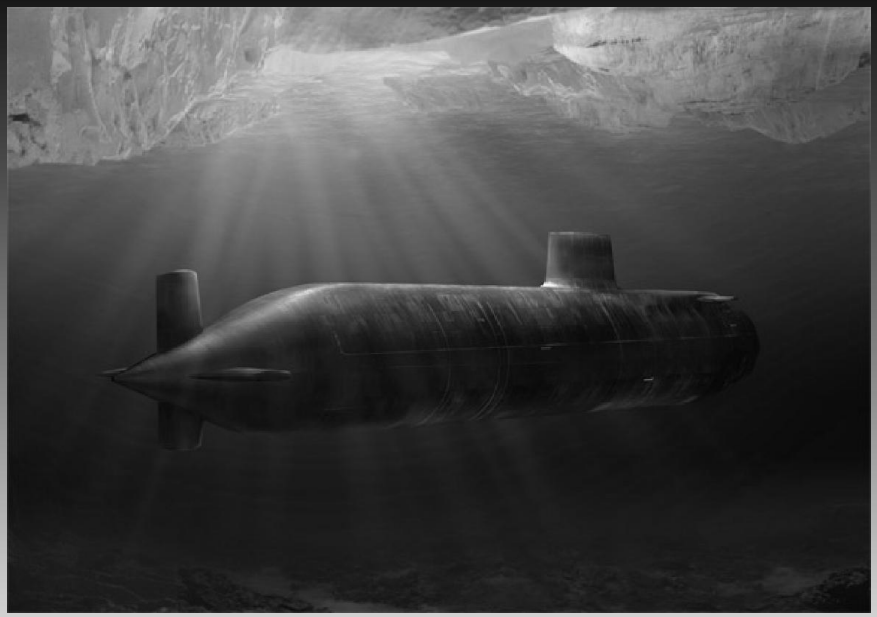
BIS: sogno o son desto?



Mercoledì, 9 aprile alle ore 14,30 – Aula 2CR

Toninelli A. - Trapasso V. - Turin M.

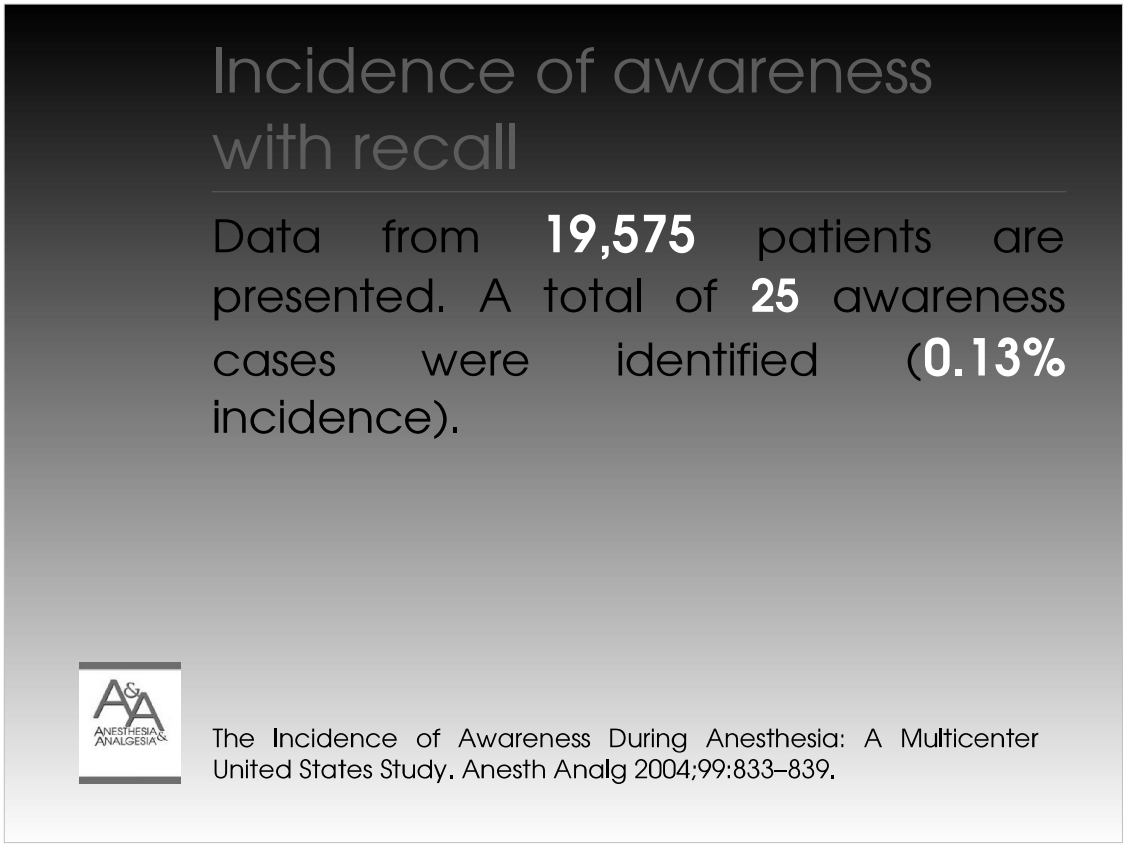
Too ... light

Definition of Anesthesia awareness

"Anesthesia awareness is currently defined as consciousness under general anaesthesia with subsequent recall of the experienced events."

Practice advisory for intraoperative awareness and brain function monitoring: a report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. Anesthesiology 2006; 104: 847–864.

Anaesthesia awareness is currently defined as consciousness under general anaesthesia with subsequent recall of the experienced events (American Society of Anesthesiologists Task Force 2006). This definition conflates intraoperative awareness (i.e. consciousness) and postoperative recall (i.e. memory).



We undertook a prospective study to determine the incidence of awareness with recall during general anesthesia in the United States. This is a prospective, nonrandomized descriptive cohort study that was conducted at seven academic medical centers in the United States. Patients scheduled for surgery under general anesthesia were interviewed in the postoperative recovery room and at least a week after anesthesia and surgery by using a structured interview. Data from 19,575 patients are presented. A total of 25 awareness cases were identified (0.13% incidence).

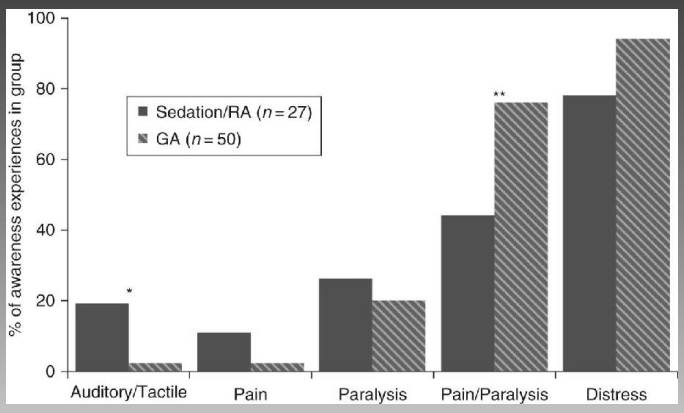
Incidence of awareness with recall

NAP5 project (the national UK survey of intraoperative awareness during general anaesthesia) have been published incidence of awareness with recall, as reported by participant anaesthetists, as low as **1:15.414**.

I. Awareness with explicit recall during general anaesthesia: current status and issues. Br. J. Anaesth. 2014;112:1-4.

ANESTHESIA AWARENESS REGISTRY
www.awaredb.org

Sensations and distress in patients with unexpected explicit recall complaints

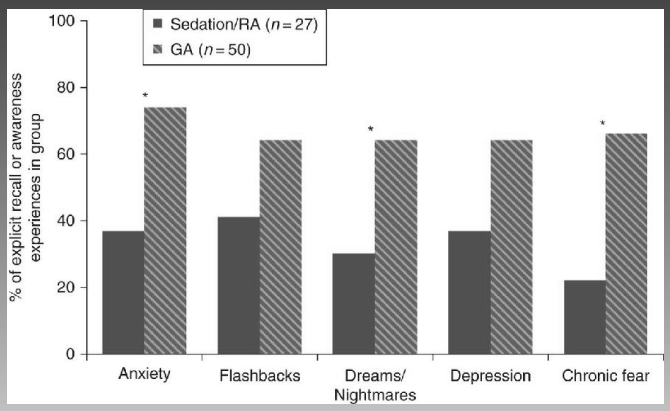


Psychological impact of unexpected explicit recall of events occurring during surgery performed under sedation, regional anaesthesia, and general anaesthesia: data from the Anesthesia Awareness Registry. Br. J. Anaesth. 2013;110:381-387.

Figure indicates the types of sensations reported by the patients as classified by the investigators using the Michigan Awareness Classification Instrument. The sensation of paralysis was reported by 70% of the patients receiving sedation (14 out of 20), and pain, with or without paralysis, was reported by 65% (13 of 20). Five out of seven patients with RA reported paralysis (two without pain (subarachnoid block) and three with pain (epidural)). The large majority (78%) of sedation/RA patients experienced distress. In contrast, nearly all (96%) of the patients who received GA reported paralysis, 78% reported pain, and 94% experienced distress. A greater proportion of sedation/RA patients experienced only auditory or tactile sensations (19% vs 2% GA, P=0.03) and a lower proportion experienced paralysis with pain (44% vs 76% GA, P<0.01).

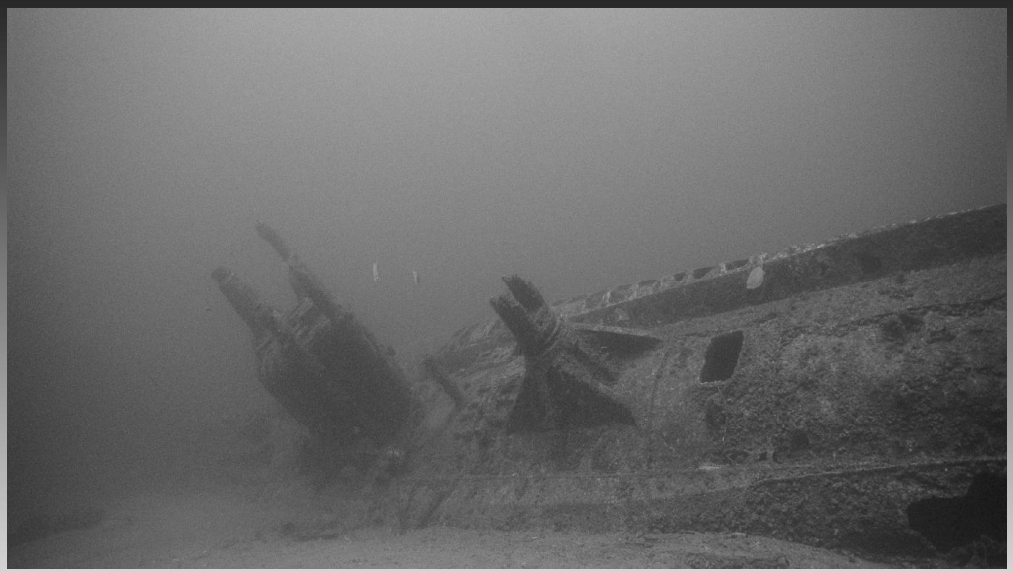
ANESTHESIA AWARENESS REGISTRY
www.awaredb.org

Psychological sequelae of unexpected explicit recall or awareness



Psychological impact of unexpected explicit recall of events occurring during surgery performed under sedation, regional anaesthesia, and general anaesthesia: data from the Anesthesia Awareness Registry Br. J. Anaesth. 2013;110:381-387.

