

# Postoperative cognitive dysfunction after cardiac surgery

## *Disfunção cognitiva após cirurgia cardíaca*

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RBCCV 44205-981

### *Abstract*

Postoperative cognitive dysfunction, frequent in cardiac surgeries, leads to major consequences. The pathophysiological processes involved in this condition are still not completely elucidated, though its multifactor character is known. Besides pre-operative factors such as age and education, some intra-operative factors are of extreme importance. However, according to a vast literature on the subject, these factors are not sufficient to totally clarify the etiology of all cases, thus suggesting a genetic basis for this neurological sequel. In this review article, we briefly assess the factors involved in this cognitive dysfunction and discuss pharmacotherapy in the prevention of this event.

**Descriptors:** Coronary artery bypass surgery. Cardiopulmonary bypass. Cognition. Cognition disorders/etiology. Heart surgery procedures/adverse effects.

### *Resumo*

Disfunção cognitiva pós-operatória é situação frequente em cirurgias cardíacas, o que pode levar a conseqüências imensuráveis para os indivíduos acometidos. Os processos fisiopatológicos envolvidos nessa condição ainda não se encontram totalmente elucidados, apresentando um caráter multifatorial. Além de fatores pré-operatórios, como idade e escolaridade, alguns fatores intra-operatórios também são de extrema importância. Entretanto, conforme ampla literatura sobre o tema, esses fatores não são capazes de esclarecer etiológicamente a totalidade dos casos, remetendo a uma base genética para essa seqüela neurológica. Nessa revisão, avaliamos fatores envolvidos na disfunção cognitiva e a terapia farmacoprotetora empregada em sua prevenção.

**Descritores:** Revascularização miocárdica. Circulação extracorpórea. Cognição. Transtornos cognitivos/etiologia. Procedimentos cirúrgicos cardíacos/efeitos adversos.

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Article received on February 25<sup>th</sup>, 2008

Article accepted on May 13<sup>th</sup>, 2008

## INTRODUCTION

Over the last few years, great interest has been paid to the study of postoperative morbidities of heart surgery due to the decline in mortality rates. Thus, one of the areas that most calls the attention is the impact of these procedures on the brain and cognitive function with serious clinical and financial implications.

In the setting of cardiovascular surgery, since the introduction of the cardiopulmonary bypass (CPB) five decades ago, reports that various patients developed some type of neurological sequel started to emerge. These sequels included from cognitive impairment to fatal strokes [1], with incidences varying from 20 to 83% [2-4] and from 1.5 to 5.2% [5,6], respectively. Hence, these are common consequences causing high costs to the public health system.

As can be seen, there is a great difference among the results published on this subject. This is mainly due to the designs of studies (prospective or retrospective), to open heart or extracardiac surgery, the presence of comorbidities, to the method and time of evaluation of the type and degree of neurological disturbances [7-9]. Thus, among the most commonly studied procedures are coronary artery bypass grafting (CABG).

Impairment of memory, concentration, language, comprehension and social integration, characterizing the so-called cognitive dysfunction (CD), are some of the most frequently affected areas in surgical interventions, situations that can occur from days to months after the surgery and remain for the rest of the life of the patient [1]. Many of these cognitive changes are temporary with resolution in between six weeks and six months after the procedure thereby minimizing medical concern of the importance of transitory cognitive deficits on the quality of life of patients [10].

The main etiology of postoperative CD remains unknown, thus supporting the hypothesis that it is a multifactorial problem [1,8,10,11]. Among the involved risk factors are pre-operative (age, education, previous diseases), intra-operative (number of emboli, duration of the procedure, arterial pressure, temperature, etc.) and post-operative (temperature) [1]. Additionally, some researchers have reported a genetic influence on the surgical outcome, in particular related to the presence of the apolipoprotein E  $\epsilon$ 4 allele [12-17].

The aim of this review article is to discuss the main factors involved in neurological lesions after heart surgery and to report the advances of pharmacotherapy in the protection of future neurological outcomes.

