PROF. DOUTOR FERNANDO FONSECA EPE
HOSPITAL

DISFUNÇÃO COGNITIVA PÓS-OPERATÓRIA

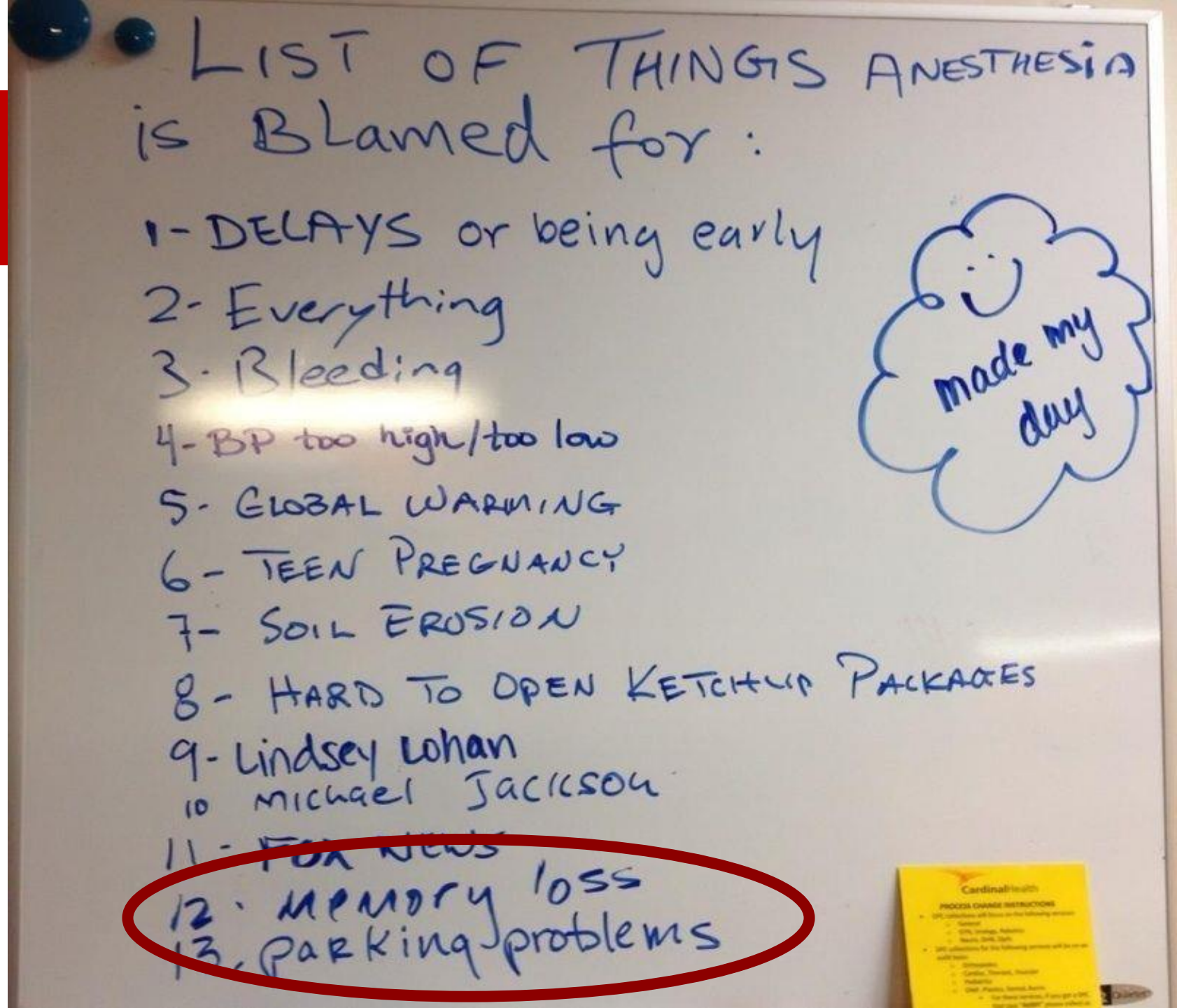
SERVIÇO DE ANESTESIOLOGIA

APRESENTAÇÃO: MIHRAN PORTUGALYAN; LUIS LOPES

DIRETORA SERVIÇO: DRA. MANUELA CASTRO

SUMÁRIO

- DEFINIÇÃO
- Incidência
- Fatores de risco
- Abordagem
- Desafios futuros



DEFINIÇÃO

- O termo DCPO foi aplicado pela 1ª vez em 1955, por Bedford na Lancet, com a designação de "*adverse cerebral effects of anesthesia on old people*";
- DCPO é uma medida objetiva, através de testes neuro-psicológicos, de declínio cognitivo pós-operatório comparado com a função cognitiva pré-operatória.

AVALIAÇÃO FUNÇÃO COGNITIVA

- Não existe um *gold standard*;
- Não existe um *timing* para avaliação pós-operatória da função cognitiva;
- Diferentes testes para diferentes domínios;
- Cada doente é o seu próprio controlo (*baseline*);
- Difícil a comparação com um grupo controlo saudável (variação sessão a sessão, variação entre população, curva de aprendizagem).

DEFINIÇÃO

- Patologia subtil com AUSÊNCIA DE SINAIS CLÍNICOS;
- Alterações da MEMÓRIA, ATENÇÃO, CONCENTRAÇÃO, RESOLUÇÃO DE PROBLEMAS, PROCESSAMENTO INFORMAÇÃO;
- Sem alterações da consciência;
- Duração semanas – meses;
- Em grande parte, reversível.