Psychological sequelae of unexpected explicit recall or awareness. Patients with unexpected explicit recall complaints after sedation/RA were less likely to report experiencing anxiety, dreams or nightmares, and chronic fear daily, weekly or monthly since their explicit recall experience compared with those with awareness during GA (*P<0.01 for each by the $\chi 2$ test).



Too ... deep

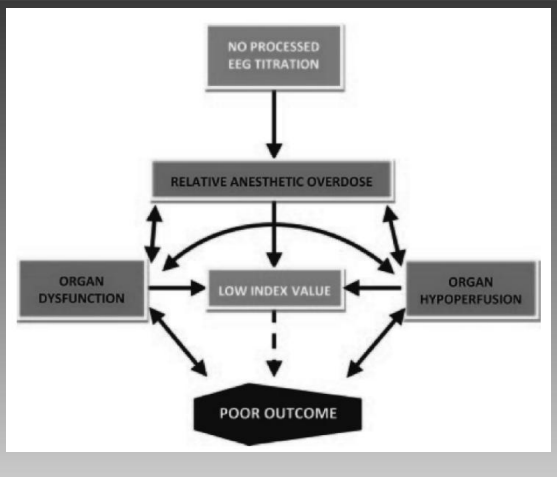
Mortality after anesthesia

Predictor	Relative risk (odds ratio) [95% CI]	*P* value
Comorbidity (3+ versus 0–2)	13.901 (7.722–25.027)	<0.0001
ASA physical status (Class 3, 4 versus Class 1)	8.300 (2.009–34.289)	0.0035
Age (65+ versus 18–39 yr)	4.459 (2.032–9.784)	0.0002
History of hepatic disease	3.591 (1.764–7.310)	0.0004
History of previous myocardial infarction	3.529 (1.733–7.183)	0.0005
History of heart disease	2.174 (1.128–4.192)	0.0204
History of hypertension	1.944 (1.162–3.254)	0.0114
Cumulative deep hypnotic time (per h)	1.335 (1.132–1.574)	0.0006
Surgical duration (per h)	1.218 (1.056–1.405)	0.0067
Intraoperative systolic blood pressure <80 mm Hg (per min)	1.044 (1.016–1.072)	0.0017
Body mass index	0.968 (0.937–1.000)	0.0494
Preoperative diastolic blood pressure	0.963 (0.942–0.985)	0.0010
Educational level (yr)	0.878 (0.794–0.972)	0.0118
Preoperative Mini-Mental State Examination (per unit)	0.829 (0.700–0.982)	0.0298
Type of surgery		
Minimally invasive or superficial versus intracavitary	0.308 (0.123–0.774)	0.0123
Orthopedic versus intracavitary	0.217 (0.086–0.545)	0.0011

Anesthetic Management and One-Year Mortality After Noncardiac Surgery. Anesth Analg 2005;100:4 –10.

Multivariate Cox Proportional Hazards modeling identified three variables as significant independent predictors of mortality: patient comorbidity (relative risk, 16.116; P < 0.0001), cumulative deep hypnotic time (Bispectral Index ® <45) (relative risk = 1.244/h; P=0.0121) and intraoperative systolic hypotension (relative risk = 1.036/min; P = 0.0125). Death during the first year after surgery is primarily associated with the natural history of preexisting conditions. However, cumulative deep hypnotic time and intraoperative hypotension were also significant, independent predictors of increased mortality.

Postoperative delirium in elderly patients



Low Bispectral Index Values and Death: The Unresolved Causality Dilemma. Anesth Analg 2011;113:660–663.

Several studies identified more important associations with poor outcome than cumulative deep hypnotic time, namely, advancing age, comorbidities including malignancy, and intraoperative hypotension. These factors have been identified before and are included in Figure under the headings "organ dysfunction" and "organ hypoperfusion."

Anesthetic agents are potent causes of arterial hypotension and any significant cerebral hypoperfusion may mean that a dose or concentration that was appropriate from an anesthetic depth perspective when the patient was normotensive is now excessive (i.e., a relative anesthetic overdose).

There is an obvious question if the hypothesis is true: What is the mechanism? At a molecular level, the deleterious effects of anesthesia are protean. Animal and some human studies have shown that anesthetics can provoke the inflammatory response, increase deposition of Alzheimer proteins, induce neuronal apoptosis, and cause prolonged postoperative cognitive dysfunction. Opioids can also induce angiogenesis and may decrease cancer survival times. The unproven clinical implication of inherent dose-dependent anesthetic toxicity is that a lower dose of anesthetic is better.

In medio stat virtus

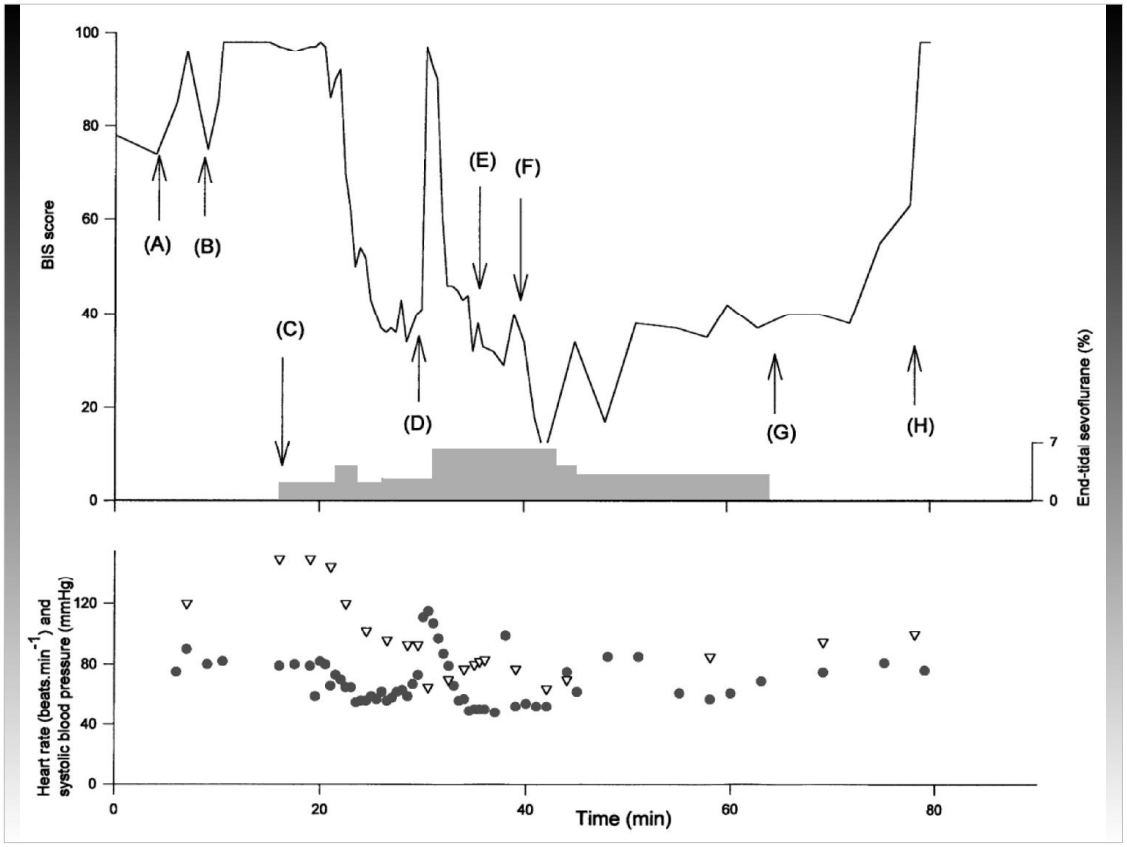


Figure (Upper) BIS scores during anaesthesia and surgery (left axis). The end-tidal sevoflurane concentration is also shown aschart (right axis). Events (A) to (H) are discussed in detail in the text: (A) venous cannulation; (B) changing the tracheostomy tube; (C) induction of anaesthesia; (D) attempted laryngoscopy; (E) second, successful laryngoscopy and insertion of the throat pack; (F) startsurgery; (G) end of surgery; (H) signs of movement of the mouth and arms.

Case report

	Adrenaline ($nmol.l^{-1}$)	Noradrenaline ($nmol.l^{-1}$)	Growth hormone ($mU.l^{-1}$)	Cortisol ($nmol.l^{-1}$)	Prolactin ($mU.ml^{-1}$)	Glucose ($mmol.l^{-1}$)
Normal range	< 1.5	< 10	< 20	140–700	< 900	< 10
Pre-operative	< 0.06	6.70	0.3	161	941	4.9
Postoperative	0.10	3.45	0.6	165	5201	5.0

J. J. Pandit. Bispectral index-guided management of anaesthesia in permanent vegetative state. Anaesthesia 2002; 57: 1190–1194.

There are three possible interpretations of our observations.

First, the diagnosis of PVS in our patient may be an over-simplification of the precise state of brain activity. It is increasingly appreciated that the term PVS might encompass a spectrum of disease. Our patient appears to fulfil all currently accepted criteria for PVS, but the term "awareness state" has been suggested as more appropriate description for some patients as this term implies some (rather than absent) cortical activity. It is reasonable to suppose on theoretical grounds that the BIS monitor might be somewhat more accurate when there is initially some (albeit low) cortical activity, rather than a complete absence of such activity. Our results might therefore be consistent with the notion that some cortical activity persists in some patients currently diagnosed with PVS.

A **second** possibility is that BIS as a technique is not robust enough to distinguish between integrated and nonintegrated cortical neuronal activity. In other words, high BIS score might indicate that the overall level of cortical activity is high (which in a normal subject implies a high level of consciousness) but a high BIS score does not necessarily indicate that this cortical activity is integrated or meaningful, especially in a subject with chronic brain disease. This is speculative, but the observation that EEG coherence (which is the extent to which EEG voltages in different parts of the brain are correlated) can be severely impaired in PVS without a significant change in the overall power spectrum (which is the analysis of the EEG voltage) current product vs. frequency vs. time) lends some support to this notion.

A **third** possibility is that the BIS profile was an artefact or coincidence.

AWARENESS

E

BIS

dott.ssa Valentina Trapasso

A rischio di Awareness:

- Pz con storia di pregressa awareness
- Pz sottoposti a interventi di cardio-chirurgia
- Pz sottoposte a parti cesarei in anestesia generale
- Pz sottoposti ad interventi con significative perdite emorragiche
- Pz che assumono significative dosi di sedativi o analgesici
- Pz che devono essere curarizzati
- Pz difficili da intubare
- Pz «fragili»:
  - -anziani
  - -cardiopatici

Lancet. 2004 May 29;363(9423):1757-63.

Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial.

Myles PS[1], Leslie K, McNeil J, Forbes A, Chan MT

The B-Aware Trial:

- **Studio multicentrico, prospettico, randomizzato, a doppio cieco**
- **2463 pazienti arruolati, tutti a rischio di awareness**

- **BIS group: 1225 pz**
- **Routine care group: 1238 pz (la profondità dell'anestesia era valutata solo attraverso i segni clinici)**

N.B. Le anestesie generali sono state sia totalmente endovenose (TIVA) che inalatorie

Lancet. 2004 May 29;363(9423):1757-63.

Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial.

