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REVIEW ARTICLE

Is there any benefit in associating neuraxial anesthesia to general anesthesia for coronary artery bypass graft surgery?☆



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KEYWORDS

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Abstract

Background and objectives: The use of neuraxial anesthesia in cardiac surgery is recent, but the hemodynamic effects of local anesthetics and anticoagulation can result in risk to patients. **Objective:** To review the benefits of neuraxial anesthesia in cardiac surgery for CABG through a systematic review of systematic reviews.

Content: The search was performed in Pubmed (January 1966 to December 2012), Embase (1974 to December 2012), The Cochrane Library (volume 10, 2012) and Lilacs (1982 to December 2012) databases, in search of articles of systematic reviews. The following variables: mortality, myocardial infarction, stroke, in-hospital length of stay, arrhythmias and epidural hematoma were analyzed.

Conclusions: The use of neuraxial anesthesia in cardiac surgery remains controversial. The greatest benefit found by this review was the possibility of reducing postoperative arrhythmias, but this result was contradictory among the identified findings. The results of findings regarding mortality, myocardial infarction, stroke and in-hospital length of stay did not show greater efficacy of neuraxial anesthesia.

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PALAVRAS-CHAVE

Anestesia geral;
Anestesia subaracnoidea;
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Revisão sistemática;
Mortalidade;
Evidências

Existe algum benefício em associar a anestesia neuroaxial à anestesia geral para revascularização miocárdica?**Resumo**

Justificativa e objetivos: O uso da anestesia neuroaxial em cirurgia cardíaca é recente, porém os efeitos hemodinâmicos dos anestésicos locais e a anticoagulação podem trazer riscos aos pacientes.

Objetivo: Revisar os benefícios da anestesia neuroaxial em cirurgia cardíaca para revascularização miocárdica por meio de uma revisão sistemática de revisões sistemáticas.

Conteúdo: Foi feita pesquisa nas bases de dados Pubmed (de janeiro de 1966 a dezembro de 2012), Embase (1974 a dezembro 2012), The Cochrane Library (volume 10, 2012) e Lilacs (1982 a dezembro de 2012) em busca de artigos de revisões sistemáticas. Foram analisadas as seguintes variáveis: mortalidade, infarto do miocárdio, acidente vascular cerebral, tempo de internação hospitalar, arritmias e hematoma peridural.

Conclusões: O uso da anestesia neuroaxial para revascularização miocárdica permanece controverso. O maior benefício encontrado por meio desta revisão foi a possibilidade de redução das arritmias pós-operatórias, porém esse resultado foi contraditório entre as evidências identificadas. Os resultados das evidências encontradas referentes à mortalidade, ao infarto do miocárdio, ao acidente vascular cerebral e ao tempo de internação hospitalar não mostraram maior efetividade da anestesia neuroaxial.

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Introduction

The technological and pharmacological advances in anesthesia and surgery over the past decades, as well as better working conditions in intensive care units decreased complications in patients undergoing cardiac surgery.^{1,2}

Neuraxial anesthesia (NA) causes sympathectomy and can improve the coronary perfusion and balance between supply and demand of myocardial oxygen and reduce the incidence of postoperative arrhythmias and perioperative heart attack.³⁻⁵ The combination of general anesthesia (GA) and NA may bring benefits to patients undergoing cardiac surgery.^{3,4}

The systematic use of anticoagulation in cardiac surgery with cardiopulmonary bypass increases the risk of hematoma and spinal cord compression when anesthesia is performed on spinal cord or nerves.⁶ The major problem with neuraxial administration of local anesthetics is systemic hypotension, which may be accompanied by decreases in coronary blood flow, as the safe level of hypotension in patients undergoing cardiac surgery is not known.⁷ If we take into account the physiological effects of local anesthetic neuraxial administration and NA management in patients with anticoagulation, it is noticed that the use of NA, i.e., thoracic epidural anesthesia (TEA) and spinal anesthesia (SA), in cardiac surgery remains controversial.^{6,7} It is necessary to analyze the existing data in the literature to identify benefits of the NA administration in cardiac surgery for coronary artery bypass grafting (CABG).

