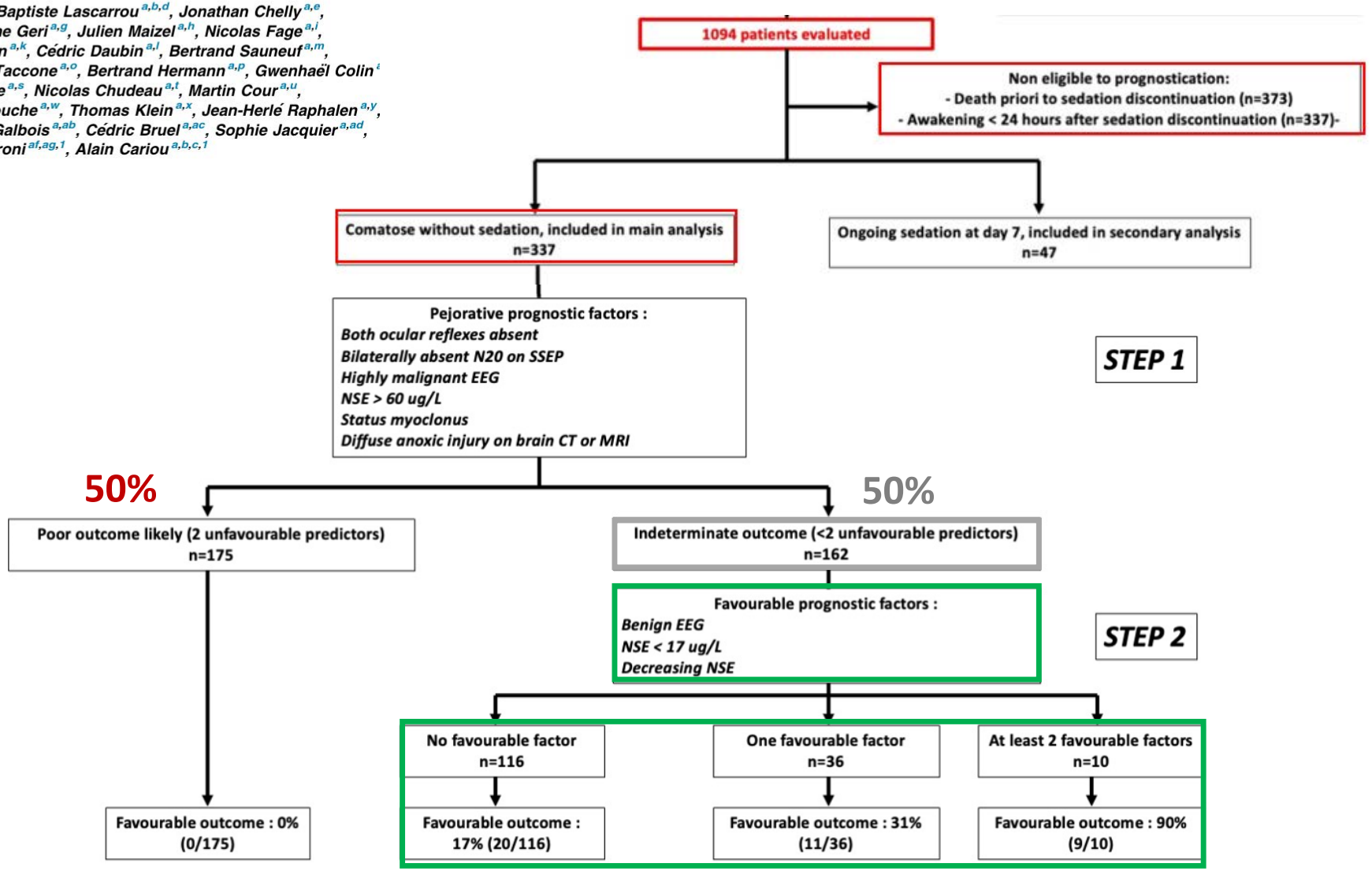
Rossetti Lancet neuro 2016
Sandroni ICM 2022
Besnard Crit Care 2025
Lagebrant Resuscitation 2025

Good outcome prediction decrease prognostic uncertainly

Performance of the ERC/ESICM-recommendations for neuroprognostication after cardiac arrest: Insights from a prospective multicenter cohort

Wulfran Bougouin[a,b,c,], Jean-Baptiste Lascarrou[a,b,d], Jonathan Chelly[a,e], Sarah Benghanem[a,f], Guillaume Geri[a,g], Julien Maizel[a,h], Nicolas Fage[a,i], Ghada Sboui[a,j], Nicolas Pichon[a,k], Cédric Daubin[a,l], Bertrand Sauneuf[a,m], Nicolas Mongardon[a,n], Fabio Taccone[a,o], Bertrand Hermann[a,p], Gwenhaël Colin[i] Olivier Lesieur[a,r], Nicolas Deye[a,s], Nicolas Chudeau[a,t], Martin Cour[a,u], Jeremy Bourenne[a,v], Kada Klouche[a,w], Thomas Klein[a,x], Jean-Herlé Raphalen[a,y], Grégoire Muller[a,z,aa], Arnaud Galbois[a,ab], Cédric Bruel[a,ac], Sophie Jacquier[a,ad], Marine Paul[a,ae], Claudio Sandroni[af,ag,1], Alain Cariou[a,b,c,1]*

