

Anestesia Neuroaxial Comparada à Anestesia Geral para Revascularização dos Membros Inferiores em Idosos. Revisão Sistemática com Metanálise de Ensaios Clínicos Aleatórios*

Neuroaxis Block Compared to General Anesthesia for Revascularization of the Lower Limbs in the Elderly. A Systematic Review with Metanalysis of Randomized Clinical Studies

Fabiano Timbó Barbosa, TSA¹, Mário Jorge Jucá², Aldemar Araújo Castro³

RESUMO

Barbosa FT, Jucá MJ, Castro AA — Anestesia Neuroaxial Comparada à Anestesia Geral para Revascularização dos Membros Inferiores em Idosos. Revisão Sistemática com Metanálise de Ensaios Clínicos Aleatórios.

JUSTIFICATIVA E OBJETIVOS: A controvérsia atual é saber se a anestesia neuroaxial (AN) é mais eficiente que a geral (AG) em idosos submetidos à cirurgia não-cardíaca. O objetivo foi determinar a eficiência da AN comparada à AG para revascularização de membros inferiores (RMI) em idosos.

MÉTODO: Utilizada estratégia de busca para as bases de dados: MEDLINE (1955 a 2007), CINHALL (1982 a 2007), Embase (1980 a 2007), LILACS (1982 a 2007) e ISI (1945 a 2007). Dois revisores analisaram independentemente os artigos em busca de ensaios clínicos aleatórios (ECA) que comparassem a AN com a AG para a RMI. O texto completo dos ECA que atendessem aos critérios de inclusão foram analisados. Discordâncias foram analisadas em reuniões de consenso. A metanálise foi realizada com o software Review Manager, por meio da razão de chances com intervalo de confiança de 95%.

RESULTADOS: Foram selecionados três artigos originais envolvendo 465 pacientes. Não houve significância estatística na metanálise das variáveis: mortalidade (OR: 0,90; IC 95%: 0,30 — 2,73; P = 0,85 raquianestesia; OR: 1,30; IC 95%: 0,38 — 4,48; P = 0,68 anestesia peridural), infarto miocárdico (OR: 1,38; IC 95%: 0,29 — 6,46; P = 0,68) e taxa de amputação dos membros inferiores (OR: 0,81; IC 95%: 0,30 — 2,19; P = 0,68 raquianestesia; OR: 0,70; IC 95%: 0,24 — 2,07; P = 0,52 anestesia peridural). Houve

significância estatística para pneumonia (OR: 0,37; IC 95%: 0,15 — 0,89; P = 0,03), porém houve heterogeneidade clínica.

CONCLUSÕES: As evidências geradas nessa metanálise foram insuficientes para demonstrar que a AN é mais eficiente, equivalente, ou menos eficiente quando comparada a AG para RMI em idosos.

Unitermos: CIRURGIA, Vascular; TÉCNICAS ANESTÉSICAS, Geral, Regional.

SUMMARY

Barbosa FT, Jucá MJ, Castro AA — Neuroaxis Block Compared to General Anesthesia for Revascularization of the Lower Limbs in the Elderly. A Systematic Review with Metanalysis of Randomized Clinical Studies.

BACKGROUND AND OBJECTIVES: Currently, it is controversial on whether neuroaxis block (NB) is more effective than general anesthesia (GA) in elderly individuals undergoing non-cardiac surgeries. The objective of this study was to determine the efficiency of NB in comparison to GA for revascularization of the lower limbs (RLL) in the elderly.

METHODS: A search of the following data base was conducted: MEDLINE (1955 to 2007), CINHALL (1982 to 2007), EMBASE (1980 to 2007), LILACS (1982 to 2007), and ISI (1945 to 2007). Two investigators undertook an independent analysis of the studies published to identify randomized clinical trials (RCTs) comparing NB with GA for RLL. The full text of the RCTs that fulfill the inclusion criteria was analyzed. Disagreements were analyzed in consensus meetings. The software Review Manager was used for the Metanalysis by means of odds ratio with a confidence interval of 95%.