DIAGNÓSTICO DIFERENCIAL

	MANIFESTAÇÕES	DIAGNÓSTICO	TEMPO	PROGNÓSTICO
DCPO	Défices cognitivos, de novo, no pós-op	Testes neuro-psicológicos pré e pós-op (MoCA, ACE-III)	Imediatamente após cirurgia, pode durar até 6 meses	Reversível em dias - meses
DELIRIUM	Défices cognitivos, **alucinações**, **flutuação estado consciência**	Escalas de delirium (Nu-DESC, Cam-ICU)	Dias – semanas (dependendo da **causa**)	Reversível, se condição subjacente for tratada
DEMÊNCIA	Falhas memória, capacidade abstração e julgamento, alterações personalidade	Testes demência (Mini-Mental State)	Progressivamente durante meses – anos	**Mau prognóstico**

Adaptado de Rundshagen, Ingrid, Postoperative Cognitive Dysfunction; Deutsches Ärzteblatt International (2014)

SUMÁRIO

- Definição
- INCIDÊNCIA
- Fatores de risco
- Abordagem
- Desafios futuros

INCIDÊNCIA

1 Semana

- Disfunção cognitiva em **25%** 1 semana após cirurgia vs 3,4% (controlo);

3 Meses

- Disfunção cognitiva em **9,9%** 3 meses após cirurgia vs 2,8% (controlo);

Moller *et al*, Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study; Lancet (1998)

INCIDÊNCIA

- DCPO associa-se a:
  - 1) Aumento risco MORTALIDADE após cirurgia cardíaca ou não cardíaca;
  - 2) Aumento risco de DEIXAR MERCADO DE TRABALHO PREMATURAMENTE;
  - 3) Aumento da DEPENDÊNCIA DE APOIOS SOCIAIS.

Steinmetz *et al*, ISPOCD Group: Long-term consequences of postoperative cognitive dysfunction; Anesthesiology (2009)
Monk *et al*, Predictors of cognitive dysfunction after major noncardiac surgery; Anesthesiology (2008)

SUMÁRIO

- Definição
- Incidência
- FATORES DE RISCO
- Abordagem
- Desafios futuros

FATORES DE RISCO

Anestesia

Cirurgia

Doente

- Idade (+++);
- Patologia cerebral, cardíaca ou vascular pré-existente;
- Défice cognitivo ligeiro pré-operatório;
- Menor escolaridade (+);
- História de abuso do álcool.

Moller *et al*; Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study; Lancet (1998)
Hudtez *et al*; Postoperative cognitive dysfunction in older patients with a history of alcohol abuse; Anesthesiology (2007)

FATORES DE RISCO

Anestesia

Cirurgia

- Cirurgias prolongadas;
- Cirurgias secundárias;

Doente

- Complicações intra ou pós-operatórias.

Rundshagen, Ingrid; Postoperative Cognitive Dysfunction; Deutsches Ärzteblatt International (2014)
Monk *et al*; Predictors of cognitive dysfunction after major noncardiac surgery; Anesthesia (2008)

FATORES DE RISCO

Anestesia

Cirurgia

Doente

- Hiperventilação
- Hipotensão
- Hipóxia
- Microembolização cerebral
- Mecanismos inflamatórios

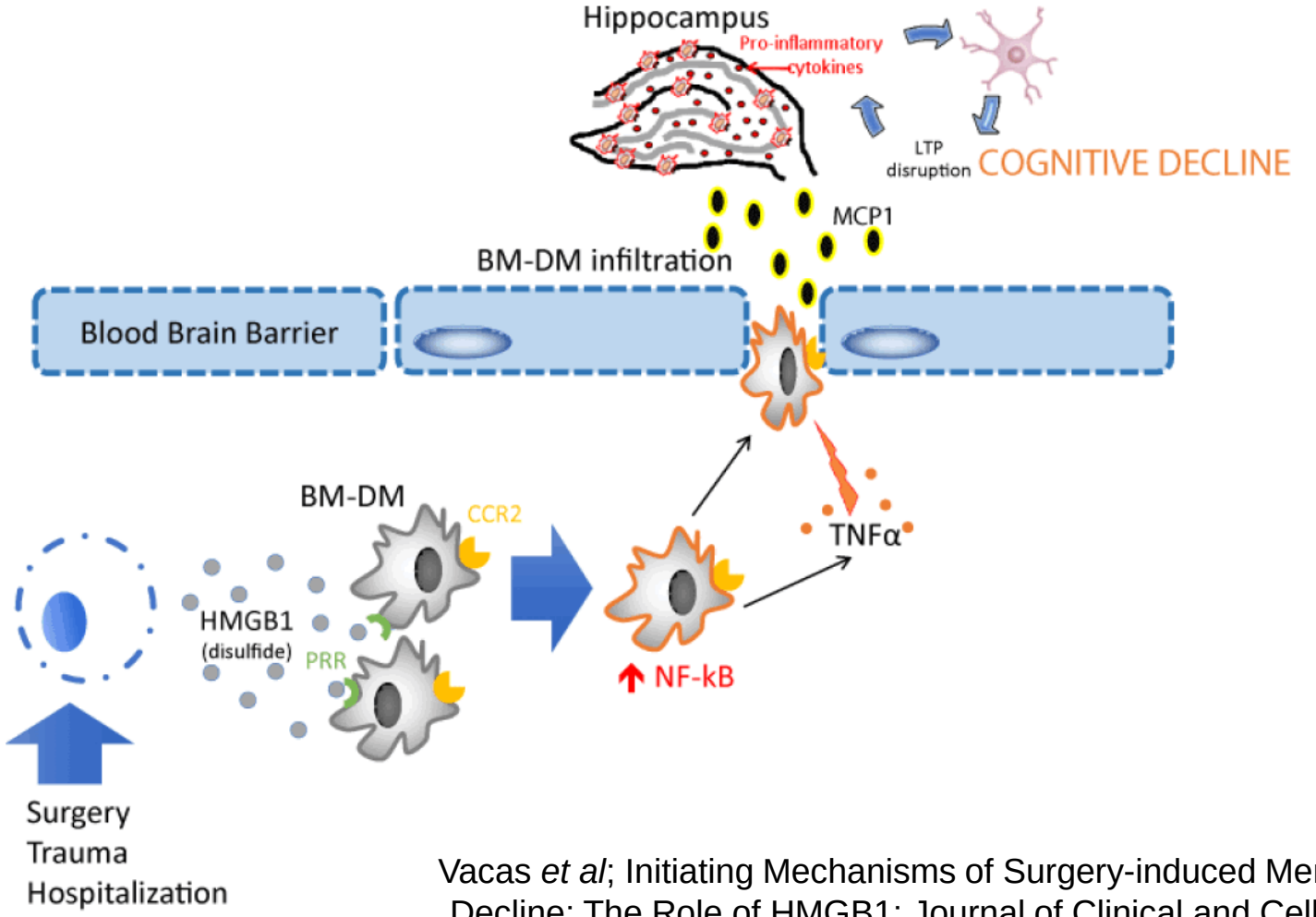
Moller *et al*, Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study; Lancet (1998)

