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REVIEW

Effect of preoperative botulinum toxin injection in the treatment of giant incisional hernias: a systematic review and meta-analysis

Yasmin Mejía-Saavedra[1] · Analý Mejía-Saavedra[1] · José Caballero-Alvarado[1,2] · Carlos Zavaleta-Corvera[3] · Víctor Lau-Torres[4] · Katherine Lozano-Peralta[1]

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Abstract

Introduction Giant incisional hernias pose a significant surgical challenge due to their high morbidity, risk of postoperative complications, and recurrence. Preoperative botulinum toxin type A (BTX-A) injection has emerged as a novel intervention to optimize fascial closure by reducing abdominal wall muscle tension, facilitating surgical repair, and potentially decreasing postoperative complications.

Objective To evaluate the effect of preoperative BTX-A injection on fascial closure rates, postoperative complications, hernia recurrence, and hospital length of stay in patients undergoing repair of giant incisional hernias.

Methods A systematic review and meta-analysis were conducted according to PRISMA guidelines. Studies assessing the outcomes of BTX-A injection in the management of giant incisional hernias were included. The primary outcomes were the rate of complete fascial closure and hernia recurrence. Secondary outcomes included postoperative complications and length of hospital stay. Risk ratios (RR) and mean differences (MD) with 95% confidence intervals (CI) were calculated using a random-effects model.

Results Five articles were selected and included in this systematic review. BTX-A injections showed a positive trend toward improved fascial closure in certain studies, although global analysis did not reveal statistically significant differences compared to controls (RR = 0.95; 95% CI: 0.90–1.01). There was no significant effect on hernia recurrence (RR = 1.02; 95% CI: 0.64–1.49). However, BTX-A significantly reduced postoperative complications (RR = 0.66; 95% CI: 0.50–0.88), with no meaningful reduction in the length of hospital stay (MD = -0.72 days; 95% CI: -1.8 to 0.36).

Conclusion Preoperative BTX-A injection is a safe adjunct but has not shown significant benefits in improving fascial closure or reducing hernia recurrence. Although it reduces postoperative complications, its overall clinical impact is limited. Current evidence does not support its routine use, and further high-quality RCTs are needed.

Keywords (DeCS/MeSH) · Hernia · Ventral · Botulinum toxins · Type A · Herniorrhaphy · Postoperative complications · Length of stay

Introduction

Giant incisional hernias remain a significant challenge for surgeons due to their complexity and the high rates of morbidity and recurrence associated with them [1]. The European Hernia Society classifies these hernias based on their width in centimeters: W1 (<4 cm), W2 (4–10 cm), and W3 (>10 cm) [2]. Other sources also categorize them as complex, large, or giant hernias [1, 3]. Giant incisional hernias are defined as those measuring more than 10 cm in width, with or without loss of domain [3]. This condition occurs when the abdominal wall defect enlarges to the point where the abdominal cavity can no longer accommodate

✉ Carlos Zavaleta-Corvera
czavaletac3@upao.edu.pe

1 Faculty of Medicine, Antenor Orrego Private University, Trujillo 13007, Peru

2 Department of Surgery, Regional Hospital of Trujillo, Trujillo 13007, Peru

3 Faculty of Medicine, Universidad Científica del Sur, Av Panamericana Sur Km 19, Lima 15067, Peru

4 Faculty of Medicine, National University of Trujillo, Trujillo 13007, Peru

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the viscera, allowing their protrusion into the hernial sac [4]. This scenario can lead to severe complications such as back pain, paradoxical respiratory movements, mesenteric edema, intestinal dysfunction, skin necrosis, enterocutaneous fistulas, and aesthetic deformities [1].

The incidence of these hernias has increased, with rates ranging from 11 to 23% within three years after the initial surgery [5]. This rise is linked to difficulties in achieving adequate fascial closure due to chronic abdominal muscle contractions, which reduce the abdominal cavity's volume [1, 4–8]. Consequences include intense postoperative pain, wound dehiscence, intra-abdominal hypertension, ventilatory compromise, abdominal compartment syndrome, and frequent recurrences. Recurrence rates range from 9 to 12% for open repairs and 7–10.6% for laparoscopic approaches [7].

Surgical treatments for giant incisional hernias include component separation techniques, retromuscular tension-free repair, mesh placement, autologous tissue repairs, and myofascial coaptation [9]. The component separation technique involves the controlled mobilization of the abdominal wall's myofascial layers (external oblique, internal oblique, and transversus abdominis) to close the hernial defect using autologous, vascularized, and innervated tissue. This approach aims to reduce tension during closure, minimize the need for prosthetic materials, and restore abdominal wall functionality. The technique can be performed via an anterior approach (Ramírez technique) or a posterior approach (transversus abdominis release, TAR), which provides additional medialization of the rectus abdominis muscles for more complex defects [9, 10]. The Ramírez technique, one of the most widely recognized and utilized for large hernial defects, involves the controlled release of the external oblique aponeurosis, facilitating medial mobilization of the myofascial layers and allowing reconstruction of the linea alba, thus restoring fascial continuity and abdominal wall function.