The aim of this article was to review the NA benefits in cardiac surgery for CABG through a systematic review of systematic reviews.

Methods

The strategy to accomplish this systematic review followed the Cochrane Collaboration guidelines.⁸ This is a systematic review of systematic reviews. The items for systematic reviews publications of Prisma statement were followed to report the results of this review.⁹

Inclusion criteria were systematic review articles of randomized controlled trials (RCTs) evaluating the use of neuraxial anesthesia in cardiac surgery for CABG. There was no language restriction. Other types of research articles were excluded from the analysis.

The identification of systematic review articles was performed by searching in electronic databases. The sources used were: Medline via PubMed (January 1966 to December 2012), Embase (1974 to December 2012), The Cochrane Library (volume 10, 2012), and Lilacs (1982 to December 2012). The search strategy used for PubMed is shown in [Table 1](#). The search strategy for Embase was: systematic review/exp and general anesthesia/exp or spinal anesthesia/exp or epidural anesthesia/exp and cardiac surgery/exp and embase/lim. 'Anesthesia' and 'cardiac surgery' terms were used for Lilacs and Cochrane Collaboration.

The published articles identified by the search strategy were selected by analysis of titles and abstracts, or both. This selection was independently made by two reviewers (Barbosa F.T. and Castro A.A.) and followed by meetings to resolve disagreements between the authors. The published systematic review articles that met the inclusion criteria were fully reviewed.

The Overview Quality Assessment Questionnaire (OQAQ) was used to assess the quality of systematic reviews with

Table 1 Search strategy for Medline via Pubmed.

Database	Terms used
Pubmed	<p><i>systematic</i>[sb] and <i>thoracic surgery</i> [Mesh Terms] or (<i>thoracic</i> [all fields] and <i>surgery</i> [all fields]) or <i>thoracic surgery</i> [all fields] or (<i>cardiac</i> [all fields] and <i>surgery</i> [all fields]) or <i>cardiac surgery</i> [all fields] or <i>cardiac surgical procedures</i> [Mesh Terms] or (<i>cardiac</i> [all fields] and <i>surgical</i> [all fields]) and <i>procedures</i> [all fields]) or <i>cardiac surgical procedures</i> [all fields] or (<i>cardiac</i> [all fields] and <i>surgery</i> [all fields]) and <i>general anaesthesia</i> [all fields] or <i>anesthesia, general</i> [Mesh Terms] or (<i>anesthesia</i> [all fields] and <i>general</i> [all fields]) or <i>general anesthesia</i> [all fields] or (<i>general</i> [all fields] and <i>anesthesia</i> [all fields])</p>

variables of interest.¹⁰ It is a 10-item questionnaire, in which the first nine questions were used to assess the search strategy, selection strategy, quality used in the review, data analysis performed, and outcomes. These questions were answered with yes, no, or partial/indeterminate. The last question focused on the systematic review overall scientific quality consists of a 7-point scale: 1–2 for extensive flaws, 2–4 for major flaws, 4–6 for minor flaws, and 6–7 for minimal flaws.

Only one reviewer assessed the methodological quality of systematic reviews. According to other authors and to facilitate interpretation of OQAQ scores, we grouped the scores as follows: 1–2 for extensive flaws, 3–4 for major flaws, 5–6 for minor flaws, and 7 for minimal flaws.^{11,12} Scores 5–6 were considered as systematic review of acceptable quality and a score of 7 as good quality.

The variables of interest to this systematic review were: mortality, myocardial infarction, stroke, hospital stay, arrhythmia, and epidural hematoma.

This review was not submitted to the Ethics Research Committee because it is a secondary data analysis. The method used was a convenience sample. The agreement between reviewers was assessed using the kappa statistic. A qualitative approach was used to evaluate the variables of interest data reported in the systematic reviews found.