Myles PS[1], Leslie K, McNeil J, Forbes A, Chan MT

The B-Aware Trial:

- **Primo outcome:**

  valutare l'incidenza di awareness nei due gruppi

  (i pz venivano intervistati a 2-6 h dall'intervento chirurgico, a 24-36 h e, infine, a 30 giorni)

- **Secondo outcome:**

  valutare i tempi di risveglio, la quantità somministrata di anestetici, l'incidenza di marcata ipotensione, l'ansia e la depressione, il gradimento del paziente la mortalità a 30 giorni.

Lancet. 2004 May 29;363(9423):1757-63.

Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial.

Myles PS[1], Leslie K, McNeil J, Forbes A, Chan MT.

The B-Aware Trial:

AWARENESS:

- **BIS group: 2 casi**
- **Routine care group: 11 casi**

RIDUZIONE DEL RISCHIO DI AWARENESS: 82%

(95% CI, 17 a 98%)

p=0.022 DIFFERENZA STATISTICAMENTE SIGNIFICATIVA!!

OR: 0.18

Lancet. 2004 May 29;363(9423):1757-63.

Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial.

Myles PS[1], Leslie K, McNeil J, Forbes A, Chan MT

The B-Aware Trial:

- **SECONDO OUTCOME:**

(risultati meno evidenti rispetto a quelli sull' awareness)

- nel BIS group vennero usate quantità inferiori di anestetici (midazolam e propofol) (p =0.017 e p =0.016)

-i tempi di risveglio furono più brevi nel BIS group (p =0.003)

- i tempi di dimissione dalla PACU furono simili

- nessuna differenza sull'incidenza di ipotensione

N Engl J Med. 2008 Mar 13;358(11):1097-108. doi: 10.1056/NEJMoa0707361.

Anesthesia awareness and the bispectral index.

Avidan MS[1], Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, Saager L, Turner MS, Rao S, Bottros M, Hantler C, Jacobsohn E, Evers AS.

The B-Unaware Trial:

- **Studio di un SINGOLO CENTRO, prospettico, randomizzato**
- **arruolati 2000 pz a elevato rischio di awareness, tutti sottoposti ad anestesia generale con isoflurano, sevoflurano o desflurano**
- **- 1000 assegnati al protocollo «BIS» (range 40-60)**

  - 1000 assegnati al protocollo »ETAG» (espirato del gas anestetico o MAC compreso tra 0.7 e 1.3)
- **i pz venivano intervistati a 24 h, tra 24 e 72 h e a 30 giorni dall'estubazione**

N Engl J Med. 2008 Mar 13;358(11):1097-108. doi: 10.1056/NEJMoa0707361.

Anesthesia awareness and the bispectral index.

Avidan MS[1], Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, Saager L, Turner MS, Rao S, Bottros M, Hantler C, Jacobsohn E, Evers AS.

The B-Unaware Trial:

RISULTATI:

- **4 pz presentarono awareness:**
  - **-2 pz appartenenti al BIS group**
  - **- 2 pz appartenenti all ' ETAG group**

RIDUZIONE DEL RISCHIO ASSOLUTO= 0%

(95% CI, -0.56 a 0.57)

INCIDENZA TOTALE DI SICURA AWARENESS = 0.21%

(95% CI, 0.08 a 0.53)

N Engl J Med. 2008 Mar 13;358(11):1097-108. doi: 10.1056/NEJMoa0707361.

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The B-Unaware Trial:

RISULTATI:

- **5 pz ebbero una possibile awareness**
  - **4 pz nel BIS group**
  - **1 pz nell'ETAG group**

INCIDENZA DELLA POSSIBILE AWARENESS NEL BIS GROUP=0.62%

INCIDENZA DELLA POSSIBILE AWARENESS NELL'ETAG GROUP=0.31%

INCIDENZA TOTALE DELLA SICURA E POSSIBILE AWARENESS=0.46%

(95% CI , tra 0.24 e 0.87)

N Engl J Med. 2008 Mar 13;358(11):1097-108. doi: 10.1056/NEJMoa0707361.

Anesthesia awareness and the bispectral index.

Avidan MS[1], Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, Saager L, Turner MS, Rao S, Bottros M, Hantler C, Jacobsohn E, Evers AS.

The B-Unaware Trial:

RISULTATI

- **BIS>60 in 1 dei 4 pz con sicura awareness e in 3 dei 9 pz con possibile o sicura awareness**
- **MAC<0.7 in 3 dei 4 pz con sicura awareness e in 7 dei 9 pz con possibile o sicura awareness**

N Engl J Med. 2008 Mar 13;358(11):1097-108. doi: 10.1056/NEJMoa0707361.

Anesthesia awareness and the bispectral index.

Avidan MS[1], Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, Saager L, Turner MS, Rao S, Bottros M, Hantler C, Jacobsohn E, Evers AS.

The B-Unaware Trial:

CONCLUSIONI:

- **Non è stata dimostrata la superiorità del BIS rispetto all'ETAG per prevenire l'awareness**
- **Nella maggior parte dei casi di sicura o possibile awareness, BIS<60!!!**

- **Lo studio ha importanti limiti:**

  Errori comuni: diagnosi soggettiva di awareness, induzione di falsi ricordi…

  E' stata praticata a tutti un'anestesia inalatoria, mai TIVA

  Studio condotto in un solo centro

CONSIDERAZIONI AUTORI

- **L'uso del BIS fornisce un falso senso di sicurezza agli anestesisti circa la prevenzione dell'awareness**
- **Costo BIS: se fosse usato in tutte le anestesie il costo eccederebbe i 360$ annui**

N Engl J Med. 2011 Aug 18;365(7):591-600. doi: 10.1056/NEJMoa1100403.

Prevention of intraoperative awareness in a high-risk surgical population.

Avidan MS[1], Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, Karl L, Kamal S, Torres B, O'Connor M, Evers AS, Gradwohl S, Lin N, Palanca BJ, Mashour GA; BAG-RECALL Research Group.

THE BAG-RECALL Study Group:

- **Trial prospettico randomizzato , cieco al valutatore, effettuato in 3 centri**
- **6100 pz prerandomizzati ad alto rischio di awareness**
- **BIS Group: 2861 pz**
- **ETAC group: 2852 pz**

Il monitoraggio BIS fu applicato a tutti i pz; nell'ETAC group il valore del BIS era oscurato mentre in entrambi i gruppi era possibile vedere l'ETAC

- **I pz venivano intervistati a 72 h dall'intervento chirurgico e a 30 gg dall'estubazione**

N Engl J Med. 2011 Aug 18;365(7):591-600. doi: 10.1056/NEJMoa1100403.

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Table 3. **Between-Group Comparison of Awareness Experiences.***

Outcome	BIS Group (N=2861)	ETAC Group (N=2852)	P Value†	Difference, BIS–ETAC
	no. (%)			*percentage points (95% CI)*
Definite awareness: primary outcome	7 (0.24)	2 (0.07)	0.98	0.17 (−0.03 to 0.38)
Definite or possible awareness: pre-specified secondary outcome	19 (0.66)	8 (0.28)	0.99	0.38 (0.03 to 0.74)
Distressing experience of awareness: post hoc secondary outcome	8 (0.28)	1 (0.04)	0.99	0.24 (0.04 to 0.45)

* BIS denotes bispectral index, and ETAC end-tidal anesthetic-agent concentration.

† One-tailed P values were calculated to test the null hypothesis that BIS is not superior to ETAC and the alternative hypothesis that BIS is superior to ETAC. A one-tailed P value of less than 0.05 with the use of Fisher's exact test would suggest that the null hypothesis should be rejected and the alternative hypothesis accepted.

N Engl J Med. 2011 Aug 18;365(7):591-600. doi: 10.1056/NEJMoa1100403.

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THE BAG-RECALL Study Group:

CONCLUSIONI:

Non è stata dimostrata la superiorità del BIS rispetto all'ETAC nella prevenzione dell'awareness intraoperatoria!

LIMITI:

- **Pz arruolati ad alto rischio di awareness**

Bispectral index for improving anaesthetic delivery and postoperative recovery (Review)

Punjasawadwong Y, Phongchiewboon A, Bunchungmongkol N

The Cochrane Library 2010, Issue 10

Bispectral index for improving anaesthetic delivery and postoperative recovery (Review)

OUTCOME PRIMARIO:

- **Valutazione Awareness**

OUTCOMES SECONDARI:

- **Consumo di anestetici**
- **Tempi di risveglio dei pz**
- **Costi dell'anestesia**

Bispectral index for improving anaesthetic delivery and postoperative recovery (Review)

MATERIALI E METODI :

- **31 trials analizzati**
- **Pz a basso e alto rischio di Awareness**
- **Pz >18 anni sottoposti ad anestesia generale**
- **Trials con almeno 2 bracci:**

  -BIS group

  -gruppo valutato attraverso standard practice (segni clinici, MAC)

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003843.

Bispectral index for improving anaesthetic delivery and postoperative recovery.

Punjasawadwong Y[1], Boonjeungmonkol N, Phongchiewboon A.

OUTCOME PRIMARIO:

- **Awareness negli studi che usavano i segni clinici come guida nella pratica clinica, l'uso del BIS ridusse il rischio di Awareness (OR 0.24)**

- **Awareness negli studi che usavano l'espirato del gas inalatorio come guida nella pratica clinica, l'uso del BIS non ridusse il rischio di Awareness (OR 1.01)**

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003843.

Bispectral index for improving anaesthetic delivery and postoperative recovery.

Punjasawadwong Y[1], Boonjeungmonkol N, Phongchiewboon A.

OUTCOMES SECONDARI (nei BIS groups):

- **Consumo di anestetici**

  -riduzione del consumo di propofol (1.44 mg/kg/h)

  (95% CI -1.95 a -0.93; I =79%)

  -riduzione del consumo di anestetici inalatori (0.14 MAC)

  (95% CI -0.22% a -0.05; I =93%)

- **Tempi di risveglio dei pz**

  -tempo di apertura occhi ridotto di 2.14 min

  -tempo di risposta al comando ridotto di 2.73 min

  -tempo di estubazione ridotto di 2.87 min

  -tempo di orientamento ridotto di 2.57 min

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003843.

Bispectral index for improving anaesthetic delivery and postoperative recovery.

Punjasawadwong Y[1], Boonjeungmonkol N, Phongchiewboon A.

OUTCOMES SECONDARI:

- **PACU : ridotta di 7.63 min**
- **Costi dell'anestesia**

-costo dei farmaci anestetici più basso nel BIS group rispetto al CS group(5.8 versus 7.5 cents/kg/h per il propofol (p <0.005)

-0.699 versus 0.984 euro/min/70 kg pz per il sevoflurano

Anesthesiology. 2012 Oct;117(4):717-25.

Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial.

Mashour GA[1], Shanks A, Tremper KK, Kheterpal S, Turner CR, Ramachandran SK, Picton P, Schueller C, Morris M, Vandervest JC, Lin N, Avidan MS

THE MACS trial

- **RTC con 21601 pz arruolati**
- **Pz non selezionati per essere a rischio di Awareness, sottoposti ad anestesia generale (sia inalatoria che TIVA)**
- **18836 pz disponibili per essere intervistati ad un mese dall'intervento**
- **9460 pz arruolati nel BIS group**
- **9376 pz arruolati nel gruppo delle concentrazioni anestetiche**

Anesthesiology. 2012 Oct;117(4):717-25.

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THE MACS trial

AWARENESS:

- 19/18836 pz (0.1%)
- 8/9460 pz del BIS group (0.08%) (95% CI 0.04 a 0.16%)
- 11/9376pz del gruppo delle concentrazioni anestetiche (0.12%) (95% CI 0.07 a 0.21%)
- p =0.48 NESSUNA DIFFERENZA STATISTICA!!