Multicenter study n=337 patients



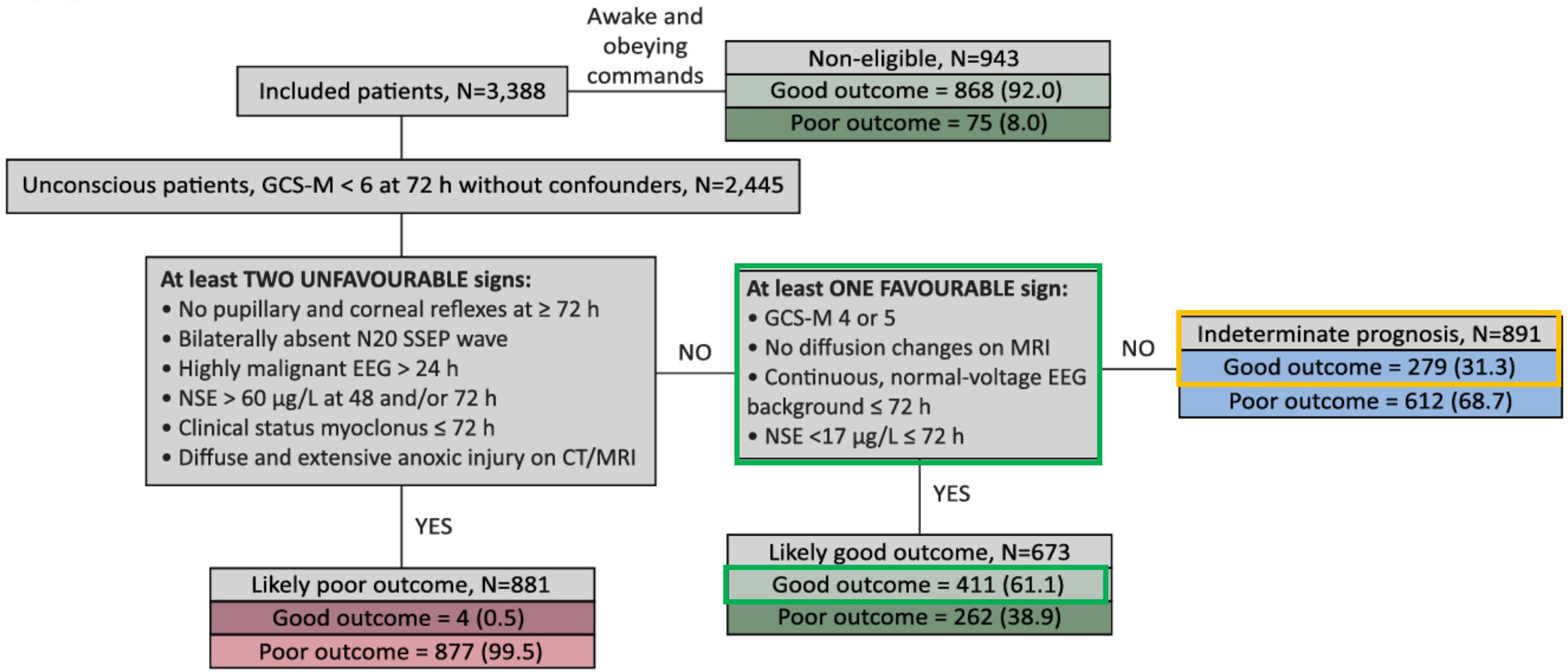
Resuscitation 2024

Good outcome prediction decrease prognostic uncertainly

Prediction of good functional outcome decreases diagnostic uncertainty in unconscious survivors after out-of-hospital cardiac arrest

Alice Lagebrant[a,b,], Claudio Sandroni[c,d], Jerry P. Nolan[e,f], Jan Bělohlávek[g,h], Alain Cariou[i], Riccardo Carrai[j], Josef Dankiewicz[a,k], Anders Morten Grejs[l,m], Antonello Grippo[j], Christian Hassager[n,o], Janneke Horn[p], Matthias Haenggi[q], Janus C. Jakobsen[r,s], Thomas R. Keeble[t,u], Hans Kirkegaard[m,v], Jesper Kjaergaard[n,o], Michael A. Kuiper[w], Byung Kook Lee[x,y], Dong Hun Lee[x,y], Helena Levin[a,z], Gisela Lilja[a,aa], Andreas Lundin[ab], Niklas Nielsen[a,ac], Sang Hoon Oh[ad], Kyu Nam Park[ad], Tommaso Pellis[ae], Chiara Robba[af,ag], Christian Rylander[ah], Seok Jin Ryu[x,y], Manoxj Saxena[ai,aj], Maenia Scarpino[j], Claudia Schrag[ak], Pascal Stammet[al,am], Christian Storm[an], Fabio Silvio Taccone[ao,ap], Matthew Thomas[aq], Erik Westhall[a,ar], Matt P. Wise[as], Chun Song Youn[ad], Paul Young[at,au,av,aw], Tobias Cronberg[a,ax], Marion Moseby-Knappe[a,ay]*

Multicenter study n=2445 patients



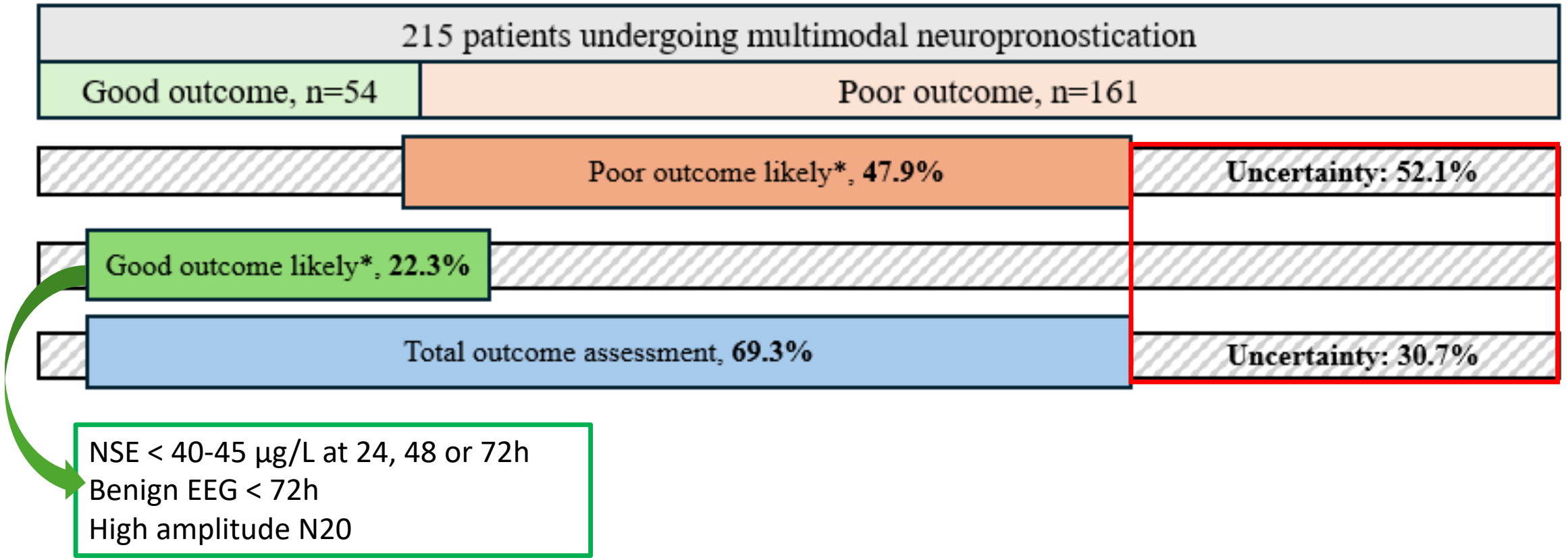
Resuscitation 2025

Good outcome prediction decrease prognostic uncertainly

Multimodal assessment of favorable neurological outcome using NSE levels and kinetics, EEG and SSEP in comatose patients after cardiac arrest

Aurélie Besnard[1], Juliette Pelle[1], Estelle Pruvost-Robieux[2,3,4], Antonin Ginguay[5], Clara Vigneron[1], Frédéric Pène[1,2], Jean-Paul Mira[1,2], Alain Cariou[1,2,6] and Sarah Benghanem[1,2,4,6*]

Cochin hospital, N=215 patients comatose after sedation weaning, with EEG, NSE and SSEP
2017 - 2023