FISIOPATOLOGIA

Anestesia

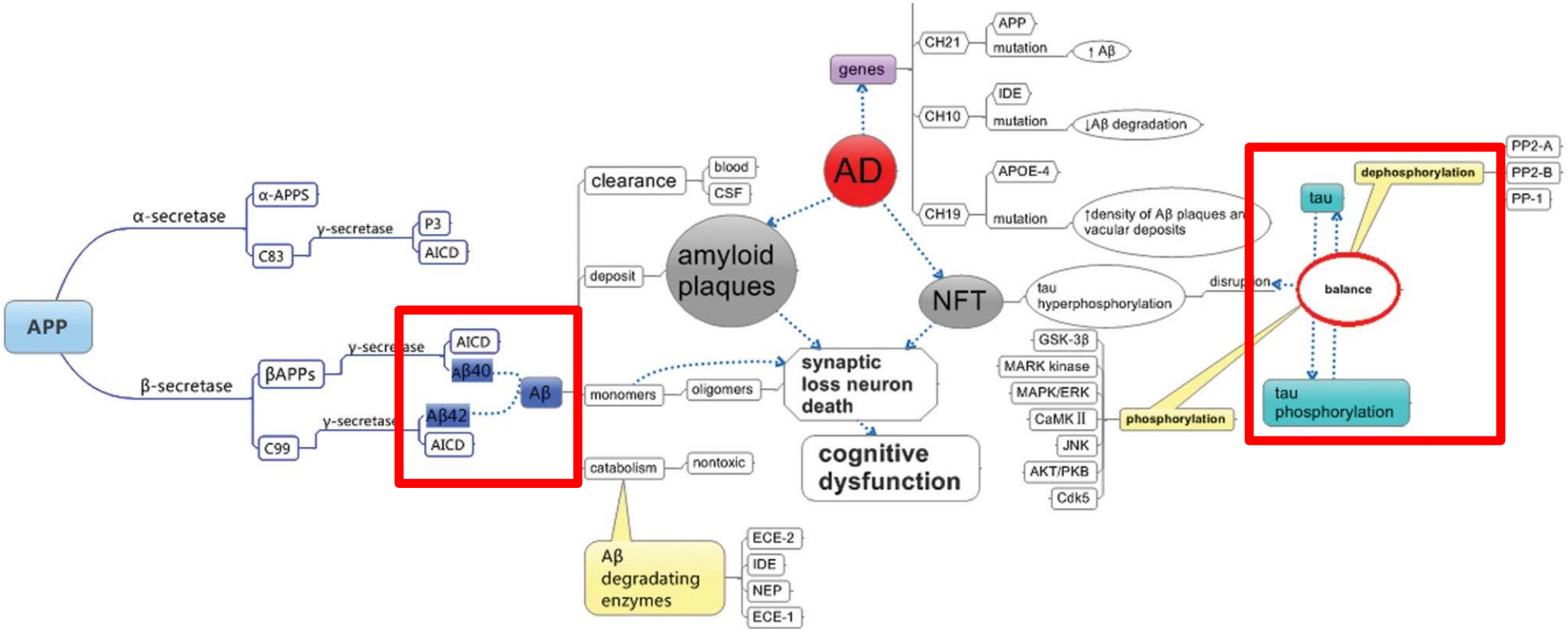
Cirurgia

Doente

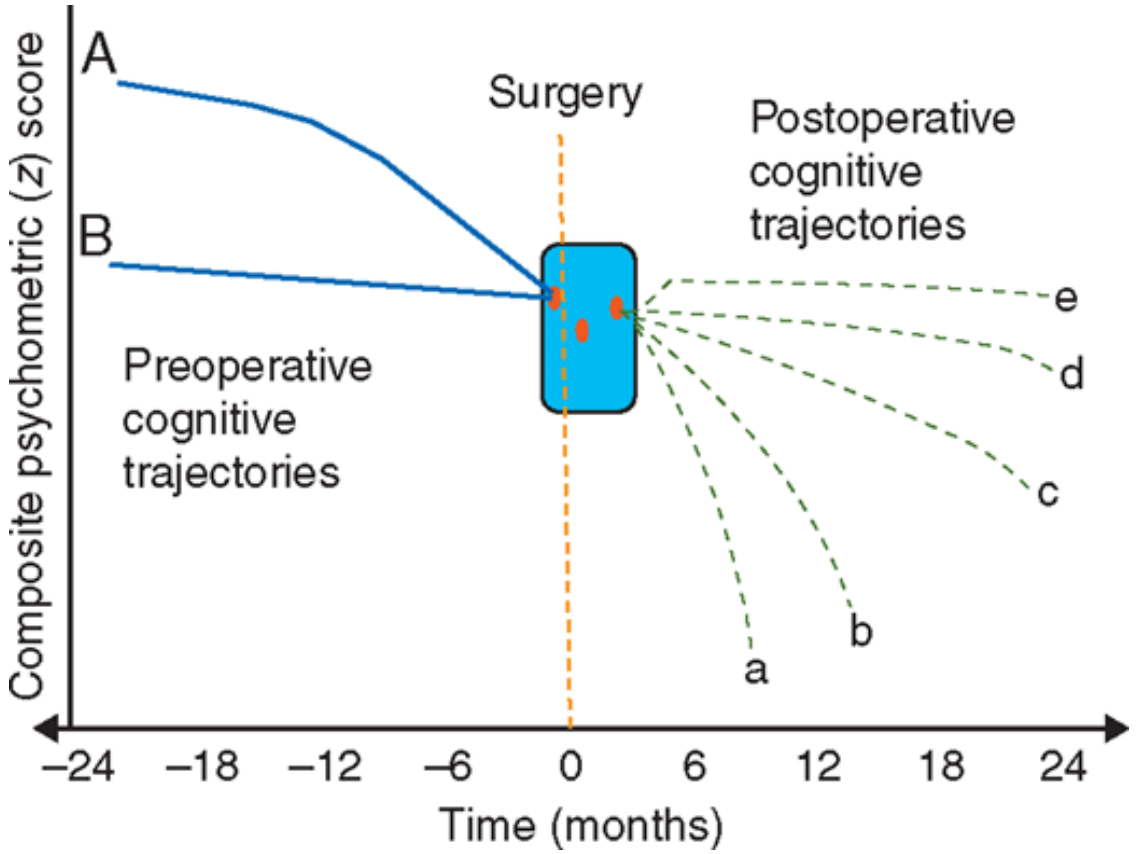


Vacas *et al*; Initiating Mechanisms of Surgery-induced Memory Decline: The Role of HMGB1; Journal of Clinical and Cellular Immunology (2016)