Anesthesiology. 2012 Oct;117(4):717-25.

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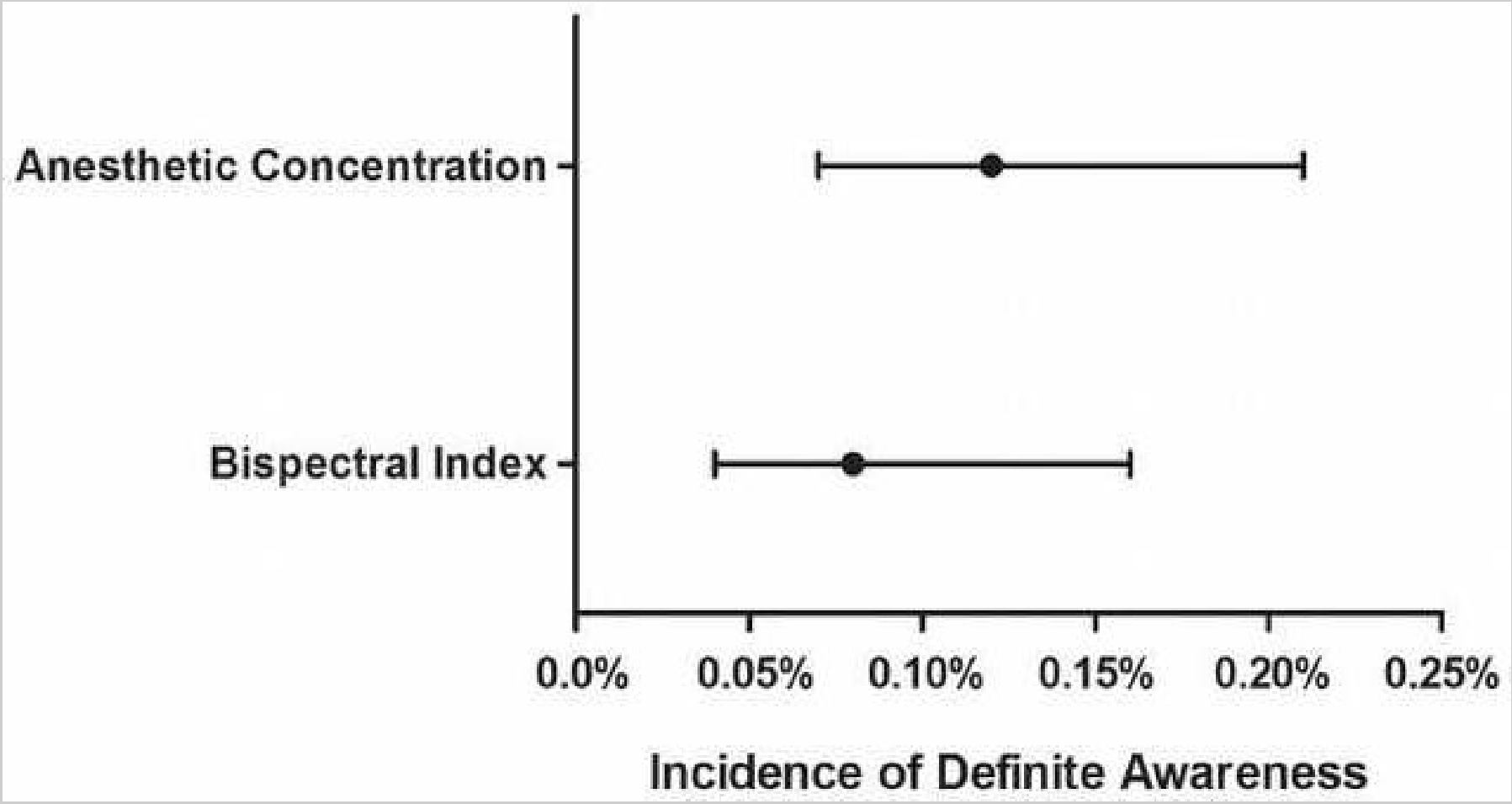

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THE MACS trial

By post hoc analysis, AWARENESS SICURA :

- **3/6076 (0.05%) nel BIS group**
- **11/9376 (0.12%) nel gruppo delle concentrazioni anestetiche**
- **5/3384 (0.15%) nel gruppo del non intervento**
- **p = 0.27 STATISTICAMENTE NON SIGNIFICATIVA!!!**

INCIDENZA DI SICURA E POSSIBILE AWARENESS:

- **0.08% nel BIS group**
- **0.20% nel gruppo delle concentrazioni anestetiche**
- **0.38% nel gruppo del non intervento**
- **p =0.006 STATISTICAMENTE SIGNIFICATIVA!!!**

Anesthesiology. 2012 Oct;117(4):717-25.

Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial.

Mashour GA[1], Shanks A, Tremper KK, Kheterpal S, Turner CR, Ramachandran SK, Picton P, Schueller C, Morris M, Vandervest JC, Lin N, Avidan MS.

THE MACS trial:

- **Il gruppo del non intervento presentò 4.7 volte in più episodi di sicura o possibile Awareness rispetto al gruppo del BIS**

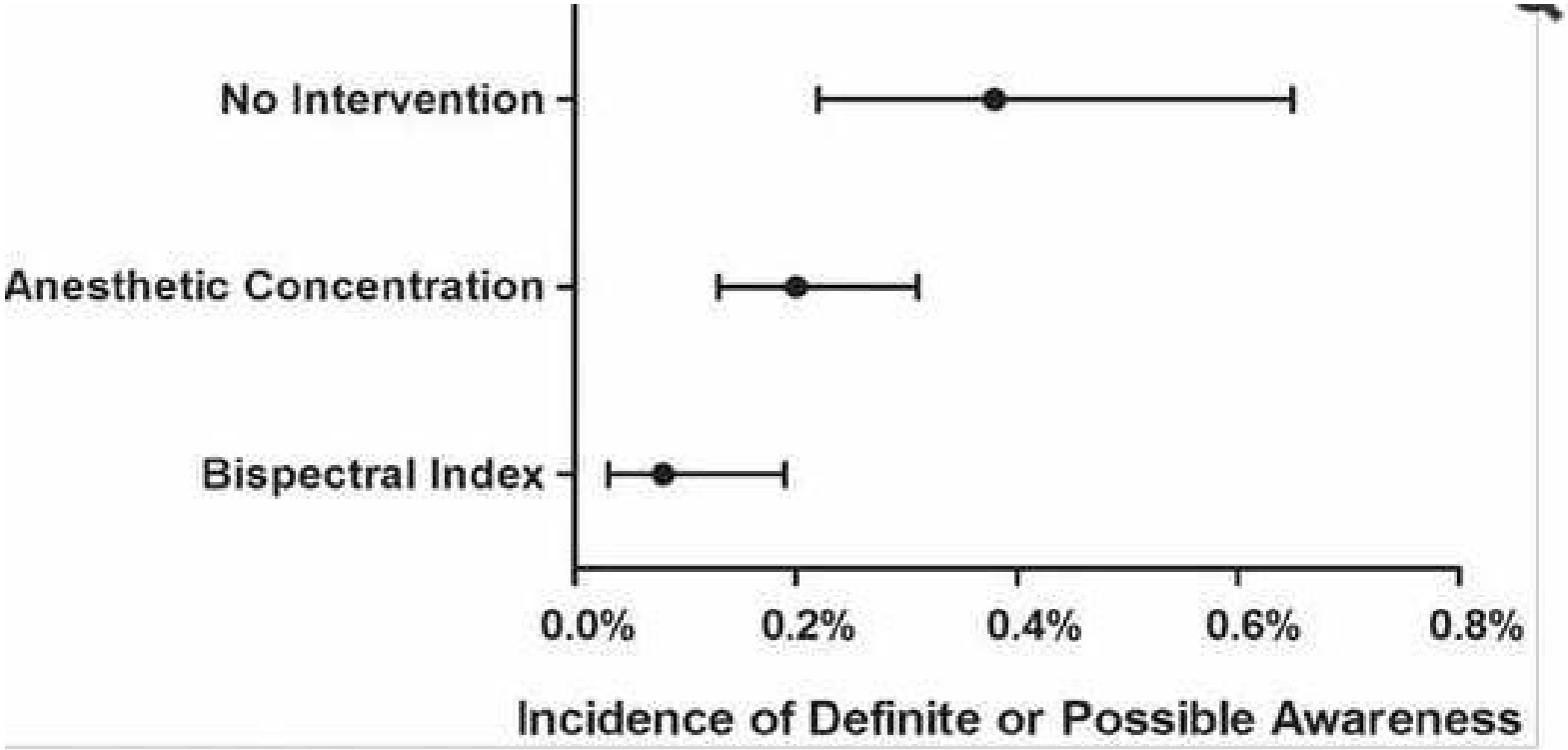
p= 0.001; 95% CI 1.7 a 13.1

DIFFERENZA STATISTICAMENTE SIGNIFICATIVA!!!

Anesthesiology. 2012 Oct;117(4):717-25.

Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial.

Mashour GA[1], Shanks A, Tremper KK, Kheterpal S, Turner CR, Ramachandran SK, Picton P, Schueller C, Morris M, Vandervest JC, Lin N, Avidan MS.



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Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial.

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THE MACS trial:

CONCLUSIONI:

- **RCT più grande mai condotto sulla prevenzione dell'Awareness su una popolazione non a rischio**
- **l'uso del BIS mostra un trend di riduzione dell'incidenza di Awareness rispetto al gruppo del non intervento**
- **L'uso del BIS non è stato associato ad una riduzione della quantità di anestetici somministrati né ad una riduzione dei tempi di risveglio o d'incidenza di nausea e vomito**

BIS – guided Anesthesia:

Low BIS ed outcomes post-operatori

- Awareness
- Drug Saving
- Reduction time of emergency, PACU stay, Nausea and Vomiting

- Delirium
- POCD (Post-Operative Cognitive Dysfunction)
- Mortality

Delirium o Stato confusionale acuto

"Alterazione dello stato di coscienza che si manifesta con alterazione dello stato di vigilanza, dell'attenzione, dell'orientamento, dell'umore, del comportamento, della coscienza di sé."

National Clinical Guideline Centre (2010). Delirium: diagnosis, prevention and management.

http://www.nice.org.uk/nicemedia/live/13060/49908/49908.pdf

Delirium post-operatorio

"Complicanza transitoria che solitamente insorge in modo acuto nelle prime 24 ore dopo l'intervento e si risolve nel giro di 72 ore."

Sieber F.E. Postoperative Delirium in the Elderly Surgical Patient. Clinical Anesthesiology 2009;27:451-64.

Fricchione GL, Nejad SH, Esses JA, et al. Postoperative delirium. American Journal of Psychiatry 2008;165:803-12.

Rudra A, Chatterjee S, Kirtania J, et al. Postoperative delirium. Indian Journal of Critical Care Medicine 2006;10:235-40.

Delirium post-operatorio: clinica

Dal punto di vista clinico i soggetti con *delirium* possono avere manifestazioni eterogenee.

A seconda del comportamento psicomotorio si distinguono tre forme:

- *delirium* ipercinetico: ansia, agitazione, disorientamento spazio-temporale, irritabilità ed aggressività;
- *delirium* ipocinetico: apatia, letargia, risposta rallentata a domande e stimoli di varia natura, riduzione dei movimenti spontanei;
- *delirium* misto: caratteristiche di entrambi i quadri descritti.

