ABSTRACT

The number of fixed segments in the surgical treatment of thoracolumbar burst fractures remains controversial. This study aims to compare the results of short and long fixation in thoracolumbar burst fractures through a meta-analysis of studies published recently. MEDLINE and Cochrane databases were used. Randomized controlled trials and non-randomized comparative studies (prospective and retrospective) were selected. Data were analyzed with the software Review Manager. There was no statistically significant difference in the Cobb angle of preoperative kyphosis. Long fixation showed lower average measurements postoperatively (MD = 1.41; CI = 0.73–2.08; p = 0.00001) and in the last follow-up (MD = 3.98; CI = 3.22–4.75; p < 0.00001). The short fixation showed the highest failure rates (RD = 4.03; CI = 1.33–12.16; p = 0.01) and increased loss of height of the vertebral body (MD = 1.24; CI = 0.49–1.98; p = 0.001), with shorter operative time (MD = −24.54; CI = −30.16–−18.91; p < 0.00001). There was no significant difference in blood loss and clinical outcomes. The high rates of kyphosis correction loss with short fixation and the lower correction rate in the immediate postoperative period were validated. There was no significant difference in the blood loss rates because arthrodesis was performed in a short segment in the analyzed studies. The short fixation was performed in a shorter operative time, as expected. No study has shown superior clinical outcomes. The short fixation had worse rates of kyphosis correction in the immediate postoperative period, and increased loss of correction in long-term follow-up, making the long fixation an effective option in the management of this type of fracture.

Keywords: Thoracolumbar fractures; Short fixation; Long fixation; Meta-analysis; Posterior fixation.

RESUMEN

El número de segmentos fijados en el tratamiento quirúrgico de las fracturas toracolombares tipo explosión sigue siendo controvertido. Este estudio tiene como objetivo comparar los resultados de la fijación corta y larga en las fracturas toracolombares tipo explosión, por medio de una metanálisis de los estudios publicados recientemente. Se utilizaron como bases de datos MEDLINE y COCHRANE. Se seleccionaron ensayos controlados randomizados y estudios comparativos no randomizados (prospectivos y retrospectivos). Los datos fueron analizados con el software Review Manager. No hubo diferencia estadísticamente significante en la medida del ángulo de Cobb de la cifosis preoperatoria. La fijación larga presentó medidas menores en el pós-operativo (MD = 1.41; IC = 0.73–2.08; p < 0.00001) y en el último seguimiento (MD = 3.98; IC = 3.22–4.75; p < 0.00001). La fijación corta presentó taxas de fracaso mayores (RD = 4.03; IC = 1.33–12.16; p = 0.01) y mayor pérdida de altura del cuerpo vertebral (MD = 1.24; IC = 0.49–1.98; p = 0.001), con menor tiempo operatorio (MD = −24.54; IC = −30.16–−18.91; p < 0.00001). No hubo diferencia estadísticamente significante en la pérdida de sangre y los resultados clínicos. Se validaron las altas tasas de pérdida de corrección de la cifosis con la fijación corta y la menor tasa de corrección en el pós-operatorio inmediato. No hubo diferencia significativa en las tasas de pérdida de sangre porque se hizo arthrodesis en un segmento corto en los estudios analizados. La fijación corta tuvo menor tiempo operatorio, como se esperaba. Ningún estudio ha demostrado resultados clínicos superiores. La fijación corta tuvo peores tasas de corrección de la cifosis en el pós-operatorio inmediato y mayor pérdida de corrección en el seguimiento a largo plazo, por lo que la fijación larga es una opción efectiva en el manejo de este tipo de fracturas.

Descritores: Fraturas toracolombares; Fixação curta; Fixação Longa; Metanálise, Fixação Posterior.
INTRODUCTION

Fractures of the vertebral spine are among the most feared lesions among patients and physicians, and their consequences can be devastating, ranging from mild pain and discomfort to serious paralysis and even death.\(^1\)\(^-\)\(^4\) Traffic accidents, falls, and sports accidents are the cause of the majority of these lesions.\(^5\)\(^-\)\(^7\) Associated injuries are common, such as rib fractures, bronchial rupture, pulmonary contusion or myocardial infarction, lesions of large vessels, cardiac tamponade and rupture of the diaphragm, in addition to fractures of the long bones. Some degree of neurological lesion is also common.\(^8\)

The majority of these fractures occur in the thoracolumbar region, presumably because this is a junction of the thoracic spine, which is relatively immobile, and the lumbar spine, which is relatively mobile.\(^9\)\(^-\)\(^10\) This is also the most common site of unstable burst fractures, representing about 15% of vertebral spine injuries.\(^7\)\(^,\)\(^11\)