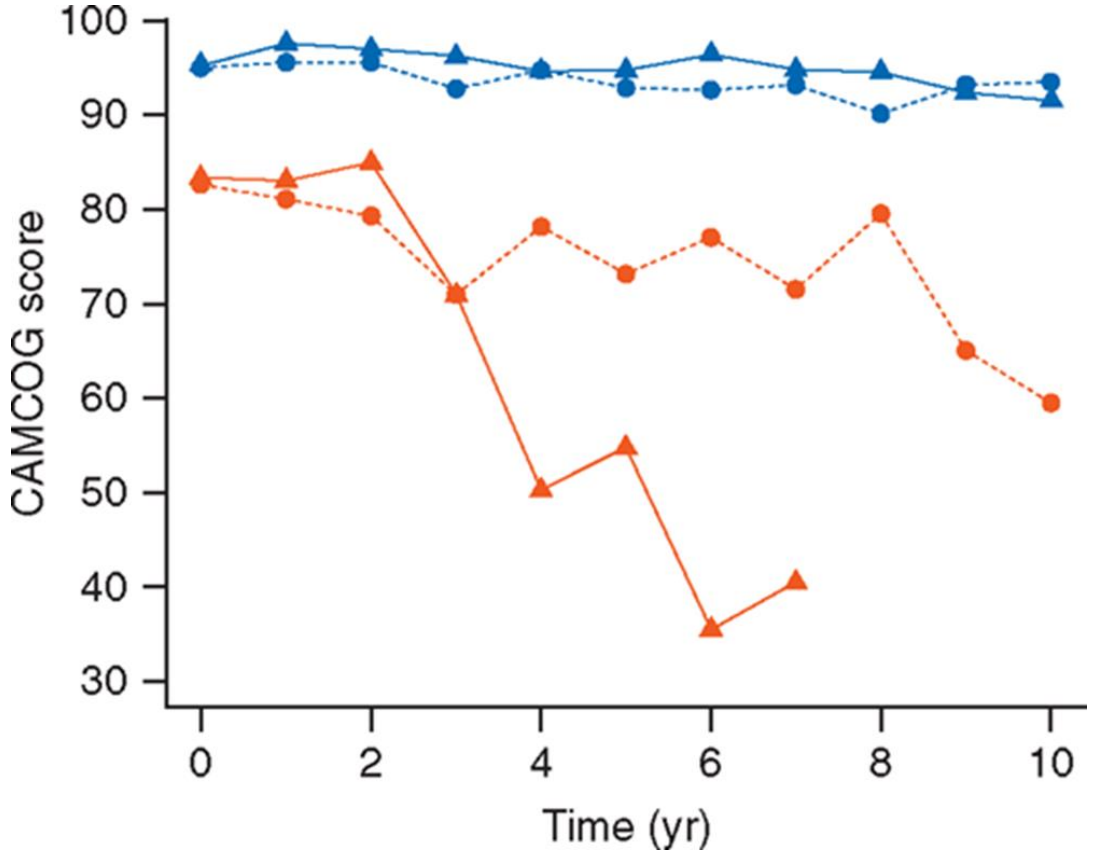
FISIOPATOLOGIA



Adaptado de Jian *et al*; Effect of the inhaled anesthetics isoflurane, sevoflurane and desflurane on the neuropathogenesis of Alzheimer's disease; Molecular Medicine Reports (2015)



Nadelson MR, Sanders RD, Avidan MS. Perioperative cognitive trajectory in adults. Br J Anaesth 2014



Patel D, Lunn AD, Smith AD, Lehmann DJ, Dorrington KL. Cognitive decline in the elderly after surgery and anaesthesia: results from the Oxford Project to Investigate Memory and Ageing (OPTIMA) cohort. Anaesthesia 2016

SUMÁRIO

- Definição
- Incidência
- Fatores de risco
- ABORDAGEM
- Desafios futuros

ABORDAGEM – PRÉ-OP

- Avaliação pré-operatória multidisciplinar (geriatra, cirurgião, anestesista, enfermeiro);
- Avaliação e correção de défices visuais ou auditivos pré-existentes;
- Controlo fatores de risco CV (HTA, obesidade, DM, tabagismo);
- Programas de abstinência alcoólica;
- Correção anemia e desequilíbrios hidroeletrolíticos.

Needham *et al*, Postoperative cognitive dysfunction and dementia: what we need to know and do; British Journal of Anaesthesia (2017)

ABORDAGEM – PRÉ-OP

- O estudo ISPOCD mostrou uma associação entre o uso pré-operatório de BENZODIAZEPINAS e uma redução na incidência de DCPO.
- Contudo, este estudo não fixou a duração e a dose de benzodiazepinas (elas próprias ligadas ao *delirium pós-operatório*).
- Estudo mais recentes, NÃO DEMONSTRARAM ESTA ASSOCIAÇÃO.

Moller *et al*, Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study; Lancet (1998)
Rasmussem *et al*, Benzodiazepines and postoperative cognitive dysfunction in the elderly. ISPOCD Group; British Journal of Anaesthesia (1999)

ABORDAGEM – PRÉ-OP

JOURNAL of ANESTHESIA and PERIOPERATIVE MEDICINE

Review Article

Perioperative Use of Benzodiazepines: A Reconsideration of Risks and Benefits

Yanzi Zhang[1], Yidan Tang[1], Jing Yang[1], Chunyu Gong[2], and Zhuo Li[3]

ABSTRACT

Aim of review: Reconsideration of Benzodiazepines (BZDs) after many years' widespread use, for development of recent new similar drugs and consideration about increased delirium with BZDs.

Methods: A comprehensive search in OVID MEDLINE, EMBASE and PubMed were performed from inception to Jan 31, 2016, the studies which involved pharmacological characteristics of BZDs and comparison among BZDs, placebo and some similar new drugs used for sedation and antianxiety in the perioperative period were included.