## Pre-operative factors

### a) Age

Age is the least controversial demographic risk factor in CD, with a proven relationship with the increase in age (Table 1). However the mechanism by which greater ages are related to postoperative CD remains unknown. Progressive atherosclerosis linked to silent cardiovascular disease and factors intrinsically related to the risk of embolization seem to be the most acceptable explanation for CD to be associated to the increase in age [4,10]. Moreover, older individuals are predisposed to present alterations in the vasculature and auto-regulation of cerebral blood flow [23], an abnormal response to pharmaceutical agents [21] and a natural reduction in the cognitive function which associated with a small postoperative cognitive impairment may cause a significant impact on the quality of life [10].

### b) Education

Another pre-operative factor that should be mentioned in the pathogenesis of CD is the level of education. The protective effect of the number of school years, according to some authors (Table 1), seems similar to that suggested in recent studies on Alzheimer's disease, although the mechanism by which this is possible requires further elucidation [24]. It is still not clearly known how a greater number of years of study implies a cognitive reserve, an improvement in evaluation abilities or an increase in the neuronal homeostasis, situations which make the patient more resistant to neuronal injury [10]. One hypothesis, that may explain this association, is based on the fact that education increases the synaptic density in the neocortex, increasing the neuronal communication and minimizing the signs of cognitive and functional impairment [27].

### c) Previous diseases

Similar to age and education, the history of comorbidities such as diabetes mellitus (DM), systemic arterial hypertension (SAH) and chronic renal failure (CRF) are factors that are implicated in postoperative neural outcomes.

The history of diabetes mellitus has received the most attention as is seen in the publications listed in Table 1. A possible mechanism which explains this association is the fact that diabetic individuals have an altered auto-regulation of cerebral blood flow, characterized by a greater extraction of oxygen during CPB [19,22] and consequently, reduced availability to the brain. Similarly, SAH and anti-hypertension therapy may be related to the cognitive outcome (Table 1), a reflection of the impaired self-regulation of the cerebral blood flow, hardening of the small cerebral arteries and generalized atherosclerotic disease existent in hypertensive individuals.

Table 1. Preoperative factors

Authors	Year	Studied variable	Participants	Neuropsychological evaluation	Results
Tuman et al. [18]	1992	Age	2000 patients submitted to CABG with CPB	-	Prevalence of CD of 8.9% for e"75 year olds, 3.6% for 65-74 year-old patients, and 0.9% for <65 year-old patients
Kadoi & Goto [19]	2006	Age	88 patients submitted to CABG	One day before and six months after surgery	Greater age [p=0.04] was more common in individuals with CD 6 months after the procedure in comparison to individuals without CD [OR=1.4; 95% IC: 1.0-1.7]
Ille et al. [20]	2007	Age	83 patients submitted to heart surgery	One day before and seven days after surgery	For elderly patients, the higher the age the higher the risk of evolving with CD
Newman et al. [3]	2001	Age, Education	261 patients submitted to CABG	One day before surgery, at release and six weeks, six months and five years after	Higher ages [p=0.01] and less education [p=0.003] after multivariate analysis were predictors of CD after five years of the surgery
Di Carlo et al. [21]	2001	Education, SAH	110 patients submitted to heart surgery	Before the surgery and six months after	Education was a protecting factor after multivariate analysis [OR per year increased = 0.53; 95% IC: 0.31-0.90]. History of SAH was a significant predictor of CD [OR = 5.3; 95% IC: 1.03 -27.6]
Ho et al. [22]	2004	Education	939 patients submitted to CABG	Before the surgery and six months after	Number of years of education was reversely related to CD in a multivariate analysis [p = 0.001]
Roach et al. [23]	1996	SAH, Age	2108 patients submitted to CABG	-	Greater age [OR = 2.2; 95% IC: 1.6 – 3.0; p<0.05] and presence of SAH at admission [OR = 3.4; 95% IC: 1.4 - 8.5; p<0.05] were considered predictors of DC
Wolman et al. [24]	1999	SAH	273 patients submitted to CABG	-	Elevated systolic arterial pressure in the pre-operative/admission in hypertensive patients was associated to CD [OR = 10.4; 95% IC: 1.8 - 59.0]
Selnes et al. [25]	1999	DM	127 patients submitted to CABG	Pre-operative , in the 1 <sup>st</sup> month and one year after the procedure	History of DM was associated with a decline in executive functions [p=0.016] and psychomotor speed [p=0.003]
Kadoi & Goto [19]	2006	DM, CRF	88 patients submitted to CABG	One day before and six months after surgery	DM [OR = 1.8; 95% IC: 1.2 – 2.4; p<0.01] and chronic renal failure [OR = 2.8; 95% IC: 2.4 - 4.3; p<0.01] were associated to CD 6 months after the surgery
Nötzold et al. [26]	2006	DM	34 patients submitted to CABG with CPB	Pre-operative, and 2 <sup>nd</sup> to 5 <sup>th</sup> postoperative days	The group of diabetic patients presented with worse cognitive performance in the immediate postoperative period when compared to non-diabetics