RESULTS: Three studies involving 465 patients were selected. Metanalysis of the following parameters did not show statistically significant differences: mortality (OR: 0.90; CI 95%: 0.30-2.73; p = 0.85 for spinal anesthesia; OR: 1.30, CI 95%: 0.38-4.48, p = 0.68, for epidural block); myocardial infarction (OR: 1.38, CI 95%: 0.29-6.46, p = 0.68); and rate of lower limb amputation (OR: 0.81, CI 95%: 0.30-2.19, p = 0.68, for spinal block; OR: 0.70, CI 95%: 0.24-2.07, p = 0.52 for epidural block). A statistically significant difference was observed for pneumonia (OR: 0.37, CI 95%: 0.15-0.89, p = 0.03); however, clinical heterogeneity was present.

CONCLUSIONS: This metanalysis did not generate enough evidence to demonstrate that NB is more efficient, equivalent, or less efficient than GA for RLL in the elderly.

Key Words: ANESTHETIC TECHNIQUES, General, Regional; SURGERY, Vascular

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ções por um ou mais problemas, tais como: o número de pacientes foi menor do que o valor apresentado pelo cálculo do tamanho da amostra, houve dificuldades no encobrimento dos pacientes e dos responsáveis pela coleta e pela análise dos dados, não houve descrição das exclusões, além da técnica de distribuição aleatória e do sigilo da alocação não terem sido completamente descritas. As limitações observadas nos artigos originais incluídos podem ter influenciado os resultados encontrados.

A análise da variável mortalidade não demonstrou haver diferença estatística entre os grupos (OR: 0,90; IC 95%: 0,30 — 2,73; $p = 0,85$ para raquianestesia; OR: 1,30; IC 95%: 0,38 — 4,48; $p = 0,68$ para anestesia peridural). Outros grandes estudos em cirurgia ortopédica já foram realizados e também não demonstraram haver diferença estatística em pacientes idosos quando se considerou a diferença de técnicas anestésicas^{13,14}. O surgimento de novos fármacos ao longo dos anos, com perfil farmacocinético mais adequado para os idosos¹, o melhor entendimento das complicações^{1,2} e as descobertas de novas estratégias protetoras^{15,16} podem justificar e até manter nos próximos anos os resultados encontrados.

Em relação à variável infarto miocárdico não houve diferença estatística entre os grupos (OR: 1,38; IC 95%: 0,29 — 6,46; $p = 0,68$). A fisiopatologia do infarto cardíaco perioperatório não está completamente elucidada, porém dois fatores parecem estar associados¹⁷: o desequilíbrio entre oferta e consumo de oxigênio miocárdico e a ruptura da placa aterosclerótica com subsequente formação de trombo e oclusão coronariana. Em anestesia essa complicação pode ocorrer pelo aumento do consumo de oxigênio, pela diminuição da oferta de oxigênio ao miocárdio ou por ambas as causas¹⁸. É plausível que o infarto miocárdico ocorra tanto na anestesia neuroaxial quanto na geral, pois o bloqueio simpático, que ocorre após o uso do anestésico local, leva à redução do retorno venoso, diminuição da pressão diastólica final do ventrículo esquerdo e hipotensão arterial sistêmica resultando em menor perfusão coronariana quando não-tratado adequadamente, e a anestesia geral pode não abolir adequadamente o *stress* cirúrgico e a resposta endócrina ao trauma. A variável taxa de amputação dos membros inferiores não demonstrou significância estatística (OR: 0,81; IC 95%: 0,30 — 2,19; $p = 0,68$ para raquianestesia; OR: 0,70; IC 95%: 0,24 — 2,07; $p = 0,52$ para anestesia peridural). O aumento do fluxo sanguíneo no local do enxerto vascular é um importante fator determinante para a vida média da patência do enxerto⁹. Os autores dessa revisão sistemática assumiram a hipótese de que o bloqueio simpático causado pelo anestésico local no canal vertebral aumentaria o fluxo nos membros inferiores e causaria menor taxa de amputação no pós-operatório, entretanto esse efeito não ficou confirmado nessa pesquisa. Os autores dos artigos originais incluídos descreveram a utilização do anestésico local em dose única, consequentemente pode-se inferir que a ação vasodilatadora nos membros inferiores não foi prolongada e isso pode jus-

tificar a ausência de significância estatística na análise dessa variável, uma vez que os autores dos artigos incluídos levaram em consideração todo o tempo de seguimento e não apenas o pós-operatório imediato.