Delirium post-operatorio: epidemiologia

Complicanza frequente, specialmente nei pz anziani

- Incidenza varia ampiamente: *dal 9 all' 87%* (in base ad età dei pz e tipo di chirurgia).
- Incidenza sottostimata: molti casi (dal 66 all'84%) non riconosciuti.
- Forma ipocinetica: sotto-diagnosticata, scambiata con depressione e demenza.

Whitlock EL, Vannucci A, Avidan MS. Postoperative delirium. Minerva Anestesiologica 2011;77:448-56.

Delirium post-operatorio: fattori di rischio

TABLE I.—*Risk factors for delirium.*

Predisposing [19]	Precipitating [19, 21]	
Reduced cognitive reserve:	Medications or medication withdrawal:	
Dementia	Anticholinergics	Psychotropic medications:
Depression	Muscle relaxants	Antidepressants
Advanced age	Antihistamines	Antiepileptics
Reduced physical reserve:	Gastrointestinal antispasmodics	Antipsychotics
Atherosclerotic disease	Opioid analgesics [29]	Benzodiazepines
Renal impairment	Antiarrhythmics	
Pulmonary disease	Corticosteroids	
Advanced age	>6 total medications	
Preoperative beta blockade [30]	>3 new inpatient medications	
Sensory impairment (vision, hearing)	Pain31	
Alcohol abuse	Hypoxemia	
Malnutrition	Electrolyte abnormalities	
Dehydration [29]	Malnutrition	
Apolipoprotein E4 genotype [32]	Dehydration [29]	
	Environmental change (e.g. ICU admission)	
	Sleep-wake cycle disturbances [33]	
	Urinary catheter use	
	Restraint use	
	Infection	

Delirium post-operatorio: diagnosi

- Diagnosi clinica, complessa.
- *Gold standard*: accertamento clinico secondo i criteri del DSM-IV (chiede tempo ed esperienza clinica in ambito psichiatrico).
- Diverse scale di valutazione validate:

  differiscono per accuratezza diagnostica, esperienza e tempo necessari per la somministrazione.

Whitlock EL, Vannucci A, Avidan MS. Postoperative delirium. Minerva Anestesiologica 2011;77:448-56.

Delirium post-operatorio: diagnosi

- *Confusion Assessment Method* (CAM)

- **CAM-ICU** → pz intubati, in ICU, in *recovery room* dopo intervento chirurgico

Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med 1990;113:941-8.

Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA 2001;286:2703-10.

Delirium post-operatorio: diagnosi

Table 1. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

Features and Descriptions	Absent	Present
I. Acute onset or fluctuating course*		
A. Is there evidence of an acute change in mental status from the baseline? B. Or, did the (abnormal) behavior fluctuate during the past 24 hours, that is, tend to come and go or increase and decrease in severity as evidenced by fluctuations on the Richmond Agitation Sedation Scale (RASS) or the Glasgow Coma Scale?		
II. Inattention†		
Did the patient have difficulty focusing attention as evidenced by a score of less than 8 correct answers on either the visual or auditory components of the Attention Screening Examination (ASE)?		
III. Disorganized thinking		
Is there evidence of disorganized or incoherent thinking as evidenced by incorrect answers to 3 or more of the 4 questions and inability to follow the commands? Questions 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does 1 pound weigh more than 2 pounds? 4. Can you use a hammer to pound a nail? Commands 1. Are you having unclear thinking? 2. Hold up this many fingers. (Examiner holds 2 fingers in front of the patient.) 3. Now do the same thing with the other hand (without holding the 2 fingers in front of the patient). (If the patient is already extubated from the ventilator, determine whether the patient's thinking is disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject.)		
IV. Altered level of consciousness		
Is the patient's level of consciousness anything other than alert, such as being vigilant or lethargic or in a stupor, or coma? Alert: spontaneously fully aware of environment and interacts appropriately Vigilant: hyperalert Lethargic: drowsy but easily aroused, unaware of some elements in the environment or not spontaneously interacting with the interviewer; becomes fully aware and appropriately interactive when prodded minimally Stupor: difficult to arouse, unaware of some or all elements in the environment or not spontaneously interacting with the interviewer; becomes incompletely aware when prodded strongly; can be aroused only by vigorous and repeated stimuli and as soon as the stimulus ceases, stuporous subject lapses back into unresponsive state Coma: unarousable, unaware of all elements in the environment with no spontaneous interaction or awareness of the interviewer so that the interview is impossible even with maximal prodding		
Overall CAM-ICU Assessment (Features 1 and 2 and either Feature 3 or 4): Yes____ No____		

Delirium post-operatorio: *outcomes*

- Aumento della morbilità.
- Aumento della durata di VAM, del ricovero in ICU, della degenza ospedaliera (e quindi dei costi).
- Aumento della mortalità: del 10-20% per ogni 48h di delirium.

Lat I, McMillian W, Taylor S, Janzen JM, Papadopoulos S, Korth L et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. Crit Care Med 2009;37:1898-905.

Gonzalez M, Martinez G, Calderon J, Villarroel L, Yuri F, Rojas C et al. Impact of delirium on short-term mortality in elderly inpatients: a prospective cohort study. Psychosomatics 2009;50:234-8.

Rudolph JL, Inouye SK, Jones RN, Yang FM, Fong TG, Levkoff SE et al. Delirium: an independent predictor of functional decline after cardiac surgery. J Am Geriatr Soc 2010;58:643-9.

Delirium post-operatorio: terapia

- Antipsicotici di I e II generazione (BDZ?)

- "As few therapeutic measures for postoperative delirium are available, prevention remains the best option".

Vidan MT, Sanchez E, Alonso M, Montero B, Ortiz J, Serra JA. An intervention integrated into daily clinical practice reduces the incidence of delirium during hospitalization in elderly patients. J Am Geriatr Soc 2009;57:2029-36.

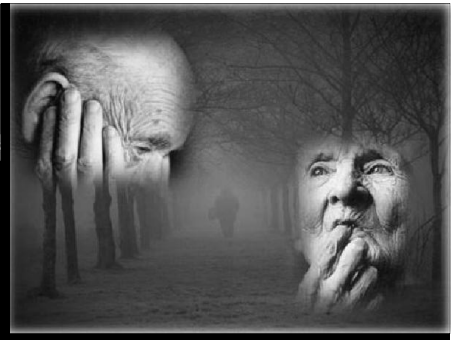
Post-operative Cognitive Dysfunction (POCD)

"Alterazione **transitoria** e **reversibile** delle funzioni cognitive (memoria, apprendimento, attenzione e percezione) - può essere accompagnata da difficoltà psicomotorie, demenza, delirio e depressione - si manifesta soprattutto nei pz anziani dopo intervento chirurgico."

Sauër AM, Kalkman C, Van Dijk D. Postoperative cognitive decline. J Anesth 2009; 23:256-9.

Hanning CD. Postoperative cognitive dysfunction. Br J Anaesth 2005; 95:82-7.

POCD: epidemiologia



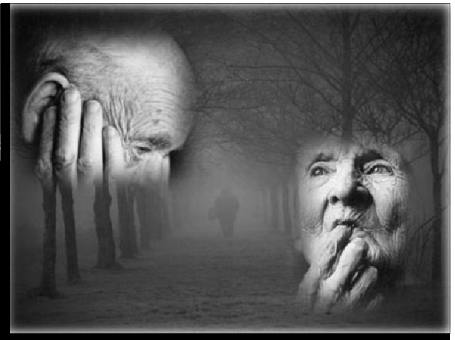
- Incidenza relativamente alta, specialmente nei pz anziani.
- Reversibile nell'arco di *1 settimana – 3 mesi* nel 20-30% dei casi.

Difficile da stimare!

- Incidenza iniziale: **25% at 2–10 days**
- Graduale risoluzione: **10% at 3 months**
  5% at 6 months

Abildstrom H, Rasmussen LS, Rentowl P, et al. Cognitive dysfunction 1–2 years after non-cardiac surgery in the elderly. ISPOCD group. International Study of Post-Operative Cognitive Dysfunction. Acta Anaesthesiol Scand 2000; 44:1246–51.

POCD: outcomes

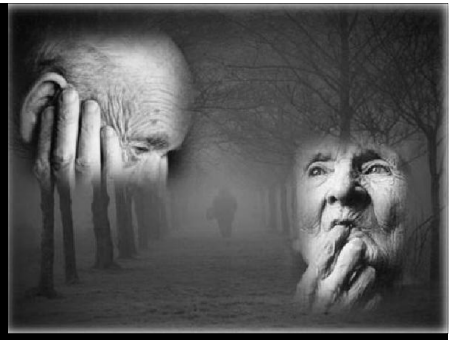


Importante problema sanitario:

- Aumento costi di **ospedalizzazione** (*maggior numero di giorni di degenza*) e di assistenza domiciliare.
- Aumento della **morbilità** e (conseguente) riduzione della qualità di vita del pz.

National Institute of Health (2010). An Update on Postoperative Cognitive Dysfunction. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2998043/

POCD: fattori di rischio



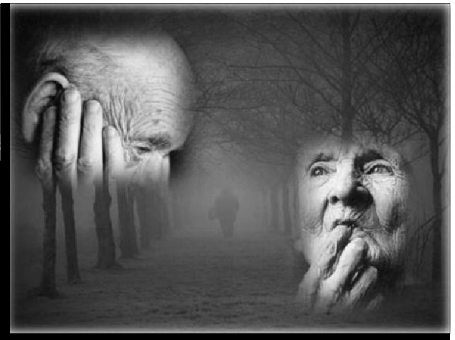
Patient-related risk factors	Supporting evidence
Age	ISPOCD, Stockton, Ancelin, Monk [2,5,91,95]
Education	ISPOCD, Monk [2,5]
Burden of illness	Monk [5]
Preoperative depression	Leung (delirium only) [96]
Preoperative cognitive impairment	
Preoperative habits and drug use	
Apolipoprotein E4	H

Proposed patient-related risk factors of POCD

ISPOCD = International Study on Post-Operat

Precipitating factors	Supporting evidence
Second operation	ISPOCD [2]
Postoperative infection	ISPOCD [2]
Respiratory complications	ISPOCD [2]
General anesthetic	?
Anesthetic type	?
Anesthetic maintenance (hypotension)	?
Pain management	Leung [98,99]

POCD: eziologia?



*The exact pathophysiology of POCD remains **undefined**.*

- Recenti studi, mostrano **in vitro** che diversi anestetici agiscono sulla oligomerizzazione del peptide β-amiloide (Aβ).
  - La produzione incontrollata, l'oligomerizzazione e la deposizione di Aβ, con successivo sviluppo di placche amiloidi, sono passi fondamentali nella genesi della *malattia di Alzheimer*.

Eckenhoff RG, Johansson JS, Wei H, et al. Inhaled anesthetic enhancement of amyloid-beta oligomerization and cytotoxicity. Anesthesiology 2004.