CAGB - coronary artery bypass grafting; CPB - Cardiopulmonary Bypass; SAH - Sistemic arterial hypertension; DM - Diabetes Mellitus; CRF - chronic renal failure; CD - Cognitive Dysfunction

## **Intra-operative factors**

### **a) Embolization**

The formation of emboli, whose genesis would be the atheroma of the aortic wall, aggregated platelets, air bubbles originating from the oxygenator and the heart chambers may be the main cause of encephalic injury and the deterioration of pre-existent lesions [8]. These are subdivided in micro and macroemboli, with the former being more relevant in the emergence of CD.

Among the types of emboli, gaseous microemboli are the most probable source of CD, an event which is difficult to diagnose in the intra-operative period. There are three main causes for the genesis of microbubbles: the oxygenator itself, the cooling process of gasses which alters their solubility with predisposition to the formation of bubbles in the blood stream and the opening of heart chambers during the surgical procedure [8].

The understanding that emboli occurring during CPB may cause CD enables the adoption of techniques such as filtering and processing of blood thereby reducing the risk of injury caused by this embolic phenomenon. However, the possible beneficial effects of these new techniques were not confirmed in the results of Rubens et al. [28], which did not show differences in the incidence of CD in individuals submitted to CPB with the processing of blood or not, thus demonstrating the necessity of a continuous evolution of technology.

### **b) Duration of the surgical procedure**

The hypothesis that CPB and the duration of the surgical procedure are related to greater microvascular obstructions by emboli suggests a relationship between these factors and the evolution to CD (Table 2).

In a recent review article, Hogue et al. [39] discussed the impact of CPB on the development of postoperative CD and stressed the importance of recent advances in technology linked to this procedure in the prevention of new neurological events. Hence, the continuous perfecting of the CPB circuit has become fundamental to diminish the migration of emboli, and so significantly collaborate to the reduction in the incidence of CD.

### **c) Arterial pressure**

The importance of the mean arterial pressure (MAP) during the surgery is also the subject of research (Table 2), with intra-operative hypertension and consequent hypoperfusion potentially causing neurological impairment [4]. It is probable that an area of the cerebral irrigated by an occluded artery is exposed to hypoperfusion if the system of collateral arteries are affected by systemic hypotension [40], thereby culminating in an unfavorable cognitive outcome.

However, there are works that do not support this hypothesis. This disparity may be due to the age of the participants of the studies [31]. Great attention should be paid to maintain an adequate MAP in elderly patients as they are more susceptible to brain lesions.

### **d) Inflammation**

Another intra-operative factor that may contribute to neurological lesions is the inflammatory response. It is well known that exposure of blood to the surfaces of the CPB circuit triggers a systemic inflammatory response [40]. In areas affected by hypoperfusion, the exposure of blood to non-endothelial surfaces activates the coagulation cascade and the fibrinolytic and complement systems, as well as favoring the release of free radicals, factors that cause deterioration of pre-existent lesions [8].