A variável pneumonia apresentou diferença estatística entre os grupos analisados (OR: 0,37; IC 95%: 0,15 — 0,89; $p = 0,03$). As complicações pulmonares pós-operatórias são mais frequentes nos pacientes idosos submetidos à anestesia geral, não só pelas alterações fisiológicas características da faixa etária avançada como pela possibilidade de ventilação mecânica prolongada após o término do procedimento¹. Na pesquisa, foi avaliada a incidência de pneumonia e observou-se que houve uma maior contribuição de um único artigo original⁸ na análise dessa variável. No artigo⁸, os autores relatam que houve um maior número de idosos e fumantes no grupo da anestesia geral sem descrição das taxas e ainda relacionaram os resultados à falta de umidificação dos vapores anestésicos. Na análise de sensibilidade percebeu-se também que houve heterogeneidade clínica em virtude das diferentes técnicas anestésicas neuroaxiais empregadas pelos autores para a comparação com a anestesia geral^{8,9}. Uma das medidas possíveis para atestar o resultado é retirar os dados do artigo original que parece ser responsável pela heterogeneidade, entretanto só é possível a realização da metanálise com os dados de pelo menos dois artigos originais.

Conclui-se, então, que as evidências geradas nessa revisão sistemática com metanálise foram insuficientes para demonstrar que a anestesia neuroaxial é mais eficiente, equivalente, ou menos eficiente quando comparada com a anestesia geral para a revascularização dos membros inferiores em pacientes idosos.

Neuroaxis Block Compared to General Anesthesia for Revascularization of the Lower Limbs in the Elderly. A Systematic Review with Metanalysis of Randomized Clinical Studies

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INTRODUCTION

Developments in surgical and anesthetic techniques decreased perioperative risks and expanded the surgical indications in the elderly¹. In the elderly, general anesthesia has been associated with postoperative respiratory complications² and for this reason neuroaxis block has been recommended as the first choice in this population³.

Regarding elderly patients, and out of the realm of vascular surgery, it has been demonstrated that the mortality asso-

ciated with neuroaxis block can be 30% lower than that of general anesthesia³ due to changes inherent to old age, greater number of comorbidities in the elderly, and their greater sensitivity to drugs^{1,3}; however, a systematic review to determine the efficiency of neuroaxis block in comparison to general anesthesia in elderly patients undergoing revascularization of the lower limbs has not been done.

The present study hypothesized that neuroaxis block is more efficient than general anesthesia for revascularization of the lower limbs in the elderly.

The objective of this study was to determine the efficiency of neuroaxis block, compared to general anesthesia, for revascularization of the lower limbs in the elderly.

METHODS

This is a systematic review and metanalysis of randomized clinical trials⁴. The study was approved by the Ethics on Research Committee of the Universidade Federal de Alagoas. The study was funded by the authors. Original clinical studies, properly randomized, comparing neuroaxis block and general anesthesia for revascularization of the lower limbs were analyzed. Studies were not restricted by the language they were written on. The confidentiality of the allocation was also evaluated.

Adequate randomized distribution was defined as the allocation process that allowed every patient to have the same probability to be allocated to the intervention or experimental group and the control group⁵.

A strategy was developed for the search of the following data base: MEDLINE (1955 to 2007), CINHAI (1982 to 2007), EMBASE (1980 to 2007), Latin American and Caribbean Literature on Health Sciences — LILACS (1982 to 2007), and ISI Web of Science (1945 to 2007). The references of the studies that fulfilled the inclusion criteria were also analyzed to identify original studies that were not identified by the search of the data.