In 1983, Denis\(^12\) proposed his "three column spine" theory, taking the sagittal plane as reference. The anterior column consists of the front half of the vertebral body and the anterior longitudinal ligament; the middle column includes the posterior half of the vertebral body and the posterior longitudinal ligament; and the posterior column includes the laminae, the facet joints, and the spinous processes with their corresponding ligaments. Thus, thoracolumbar burst fracture was defined as a lesion that involves the anterior and middle columns. A burst fracture is characterized by displacement or rotation of the posterior cortical of the vertebral body, compressing the spinal canal and altering the stability of vertebral spine. There is a greater concentration of load directly on the middle spine during the axial trauma, in the region comprised of the vertebral pedicles, which results in their pulling apart, and retropulsion of fragments from the posterior portion of the vertebral body toward the spinal canal. Denis considered thoracolumbar burst fractures to be unstable, as they involve at least two of his "columns".\(^12\)

There are still controversies in relation to the stability criteria and the treatment options for burst fractures.\(^11\)\(^-\)\(^14\) Radiographic signs that include enlargement of the interspinous and interlaminar space, translation of the vertebral body greater than 2 mm, kyphosis greater than 20 degrees, loss of height or compression of the spinal canal of more than 50%, and fracture of the articular processes, are the most widely accepted parameters for the assessment of stability of the fracture.\(^15\)\(^,\)\(^16\)

Although many studies have obtained good results with conservative treatment of thoracolumbar burst fractures,\(^17\)\(^-\)\(^19\) most authors agree that surgical treatment is necessary for unstable burst fractures.\(^20\)\(^-\)\(^21\) Surgical intervention can decompress neural elements, restore the height of the vertebral body, correct and prevent angular deformity, and promote stability of the vertebral spine, allowing early mobilization and promoting neurological improvement.\(^22\)\(^,\)\(^23\)

The best option for surgical treatment of thoracolumbar fractures remains controversial, despite the greater knowledge of biomechanics and advances in surgical techniques. To date, no one method has proven to be the most suitable for the treatment of all types of lesions of the vertebral spine.\(^24\)\(^,\)\(^25\)

Anterior and posterior approaches are associated with satisfactory results in the treatment of thoracolumbar injuries. However, they are not without complications, depending on various clinical and radiographic factors such as the patient’s age, degree of impairment of the medullary canal, sagittal index, height of the vertebral body, degree of integrity of posterior elements and presence of neurological deficit.\(^26\)\(^,\)\(^27\) Posterior instrumentation is recommended by many authors, based on the excellent results achieved in terms of stability of the spine, anatomical alignment, postoperative neurological improvement, and low patient morbidity.\(^27\)\(^-\)\(^28\)

Numerous pedicular fixation methods through a posterior approach have been described.\(^24\)\(^,\)\(^25\) One of the main differences between them is the number of fixed segments.\(^30\) Short fixations, with fewer stabilized and fused uninjured segments, can preserve the maximum thoracolumbar movement. However, unacceptable failure rates have been demonstrated in this kind of fixation, particularly in terms of the loss of correction of the kyphosis produced by the fracture.\(^31\)

The aim of this study is to compare the results of surgical treatment of thoracolumbar burst fractures using the posterior approach with short versus long fixation, through a meta-analysis of recent published studies.

MATERIALS AND METHODS

Search Strategies

A literature search was performed using the MEDLINE databases and the center for clinical trials records of COCHRANE. We used the search terms "thoracolumbar fractures", "short-segment" and "long-segment", in different combinations. We also conducted a direct search of the studies included in the references to the articles found in the initial search. There was no restriction as to the language of the publication. The titles and abstracts of the works found in the electronic searches were evaluated. The full texts were then obtained for the articles selected.

Selection Criteria and Quality Evaluation

Finding only a small number of available controlled, randomized studies, we included also non-randomized comparative studies (prospective and retrospective). The inclusion criteria used were: 1) making a comparison between long and short fixation of fractures of the thoracolumbar junction; 2) evaluating adult patients with non-pathological thoracolumbar fractures; 3) Posterior approach with pedicular fixation as the sole technique chosen for the treatment; 4) complete articles in full. Articles with one of the following characteristics were excluded: 1) Biomechanical studies in cadavers, opinions and case reports; 2) repeated studies; 3) studies with the same (or part of) the patients from works already selected.