The release of inflammatory mediators due to CPB seems to be temperature-dependent, with reductions in the inflammatory response in hypothermic CPB. Hence, a better understanding of the factors involved in CPB and the adoption of therapeutic interventions with the aim of attenuating the inflammatory response may be strategically useful to diminish cerebral lesions [1].

### **e) Hyperglycemia**

Another factor common in heart surgeries is hyperglycemia (blood sugar > 200 mg/dL), a phenomenon with neurological consequences, although not totally understood, that may greatly influence the cerebral metabolism [34]. Initially, high levels of blood sugar lead to an increase in the availability of substrate for the production of lactate in the anaerobic metabolism, a common phenomenon during ischemic processes. Consequently, the resulting acidosis interferes in glycolysis, proteic synthesis, homeostasis, enzymatic functions and in other cell processes [41], which lead to an expansion of the ischemic area [42]. Additionally, there is evidence that link hyperglycemia to an increase in the release of excitatory amino acids, a greater inflammatory response and an increase in the production of corticosteroids, facts that allied to factors described below may contribute to a higher incidence of postoperative CD [34].

### **F) Temperature: hyperthermia**

The effect of temperature during and after CPB on the postoperative cognitive result remains of great interest. With the adverse effects caused by hyperthermia, the significant influence of temperature on the cerebral response to existing damage seems to be of great value.

Table 2. Intra-operative factors

Authors	Year	Studied variable	Participants	Neuropsychological evaluation	Results
Ille et al. [20]	2007	Duration of procedure	83 patients submitted to heart surgery	One day before and seven days after surgery	For elderly individuals submitted to heart surgery the duration time of the procedure is directly related to CD
Stroobant et al. [29]	2005	Use or not of CPB	50 patients submitted to heart surgery [38 with and 12 without CPB]	Pre-operative, 6 <sup>th</sup> day and six months after the procedure	Six days after surgery, the prevalence of CD was not different between those with and without CPB. After six months, neurological sequels were present in 31.8% of those submitted to CPB and in 9.1% of those not submitted to CPB
Yin et al. [30]	2007	Use or not of CPB	40 male patients submitted to CABG [20 with and 20 without CPB]	Pre-operative, 7-10 days after the procedure	The incidence of neuropsychological tests was higher in individuals submitted to CABG with CPB when compared to those without CPB
Newman et al. [31]	1995	MAP	237 patients submitted to CABG	Pre-operative and at hospital release	Multivariate analysis demonstrated that the MAP was not associated to cognitive impairment
Gold et al. [32]	1995	MAP	240 patients submitted to CABG with CPB	-	Lower incidence of neurological complications in the group of individuals submitted to CABG with MAP between 80 and 100 mmHg, when compared to the group with MAP between 50 and 60
Gottesman et al. [33]	2007	MAP	15 patients high risk for strokes submitted to CABG	1-2 days before the surgery and 3-5 days after the procedure	A drop in the PAM in relation to the basal measurement is associated to worse cognitive performance
Puskas et al. [34]	2007	Hyperglycemia	525 patients submitted to CABG with CPB	Before the surgery and six weeks after	Among non-diabetic individuals, hyperglycemia was associated to CD after six weeks [p=0.035]
Grigore et al. [35]	2001	Temperature	237 patients submitted to CABG with CPB	Pre-operative and six weeks after	There was no difference in the cognitive outcome between the groups submitted to normothermic and hypothermic CPB
Boodhwani et al. [36]	2006	Temperature	448 patients submitted to CABG	Pre- and post-operative	The presence of normothermia during CABG was associated to CD [OR = 1.5, 95% IC: 1.01 - 1.31]
Boodhwani et al. [37]	2007	Temperature	267 patients submitted to heart surgery	Pre-operative and three months after hospital release	There was no difference in the incidence of CD between patients submitted to nasopharyngeal temperature (T) of 34° and those submitted to T = 37° in the intra-operative period
Nathan et al. [38]	2007	Temperature	131 patients submitted to CABG with CPB	Pre-operative, one week and five years after	There was evidence of neuroprotection after one week in individuals submitted to hypothermia [T = 34°] when compared to those with T = 37°. The result after five years was inconclusive