NSE < 40-45 µg/L at 24, 48 or 72h
Benign EEG < 72h
High amplitude N20

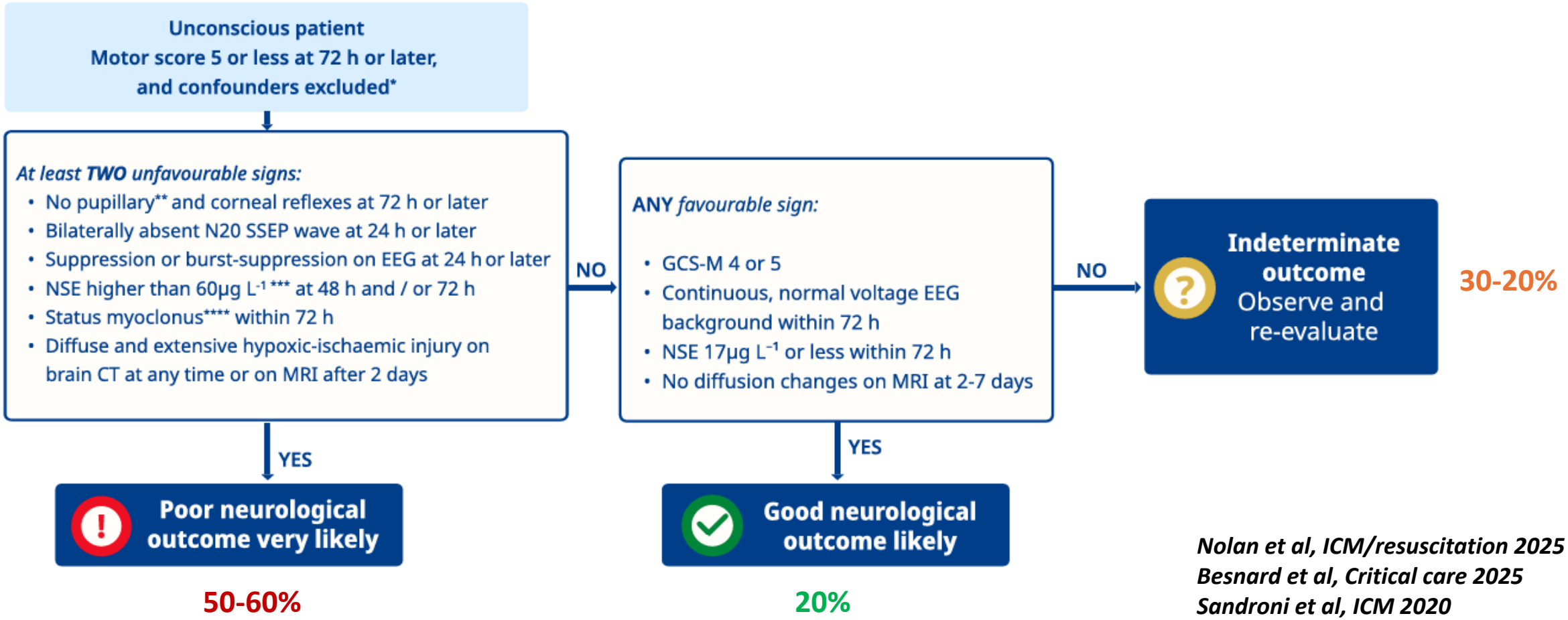
Critical care, 2025

Good outcome prediction decrease prognostic uncertainly

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2025 Post-Resuscitation Care ☆

Jerry P. Nolan[a,b,#,], Claudio Sandroni[c,d,#], Alain Cariou[e], Tobias Cronberg[f], Sonia D'Arrigo[b,c], Kirstie Haywood[g], Astrid Hoedemaekers[h], Gisela Lilja[i,j], Nikolaos Nikolaou[k], Theresa Mariero Olasveengen[l], Chiara Robba[m], Markus B. Skrifvars[n], Paul Swindell[o], Jasmeet Soar[p]*

GUIDELINES 2025 EUROPEAN RESUSCITATION COUNCIL

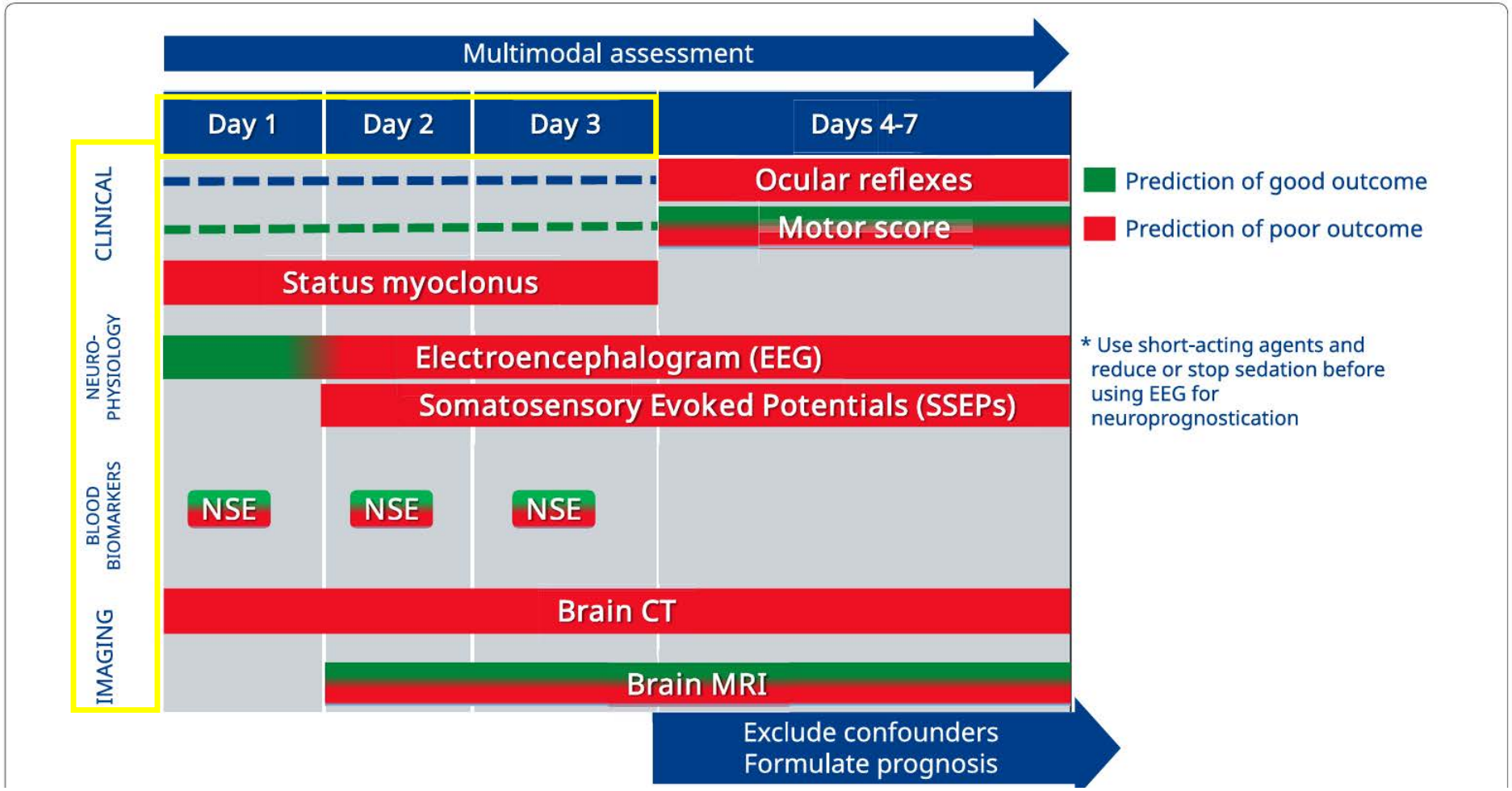


Nolan et al, ICM/resuscitation 2025
Besnard et al, Critical care 2025
Sandroni et al, ICM 2020
Bougouin et al, resuscitation 2024
Lagebrant et al, resuscitation 2025

Timing for recording multimodal predictors of neurological outcome

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2025 Post-Resuscitation Care ☆

Jerry P. Nolan[a,b,#,], Claudio Sandroni[c,d,#], Alain Cariou[e], Tobias Cronberg[f], Sonia D'Arrigo[b,c], Kirstie Haywood[g], Astrid Hoedemaekers[h], Gisela Lilja[i,j], Nikolaos Nikolaou[k], Theresa Mariero Olasveengen[l], Chiara Robba[m], Markus B. Skrifvars[n], Paul Swindell[o], Jasmeet Soar[p]*



Nolan et al, ICM/resuscitation 2025

How can we improve the challenge of neuroprognostication ?