Inclusion criteria were as follows: original randomized clinical trials, age above 65 years, and comparing neuroaxis block and general anesthesia. Exclusion criteria included: inadequate randomized distribution, studies with incomplete description, and whenever patients from one of the study groups received combined neuroaxis block and general anesthesia.

Titles and summaries of all studies identified by the search were independently reviewed by two investigators. Afterwards, the full text of this group of studies was requested to evaluate the randomization. Data from studies with adequate randomized distribution were recorded on a standardized form developed by the authors, analyzed, and underwent statistical analysis. The following phases were followed by consensus meetings among the authors.

The Cochrane collaboration's software, Review Manager⁶, was used for the statistical analysis. Sensitivity evaluation was planned to explore heterogeneity sources when present. Statistical heterogeneity was quantified by the Chi-square (χ^2) and Higgins (I^2) tests⁷. Odds ratio (OR) with 95% confidence interval (CI) was used to evaluate the statistical difference among the groups analyzed. The random effects model was used.

The primary parameters of the present study included: mortality, myocardial infarction, stroke, muscular paralysis, and postoperative rate of lower limb amputation. Secondary parameters included: length of hospitalization, postoperative cognitive dysfunction, postoperative infection, pneumonia, hematoma of the neuroaxis, and complications in the recovery room.

RESULTS

The literature search identified 3,913 studies but, based on the inclusion criteria, only 21 were selected. Complete review of those studies showed that three of them, with a total of 465 patients, had adequate randomized distribution and were included in the present study (Table I)⁸⁻¹⁰. The references of those three studies, for a total of 158, were also analyzed and two were selected; however, they had already been identified by the search.

The incidence of stroke, muscle paralysis, postoperative cognitive dysfunction, neuroaxis neuroma, complications in the recovery room, degree of satisfaction, postoperative pain, urinary retention, blood transfusion, and length of hospitalization were not analyzed due to the lack of data in the three studies mentioned above.

The spinal block group had a mortality rate of 5%, in the epidural block group it was 4%, and in the general anesthesia group 6% ($p = 0.85$) and 3% ($p = 0.68$) when compared to the spinal and epidural blocks, respectively, and statistically significant differences were not observed (Figure 1).

Table I – List of Original Studies Included in the Assessment and Number of Patients in Each Group

Study	Sample size		Total
	Neuroaxis block	General anesthesia	
Cook et al. ⁸	50	51	101
Christopherson et al. ⁹	49	51	100
Pierce et al. ¹⁰	168	96	264
Total	267	198	465

Myocardial infarction had an incidence of 4% in the neuroaxis block group and 3% in the general anesthesia group ($p = 0.68$), but this difference was not statistically significant (Figure 2).

Lower limb amputation had an incidence of 6% in the spinal block group, 4% in the epidural block group, and 7% in the general anesthesia group ($p = 0.68$), when compared with the spinal block group, and 6% ($p = 0.52$) when compared with the epidural block group. Those differences were not statistically significant (Figure 3).

The neuroaxis block group had a 9% incidence of pneumonia, while the general anesthesia group had an incidence of

20% ($p = 0.03$); the difference was statistically significant and favored the neuroaxis block (Figure 4).

Heterogeneity was not observed in the statistical analyses, but clinical heterogeneity was seen for pneumonia due to the different techniques of neuroaxis block used. One study used spinal block⁹ and another used epidural block⁹.

DISCUSSION

The importance of the choice of anesthetic technique for lower limb revascularization has been debated for several years. During this period, clinicians developed strong convic-