CABG - coronary artery bypass grafting; CPB - Cardiopulmonary Bypass; MAP - Mean Arterial Pressure; CD - Cognitive Dysfunction

Several mechanisms may explain the role of hyperthermia and its influence on the brain [43]. Sternau et al. [44], in an experimental study, demonstrated that the release of neurotransmitters in toxic amounts is accentuated by hyperthermia. Similarly, hyperthermia, when compared to normothermia, is associated to a higher release of free radicals [45], an exaggerated increase in the hematoencephalic barrier permeability [46] and enlargement of the ischemic areas by increasing ischemic depolarization [47]. Apart from these effects identified in experimental models, hyperthermia after strokes is associated to an increase in the area of infarction, thus contributing to higher morbidity and mortality rates [43].

Among the neuroprotector factors, hypothermia is the only one that reduces the energy consumption, which is directly related to the maintenance of cell integrity. Thus, this improves the cerebral and myocardial tolerance to the ischemic process [48]. In moderate hypothermia, self-regulation of the cerebral blood flow is intimately correlated to the cerebral metabolic rate, a condition not seen in situations of extreme hypothermia [4]. However, the beneficial effects of maintaining low temperatures are still controversial and there are disadvantages according to some authors (Table 2), with the necessity of rewarming to a normothermic temperature being the most important.

### Postoperative factors

Among the postoperative factors related to CD, studies

in respect to hypoxia and the CPB rewarming temperature are highlighted [31,43,48,49]. Browne et al. [49] found that postoperative hypoxia is a risk factor for the development of early CD, a fact confirmed by Hopkins et al. [50], who demonstrated, in individuals submitted to cerebral hypoxia, alterations in the structure of the hippocampus associated to CD. However, these findings were not confirmed by Moller et al. [51], who, on excluding individuals submitted to heart surgery from their work, did not evaluate an important factor related to CD, that is CPB and the consequent postoperative hypoxia. Hence, clearer evidence is necessary to elucidate the role of this condition in the development of CD.

On the other hand, according to what was discussed for the intra-operative factors, the most important adverse effect of the maintenance of low temperatures in CPB is the necessity of rewarming. During rewarming from hypothermic CPB, there may be an overload of cerebral temperature due to the aggressive rewarming process aimed at reducing the time of CPB and of the surgical procedure [40]. Moreover, the speed of rewarming is directly related to jugular desaturation [52], which in turn is associated to cognitive performance [53]. Another important fact in the pathogenesis of cerebral damage is the speed at which the rewarming rate is established, a condition related to the development of CD at a very early stage in the postoperative period (Table 3).

Table 3. Postoperative factors

Authors	Year	Studied variable	Participants	Neuropsychological evaluation	Results
Newman et al. [31]	1995	Temperature	237 patients submitted to CPB	Preoperative and at hospital release	Multivariate analysis demonstrated that the rate of rewarming was not associated to cognitive impairment
Grigore et al. [48]	2002	Temperature	165 patients submitted to CABG	Preoperative and six weeks after	Individuals submitted to slower rewarming had a better cognitive performance in the postoperative period [p=0.05]
Grocott et al. [43]	2002	Temperature	300 patients submitted to CABG with CPB	Preoperative and six weeks after	A higher temperature in the postoperative period was associated to a greater prevalence of CD [p=0.05]
Browne et al. [49]	2003	Hypoxia	175 patients submitted to CABG	Preoperative, five days and three months after hospital release	There was a significant correlation between CD and hypoxia five days after CABG

CABG - coronary artery bypass grafting; CPB - Cardiopulmonary Bypass; CD - Cognitive Dysfunction