Despite their effectiveness, these techniques are associated with high postoperative morbidity rates of up to 30% [3, 5, 11]. To overcome these limitations, preoperative techniques such as botulinum toxin type A (BTX-A) injection and progressive pneumoperitoneum have been proposed. This systematic review focuses on the use of BTX-A, a neurotoxin derived from *Clostridium botulinum* that inhibits the release of acetylcholine at presynaptic nerve terminals, causing localized muscle paralysis [7, 9, 10, 12]. Its preoperative use relaxes the lateral abdominal wall muscles, increases abdominal compliance, reduces the size of the defect, and facilitates effective fascial closure [13, 14]. This chemical component separation effect peaks between 2 and 4 weeks post-injection and typically lasts for 2 to 5 months [9, 10], with some studies reporting effects lasting up to 6 months [3, 13, 14]. A distinctive feature of BTX-A is its localized pharmacological action, with a diffusion area limited to 2 cm around the injection site, providing additional safety for patients [15].

BTX-A injection is contraindicated in patients with neuromuscular diseases such as myasthenia gravis, amyotrophic lateral sclerosis, or polyneuropathies due to the risk of worsening these conditions. It is also restricted in pregnant or breastfeeding women, as there is insufficient evidence regarding its safety in these populations [12]. The procedure is typically performed four weeks before the scheduled surgery under ultrasound guidance, targeting the three lateral muscle layers: external oblique, internal oblique, and transversus abdominis [9, 16].

Recent studies have demonstrated the effectiveness of BTX-A. PHF Amaral et al. (2024) reported successful fascial closure in 92.6% of patients treated with BTX-A, with a significant reduction in hernia width and elongation of the lateral abdominal muscles [17]. Nielsen et al. (2020) observed a 100% fascial closure rate with no adverse events related to BTX-A administration [18]. Similarly, Elstner et al. (2016) reported a significant increase of 4.2 cm in lateral abdominal wall length and a reduction of up to 58% in defect size, achieving tension-free fascial closure in all cases [19]. Faisal F. et al. (2015) documented a notable elongation of the lateral muscles and no early recurrences in patients treated with mesh repairs [20].

Key factors such as the ability to achieve complete fascial closure, reduce postoperative complications, and shorten hospital stays are critical when evaluating the effectiveness of BTX-A as a preoperative technique [21–23]. Despite its potential, the lack of robust evidence limits its widespread adoption. Therefore, this systematic review and meta-analysis aim to update current knowledge, address gaps in the scientific literature, and provide surgeons with an additional preoperative tool to plan surgical procedures more effectively, improve clinical outcomes, and facilitate patient recovery.

Materials and methods

Study design

This systematic review and meta-analysis were conducted following the PRISMA 2020 guidelines. This review was conducted as a secondary study synthesizing evidence from primary research articles. The objective was to evaluate the effect of preoperative BTX-A injections on surgical outcomes in patients undergoing repair for giant incisional

hernias. The protocol was designed using the PICO framework to define the research question and eligibility criteria clearly.

Eligibility criteria

Studies were selected based on predefined inclusion and exclusion criteria. Eligible studies included adult patients (≥18 years old) diagnosed with giant incisional hernias, defined as defects larger than 10 cm in width, with or without loss of domain. The intervention of interest was preoperative BTX-A injection before surgical hernia repair, compared with conventional surgical treatment without BTX-A injection. The primary outcomes assessed were the rate of fascial closure and hernia recurrence, while secondary outcomes included postoperative complications (such as seroma, hematoma, and surgical site infection) and length of hospital stay.

Studies were eligible for inclusion if they were randomized controlled trials (RCTs), cohort studies, case-control studies, or propensity score-matched analyses. Only studies reporting at least one of the predefined outcomes were considered. Excluded studies comprised case reports, case series, narrative reviews, scoping reviews, systematic reviews, editorials, and letters to the editor. Additionally, studies involving pediatric populations, non-comparative research, or those lacking complete data were excluded.

Information sources and search strategy

A comprehensive literature search was performed in the following databases: PubMed, Scopus, Web of Science, Embase, Ovid MEDLINE, and the Cochrane Library. Manual searches of the gray literature and reference lists from relevant reviews were also conducted to identify additional studies. The search strategy incorporated a combination of Medical Subject Headings (MeSH) and DeCS terms. Key search terms included "Incisional Hernia," "Giant Incisional Hernia," "Ventral Hernia Repair," "Botulinum Toxins, Type A," "Botulinum Toxin Injection," and "Clostridium botulinum Toxin A." No language restrictions were applied, and no date filters were imposed to ensure the inclusion of all relevant literature.