1. Assess markers of good outcome

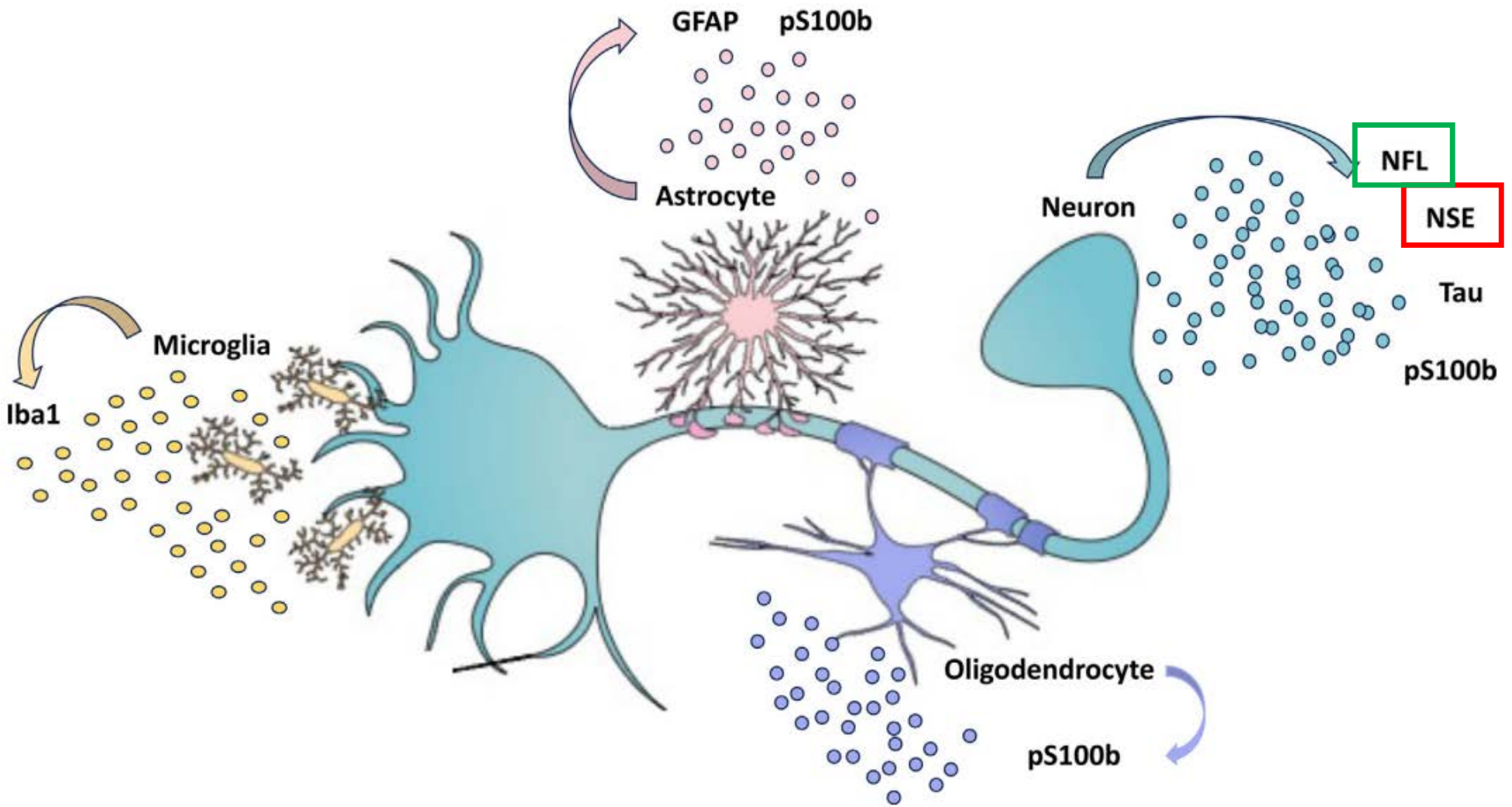
2. identify **new prognostic markers**

New prognostic markers: biomarkers

Biomarkers for neuroprognostication: The time has come for the new wave.

Benghanem S, Pelle J, Cariou A.

Resuscitation. 2023 Dec;193:110028. doi: 10.1016/j.resuscitation.2023.110028. Epub 2023 Nov 3.



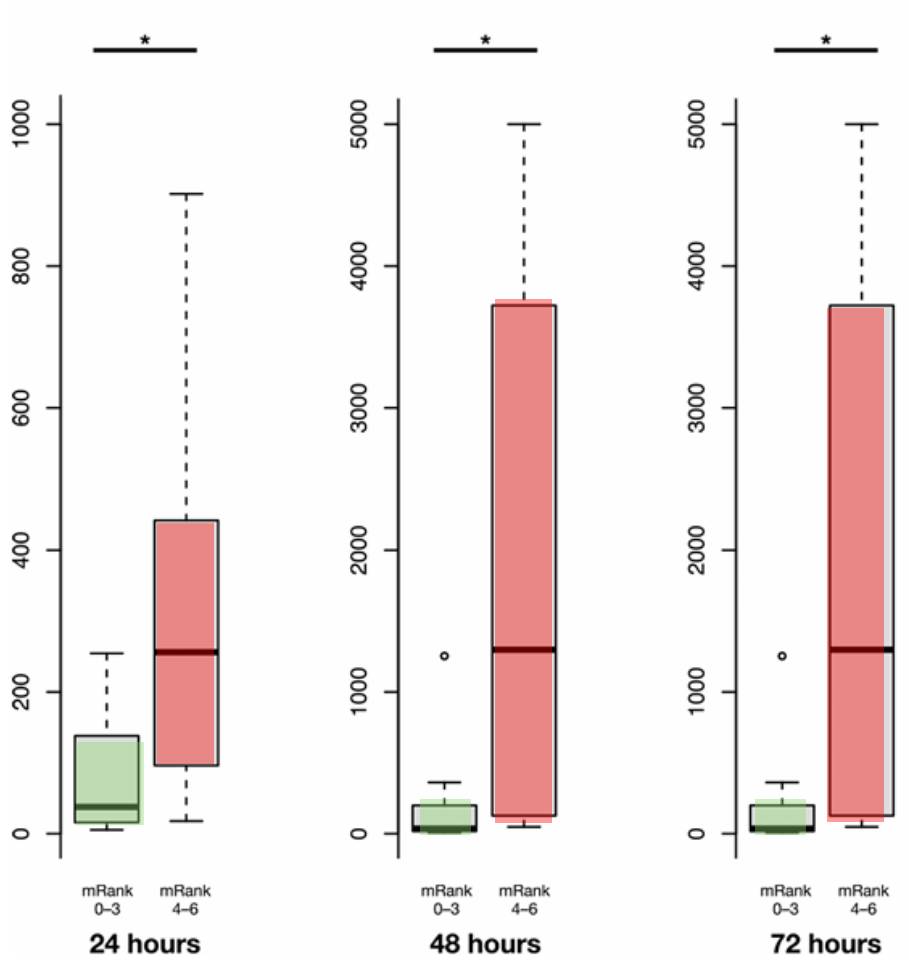
Resuscitation 2023

Neuro-filament chain light - NFL

Absolute blood levels and kinetics of neurofilament light (NFL) chains for neurological prognosis in comatose patients after cardiac arrest