Recent findings: Routine use of BZDs as a sedative and antianxiety premedication is lack of benefits. BZDs did not improve the self-reported patient experience the day after surgery, but was associated with a lower rate of early cognitive recovery. Large numbers of using of other sedation drugs such as Propofol or Dexmedetomidine are replacing the using of BZDs for postoperative sedation. BZDs are important anesthesia-related predictors of postoperative delirium. Compared with those new drugs in sedation and anti-anxiety, BZDs has gradually lost its market.

Conclusion: As the developing of anesthesia monitoring technique and more beneficial pharmaceutical, the perioperative application of BZDs should be used with caution. (Funded by the National Natural Science Foundation of China.)

Zhang *et al*, Perioperative Use of Benzodiazepines: A Reconsideration of Risks and Benefits. Journal of Anesthesia and Perioperative Medicine (2018)

ABORDAGEM – INTRA-O

- ANESTESIA GERAL

  VS LOCO-REGIONAL

- Anestesia balanceada

  vs endovenosa

- Monitorização

- Adjuvantes

Postoperative Cognitive Dysfunction Is Independent of Type of Surgery and Anesthetic

Lisbeth Evered, BSc, MBiostat,* David A. Scott, MB, BS, PhD, FANZCA,*
Brendan Silbert, MB, BS, FANZCA,* and Paul Maruff, PhD†

BACKGROUND: Postoperative cognitive dysfunction (POCD) has been documented after cardiac and noncardiac surgery. The type of surgery and anesthetic has been assumed to be associated with the incidence but there are few prospective data comparing the incidence after different procedures. In this study, we sought to determine the association of the type of surgical procedure and anesthesia on the incidence of POCD after procedures involving light sedation, general anesthesia for noncardiac surgery, and general anesthesia for cardiac surgery involving cardiopulmonary bypass.

METHODS: Eight neuropsychological tests were administered at baseline and at 7 days and 3 months postoperatively to subjects from 3 procedure groups and a nonoperative control group. Reliable change index was used to calculate POCD. The study sample consisted of subjects involved in 3 separate trials investigating coronary angiography (CA) (percutaneous diagnostic procedure) under sedation, major noncardiac surgery (total hip joint replacement [THJR] surgery) under general anesthesia, and coronary artery bypass graft (CABG) surgery under general anesthesia.

RESULTS: Data were collected from 644 patients in the patient groups and 34 subjects in the control group. Neuropsychological results were available for POCD at day 7 for THJR surgery (n = 162) and CABG surgery (n = 281). The incidence of POCD at day 7 was 17% for THJR surgery and 43% for CABG surgery (adjusted odds ratio = 0.2, 95% confidence interval [CI]: 0.1, 0.4; $P <$ 0.01). At 3 months, the incidence of POCD for all groups combined (n = 636) was 17% (21% for CA under sedation, 16% for THJR surgery, and 16% for CABG surgery). The mean (95% CI) for the difference in proportions of POCD among groups was 0.00 (−0.07, 0.07) (P = 0.91) for CABG versus THJR; −0.05 (−0.12, 0.03) (P = 0.21) for CABG versus CA; and −0.05 (−0.13, 0.03) (P = 0.24) for THJR versus CA. There were no significant differences among groups (adjusted odds ratio = 1.21, 95% CI: 0.94, 1.55; P = 0.13).

CONCLUSIONS: The incidence of POCD in old and elderly patients at day 7 was higher after CABG surgery than THJR surgery, but POCD at 3 months was independent of the nature or the type of procedure or anesthetic when comparing CA, THJR, and CABG surgery groups. Cardiovascular risk factors were not predictive of POCD after any procedure. (Anesth Analg 2011;112:1179–85)

Evered *et al*; Postoperative Cognitive Dysfunction Is Independent of Type of Surgery and Anesthetic; Anesthesia and Analgesia (2011)

ABORDAGEM – INTRA-C

- ANESTESIA GERAL VS LOCO-REGIONAL
- Anestesia balanceada vs endovenosa
- Monitorização
- Adjuvantes

British Journal of Anaesthesia 113 (5): 784–91 (2014)
Advance Access publication 27 June 2014 · doi:10.1093/bja/aeu163

BJA

CLINICAL PRACTICE

Incidence of postoperative cognitive dysfunction after general or spinal anaesthesia for extracorporeal shock wave lithotripsy

B. S. Silbert[1,2]*, L. A. Evered[1,2] and D. A. Scott[1,2]

Editor's key points

- Aspects of general anaesthesia might contribute to postoperative cognitive dysfunction (POCD).
- This study found that avoiding general anaesthesia did not reduce the risk of POCD.
- Other factors, perhaps the inflammatory response to surgery, and hospitalization, might contribute to POCD.

Background. Since general anaesthesia invariably accompanies surgery, the contribution of each to the development of postoperative cognitive dysfunction (POCD) has been difficult to identify.

Methods. A prospective randomized controlled trial was undertaken in elderly patients undergoing extracorporeal shock wave lithotripsy (ESWL). Between 2005 and 2011, 2706 individuals were screened to recruit 100 eligible patients. Patients were randomly assigned to receive general or spinal anaesthesia alone. A battery of eight neuropsychological tests was administered before operation and at 7 days and 3 months after operation. The reliable change index was used to calculate the incidence of POCD. Intention-to-treat analysis was used to compare rates of POCD.

Results. Futility analysis led to stopping of the trial after recruitment of 100 patients. Fifty patients were randomly assigned to general anaesthesia, and 48 patients to spinal anaesthesia without sedation or postoperative opioids. At 3 months, POCD was detected in 6.8% [95% confidence interval (CI): 1.4–18.7%] of patients in the general anaesthesia group and 19.6% (95% CI: 9.4–33.9%) in the spinal group ($P=0.07$). At 7 days after operation, the incidence of POCD was 4.1% (95% CI: 0.5–14%) in the general anaesthesia group and 11.9% (95% CI: 4.0–26.6%) in the spinal group ($P=0.16$).

Conclusions. We found no significant difference in the rates of POCD when comparing general anaesthesia with spinal anaesthesia, suggesting that the surgical or procedural process itself may contribute to the development of POCD.