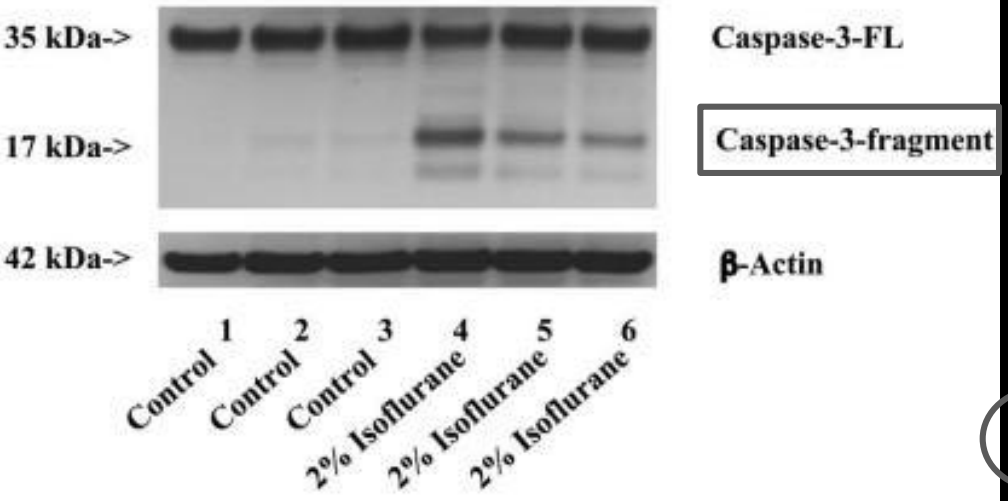
Mandal PK, Fodale V. Smaller molecular-sized anaesthetics oligomerize Aβ peptide simulating Alzheimer's disease: a relevant issue. Eur J Anaesthesiol 2009.

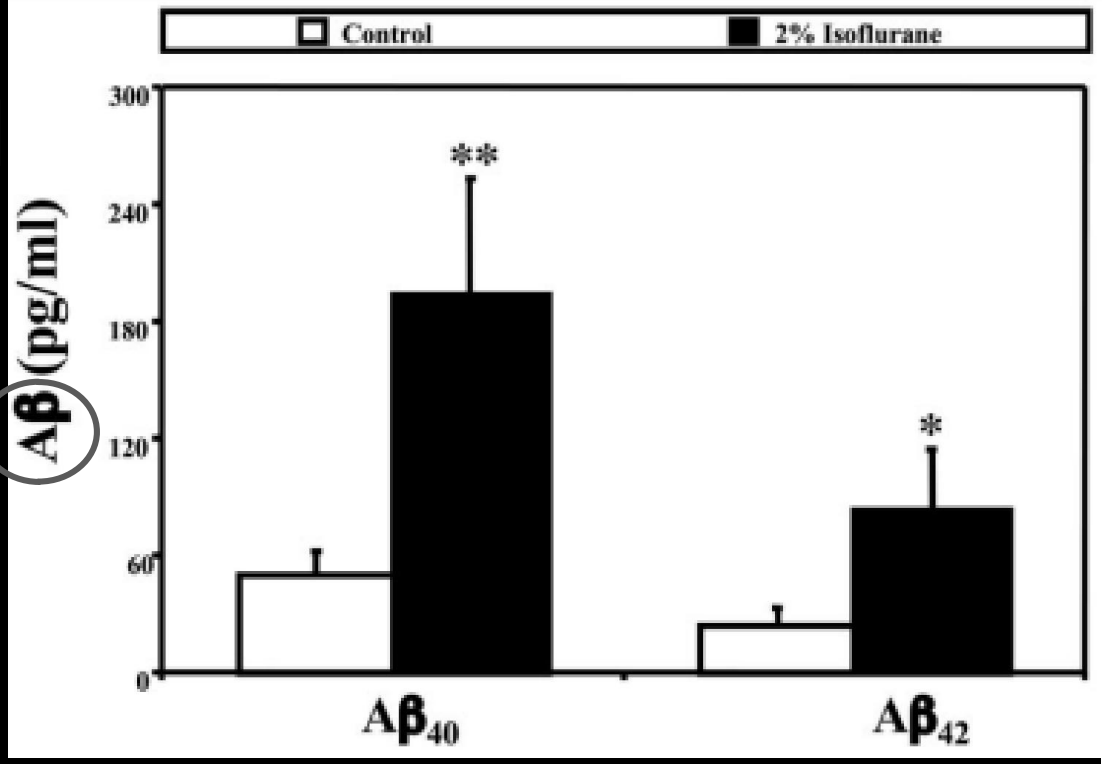
Anesthesiology 2006; 104:988–94

The Common Inhalation Anesthetic Isoflurane Induces Apoptosis and Increases Amyloid β Protein Levels

Zhongcong Xie, M.D., Ph.D.,* Yuanlin Dong, M.D., M.S.,† Uta Maeda, ‡ Paul Alfille, M.D.,§ Deborah J. Culley, M.D.,‖ Gregory Crosby, M.D.,# Rudolph E. Tanzi, Ph.D.**

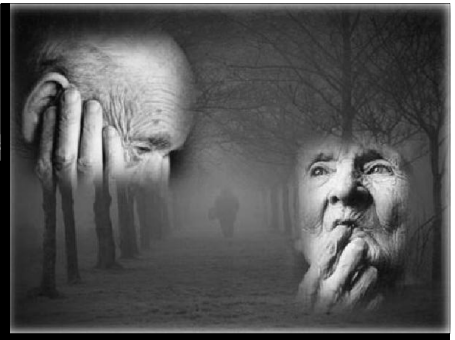
Methods: H4 human neuroglioma cells stably transfected to express human full-length wild-type amyloid precursor protein (APP) were exposed to 2% isoflurane for 6 h. The cells and





Results: Two percent isoflurane caused apoptosis, altered processing of APP, and increased production of Aβ in H4 human neuroglioma cell lines. Isoflurane-induced apoptosis was

POCD: diagnosi complessa!



- Test neuropsicologici pre- e post- operatori, quali?

Logical Memory Test, CERAD word list memory, Boston Naming test, Category Fluency test, Digit Span Test, Trail making test, Digit symbol substitution test...

- *"Quanto declino"* deve verificarsi?

- Tempi di somministrazione *(h del giorno, timing pre operatorio, durata del follow-up)*

- *Criteri di inclusione ed esclusione*

Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth 2009; 103 (Suppl. 1): i41–i46 .

British Journal of Anaesthesia **110** (S1): i98–i105 (2013)
Advance Access publication 28 March 2013 · doi:10.1093/bja/aet055

BJA

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

F. M. Radtke[1†], M. Franck[1†], J. Lendner[1], S. Krüger[1], K. D. Wernecke[2] and C. D. Spies[1*]

[1] Department of Anaesthesiology and Surgical Intensive Care Medicine, Campus Charité Mitte and Campus Virchow-Klinikum, Charité-Universitätsmedizin Berlin, Charitéplatz 1, Berlin 10117, Germany
[2] Charité-Universitätsmedizin Berlin and SoStAna GmbH, Wildensteiner Straße 27, Berlin 10318, Germany

* Corresponding author. E-mail: claudia.spies@charite.de

Studio randomizzato controllato (RCT)

- **2** ospedali universitari di Berlino
- between March 2009 and May 2010, and the follow-up was until August 2010

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

The aim of the study

"To assess whether BIS-guided anaesthesia vs routine care reduces the incidence of postoperative delirium in elderly patients"

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

METODI

Criteri di inclusione

- Età > 60 aa
- Interventi in elezione (durata prevista > 60 min)
  - Ch generale, addominale, toracica, vascolare
  - Ortopedia, ORL
  - Ginecologia, Urologia

Criteri di esclusione

- MMSE < 24
- Storia di deficit neurologici (per es. stroke)
- Interventi non in AG (per es. AL, ALR)
- Pz che non parlano la lingua locale
- Pz impossibilitati a fornire il consenso scritto

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

METODI

Intraoperative conduction

- AG inalatoria o TIVA
- BIS-open group: BIS data were allowed to be included into the management of anaesthesia
- BIS-blinded group: BIS monitor value was concealed

In both groups, BIS-data were recorded at minimum intervals of 1 min.

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

METODI

Assessment of *delirium*

- by trained medical personnel, instructed and supervised by a psychiatrist, unaware of the treatment group
- According to the DSM IV
- twice daily (morning and night) from the 1° to the 7° postoperative day

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

METODI

Assessment of *POCD*

- Neuropsychological test battery:
  - A Motor Screening Test
  - Two tests of visual memory (pattern recognition memory and spatial recognition memory)
  - A test of attention (choice reaction time)
- Administered the evening before surgery, as well as 7 days and 3 months after surgery

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

The trial was stopped early because of limited funding.

1155 pz analizzati vs. 1522 pz previsti
(secondo il calcolo della dimensione campionaria)

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

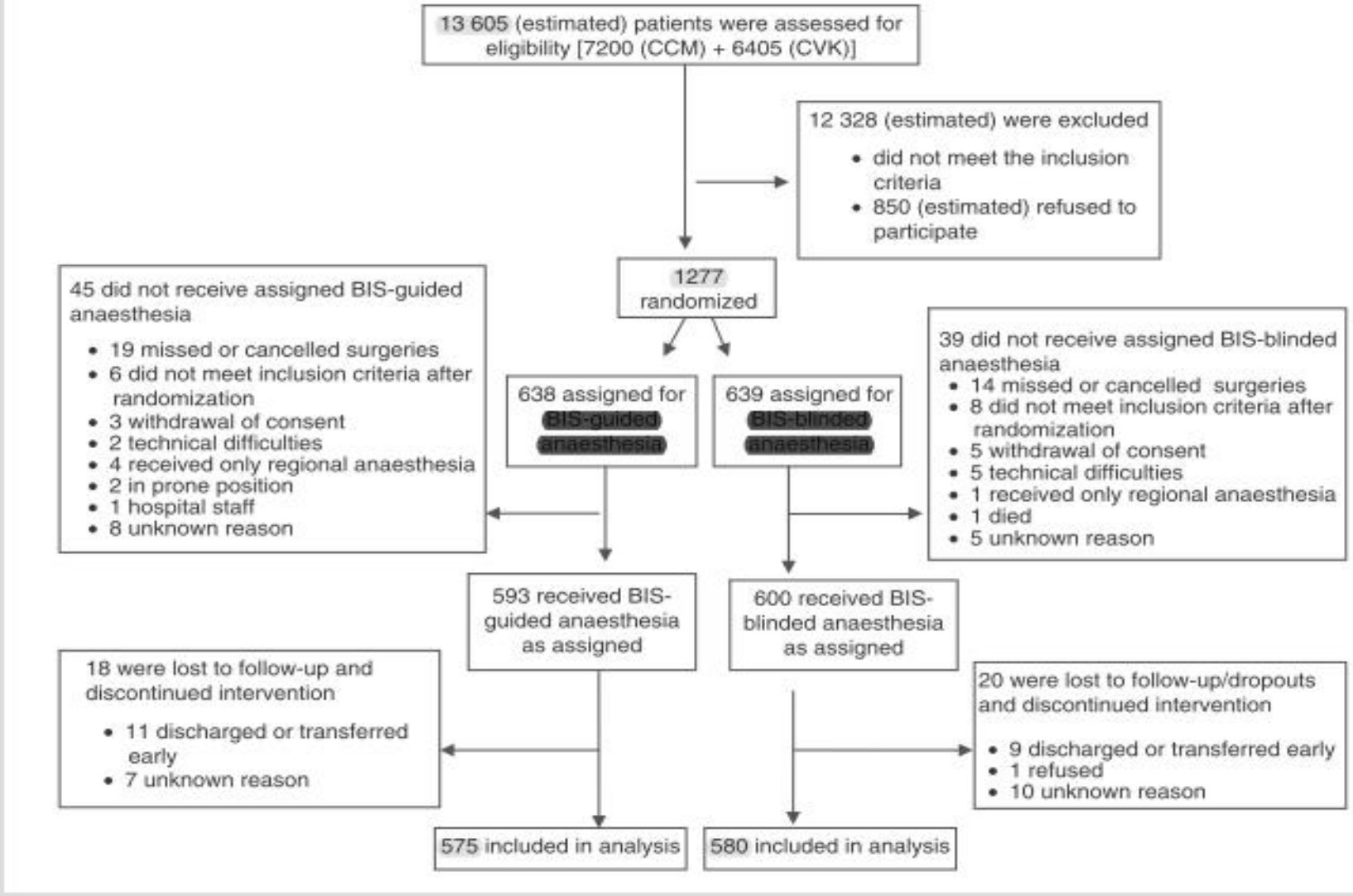


Fig 1 Screening, randomization, and the follow-up.