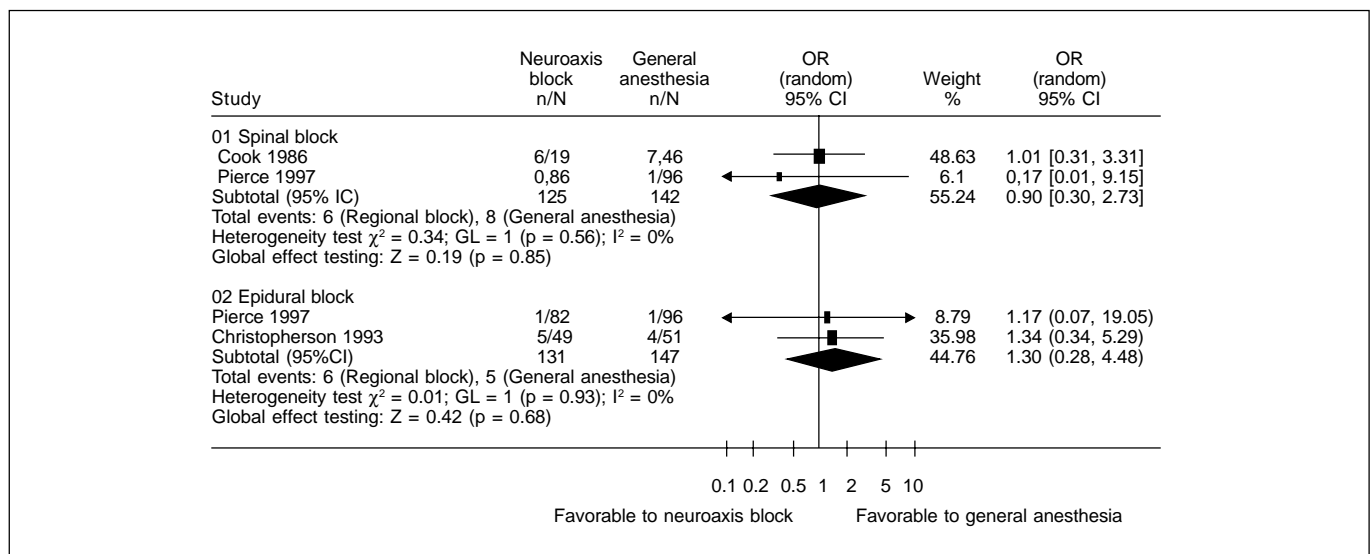


Figure 1 – Metaanalysis of Mortality in all Three Studies

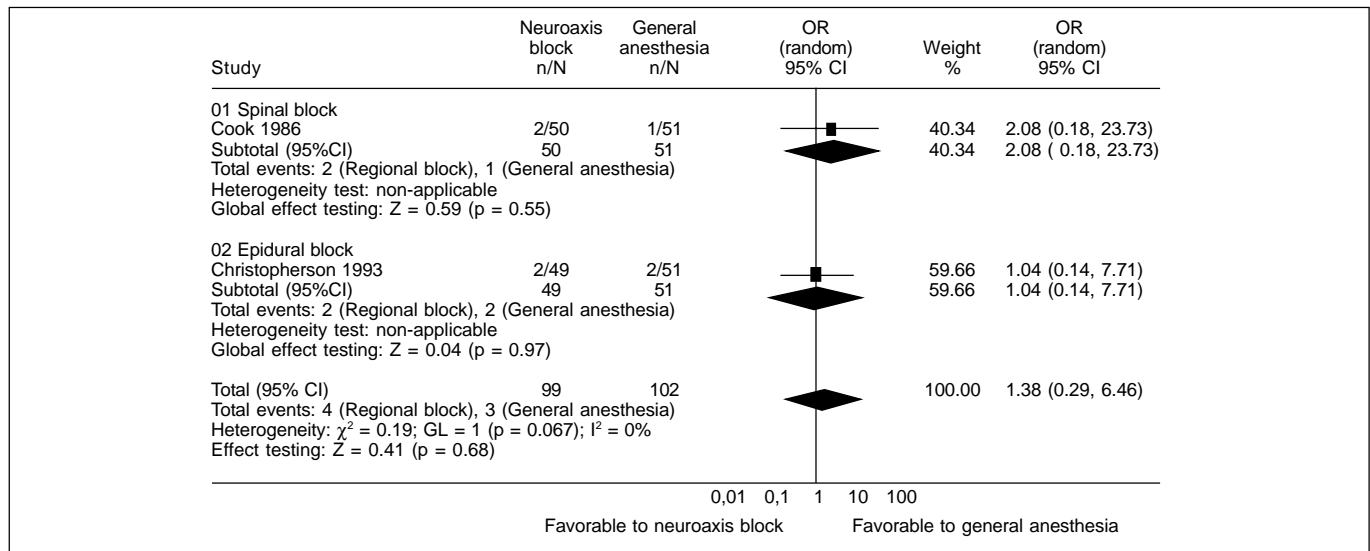


Figure 2 – Metaanalysis of Myocardial Infarction in Two Studies