Timothée Ayasse[1], Maxime Touron[1], Marie-Céline Blanc[2], Estelle Pruvost-Robieux[3,4,5], Jean-Baptiste Lascarrou[6], Clara Vigneron[1], Jean-Paul Mira[1,4], Frédéric Pène[1,4], Alain Cariou[1,4,7,8] and Sarah Benghanem[1,4,5,8*]

Monocentric prospective study at Cochin hospital
n = 67 patients comatose after CA with at least one NFL level, 2023 -2024



Time, h	AUC
24	0.80 [0.68–0.93]
48	0.88 [0.77–0.98]
72	0.90 [0.81–1.00]

Annals of intensive care 2025

	Mosebby Knappe JAMA Neuro 2019	Levin et al Critical care 2025	Klitholm et al Resuscitation 2023	Ayasse et al, Annals of intensive care 2025	Czimmeck et ak Resuscitation 2025	Pussinen et al Resusictation 2025	Synthèse
poor outcome Sp=100% 24h	> 1232	NA	> 608	>1121	>2000	>112	>1000
poor ouctome Sp 100% 48h	>1539	>336 OHCA >640 IHCA	> 720	>1324	>2000	>229	>1000
poor ouctome Sp 100% 72h	> 1756	NA	> 920	>510	>2000	>331	>1000
poor outcome Sp 95% 24h	> 286	NA	NA	>250	NA	> 48	>200
poor ouctome Sp 95% 48h	>499	>220 OHCA >323 IHCA	NA	>383	NA	>80	>400
poor ouctome Sp 95% 72h	> 590	NA	NA	>406	NA	> 236	>500

	Mosebby Knappe ICM 2021	Levin et al Critical care 2025	Klitholm et al Resuscitation 2023	Ayasse et al, Annals Of intensive care 2025	Czimmeck et ak Resuscitation 2025	Pussinen et al Resuscitation 2025	Synthèse
Good outcome 24h	< 55 VPP: 72.5% Se: 95.4%	<12 Sp: 60% Se:80%	NA	<82 VPP: 65% Sp: 75% Se: 81%	<55 VPP: 89% Sp: 48% Se: 95%	<48 Sp: 90% Se 95%	<55
Good ouctome 48h	< 55 VPP: 66.4% Se: 96%	<45 Sp: 88% Se: 80%	NA	<307 VPP: 91% Sp: 88% Se: 78%	<55 VPP: 89% Sp: 48% Se: 95%	<52 Sp: 89% Se: 95%	<150
Good ouctome 72H	< 55 VPP: 63.4% Se: 96.5%	<388 Sp: 100% Se: 80%	NA	<459 VPP: 71% Sp: 83% Se: 100%	<55 VPP: 89% Sp: 48% Se: 95%	<55 Sp: 85% Se: 95%	<400

CINEFIL study, prospective multicentric study (Cochin, Necker, HEGP) : prognostic value of NFL from T0 to D7

AfterROSC is a research network associating physicians from 26 intensive care units in France and Belgium. The main objectives are to promote /develop research and teaching in the post cardiac arrest care setting.

Avis neuropronostication du réseau After Rosc
Discussion multidisciplinaire via télémédecine dans les 48 heures post sollicitation

Une seule adresse : avis@afterrosc.org

14 membres de la RCP neuropronostication :

- **Dr Sarah Benghanem (MIR Cochin)**
- **Dr Wulfran Bougouin (Réanimation Massy)**
- **Pr Alain Cariou (MIR Cochin)**
- **Dr Jonathan Chelly (Réanimation, Toulon)**
- **Dr Charlotte Calligaris (Neuro-réanimation, Ste Anne)**
- **Dr Cédric Daubin (Réanimation, Caen)**
- **Dr Nicolas Deye (MIR, Lariboisière)**
- **Pr Martin Dres (MIR Pitié Salpêtrière)**
- **Pr Guillaume Géri (Réanimation Clinique Ambroise Paré)**
- **Dr Bertrand Hermann (MIR HEGP)**
- **Pr Jean Baptiste Lascarrou (MIR Nantes)**
- **Dr Marine Paul (Réanimation, Versailles)**
- **Dr Jean Raphalen (Réanimation Necker)**
- **Pr Benjamin Rohaut (MIR-neuro, Pitié Salpêtrière)**

Summary

- 72h after CA is the best time point
- Some indicators collected at 24h after CA: myoclonus, NSE, EEG, SSEPs

- Multimodal approach for poor outcome prediction: at least 2 variables
- Markers of good outcome reduce prognostic uncertainly:

benign EEG < 72h, low NSE, descending trend of NSE, high N20 amplitude, normal or subnormal MRI

- Indeterminate outcome : observe and re-evaluate

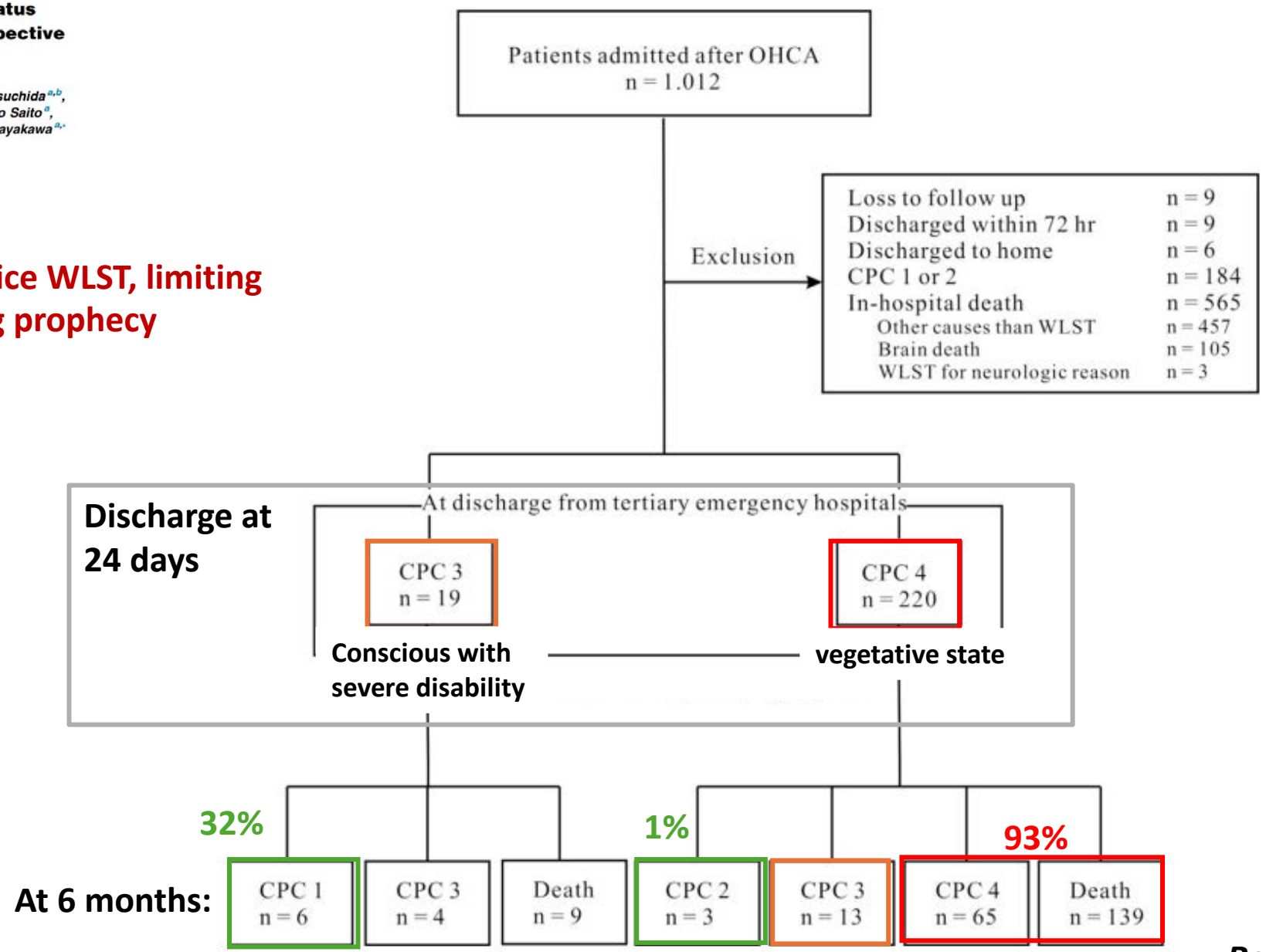
- « New » markers of interest: NFL = marker with the highest prognostic value, compared to all others variables