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

Assessment of *delirium*

Postoperative delirium was detected

- In 95 patients (16.7%) in the intervention group
- In 124 patients (21.4%) in the control group

P=0.036

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

Assessment of *delirium*

I pazienti con *delirium* ebbero:

- Maggiore durata del ricovero
- Aumento dell' incidenza di **POCD** a 7 giorni e a 3 mesi post-intervento
- Maggiore **mortalità**

P=0.015; OR= 2.05; CI=1.15–3.65

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

Assessment of *POCD*

POCD, at the 7th day, was detected

- In 70 patients (18.1%) in the intervention group
- In 90 patients (23.9%) in the control group

P=0.062 → *"was increased **in tendency** in the BIS-blinded group"*

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RISULTATI

Assessment of *POCD*

POCD, at 3 months after surgery, was detected

- In 21 patients (8.0%) in the intervention group
- In 28 patients (10.3%) in the control group

P=0.372 → *"BIS monitoring **did not** alter the incidence of POCD"*

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction *POST HOC analysis*

Analisi multivariata: *delirium & mortalità (a 3 mesi)*

With respect to the primary endpoint (POD), the following features resulted:

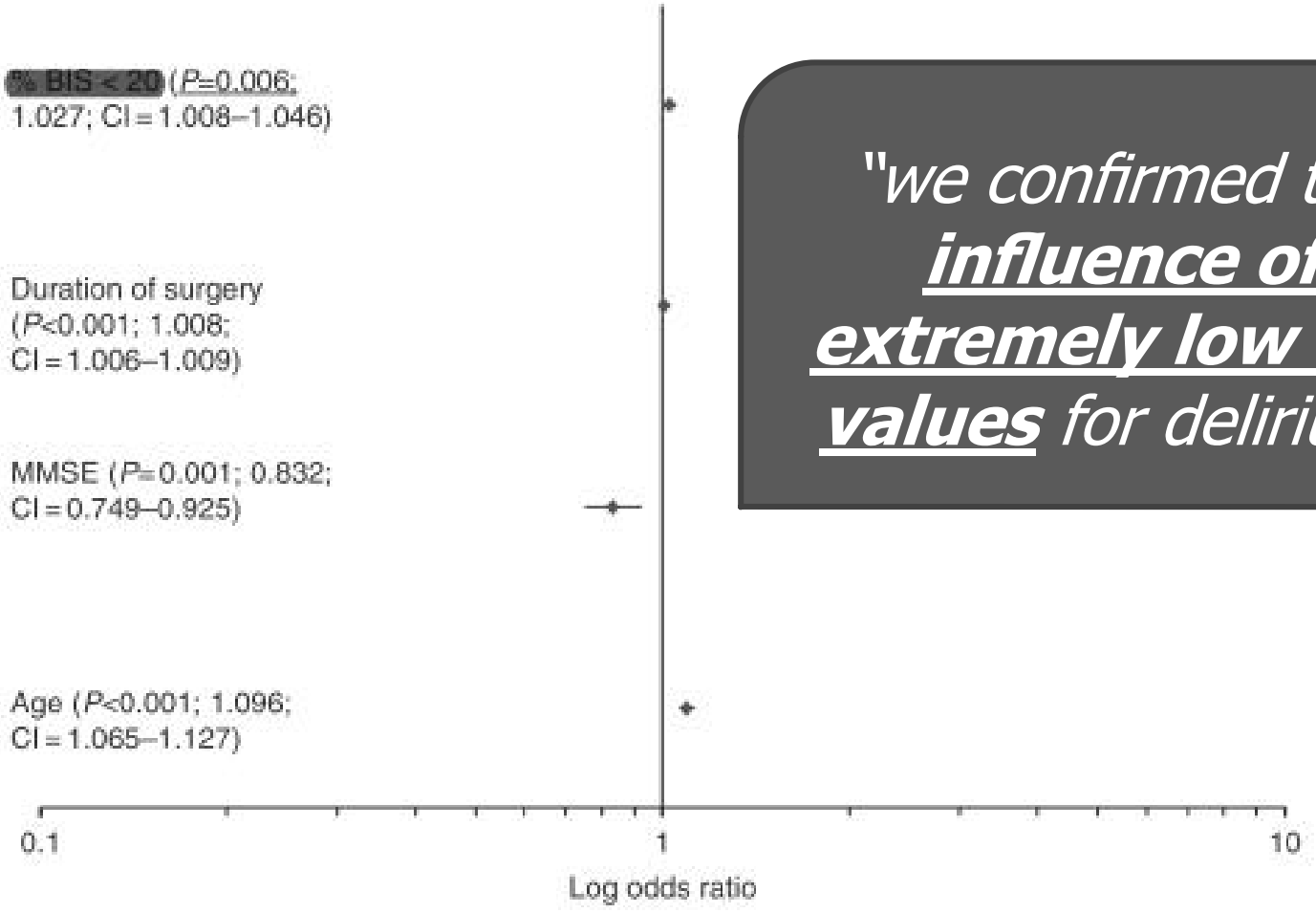
- BIS open vs blinded
- % BIS < 20
- Age
- MMSE values
- Duration of surgery
- ASA physical status

For reasons of comparability, we chose the same features in the calculation of mortality.

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

POST HOC analysis

Analisi multivariata: *delirium*

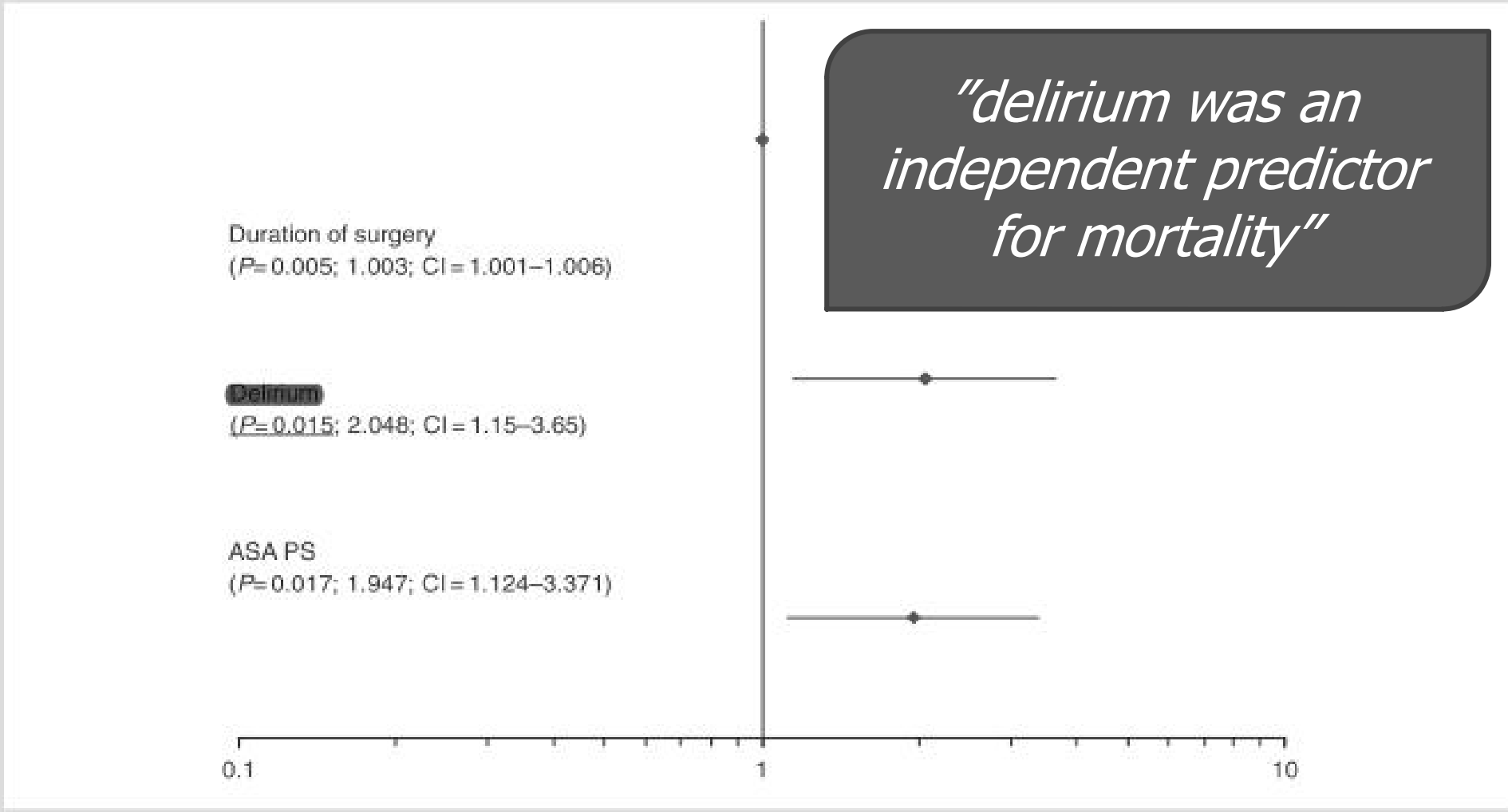


*"we confirmed the **influence of extremely low BIS values** for delirium"*

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

POST HOC analysis

Analisi multivariata: mortalità (a 3 mesi)



"delirium was an independent predictor for mortality"

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction **CONCLUSIONI**

*"Intraoperative neuromonitoring is correlated with a **lower incidence of delirium**, possibly by reducing extreme low BIS values."*

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,†*
Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA, and the CODA Trial Group*

Cognitive Dysfunction after Anesthesia (CODA)

Studio randomizzato controllato (RCT)

- 2 ospedali universitari di Hong Kong
- between January 2007 and December 2009

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

The aim of the study

"To determine whether BIS-guided anaesthesia decreases the incidence of POCD and postoperative delirium in elderly patients undergoing major surgery"

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

- Primary outcome:

  POCD at 3 months after surgery

- Secondary outcomes:
  - POCD at 1 week
  - Delirium in hospital
  - The rate and the quality of recovery (QoR)

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

METODI

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

Criteri di inclusione

- Età > 60 aa
- Interventi di chirurgia maggiore in elezione (durata prevista > 120 min)

Criteri di esclusione

- Pz analfabeti, con difficoltà linguistiche
- Pz gravemente ipoacusici e/o ipovedenti
- Pz con disturbi psichiatrici noti
- Pz con demenza o disturbi di memoria
- MMSE < 24

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

METODI

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

Assessment of *POCD*

- 3 Neuropsychological tests:
  - Verbal fluency test: to name as many words as possible from a predefined category (eg, animals) within 60 seconds
  - Chinese auditory verbal learning test: word-list learning to assesses verbal learning, retention, recognition memory
  - Color trial making: to test the psychomotor speed
- Administered within a week before surgery, and at 1 week and 3 months after surgery
- Chinese version of the cognitive failure questionnaire (CFQ) to indicate potential subjective problems