Results

The search for systematic reviews through the analysis of titles and abstracts identified 1469 articles: 622 in Pubmed, 651 in Embase, 53 in Cochrane Collaboration, and 143 in Lilacs. We excluded 1463 articles for not meeting inclusion criteria. Two articles were excluded during the full text review for not being systematic reviews. Four systematic reviews were selected for analysis of the variables at the end of the process.^{13–16} The kappa concordance index was 0.75.

Table 2 shows the frequency of responses to OQAQ. After the methodological quality assessment, three systematic reviews were classified as having minor flaws^{13,15,16} and one as having minimal flaws.¹⁴

Table 3 shows the characteristics of systematic reviews included for analysis of variables. There was planning to analyze the epidural hematoma variable in systematic reviews, but this variable was not reported in the randomized clinical trials included in these reviews.

Mortality was assessed in three systematic reviews. Liu et al.¹³ reported that odds ratio was 1.56 (95% CI: 0.35–6.91; $p=0.56$) for epidural anesthesia and 0.88 (95% CI: 0.13–5.72; $p=0.89$) for spinal anesthesia. Zangrillo et al.¹⁴ reported that the risk difference for spinal anesthesia was 0.00 (95% CI: –0.02 to +0.02; $p=1.0$). Svircevic et al.¹⁵ reported that relative risk for epidural anesthesia was 0.81 (95% CI: 0.40 to –1.64; p not provided).

Myocardial infarction was assessed in three systematic reviews. Liu et al.¹³ reported that odds ratio for epidural anesthesia was 0.74 (95% CI: 0.34–1.59; $p=0.44$) and 0.75 (95% CI: 0.24–2.31; $p=0.61$) for spinal anesthesia. Zangrillo et al.¹⁴ reported that the risk difference for spinal anesthesia was 0.00 (95% CI: –0.03 to +0.02; $p=0.77$). Svircevic et al.¹⁵ reported that relative risk for epidural anesthesia was 0.80 (95% CI: 0.52 to –1.24; p not provided).

Stroke was assessed in one systematic review. Svircevic et al.¹⁵ reported that relative risk for epidural anesthesia was 0.59 (95% CI: 0.24 to –1.46; p not provided).

Hospital stay was assessed in one systematic review. Zangrillo et al.¹⁴ reported that weighted mean difference for spinal anesthesia was –0.28 days (95% CI: –0.68 to 0.13; $p=0.18$).

Arrhythmia was assessed in three systematic reviews. Liu et al.¹³ reported that odds ratio for epidural anesthesia was 0.52 (95% CI: 0.29–0.93; $p=0.03$) favorable to the epidural anesthesia group. The same benefit was not observed in studies considering spinal anesthesia with an odds ratio of 0.81 (95% CI: 0.42–1.53; $p=0.51$). Svircevic et al.¹⁵ demonstrated that relative risk for epidural anesthesia was 0.68 (95% CI: 0.50 to –0.93; p not provided). Gu et al.¹⁶ demonstrated that relative risk for epidural anesthesia was 0.61 (95% CI: 0.33–1.12; $p=0.11$).

Discussion

Inadequate pain control in patients undergoing cardiac surgery may increase morbidity due to adverse hemodynamic effects, increased metabolic and immune response to trauma, and hemostatic abnormalities.¹⁷ Aggressive postoperative pain management may improve clinical outcomes in high risk patients undergoing cardiac surgery.¹⁸ Although the adverse effects and the likelihood of prolonged intubation and mechanical ventilation of opioids are known, the use of intravenous opioids is a traditional choice.¹⁷ During the last decades, SA and TEA are gaining space in this scenario for providing adequate analgesia, even with the knowledge that these anesthetic techniques are not without risks.⁷

Activation of cardiac sympathetic innervation causes coronary vasoconstriction and decreased response of these vessels to vasodilation agents, changing the balance between myocardial oxygen supply and demand.¹⁹ Cardiac

Table 2 Frequency of the OQAQ answers.