NEUROAXIS BLOCK COMPARED TO GENERAL ANESTHESIA FOR REVASCULARIZATION OF THE LOWER LIMBS IN THE ELDERLY.
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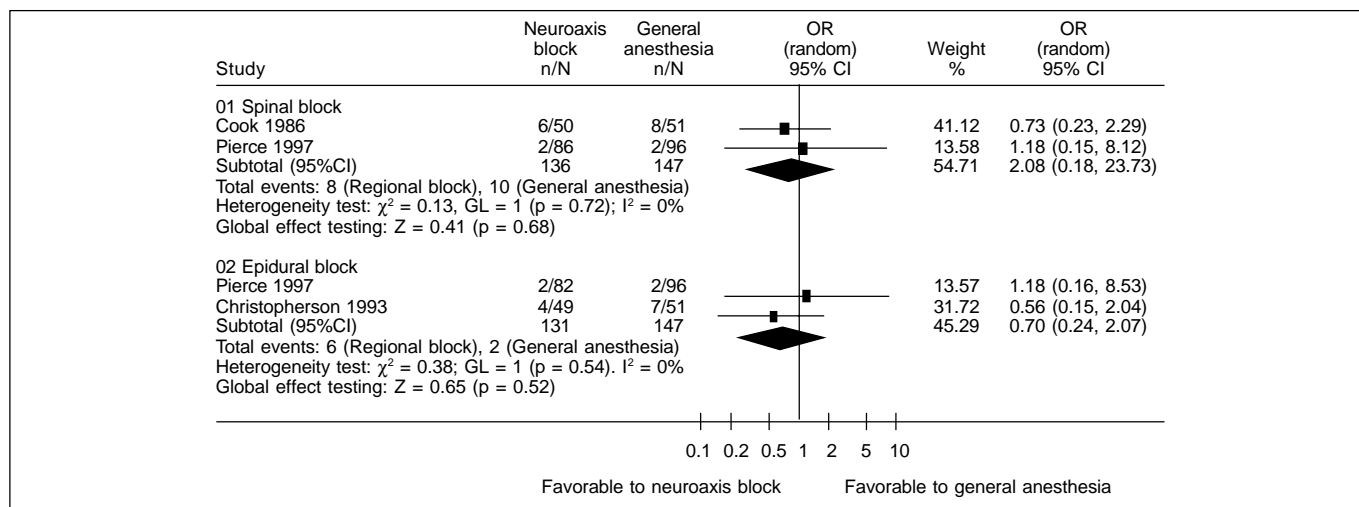