To evaluate the methodological quality of the studies included, we used different tools, according to the presence or not of randomization. For the non-randomized studies, the MINORS\(^32\) score was used, with a possible maximum of 24 points. For randomized prospective controlled studies, we used the Detsky Quality Scale\(^33\) which has a total score of 20 for possible assays and 21 for negative ones. Studies with values higher than 75% of the maximum score for the above scales were considered high quality.

Data Extraction

Information was collected on the study design, patients’ profile, inclusion and exclusion criteria, interventions, outcomes and clinical and radiographic follow-up (duration and rate of loss).

Analysis of the data and statistical methods

The data were analyzed using the software Review Manager (RevMan) 5.1, with guidance from the Cochrane. We evaluated the heterogeneity of articles using the standard Chi square test, considering a statistical significance of p>0.05, and measurement of I\(^2\), in which values higher than 50% were considered substantial heterogeneity. In the existence of heterogeneity, we applied random effects to the data selected. Otherwise, we used the fixed effects model. Differences in risk and 95% confidence interval (CI) were calculated for the dichotomous outcomes, and the median and 95% CI were calculated for the continuous outcomes.

RESULTS

The search strategy identified 476 articles, five of which met the pre-defined inclusion criteria pre-defined for the extraction of the data to be used in this meta-analysis. (Figure 1)

After compiling the contents obtained in these studies, we ob-
tained a total of 189 patients, of which 91 underwent short fixation and 98 were treated with long fixation. The scores for the quality assessment ranged between 67% and 85% of the maximum scores for the scales used. The patient characteristics were similar in the majority of the groups evaluated. The mean age ranged from 32 to 44.8 years. A predominance of female patients was found only in the short fixation group of the study of Serín et al. and in the article of Guven et al. The first lumbar vertebra was the one most affected in all groups. The follow-up times ranged from 12 to 52 months. (Table 1)

Radiographic Evaluation

Local kyphosis, measured through the upper plateau of upper vertebra to the fractured level, and the lower plateau of the lower vertebra to the fractured level, as described by the Cobb method, was evaluated in all studies. There was no statistically significant difference in the evaluation of preoperative Cobb angle. In the postoperative evaluation the long fixation group presented smaller average measurements than those of the short fixation group (MD = 1.41; CI = 0.73 - 2.08; p < 0.0001). In the analysis of Cobb angle of the last segment, the short fixation group obtained larger measurements (MD = 3.98; CI = 3.22 - 4.75; p < 0.0001). (Tables 2, 3 and 4)

Altay et al., Serín et al. and Tezeren et al. defined fixation failure as loss of kyphosis as correction of 10 degrees or more. According to this criterion, the short fixation group presented higher failure rates higher than the long fixation group (RD = 4.03; CI = 1.33 - 12.16; p = 0.01). (Table 5)

Table 1. Characteristics of the studies included.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Nationality</th>
<th>Study Design</th>
<th>Quality Scale</th>
<th>Groups</th>
<th>No of Patients</th>
<th>Mean age (years)</th>
<th>Sex M-F</th>
<th>Fracture level</th>
<th>Follow-up time (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapkas et al</td>
<td>2010</td>
<td>Greece</td>
<td>Prospective Non-Randomized</td>
<td>18/24 (75%)</td>
<td>Short fixation 20</td>
<td>33 (13-52)</td>
<td>(12/08)</td>
<td>L1 = 23</td>
<td>34 (25-70)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long fixation 30</td>
<td>35 (17-55)</td>
<td>(20/10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serín et al</td>
<td>2004</td>
<td>Turkey</td>
<td>Prospective Non-Randomized</td>
<td>19/24 (79%)</td>
<td>Short fixation 12</td>
<td>32.4 (+/-9.5)</td>
<td>(4/8)</td>
<td>L1 = 6</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long fixation 10</td>
<td>35.5 (+/-13.6)</td>
<td>(7/3)</td>
<td>L1 = 4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Altay et al</td>
<td>2007</td>
<td>Turkey</td>
<td>Retrospective</td>
<td>16/24 (67%)</td>
<td>Short fixation 32</td>
<td>42.6 (+/-14.9)</td>
<td>(19/13)</td>
<td>L1 = 13</td>
<td>36 (18-58)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long fixation 31</td>
<td>44.8 (+/-14.9)</td>
<td>(18/13)</td>
<td>L1 = 16</td>
<td>33 (18-58)</td>
<td></td>
</tr>
<tr>
<td>Tezeren et al</td>
<td>2005</td>
<td>Turkey</td>
<td>Prospective randomized</td>
<td>15/20 (75%)</td>
<td>Short fixation 9</td>
<td>32 (+/-13)</td>
<td>(7/2)</td>
<td>L1 = 7</td>
<td>29 +/-5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long fixation 9</td>
<td>34 (+/-11)</td>
<td>(8/1)</td>
<td>L1 = 7</td>
<td>29 +/-4</td>
<td></td>
</tr>
<tr>
<td>Guven et al</td>
<td>2009</td>
<td>Turkey</td>
<td>Prospective randomized</td>
<td>17/20 (85%)</td>
<td>Short fixation 18</td>
<td>37.4 (+/-3.7)</td>
<td>13.23</td>
<td>L1 = 10</td>
<td>48.1 +/- 13.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long fixation 18</td>
<td>40.8 (+/-7.2)</td>
<td></td>
<td>L1 = 7</td>
<td>52.1 +/- 13.8</td>
<td></td>
</tr>
</tbody>
</table>