### Genetic factors

Although a large number of factors may predict the risk of CD after surgical procedures, these factors contribute to about 10% to 40% of the analyzed models, findings that indicate that other factors may influence impairment [10]. Among the possible genetic polymorphisms that may influence postoperative CD, special attention should be paid to the  $\epsilon 4$  allele of apolipoprotein E (apo  $\epsilon 4$ ). This polymorphism is well known as a risk factor for Alzheimer's disease and for neurodegenerative disorders [54]. In an analysis associating the presence of apo  $\epsilon 4$  with CD, the results are controversial (Table 4) so other etiological factors associated to the development of CD should be included in studies.

Because of this, several other genetic factors have been associated to CD, although many of these more recent studies are limited either due to small sample sizes or because they analyze genes in isolation (instead of several genes), or by the methodology employed [55]. Another

studied polymorphism is the phospholipases A2, which, when present, is associated to lower scores in mental state evaluation examinations [56].

Summed to the aforementioned genetic polymorphisms, the genetic influence of the inflammatory response to CPB has also been stressed as in the cases of interleukin-6, C-reactive protein (CRP) and tumoral necrosis factor-alpha, with the study of these variants being important not only as they associate polymorphisms to an increased inflammatory response but as they link, consequent to this, inflammatory response to side effects related to heart surgery [55]. Hence, a recent publication by Mathew et al. [57] deserves special attention. In this work 37 polymorphisms of simple nucleotides (SNPs) were genotyped for 513 patients submitted to CABG with CPB. The association between these SNPs and cognitive impairment was tested six months after surgery by multiple logistic regression adjusted by age, education, basal cognitive level and populational structure. A significant

Tabela 4. Fatores genéticos

Authors	Year	Studied variable	Participants	Neuropsychological evaluation	Results
Tardiff et al. [14]	1997	ApoE	65 patients submitted to CABG	Preoperative and six weeks after the procedure	Polymorphisms of Apo E are related to postoperative CD
Steed et al. [15]	2001	ApoE	111 patients submitted to CABG	Preoperative and 4-7 weeks after the procedure	There was no relationship between cognitive impairment and the alleles of Apo E
Robson et al. [16]	2002	ApoE	86 patients submitted to CABG	One day before and three months after the surgical procedure	There was no relationship between carriers of Apo E $\epsilon 4$ and cognitive function/impairment after the surgery
Askar et al. [17]	2005	ApoE	78 patients submitted to heart surgery	One day before, at hospital release and three months after surgery	There was no statistically significant difference between the individuals with the $\epsilon 4$ allele and those without
Lelis et al. [13]	2006	ApoE	87 individuals submitted to CABG	MMSE and Glasgow Coma Scale in the preoperative, after 24h and on the 6 <sup>th</sup> postoperative day	A presence of apo $\epsilon 4$ was associated to a worse MMSE score [p=0.04] suggesting an association between this allele and the early development of CD
Tagarakis et al. [12]	2007	ApoE	137 individuals	At admission and one month after surgery	There was no relationship between cognitive impairment and the presence of the Apo E $\epsilon 4$

CABG - coronary artery bypass grafting; CPB - Cardiopulmonary Bypass; ApoE - Apolipoprotein; CD - Cognitive Dysfunction; MMSE - Mini Mental State Examination

relationship was obtained among carriers of lower alleles of CRP and a reduction of risk for CD (Odds Ratio = 0.37; 95% CI: 0.16–0.78; p-value = 0.013). In carriers of these lower alleles, the pre-operative levels of CRP were lower, ratifying biological support for the observed allelic association.

With advances in technology, the simultaneous investigations of several genes has become more scientifically and economically viable enabling the establishment of how a genetic factor is capable of affecting outcomes.

### Pharmacotherapy protection

With knowledge of the risk factors, it is possible to predict those individuals who have a greater chance of evolving with CD and so institute protective measures thereby reducing sequels and avoiding irreversible brain injury. Neuroprotection therapy aims at minimizing the activation of toxic processes and to increase the endogen mechanisms of protection [1].