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

METODI

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

Assessment of *delirium*

- Using the CAM-ICU
- daily in the mornings after surgery

Assessment of the QoR

- Using the Chinese QoR score

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RISULTATI

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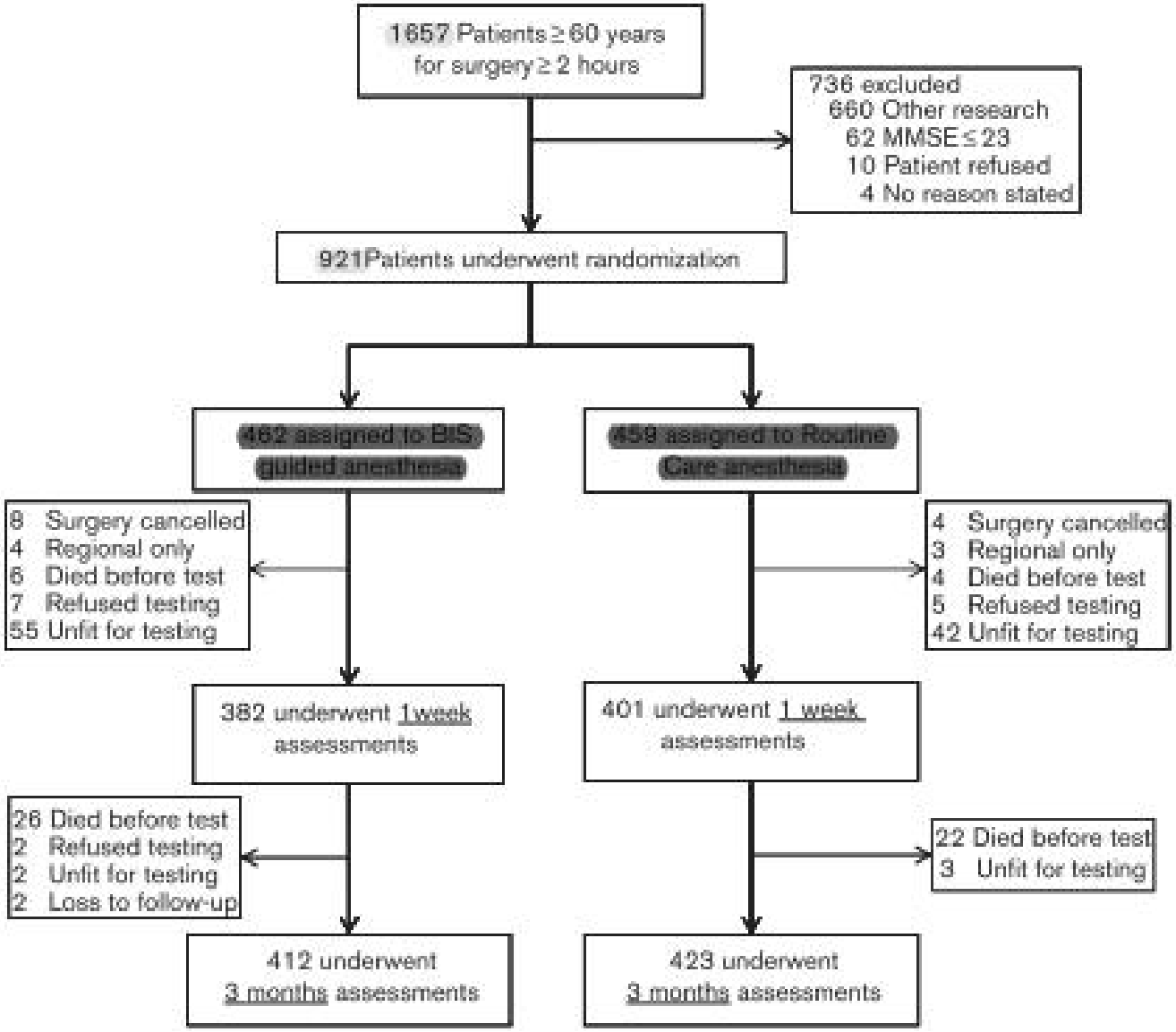

921 patients included in the CODA Trial

(85.0% and 90.7% of patients completed the 1-week and 3-month assessments)

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Assessment of POCD and *delirium*

TABLE 4. Postoperative Cognitive Outcomes

	BIS Group	Routine Care Group	Odds Ratio (95% CI)	*P*
Cognitive failure questionnaire at 3 mo after surgery				
No./total no. (%)	29/412 (7.0%)	31/423 (7.3%)	0.95 (0.41-1.98)	0.14
Delirium				
No/total no. (%)	70/450 (15.6%)	109/452 (24.1%)	0.58 (0.41-0.80)	0.01
Postoperative cognitive dysfunction				
1 wk after surgery				
No./total no. (%)	83/382 (21.7%)	93/401 (23.1%)	0.92 (0.66-1.29)	0.06
3 mo after surgery				
No./total no. (%)	42/412 (10.2%)	62/423 (14.7%)	0.62 (0.39-0.97)	0.02

BIS indicates bispectral index.

BIS-guided anesthesia reduced the rates of POCD up to 3 months after surgery.

RRA =4.5% → NNT=23

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Rate and Quality of Recovery

TABLE 5. Recovery Profiles and Postoperative Complications

	BIS Group	Routine Care Group	*P*
No. patients	450	452	
PACU admission, no.(%)	336 (74.7)	332 (73.4)	0.56
Time to eye opening (min)*	10 (7-15)	15 (10-21)	<0.001†
Time to discharge from PACU (min)*	80 (65-105)	92 (70-120)	<0.001†
Intensive care unit admission, no.(%)	113 (25.1)	120 (26.6)	0.56
Time to tracheal extubation (h)*	0.4 (0.2-4.5)	2.5 (0.2-7.9)	0.91†
Intensive care unit stay (d)*	2.0 (1.9-2.1)	2.0 (1.8-2.1)	0.06†
Hospital stay (d)*	7 (5-10)	8 (6-12)	0.98†
Quality of recovery score (out of 18)			
Day 1	11.8 ± 2.1	9.8 ± 2.4	<0.001
Hospital discharge	16.3 ± 1.7	15.3 ± 2.1	<0.001
Short-form health survey SF-36 at 3 mo after surgery:			
Physical summary measures	47.4 ± 9.2	45.1 ± 10.2	0.002
Mental summary measures	50.2 ± 12.1	52.1 ± 10.9	0.053

BIS monitoring shortened recovery times in PACU.
QoR score were reported better after BIS-guided anesthesia.

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

POST HOC analysis

Analisi multivariata: POCD a 3 mesi

TABLE 6. Risk Factors of Cognitive Dysfunction at 3 Months After Surgery (n = 835)

		Univariate Analysis		Multivariable Analysis	
Risk Factors	**Summary Statistics***	**Odds Ratio**	***P***	**Odds Ratio**	***P***
Age (y)					
No POCD	67 ± 7.9				
POCD	68 ± 8.9	1.02 (1.00-1.04)	0.02	1.04 (1.01-1.08)	0.01
Education (y)					
No POCD	7.2 ± 4.0				
POCD	6.1 ± 4.2				
Male sex (n = 475), no. (%)					
No POCD	453 (62.1)				
POCD	62 (58.8)				
Postoperative infection, no. (%)					
No POCD	114 (15.6)				
POCD	33 (31.7)				
Respiratory complication, no. (%)					
No POCD	86 (11.8)				
POCD	20 (18.5)				
Delirium, no. (%)					
No POCD	94 (12.9)				
POCD	68 (64.4)	12.26 (7.50-20.0)	<0.001	9.58 (4.62-19.9)	<0.001
Intraoperative BIS value					
No POCD	48.2 ± 6.2				
POCD	37.4 ± 3.9	0.65 (0.59-0.70)	<0.001	0.93 (0.85-0.97)	<0.001
Time with BIS < 40 (h)					
No POCD	0.3 ± 0.5				
POCD	0.7 ± 0.6	1.21 (1.01-1.30)	0.03	1.11 (1.01-1.96)	0.04
End-tidal volatile concentration (MAC equivalents)					
No POCD	0.74 ± 0.25				
POCD	1.16 ± 0.31	8.48 (5.15-13.97)	<0.001	2.31 (1.15-15.6)	0.03

"... among these factors, large doses of anesthetic, low average BIS value, long period of deep anesthesia (BIS < 40)"

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

POST HOC analysis

Analisi multivariata: *Delirium*

TABLE 7. Risk Factors of Postoperative Delirium (n = 902)

		Univariate Analysis		Multivariable Analysis	
Risk Factors	**Summary Statistics***	**Odds Ratio**	***P***	**Odds Ratio**	***P***
Age (y)					
No delirium	68 ± 8.1				
Delirium	69 ± 9.0	1.03 (1.00-1.05)	0.05		
Education (y)					
No delirium	6.9 ± 4.1				
Delirium	6.4 ± 4.3	0.97 (0.94-1.01)	0.06		
Male sex (n = 475), no. (%)					
No delirium	443 (61.1)				
Delirium	113 (64.2)	0.88 (0.63-1.24)	0.48		
Postoperative infection, no. (%)					
No delirium	128 (17.7)				
Delirium	51 (28.4)	1.86 (1.28-2.71)	0.001		
Respiratory complication, no. (%)					
No delirium	108 (14.9)				
Delirium	37 (20.8)	1.49 (0.98-2.26)	0.06		
Intraoperative BIS value					
No delirium	47.8 ± 6.5				
Delirium	37.7 ± 7.3	0.87 (0.84-0.89)	<0.001	0.91 (0.87-0.96)	<0.001
Time with BIS < 40 h					
No delirium	0.3 ± 0.4				
Delirium	0.8 ± 0.5	3.70 (2.00-8.11)	<0.001	2.05 (1.02-4.16)	0.03
End-tidal volatile concentration (MAC equivalents)					
No delirium	0.76 ± 0.27				
Delirium	1.01 ± 0.34	6.81 (2.21-22.7)	<0.001	1.15 (1.05-7.34)	0.04

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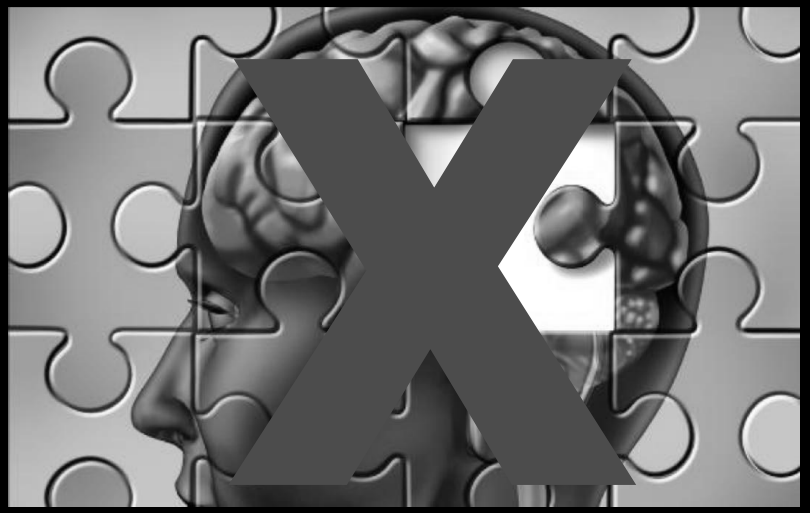
Conclusioni

"For every 1000 elderly pts, titrating anesthetic to maintain BIS between 40 and 60 would prevent 23 pts from POCD at 3 months and 83 pts from delirium."



Grazie per l'attenzione