Table 02. Forest plot showing the preoperative Cobb angle.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Short Fixation</th>
<th>Long Fixation</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (Degrees)</td>
<td>SD Degrees</td>
<td>Total Mean (Degrees)</td>
<td>SD Degrees</td>
</tr>
<tr>
<td>Altay 2007</td>
<td>20.7</td>
<td>4.6</td>
<td>32</td>
<td>18.9</td>
</tr>
<tr>
<td>Guven 2009</td>
<td>21.3</td>
<td>11.1</td>
<td>18</td>
<td>20.6</td>
</tr>
<tr>
<td>Sapkas 2010</td>
<td>17</td>
<td>7</td>
<td>20</td>
<td>17.5</td>
</tr>
<tr>
<td>Serín 2004</td>
<td>18</td>
<td>6.8</td>
<td>12</td>
<td>19.1</td>
</tr>
<tr>
<td>Tezeren 2005</td>
<td>19</td>
<td>1</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>91</td>
<td>98</td>
<td>91</td>
<td>91</td>
</tr>
</tbody>
</table>

Heterogeneity:
Chi² = 4.35, df = 4 (P = 0.36); I² = 8%
Test for overall effect:
Z = 0.35 (p = 0.73)
Guven and col.,47 Serín et al.,31 Tezeren et al.,48 assessed the loss of height of the vertebral body. The group also presented poor short fixations in the analysis of postoperative results (MD =1.24; CI = 0.49 - 1.98; p = 0.001) and in the last segment (MD = 6.53; CI = 5.82 - 7.24; p< 0.00001). (Tables 6, 7 and 8)

Surgical time
Four clinical trials evaluated the surgical time (Guven et al.,47 Serín et al.,31 Tezeren et al.,48 Sapkas et al.49 The short fixation group obtained lower mean surgical times, compared with the long fixation group, with statistically significant difference (MD = -24.54; CI = -30.16 - 18.91; p<0.0001). (Table 9)

Blood loss
Guven et al.,47 Sapkas et al.,49 Tezeren et al.,48 assessed blood loss, and found no statistically significant difference between the groups. (Table 10)

Table 03. Forest plot showing the postoperative Cobb angle.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Short Fixation</th>
<th>Long Fixation</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (Degrees)</td>
<td>SD (Degrees)</td>
<td>Total Mean (Degrees)</td>
<td>SD (Degrees) Total</td>
</tr>
<tr>
<td>Altay 2007</td>
<td>7.8</td>
<td>5.3</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>Guven 2009</td>
<td>8.5</td>
<td>2.2</td>
<td>18</td>
<td>6.5</td>
</tr>
<tr>
<td>Sapkas 2010</td>
<td>5</td>
<td>3.5</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Serín 2004</td>
<td>6.5</td>
<td>3.8</td>
<td>12</td>
<td>7.6</td>
</tr>
<tr>
<td>Tezeren 2005</td>
<td>4</td>
<td>1</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>91</td>
<td>98</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² 5.46, df = 4 (P = 0.24); I² = 27%
Test for overall effect: Z = 4.07 (P < 0.0001)

Table 04. Forest plot showing the follow-up Cobb angle.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Short Fixation</th>
<th>Long Fixation</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (Degrees)</td>
<td>SD (Degrees)</td>
<td>Total Mean (Degrees)</td>
<td>SD (Degrees) Total</td>
</tr>
<tr>
<td>Altay 2007</td>
<td>13</td>
<td>6.2</td>
<td>32</td>
<td>8.1</td>
</tr>
<tr>
<td>Guven 2009</td>
<td>12.2</td>
<td>3.6</td>
<td>18</td>
<td>8.2</td>
</tr>
<tr>
<td>Sapkas 2010</td>
<td>8.5</td>
<td>6</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>Serín 2004</td>
<td>16.7</td>
<td>8</td>
<td>12</td>
<td>12.4</td>
</tr>
<tr>
<td>Tezeren 2005</td>
<td>10</td>
<td>1</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>91</td>
<td>98</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² 1.42, df = 4 (P = 0.84); I² = 0%
Test for overall effect: Z = 10.16 (P < 0.00001)