Initially, effort was focused on anesthetics (thiopental

and propofol), based on the hypothesis that a reduced cerebral metabolic demand would provide greater resistance to ischemic events [39]. However, the results were not very satisfactory [58,59]. Other clinical trials had promising results [60-62], suggesting that pharmacological agents, such as remacemide, a glutamate neurotransmitter antagonist (released during the ischemic process and responsible for the rapid inflow of calcium to cells) and lidocaine (at antiarrhythmic doses) may be useful in neuroprotection therapy (Table 5).

With the exception of some anesthetics, many of the neuroprotecting agents studied in heart surgery were originally developed for the treatment of strokes [4]. Unhappily, the divergence of factors related to brain damage implicate a difficulty in their utilization and, in most cases, the results are disappointing. A possible explanation for these results, apart from the limited sample size, is that the treatment is directed to a specific target, in detriment to a much more complex process which occurs simultaneously.

Tabela 5. Fármacos neuroprotetores

Authors	Year	Studied variable	Participants	Neuropsychological evaluation	Results
Zaidan et al. [58]	1991	Thiopental	300 patients submitted to CABG	Before, on the 2 <sup>nd</sup> and 5 <sup>th</sup> postoperative days	There were no differences in the cognitive outcomes between the group that took thiopental and the placebo group
Arrowsmith et al. [61]	1998	Remacemide	171 patients submitted to CABG	Before and eight weeks after the procedure	Patients taking remacemide had a better cognitive performance than the placebo group
Roach et al. [59]	1999	Propofol	225 patients submitted to valve surgery	Preoperative, on the 1 <sup>st</sup> , 5 <sup>th</sup> -7 <sup>th</sup> and 50 <sup>th</sup> -70 <sup>th</sup> postoperative days	There were no differences in cognitive complications between the groups treated with propofol and placebo
Mitchell et al. [62]	1999	Lidocaine	65 patients submitted to valve surgery	Preoperative, 10 days, 10 weeks and six months after the procedure	Individuals who received lidocaine during anesthesia presented with a better cognitive performance than the individuals who received placebo
Wang et al. [60]	2002	Lidocaine	88 patients submitted to CABG with CPB	Before and nine days after surgery	The proportion of patients with postoperative CD was smaller in the group who used lidocaine compared to the placebo group [18.6% vs. 40.0%; p=0.028]

CAGB - coronary artery bypass grafting; CPB - Cardiopulmonary Bypass; CD - Cognitive Dysfunction

## CONCLUSION

Although heart surgery procedures have gone through major technological changes in recent decades, postoperative cognitive dysfunction remains a common event and causes severe lesions characterized by varying degrees of cognitive loss in a significant number of individuals. Despite of many studies, the physiopathology of these neurological events has not been clearly determined yet, and so the presence of pre-operative, intra-operative and postoperative risk factors as well as a genetic basis is implicated in this disease. Another important observation to be considered is the lack of definition in respect to the ideal pharmacological agent to reduce the incidence of cognitive dysfunction, which suggests the necessity of further studies in this area because of the highly significant number of heart surgeries.

In respect to the most severe events (for example strokes), although they are not the focus of this review article, some brief considerations should be mentioned. The elucidation of the exact physiopathologic mechanism of postoperative cognitive dysfunction helps us to understand factors related to the occurrence of more serious events, as well as how the development of pharmacotherapy to protect against cognitive dysfunction may also contribute to the development of prophylactic measures in the development of strokes.

In conclusion, a continuous process of perfecting tools and techniques utilized during surgical procedures is necessary, thereby contributing to less aggression to the organism of the patient and a progressive reduction in the incidence of neurological complications. Hence, the association of prophylactic measures and a better understanding of the risk factors associated to postoperative cognitive dysfunction will lead to surgical interventions with lower incidences of complications and consequent reductions in hospital costs and improvements in the quality of life of patients.

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