Figure 3 – Metanalysis of the Rate of Lower Limb Amputation in Two Studies

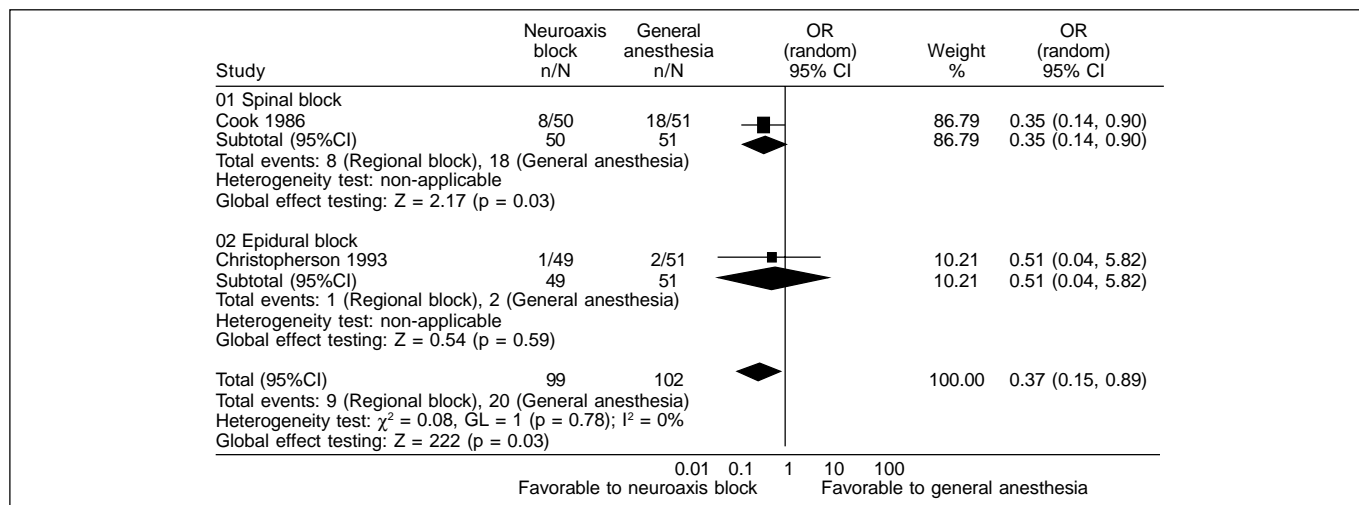


Figure 4 – Metanalysis of Pneumonia in Two of the Studies

tions that one should prefer techniques involving the neuroaxis¹¹. In the elderly, results from some research centers have demonstrated that postoperative cardiovascular mortality and morbidity of lower limb revascularization do not differ among the different anesthetic techniques used¹²; however, a systematic review has not been conducted to corroborate those results in the elderly.

In the present study, 3,913 scientific studies were identified, but only three⁸⁻¹⁰ fulfilled the inclusion criteria. Those studies had limitations due to one or more problems, such as: the number of patients was smaller than that predicted by calculating the sample size, difficulties with the double-blind nature of the study in the collection and analysis of the data, exclusions were not described, and the random distribution method and confidentiality were not completely described.

The limitations observed in those studies might have influenced their results.

Analysis of the mortality did not show statistically significant differences between both groups (OR: 0.90, CI 95%: 0.30-2.73, $p = 0.85$ for spinal blocks; OR: 1.30, CI 95%: 0.38- 4.48, $p = 0.68$ for epidural blocks). Other large studies on orthopedic surgery also failed to show statistically significant differences among the different anesthetic techniques in the elderly^{13,14}. The development of new drugs with a pharmacokinetic profile more suitable to be used in the elderly¹, better understanding of complications^{1,2}, and the discovery of newer protective strategies^{15,16} can justify and even maintain the same results in the next few years.

The incidence of myocardial infarction did not show statistically significant differences between the groups (OR: 1.38,

CI95%: 0.29-6.46, $p = 0.68$). The pathophysiology of perioperative myocardial infarction has not been completely elucidated; however, it seems to be associated with two factors¹⁷: imbalance between myocardial oxygen delivery and consumption, and rupture of the atheromatous plaque with the consequent thrombus formation and coronary obstruction. In anesthesia, this complication can be secondary to the increased oxygen consumption, reduction of oxygen delivery to the myocardium, or both¹⁸. Myocardial infarction can develop in both neuroaxis block and general anesthesia, since the sympathetic blockade seen after the use of local anesthetics can cause a reduction in venous return and left ventricular end-diastolic pressure, and hypotension, resulting in a reduction in coronary perfusion, when it is not properly treated, and general anesthesia might not be able to cause enough reduction in the surgical stress and endocrine response to trauma.