Silbert *et al*; Incidence of Postoperative Cognitive Dysfunction After General or Spinal Anaesthesia for Extracorporeal Shock Wave Lithotripsy; British Journal of Anaesthesiology (2014)

ABORDAGEM – INTRA-OP

- Anestesia geral vs loco-regional
- ANESTESIA BALANCEADA VS ENDOVENOSA
- Monitorização
- Adjuvantes

Cochrane Library

Cochrane Database of Systematic Reviews

Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery (Review)

Miller D, Lewis SR, Pritchard MW, Schofield-Robinson OJ, Shelton CL, Alderson P, Smith AF

Authors' conclusions

We are uncertain whether maintenance with propofol-based TIVA or with inhalational agents affect incidences of postoperative delirium, mortality, or length of hospital stay because certainty of the evidence was very low. We found low-certainty evidence that maintenance with propofol-based TIVA may reduce POCD. We were unable to perform meta-analysis for intraoperative hypotension or length of stay in the PACU because of heterogeneity between studies. We identified 11 ongoing studies from clinical trials register searches; inclusion of these studies in future review updates may provide more certainty for the review outcomes.

Miller *et al*; Intravenous versus inahalational maintenance of anaesthesia for posoperative cognitive outcomes in elderly people undergoing non-cardiac surgery (Review); Cochrane Database of Systematic Reviews (2018)

ABORDAGEM – INTRA-OP

- Anestesia geral vs loco-regional
- ANESTESIA BALANCEADA VS ENDOVENOSA
- Monitorização
- Adjuvantes

Because the target organ of all anesthetic agents is the brain, anesthetic agents have been circumstantially implicated. There have been conflicting claims of better outcomes with sevoflurane and propofol,[60,61] but there is at present no convincing evidence that a specific general anesthetic, either intravenous or volatile, leads to POCD more than any other.

Needham *et al*, Postoperative cognitive dysfunction and dementia: what we need to know and do; British Journal of Anaesthesia (2017)
Evered *et al*, Postoperative Cognitive Dysfunction and Noncardiac Surgery; Anesthesia and Analgesia (2018)

ABORDAGEM – INT

- Anestesia geral vs loco-regional
- Anestesia inalatória vs endovenosa
- MONITORIZAÇÃO
- Adjuvantes

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*

Background: Previous clinical trials and animal experiments have suggested that long-lasting neurotoxicity of general anesthetics may lead to postoperative cognitive dysfunction (POCD). Brain function monitoring such as the bispectral index (BIS) facilitates anesthetic titration and has been shown to reduce anesthetic exposure. In a randomized controlled trial, we tested the effect of BIS monitoring on POCD in 921 elderly patients undergoing major noncardiac surgery.

Methods: Patients were randomly assigned to receive either BIS-guided anesthesia or routine care. The BIS group had anesthesia adjusted to maintain a BIS value between 40 and 60 during maintenance of anesthesia. Routine care group had BIS measured but not revealed to attending anesthesiologists. Anesthesia was adjusted according to traditional clinical signs and hemodynamic parameters. A neuropsychology battery of tests was administered before and at 1 week and 3 months after surgery. Results were compared with matched control patients who did not have surgery during the same period. Delirium was measured using the confusion assessment method criteria.

Results: The median (interquartile range) BIS values during the maintenance period of anesthesia were significantly lower in the 14.7%; adjusted odds ratio 0.67; 95% confidence interval, 0.32-0.98; $P = 0.025$).

Conclusions: BIS-guided anesthesia reduced anesthetic exposure and decreased the risk of POCD at 3 months after surgery. For every 1000 elderly patients undergoing major surgery, anesthetic delivery titrated to a range of BIS between 40 and 60 would prevent 23 patients from POCD and 83 patients from delirium.

Key Words: postoperative cognitive dysfunction, depth of anesthesia, bispectral index, anesthetic toxicity, delirium, postoperative complications

(*J Neurosurg Anesthesiol* 2013;25:33–42)

It is widely believed that the effects of general anesthesia are temporary and that they disappear as the drugs are cleared from the body. There is, however, strong evidence from animal experiments to suggest that standard doses of routine anesthetics may produce long-lasting learning and memory impairments that persist for weeks or months after anesthetic exposure.[1–4] This is associated with τ-hyperphosphorylation,[5–7] caspase-3 activation,[8–11]

Chan *et al*; BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline; Journal of Neurosurgical Anesthesiology (2013)

ABORDAGEM – INTRA

- Anestesia geral vs loco-regional
- Anestesia inalatória vs endovenosa
- MONITORIZAÇÃO
- Adjuvantes

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*]

Editor's key points

- Postoperative delirium is a common complication of surgery and anaesthesia in the elderly.
- Anaesthetic agents may have harmful effects on the ageing brain.
- Titration of anaesthetic dose according to a measure of anaesthetic depth may help avoid excessive doses.
- The current study addressed the hypothesis that the depth of anaesthesia monitoring reduces the incidence of delirium.

Background. Postoperative delirium in elderly patients is a frequent complication and associated with poor outcome. The aim of this parallel group study was to determine whether monitoring depth of anaesthesia influences the incidence of postoperative delirium.

Methods. Patients who were planned for surgery in general anaesthesia expected to last at least 60 min and who were older than 60 yr were included between March 2009 and May 2010. A total of 1277 patients of a consecutive sample were randomized (n=638 open, n=639 blinded) and the data of 1155 patients were analysed (n=575 open, n=580 blinded). In one group, the anaesthesiologists were allowed to use the bispectral index (BIS) data to guide anaesthesia, while in the other group, BIS monitoring was blinded. Cognitive function was evaluated at baseline, 1 week, and 3 months after operation.

Results. Delirium incidence was lower in patients guided with BIS. Postoperative delirium was detected in 95 patients (16.7%) in the intervention group compared with 124 patients (21.4%) in the control group (P=0.036). In a multivariate analysis, the percentage of episodes of deep anaesthesia (BIS values <20) were independently predictive for postoperative delirium (P=0.006; odds ratio 1.027). BIS monitoring did not alter the incidence of postoperative cognitive dysfunction (7th day P=0.062; 90th day P=0.372).

Conclusions. Intraoperative neuromonitoring is associated with a lower incidence of delirium, possibly by reducing extreme low BIS values. Therefore, in high-risk surgical patients, this may give the anaesthesiologist a possibility to influence one precipitating factor in the complex genesis of delirium.