Topic for analysis	Liu et al. ¹³	Zangrillo et al. ¹⁴	Svircevic et al. ¹⁵	Gu et al. ¹⁶
1. Reported search methods	No	Yes	Yes	No
2. Comprehensive search	Undetermined	Yes	Yes	Undetermined
3. Inclusion criteria reported	Yes	Yes	Yes	Yes
4. Avoided selection bias	Undetermined	Yes	Yes	Undetermined
5. Validity criteria reported	Undetermined	Yes	Undetermined	Undetermined
6. Adequately assessed validity	Undetermined	Yes	Undetermined	Yes
7. Reported combined methods	Yes	Yes	Yes	Yes
8. Combining results properly	Yes	Yes	Yes	Yes
9. Conclusions supported by data	Yes	Yes	Yes	Yes

sympathetic activation is considered as a central mechanism for the emergence of postoperative myocardial infarction.¹⁹ The blockade of sympathetic fibers T1 to T5 reduces the surgical stress response, increases the diameter of epicardial stenotic segments of coronary circulation, decreases myocardial oxygen consumption, and improves left ventricular function.¹⁷

SA can adequately reduce the surgical stress response, but the hemodynamic changes, such as the emergence of systemic hypotension and bradycardia associated with other effects of total sympathectomy, may bring harm to patients undergoing CABG.¹⁷ Two double-blind, placebo-controlled RCTs attracted the attention of researchers for adequate analgesia achieved with the isolated use of neuraxial opioids.^{20,21} One of the RCTs reported that the use of morphine 0.5 mg before induction of general anesthesia can reduce the time of tracheal intubation and decrease the duration of mechanical ventilation.²⁰ Although this beneficial effect may have occurred, it was not found in other studies and was considered controversial.²¹⁻²³

TEA can adequately reduce the surgical stress response and hemodynamic changes, such as the emergence of systemic hypotension and bradycardia, did not seem to bring harm to patients undergoing myocardial revascularization

with reports in the literature of beta-blockers dose reduction in patients undergoing CABG.¹⁷ Three RCTs reported that postoperative analgesia is effective with this technique; however, there was divergence regarding analgesia duration, which was different between these studies.²⁴⁻²⁶ The common benefit among these RCTs was the reduced tracheal intubation time and decreased mechanical ventilation time.

Systematic reviews use the available literature data by combining results from studies in order to resolve conflicts in medical knowledge.¹² A systematic review can improve the analysis statistical power, which cannot be achieved in primary isolated studies and thus help to choose the most appropriate interventions for populations of interest.⁸ Four systematic reviews assessing the use of NA in patients undergoing CABG were identified.¹³⁻¹⁶

A systematic review published in 2004 assessed the use of epidural analgesia compared with intravenous opioid.¹³ The authors concluded that the use of NA is favorable, considering the time to tracheal extubation, postoperative pulmonary complications, and postoperative cardiac arrhythmias. That review examined studies that combined results of patients who were and who were not undergoing cardiopulmonary bypass (CPB). The surgical stress cannot be

Table 3 Characteristics of systematic reviews included for analysis of variables.

Study	Participants	Intervention	Comparison	Variables	n (N)
Liu et al. ¹³	Adults, coronary insufficiency, CPB	GA + EA, GA + SA	GA	Mortality, heart attack, arrhythmias, pulmonary complications	1846 (32)
Zangrillo et al. ¹⁴	Adults, cardiac surgery with or without CPB, myocardial ischemia, valve replacement	GA + SA	GA	Mortality, heart attack, hospital stay, length of stay in ICU, arrhythmias, complications	1106 (25)
Svircevic et al. ¹⁵	Over 18 years, cardiac surgery	GA + EA	GA	Mortality, heart attack, CVA, supraventricular tachycardia, respiratory complications	2731 (28)
Gu et al. ¹⁶	Over 18 years, coronary insufficiency, CPB, CPB	GA + EA	GA	Postoperative atrial fibrillation	540 (5)

n, number of participants; N, numbers of included studies; CPB, cardiopulmonary bypass; GA, general anesthesia; EA, epidural anesthesia; SA, spinal anesthesia; ICU, intensive care unit; CVA, cerebrovascular accident.