Table 05. Forest plot showing fixation failure.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Short Fixation</th>
<th>Long Fixation</th>
<th>Risk ratio</th>
<th>Risk ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Altay 2007</td>
<td>6</td>
<td>32</td>
<td>2</td>
<td>31</td>
</tr>
<tr>
<td>Serín 2004</td>
<td>5</td>
<td>12</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Tezeren 2005</td>
<td>5</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>53</td>
<td>50</td>
<td>100.0%</td>
<td>4.03 (1.33, 12.16)</td>
</tr>
<tr>
<td>Total events</td>
<td>16</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00, Chi² = 0.71, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 2.47 (P = 0.01)
Clinical Evaluation

Different instruments were used for to assess the clinical results (pain scale of Denis, Likert questionnaire, Low Back Outcome Score - LBOS), making statistical analysis more difficult. No study found statistically significant difference in clinical outcomes.

DISCUSSION

The treatment of thoracolumbar fractures remains controversial, despite the increase of open-surgery following the introduction of surgical instrumentation. The Harrington system, initially developed to treat scoliosis, in 1958, was later adapted for spinal fractures, and was gradually replaced by pedicle screws, as described by Boucher in 1959. In 1963, Roy-Camille et al. described the association of plates with the pedicle screw. In 1985, Dick et al. described a new instrumentation technique, known as “internal fixation”, and proposed, through it, a short fixation method for the treatment of spinal fractures.

Initially, short instrumentation was considered a method of instrumentation that would bring the advantages of sparing arthrodesis levels in the surgical treatment of spinal fractures. However, subsequent work showed high rates of failure of this technique. A greater kyphotic deformity would result in higher anterior vertebral stress transmitted to the pedicle screws, which would explain these failures. Long fixation distributes the stress between the screws, and also promotes greater correction of the kyphotic deformity, which decreases the demand for instrumentation material and, consequently, the chance of failure.

Yu et al. and McLain et al. showed high rates of loss of kyphosis correction during follow-up of patients submitted to short posterior fixation. These results were validated in our study, in which the analysis of the studied data enabled us to confirm sta-
THORACOLUMBAR BURST FRACTURES, SHORT X LONG FIXATION: A META-ANALYSIS

Statistical significance not only for loss of kyphosis correction, with \( p < 0.00001 \), but also a lower rate of correction rate measured immediately after surgery (\( p < 0.0001 \)).

Alanay et al. \(^{42} \) defined fixation failure as loss of kyphosis correction of more than 10º. That study obtained fixation failure rates of 40% and 50% in each group. In our meta-analysis, we were able to use this criterion in three of the studies, with the statistical analysis showing a high failure rate in short fixation during the patient follow-up, with statistical significance (relative risk of 4.03 \([1.33 - 12.16]\) and \( p < 0.01 \)).

Although it is a surgical technique that requires lower intervention and less instrumentation, the short fixation group did not obtain a statistically significant difference in terms of blood loss. This can be explained by the fact that the arthrodesis was performed on one segment only in all the studies analyzed, regardless of whether the fixation was long or short.

As expected, because it uses less instrumentation, short fixation was superior in the analysis of surgery times. It resulted in shorter surgery times, with a mean difference of 24.54 minutes \([30.16 - 18.91]\) (\( p < 0.00001 \)).

Despite the better radiographic results of long fixation, no study demonstrated superiority any of the fixation types compared, in terms of clinical and functional results. The different parameters used to analyze the clinical results in the works evaluated did not allow for comparison of these data.

CONCLUSION

This meta-analysis demonstrates that the surgical treatment of unstable thoracolumbar burst fractures using a short fixation presented poorer rates of kyphosis correction immediately after surgery, and greater loss of this correction in the long-term follow-up of patients, compared to long fixation. These radiographic findings make long fixation an effective option in the management of thoracolumbar burst fractures type. Despite the higher rate of failures with short fixation, it has shorter surgical times. The clinical outcome could not be evaluated in this meta-analysis, although no statistically significant differences were shown in the data for the studies evaluated.

All authors declare no potential conflict of interest concerning this article.

CONTRIBUTIONS OF THE AUTHORS: Each author made a significant individual contribution to the development of the manuscript. CAAF carried out the research, production, editing and supervision. FCS and gOP carried out the research and production.
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