Radtke *et al*; Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction; British Journal of Anaesthesiology (2013)

ABORDAGEM – INTRA-OP

- Anestesia geral vs loco-regional
- Anestesia inalatória vs endovenosa
- MONITORIZAÇÃO
- Adjuvantes

Cochrane Library

Cochrane Database of Systematic Reviews

Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults (Review)

Punjasawadwong Y, Chau-in W, Laopaiboon M, Punjasawadwong S, Pin-on P

Authors' conclusions

There is moderate-quality evidence that optimized anaesthesia guided by processed EEG indices could reduce the risk of postoperative delirium in patients aged 60 years or over undergoing non-cardiac surgical and non-neurosurgical procedures. We found moderate-quality evidence that postoperative cognitive dysfunction at three months could be reduced in these patients. The effect on POCD at one week and over one year after surgery is uncertain. There are no data available for patients under 60 years. Further blinded randomized controlled trials are needed to elucidate strategies for the amelioration of postoperative delirium and postoperative cognitive dysfunction, and their consequences such as dementia (including Alzheimer's disease (AD)) in both non-elderly (below 60 years) and elderly (60 years or over) adult patients. The one study awaiting classification and five ongoing studies may alter the conclusions of the review once assessed.

Punjasawadwong *et al*; Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults (Review); Cochrane Database of Systematic Reviews (2018)

ABORDAGEM –

- Anestesia geral vs loco regional
- Anestesia inalatória vs endovenosa
- Monitorização
- ADJUVANTES

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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2009.01978.x

Ketamine attenuates post-operative cognitive dysfunction after cardiac surgery

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Department of Anesthesiology, Clement J. Zablocki Veterans Administration Medical Center, Milwaukee, WI

Background: Post-operative cognitive dysfunction (POCD) commonly occurs after cardiac surgery. Ketamine exerts neuroprotective effects after cerebral ischemia by anti-excitotoxic and anti-inflammatory mechanisms. We hypothesized that ketamine attenuates POCD in patients undergoing cardiac surgery concomitant with an anti-inflammatory effect.
Methods: Patients randomly received placebo (0.9% saline; $n = 26$) or an i.v. bolus of ketamine (0.5 mg/kg; $n = 26$) during anesthetic induction. Anesthesia was maintained with isoflurane and fentanyl. A nonsurgical group ($n = 26$) was also included as control. Recent verbal and nonverbal memory and executive functions were assessed before and 1 week after surgery or a 1-week waiting period for the nonsurgical controls. Serum C-reactive protein (CRP) concentrations were determined before surgery and on the first post-operative day.
Results: Cognitive dysfunction was observed in 19 patients in the placebo group and only in seven patients in the ketamine group compared with the nonsurgical controls ($P < 0.001$, Fisher's exact test). Cognitive performance was also significantly different between the placebo- and the ketamine-treated groups based on all z-scores ($P < 0.001$, Mann–Whitney U-test). Pre-operative CRP concentrations were similar ($P < 0.33$, Mann–Whitney U-test) in the placebo- and ketamine-treated groups. The post-operative CRP concentration was significantly ($P < 0.01$, Mann–Whitney U-test) lower in the ketamine-treated than in the placebo-treated group.
Conclusions: Ketamine attenuates POCD 1 week after cardiac surgery and this effect may be related to the anti-inflammatory action of the drug.

ABORDAGEM – IN

- Anestesia geral vs loco regional
- Anestesia inalatória vs endovenosa
- Monitorização
- ADJUVANTES

Systematic Review and Meta-Analysis

Medicine®

OPEN

Effect of parecoxib in the treatment of postoperative cognitive dysfunction

A systematic review and meta-analysis

Song Huang, MD[a], Haijun Hu, MD[a], Yue-Hong Cai, MD[b], Fuzhou Hua, PhD[a,*]

Abstract

Background: Parecoxib is a selective cyclooxygenase (COX)-2 inhibitor widely used as an analgesia technique in perioperative period for its potent anti-inflammatory and analgesic effects. However, litter is known about its effect on postoperative cognitive dysfunction (POCD). The purpose of this meta-analysis of randomized controlled trials (RCTs) was to evaluate the effect of parecoxib in the treatment of postoperative cognitive dysfunction.

Methods: We searched PubMed, Cochrane Library and Embase databases for relevant studies up to October 2017. We selected fixed-effect model for analysis of data heterogeneity. Statistical analyses were performed by using Review Manager Version 5.3 for Windows.

Results: Four RCTs with 904 patients that underwent surgical operations were included. The meta-analysis demonstrated parecoxib could significantly decrease the incidence of POCD on postoperative day 1, day 3, day 5, and day 7 when compared with control treatment; IL-6 and S100β concentrations were lower up to postoperative day 2. The consumption of morphine, fentanyl and tramadol in parecoxib groups were lower than control groups.

Conclusion: Our meta-analysis suggested that the administration of Parecoxib was effective in treating early POCD within 7 days and reducing IL-6 and S100β concentrations within 2 days after operations. Nevertheless, our current study with some limitations such as the small sample size only provided limited quality of evidence, confirmation from further meta-analysis with large-scale, well-designed RCTs is required.

Abbreviations: BBB = blood-brain barrier, IL-1 = interleukin-1, NSE = neuron-specific enolase, POCD = postoperative cognitive dysfunction, RCTs = randomized controlled trials, RR = risk ratio, TNF-α= tumor necrosis factor.