HIBI: Time is brain !

Delayed neurologic improvement and long-term survival of patients with poor neurologic status after out-of-hospital cardiac arrest: A retrospective cohort study in Japan

Mariko Hayamizu[a], Akira Kodate[b], Hisako Sageshima[b], Takumi Tsuchida[a,b], Yoshinori Honma[a], Asumi Mizugaki[a], Tomonao Yoshida[a], Tomoyo Saito[a], Kenichi Katabami[a], Takeshi Wada[a], Kunihiko Maekawa[a], Mineji Hayakawa[a,]*

Countries do not practice WLST, limiting the risk of self-fulfilling prophecy

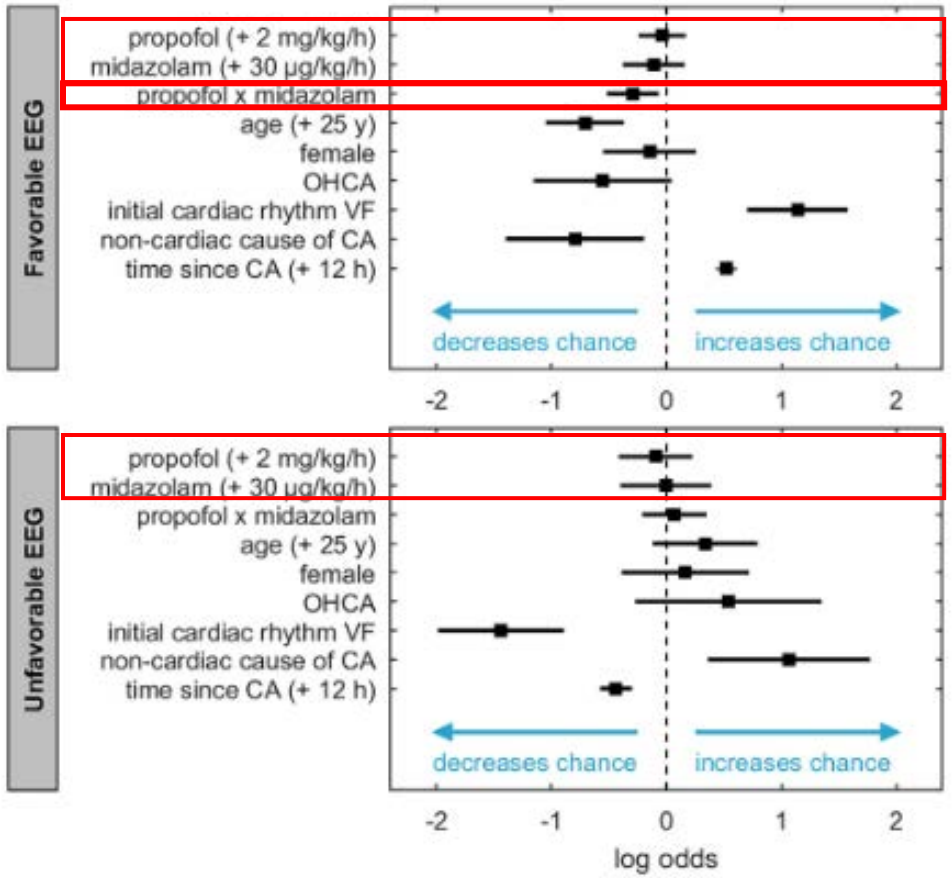


Resuscitation 2023

Propofol does not affect the reliability of early EEG for outcome prediction of comatose patients after cardiac arrest

Barry J. Ruijter [a,*], Michel J.A.M. van Putten [a,b], Walter M. van den Bergh [c], Selma C. Tromp [d], Jeannette Hofmeijer [a,e]

Multivariate analysis



Highest median doses:

- **Continuous EEG pattern: 2.67mg/kg/h**
- **burst suppression: 2.07mg/kg/h**
- **Generalized suppression: 1.94 mg/kg/h**

Light to moderate sedation use in post CA care does probably not affect predictive value of EEG