the same among patients who underwent CPB and those who were not submitted to CPB and this may influence the results when combined in meta-analysis. Therefore, it would have been more prudent if the authors had analyzed data from two types of patients separately. The analysis regarding the quality of included studies was not described. Studies with dubious quality may have been analyzed together with good quality studies and affected meta-analysis results.

A systematic review published in 2009 assessed the use of SA in cardiac surgery.¹⁴ The authors concluded that the use of NA is unfavorable considering mortality, myocardial infarction, and hospital stay. That review evaluated studies in the setting of cardiac surgery and not individualized for myocardial revascularization. Patients undergoing heart valve surgery may have a different postoperative course than those undergoing CABG and it is difficult to individualize the results.

A systematic review published in 2011 assessed the use of epidural analgesia compared with general anesthesia.¹⁵ The authors concluded that the use of NA is favorable considering the reduced risk of postoperative supraventricular arrhythmias and respiratory complications. That review evaluated studies in cardiac surgery setting and not individualized for myocardial revascularization. The authors created their own tool to assess the methodological quality of the included studies and did not describe the process of validation of this tool. A non-validated tool may not accurately reproduce the variable of interest. Quality analysis occurred for items of internal validity of randomized controlled trials; however, the analysis could have been more complete if the items of external validity and statistical data were also evaluated.

The most recent systematic review was published in 2012 and assessed the use of TEA compared with general anesthesia.¹⁶ The authors assessed only the presence of postoperative atrial fibrillation and concluded that the use of NA is not favorable. They reported the existence of statistical heterogeneity, but did not identify its origin. Methodological quality analysis was done properly, but did not help to identify the heterogeneity source. The result of meta-analysis with heterogeneity should be viewed with caution and may not even be considered; however, it can guide authors of future research about the presence of faulty points to be avoided.⁸

The implications for clinical practice after this systematic review is that the results in the literature to date should be viewed with reservations and the anesthesiologist should consider his clinical practice and the care offered by the health service in decision making regarding the patient undergoing cardiac surgery. The variables that showed positive results did not contribute to improve important clinical outcomes, such as mortality, myocardial infarction, stroke, hospital stay, and even the degree of patient satisfaction. The identified systematic review results were contradictory.

The risk of neuraxial hematoma was estimated by mathematical methods in a study conducted in 2000.²⁷ Maximum risk after full heparinization was estimated at 1:2400 and neuraxial instrumentation at 1:1000. Some precautions are suggested, such as using neuraxial technique when there is laboratory indication of normality for coagulation tests, delaying procedures when puncture is traumatic, and waiting at least 60 min after NA to perform full heparinization.¹⁷

The main clinical implication for future research in this clinical setting refers to the need for new RCTs with adequate statistical power and focusing on important clinical variables, such as mortality, myocardial infarction, stroke, hospital stay, arrhythmias, and epidural hematoma. Sample size: 284 participants are needed in each group considering 1% mortality in neuraxial anesthesia group, 5% mortality in general anesthesia group, 80% statistical power, and 5% significance level.

Conclusion

The use of neuraxial anesthesia in cardiac surgery remains controversial. The greatest benefit found by this review was the possibility of reducing postoperative arrhythmias; however, this benefit was contradictory between the identified outcomes. The outcomes found regarding mortality, myocardial infarction, stroke, and hospital stay were not more effective than neuraxial anesthesia.

Conflicts of interest

The authors declare no conflicts of interest.

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