The rate of lower limb amputation did not show statistically significant differences (OR: 0.81, CI 95%: 0.30-2.19, $p = 0.68$ for spinal blocks; OR: 0.70, CI95%: 0.24-2.07, $p = 0.52$ for epidural block). The increase in blood flow at the vascular graft is an important determinant factor for the mean life of graft patency⁹. The authors of this systematic review assumed the hypothesis that the sympathetic blockade caused by the local anesthetic in the vertebral canal would increase blood flow in the lower limbs, leading to a lower incidence of postoperative amputation; however, the present study did not corroborate this effect. The use of a single dose of local anesthetic was described by the authors of those studies; therefore, one might infer that the vasodilation in the lower limbs was not prolonged, and this could justify the absence of statistically significant differences in the analysis of this parameter, since the authors considered the entire follow-up period and not only the immediate postoperative period.

The development of pneumonia showed statistically significant differences between the groups analyzed (OR: 0.37, CI 95%: 0.15-0.89, $p = 0.03$). Postoperative pulmonary complications are more common in elderly patients undergoing general anesthesia, not only due to physiological changes characteristic of aging, but also due to the possibility of prolonged mechanical ventilation after the procedure¹. The present study evaluated the incidence of pneumonia, and a greater contribution from one study⁸ was observed. In that study⁸, the authors report a greater number of elderly individuals and smokers in the general anesthesia group, but they did not describe the rate and correlated their results to the lack of humidification of the anesthetic gases. Analysis of the sensitivity also demonstrated clinical heterogeneity due to different techniques of neuroaxis blockade used by the authors to compare with general anesthesia^{8,9}. Removal of data from the original assay responsible for the heterogeneity is one of the possible measures to test the results; however, meta-analysis can only be done with the data of at least two studies. We concluded that the evidence generated by this systematic revision with meta-analysis was not enough to demonstrate

whether neuroaxis block is more efficient, equivalent, or less efficient than general anesthesia in lower limb revascularization in the elderly.

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RESUMEN

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NEUROAXIS BLOCK COMPARED TO GENERAL ANESTHESIA FOR REVASCLARIZATION OF THE LOWER LIMBS IN THE ELDERLY.
A SYSTEMATIC REVIEW WITH METANALYSIS OF RANDOMIZED CLINICAL STUDIES

JUSTIFICATIVA Y OBJETIVOS: La controversia actual es saber si la anestesia neuroaxial (AN) es más eficaz que la anestesia general (AG) en ancianos sometidos a la cirugía no cardíaca. El objetivo fue determinar la eficacia de la AN comparada con la AG para revascularización de miembros inferiores (RMI) en ancianos.

MÉTODO: Utilizada la estrategia de búsqueda para las bases de datos: MEDLINE (1955 a 2007), CINHALL (1982 a 2007), EMBASE (1980 a 2007), LILACS (1982 a 2007) y ISI (1945 a 2007). Dos revisores analizaron independientemente los artículos en busca de ensayos clínicos aleatorios (ECA) que comparasen la AN con la AG para la RMI. Se analizó el texto completo de los ECA que respetasen los criterios de inclusión. Las discordancias se analizaron en reuniones consensuales. El metanálisis fue realizado con el software Review Manager, por medio de la razón de chances con intervalo de confianza de un 95%.

RESULTADOS: Se seleccionaron tres artículos originales con 465 pacientes. No hubo significancia estadística en el metanálisis de las variables: mortalidad (OR: 0,90; IC 95%: 0,30 - 2,73; P = 0,85 raquianestesia; OR: 1,30; IC 95%: 0,38 - 4,48; P = 0,68 anestesia epidural), infarto miocárdico (OR: 1,38; IC 95%: 0,29 - 6,46; P = 0,68) y tasa de amputación de los miembros inferiores (OR: 0,81; IC 95%: 0,30 - 2,19; P = 0,68 raquianestesia; OR: 0,70; IC 95%: 0,24 - 2,07; P = 0,52 anestesia epidural). Hubo una significancia estadística para neumonía (OR: 0,37; IC 95%: 0,15 - 0,89; P = 0,03), sin embargo, hubo heterogeneidad clínica.

CONCLUSIONES: Las evidencias generadas en este metanálisis fueron insuficientes para demostrar que la AN es más eficiente, equivalente, o menos eficiente cuando se le compara con la AG para RMI en ancianos.