Clin neurophysiol 2019

Accompagner la récupération neurologique des survivants post ACR

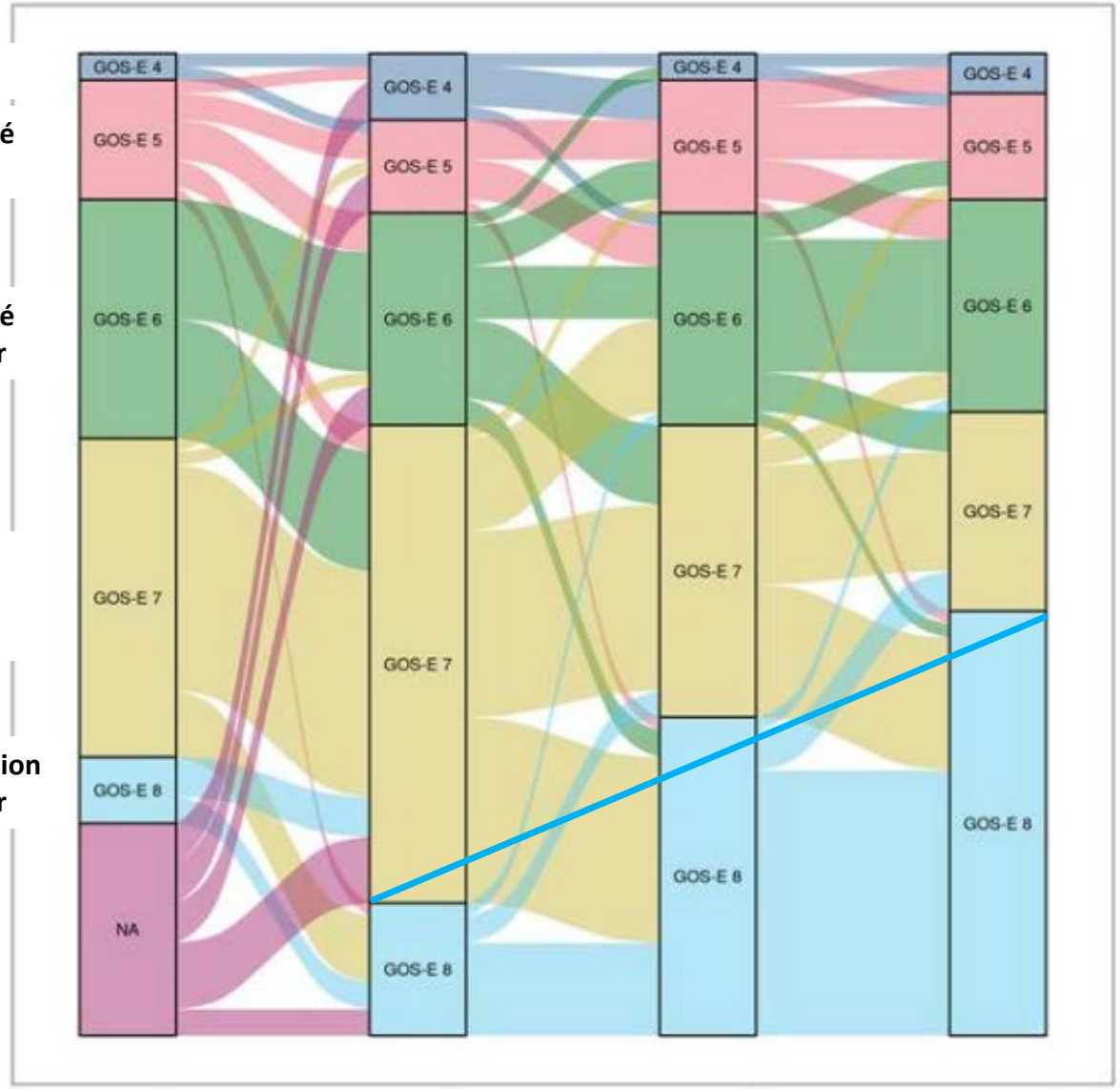
Handicap sévère

Handicap modéré
Niveau inférieur

Handicap modéré
Niveau superieur

Bonne
récupération
Niveau inférieur

Bonne récupération
Niveau supérieur



Etude prospective multicentrique
N=98 patients GOSE 4-8 à 3 mois
Suivi en rééducation jusqu'à 18 mois

Consultation post ACR (Sainte Anne, T Sharshar, C Legouy, S Barthelemy)

Détection des séquelles psycho-cognitives

Mise en place d'un réseau de soin « post ACR » pour ces patients

Peskine, Cariou et al, Chest 2020

Continuous EEG ?

Continuous vs Routine Electroencephalogram in Critically Ill Adults With Altered Consciousness and No Recent Seizure
A Multicenter Randomized Clinical Trial

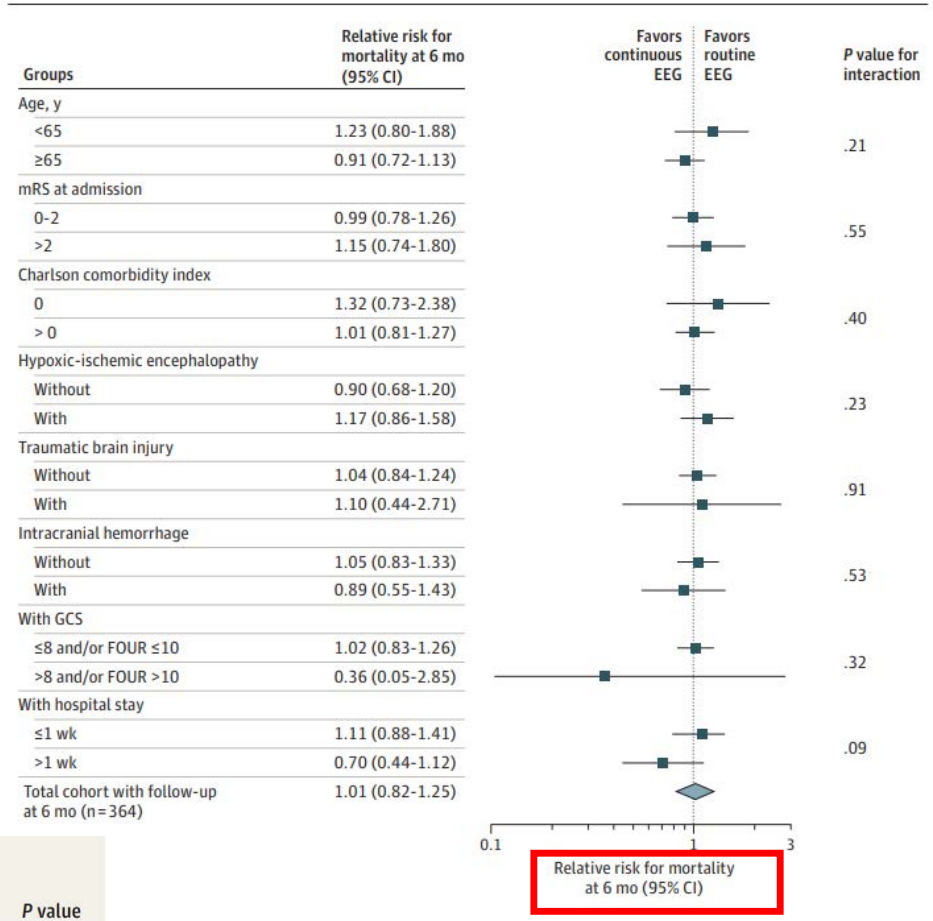
Andrea O. Rossetti, MD; Kaspar Schindler, MD, PhD; Raoul Sutter, MD; Stephan Rüegg, MD; Frédéric Zubler, MD, PhD; Jan Novy, MD, PhD; Mauro Oddo, MD; Loane Warpelin-Decrausaz, PhD; Vincent Alvarez, MD

CERTA randomized trial, continuous EEG for 30 to 48h vs two EEG of 20 minutes
N=368 patients with brain injuries

Table 1. Baseline Patient Characteristics

Characteristic	EEG, No. (%)	
	Routine (n = 183)	Continuous (n = 185)
Female	61 (33.3)	62 (33.5)
Age, mean (SD), y	63.7 (15.3)	63.8 (14.6)
Final neurologic diagnosis		
Hypoxic-ischemic encephalopathy	53 (28.9)	60 (32.4)
Brain trauma	17 (9.3)	32 (17.3)
Intracranial hemorrhage	40 (21.9)	47 (25.4)
Ischemic stroke	18 (9.8)	10 (5.4)
Toxic-metabolic, not primarily involving brain	14 (7.7)	9 (4.9)
Other	41 (22.4)	27 (14.6)
Time of EEG after admission, median (range), h	60.3 (1.0-890.0)	57.5 (0.7-2116.7)

Outcome	No. (%)		Relative risk (95% CI)	*P* value
	rEEG (n = 183)	cEEG (n = 185)		
Features of ictal-interictal continuum detected, without seizures/SE	102 (55.7)	128 (69.2)	1.24 (1.06-1.46)	.009
Seizures/SE detected	8 (4.4)	29 (15.7)	3.59 (1.68-7.64)	.001
Changes in antiseizure drug prescription within 60 h following start of EEG intervention[b]	21 (11.5)	39 (21.1)	1.84 (1.12-3.00)	.01