Huang *et al*; Effect of parecoxib in the treatment of postoperative cognitive dysfunction; Medicine (2019)

ABORDAGEM –

- Anestesia geral vs loco regional
- Anestesia inalatória vs endovenosa
- Monitorização
- ADJUVANTES

The Effect of Lidocaine on Early Postoperative Cognitive Dysfunction After Coronary Artery Bypass Surgery

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We investigated the effect of lidocaine on the incidence of cognitive dysfunction in the early postoperative period after cardiac surgery. One-hundred-eighteen patients undergoing elective coronary artery bypass surgery with cardiopulmonary bypass (CPB) were randomized to receive either lidocaine (1.5 mg/kg bolus followed by a 4 mg/min infusion during operation and 4 mg/kg in the priming solution of CPB) or placebo. A battery of nine neuropsychological tests was administered before and 9 days after surgery. A postoperative deficit in any test was defined as a decline by more than or equal to the preoperative SD of that test in all patients. Any patient showing a deficit in two or more tests was defined as having postoperative cognitive dysfunction. Eighty-eight patients completed pre- and postoperative neuropsychological tests. Plasma lidocaine concentrations (μg/mL) were 4.78 ± 0.52 (mean ± SD), 5.38 ± 0.95, 4.52 ± 0.39, 5.82 ± 0.76, and 7.10 ± 1.09 at 10 min before CPB; 10, 30, and 60 min of CPB; and at the end of operation, respectively. The proportion of patients showing postoperative cognitive dysfunction was significantly reduced in the lidocaine group compared with that in the placebo group (18.6% versus 40.0%; $P = 0.028$). We conclude that intraoperative administration of lidocaine decreased the occurrence of cognitive dysfunction in the early postoperative period.

(Anesth Analg 2002;95:1134–41)

ABORDAGEM – INTRA-OP

- Anestesia geral vs loco regional
- Anestesia inalatória vs endovenosa
- Monitorização
- ADJUVANTES

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REPORTS OF ORIGINAL INVESTIGATIONS

Effect of intravenous lidocaine on the transcerebral inflammatory response during cardiac surgery: a randomized-controlled trial

Abstract

Purpose *Postoperative cognitive dysfunction (POCD) occurs frequently after cardiac surgery. The pathophysiology of POCD remains elusive, but previous work showed that intravenous lidocaine may be protective against POCD, possibly by modulating cerebral inflammation. We hypothesized that intravenous lidocaine would attenuate the cerebral inflammatory response to cardiopulmonary bypass (CPB) by reducing the transcerebral activation gradients of platelets, leukocytes, and/or platelet-leukocyte conjugates.*

Methods *We studied 202 patients undergoing cardiac surgery with CPB in this prospective randomized double-blinded placebo-controlled trial. Subjects were randomized to receive either intravenous lidocaine (bolus + 48-hr infusion) or placebo (identical infusion volume and duration). Paired jugular venous and radial arterial blood samples were drawn at several time points and analyzed by fluorescence-activated cell sorting to identify activated platelets and platelet-leukocyte conjugates. Transcerebral activation gradients were calculated by subtracting arterial values from venous values and were compared between groups using repeated measures regression models with covariate adjustment for age, sex, surgery type, and CPB duration.*

Results *Beginning after aortic cross-clamp release and peaking ten minutes after the termination of CPB, the mean (SD) transcerebral activation gradient of platelet-monocyte conjugates decreased in lidocaine-treated vs placebo-treated patients [−1.84 (11.47) mean linear fluorescence intensity (MLFI) vs 1.46 (13.88) MLFI, respectively; mean difference, −4.08 MLFI; 95% confidence interval, −7.86 to −0.29; P = 0.03). No difference was seen at any time point for activated platelets or for platelet-neutrophil conjugates.*

Conclusion *While lidocaine did not affect the systemic or transcerebral activation of platelets or leukocytes, we did observe a reduction in the transcerebral activation of platelet-monocyte conjugates after aortic cross-clamp release. This may be a manifestation of reduced cerebral inflammation during cardiopulmonary bypass in response to treatment with lidocaine. This trial was registered at ClinicalTrials.gov (NCT00938964).*

A list of all members of the Neurologic Outcome Research Group is given in the Appendix.

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ABORDAGEM – INTRA-OP

- Anestesia geral vs loco regional
- Anestesia inalatória vs endovenosa
- Monitorização
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Abstract

Postoperative cognitive dysfunction (POCD) is a multifactorial adverse event most frequently in elderly patients. This study evaluated the effect of dexamethasone on POCD incidence after noncardiac and nonneurologic surgery. METHODS: One hundred and forty patients (ASA I-II; age 60–87 years) took part in a prospective phase III, double blind, randomized study involving the administration or not of 8 mg of IV dexamethasone before general anesthesia under bispectral index (BIS) between 35–45 or 46–55. Neuropsychological tests were applied preoperatively and on the 3rd, 7th, 21st, 90th and 180th days after surgery and compared with normative data. S100β was evaluated before and 12 hours after induction of anesthesia. The generalized estimating equations (GEE) method was applied, followed by the posthoc Bonferroni test considering $P<0.05$ as significant. RESULTS: On the 3rd postoperative day, POCD was diagnosed in 25.2% and 15.3% of patients receiving dexamethasone, BIS 35–45, and BIS 46–55 groups, respectively. Meanwhile, POCD was present in 68.2% and 27.2% of patients without dexamethasone, BIS 35–45 and BIS 46–55 groups ($p<0.0001$). Neuropsychological tests showed that dexamethasone associated to BIS 46–55 decreased the incidence of POCD, especially memory and executive function. The administration of dexamethasone might have prevented the postoperative increase in S100β serum levels. CONCLUSION: Dexamethasone can reduce the incidence of POCD in elderly patients undergoing surgery, especially when associated with BIS 46–55. The effect of dexamethasone on S100β might be related with some degree of neuroprotection.

Valentin *et al*; Effects of Single Low Dose of Dexamethasone before Noncardiac and Nonneurologic Surgery and General Anesthesia on Postoperative Cognitive Dysfunction – A Phase III Double Blind, Randomized Clinical Trial; PLoS One (2016)

ABORDAGEM – PÓS-OP

- **NUTRIÇÃO**
- **EXERCÍCIO FÍSICO**
- **TREINO COGNITIVO**
- **CONTROLO FATORES DE RISCO VASCULARES E METABÓLICOS**
- **INTERAÇÃO SOCIAL**

SUMÁRIO

- Definição
- Incidência
- Fatores de risco
- Abordagem
- DESAFIOS FUTUROS

DESAFIOS FUTUROS

- Definição universal;
- Estudos prospetivos longitudinais
- Biomarcadores;
- Novas terapêuticas.

Evered *et al*; Cerebrospinal Fluid Biomarker for Alzheimer Disease Predicts Postoperative Cognitive Dysfunction; Anesthesiology (2016)
Evered *et al*; Association of Changes in Plasma Neurofilament Light and Tau Levels With Anesthesia and Surgery: Results From the CAPACITY and ARCADIAN Studies; JAMA Neurology (2018)