JAMA neuro 2020
Urbano et al Resuscitation 2023

MRI: diffusion tensor

Use of brain diffusion tensor imaging for the prediction of long-term neurological outcomes in patients after cardiac arrest: a multicentre, international, prospective, observational, cohort study

*Lionel Velly, Vincent Perlbarg, Thomas Boulier, Nicolas Adam, Sebastien Delphine, Charles-Edouard Luyt, Valentine Battisti, Gregory Torkomian, Charlotte Arbelot, Russell Chabanne, Betty Jean, Carol Di Perri, Steven Laureys, Giuseppe Citerio, Alessia Vargiolu, Benjamin Rohaut, Nicolas Bruder, Nadine Girard, Stein Silva, Vincent Cottenceau, Thomas Tourdias, Olivier Coulon, Bruno Riou, Lionel Naccache, Rajiv Gupta, Habib Benali, Damien Galanaud, Louis Puybasset, for the MRI-COMA Investigators**

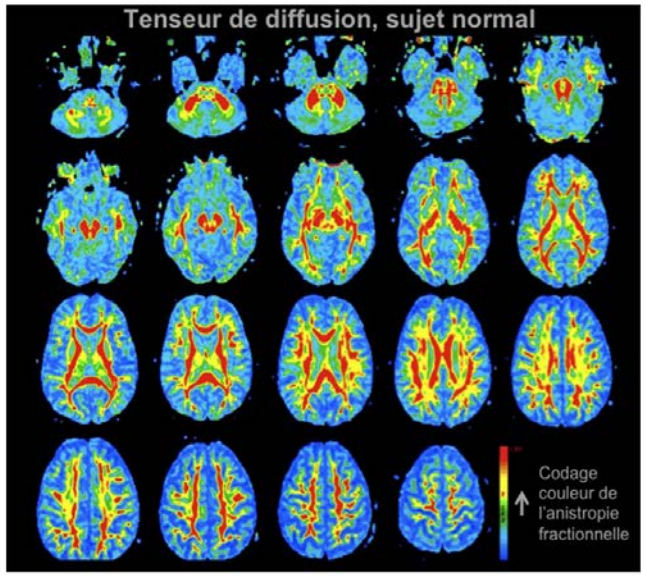


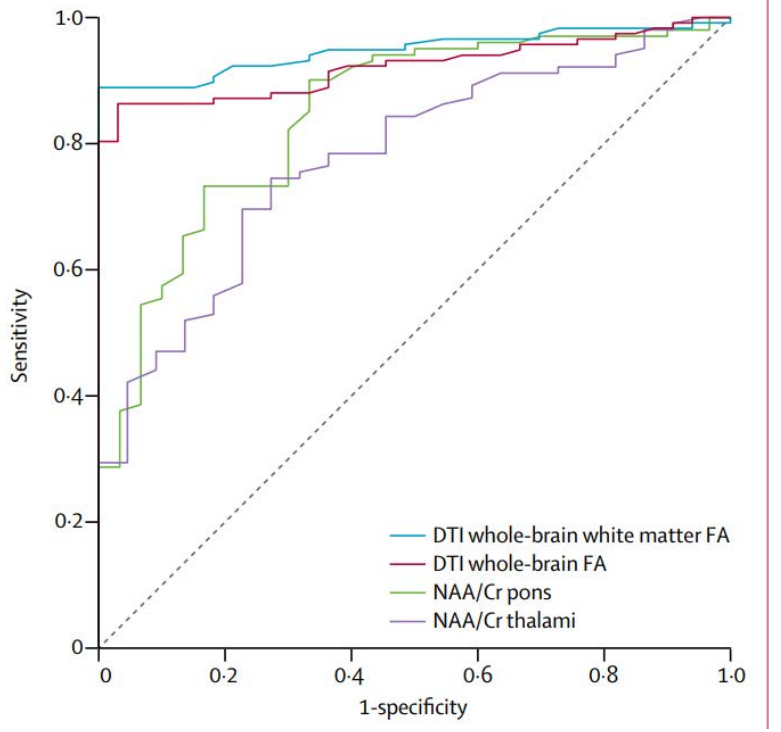
Figure 2 Aspect normal du tenseur de diffusion. Le tenseur de diffusion chez un sujet normal montre des zones très riches en faisceaux de fibres nerveuses (rouge). Le corps calleux, les régions sous-corticales notamment pariéto-occipitales et le tronc cérébral sont des zones où cheminent ces faisceaux (rouge). D'autres zones sont plus pauvres en fibres nerveuses (bleu).

Weiss et al, MRI for the prognosis of traumatic brain injury, revue MIR

Prospective multicenter study N= 150
MRI between > day 7 and day 28 after CA

WWM-FA value < 0.86 for poor outcome prediction

AUC 0.95, 95% CI 0·91–0·98



Actually, research tools with limited accessibility

Cardiac arrest: Pupillary reflexes assessment

ORIGINAL

Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double-blinded study

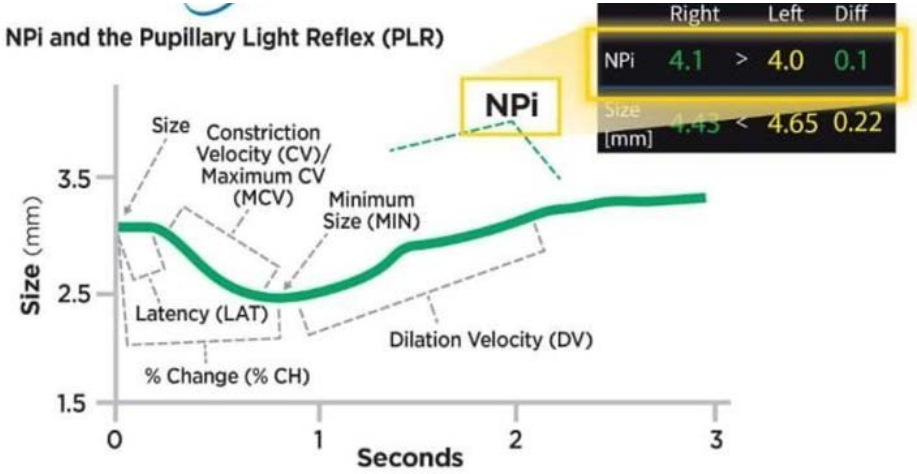
Mauro Oddo[1*], Claudio Sandroni[2], Giuseppe Citerio[3,4], John-Paul Mirozi[1], Janneke Horn[5], Malin Rundgren[6], Alain Cariou[7,8], Jean-François Payen[9], Christian Storm[10], Pascal Stammet[11] and Fabio Silvio Taccone[12]

=> Automated pupillometry is quantitative, reproductible and detect minimal changes

=> Neurological pupil index NPI: incorporates all components of the pupillary light reflex

=> NPi ranging from 0 (abolished) to 5 (normal)

=> NPi ≥ 3: normal pupillary light reactivity



- Prospective international multicenter study
- N=456 comatose resuscitated patients
- Automated pupillometry with NPi ≤ 2/5: FPR 0%
- Standard pupillary light reflex assessment: FPR 6%

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