Study selection process

All retrieved articles were imported into the Rayyan QCRI platform for systematic screening. Duplicate records were automatically removed, and the remaining titles and abstracts were independently screened by two reviewers for eligibility. Full-text articles of potentially relevant studies were retrieved for a detailed assessment. Disagreements between reviewers were resolved through discussion or consultation with a third reviewer. The selection process was documented using a PRISMA flow diagram, which outlined the number of studies screened, excluded, and ultimately included in the review.

Data extraction process

Two reviewers independently extracted data using a standardized data collection form developed in Microsoft Excel 2019. The extracted information included the following: Study characteristics: first author, year of publication, country, study design, sample size, and duration of follow-up. Patient characteristics: number of participants in the intervention and control groups, mean age, and sex distribution. Intervention details: BTX-A dosage, injection site, timing before surgery (in weeks), and whether ultrasound guidance was used. Surgical technique: details on the type of surgical repair (e.g., component separation, mesh placement, or retromuscular repair). Clinical outcomes: fascial closure rate, hernia recurrence rate, postoperative complications (seroma, hematoma, surgical site infection, mesh infection), and length of hospital stay (in days).

Risk of bias assessment

The methodological quality of the included studies was independently assessed by two reviewers. Randomized controlled trials (RCTs) were evaluated using the Cochrane Risk of Bias 2 (ROB-2) tool, which considers factors such as random sequence generation, allocation concealment, blinding of participants and outcome assessors, completeness of outcome data, selective reporting, and other potential sources of bias. Non-randomized studies were assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool, which evaluates confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selection of reported results. Any disagreements were resolved through discussion or adjudication by a third reviewer.

Data synthesis and statistical analysis

Data analysis was performed using Review Manager (RevMan) 5.4. Dichotomous outcomes, such as fascial closure, hernia recurrence, and postoperative complications, were expressed as Risk Ratios (RR) with 95% Confidence Intervals (CI). Continuous outcomes, such as the length of hospital stay, were analyzed using Mean Differences (MD) and 95% CI. A random-effects model (Mantel-Haenszel method) was applied to account for heterogeneity across studies.

Heterogeneity was quantified using the I^2 statistic. An I^2 value of less than 30% was considered low heterogeneity, between 30% and 60% was considered moderate, and greater than 60% indicated high heterogeneity. Subgroup analyses were conducted when possible based on study design (RCTs vs. observational studies), presence of loss of domain, and type of surgical repair technique. Sensitivity analyses were also performed to assess the robustness of the results by excluding studies with a high risk of bias. Publication bias was evaluated using funnel plots if at least 10 studies were available for analysis.

Ethical considerations

Since this study was based on the analysis of previously published data, no ethical approval was required. The research adhered to ethical principles as outlined in the Declaration of Helsinki, ensuring that all included studies had received appropriate ethical approval in their original contexts.

Registration

This systematic review and meta-analysis were registered in the International Prospective Register of Systematic Reviews (PROSPERO) to ensure methodological transparency and minimize the risk of duplication.

Results

Article selection

The PRISMA flow diagram was used for article selection. A comprehensive search was conducted across multiple databases, including PubMed, Scopus, Ovid Medline, Web of Science, Cochrane, and Embase, following a predefined search strategy. A total of 739 articles were initially identified (Fig. 1). After removing 327 duplicate articles, 412 studies remained for screening. Of these, 400 were excluded based on title, abstract, and keywords. The full texts of the remaining 12 articles were assessed, and 7 were excluded. Ultimately, 5 articles were selected and included in this systematic review.

Characteristics of included studies

The included studies represent a variety of methodological designs and geographic contexts. One was a propensity score-matched study conducted in the United States by Eva Barbara et al. [27], one was a prospective cohort study from Spain by José Bueno et al. [24], one was a prospective, single-blind, intra-patient comparison study by Soo Hyun et al. in South Korea [25], one was a retrospective cohort study conducted in the United States by Lucas Fair et al. [26], and one was a case-control study by Benjamin Zendejas et al., also from the United States [16].

Across all studies, BTX-A was used as a preoperative adjunct to facilitate fascial closure and reduce postoperative complications in patients with large hernia defects. The characteristics of the patients and hernias varied between studies. Eva Barbara et al. [27] analyzed 220 patients and reported an average hernia width of 14.1 cm and a mean volume of 1,405 cm^3. José Bueno et al. [24], in a cohort of 80 patients, described mean hernia widths of 15.7 cm (without BTX-A) and 15.5 cm (with BTX-A), while Benjamin Zendejas et al. [16] noted defect areas averaging 117.5 cm^2 and 59.7 cm^2 for control and intervention groups, respectively. In contrast, Soo Hyun et al. [25] included a small sample ($n = 10$) with moderate hernia widths ranging from 4 to 8 cm (Table 1). There was notable variation in the dosage and timing of BTX-A injection. Doses ranged from 150 to 500 IU, typically administered 3 to 6 weeks before surgery, although in one study [16], some injections were administered just one day prior. The most frequently targeted muscle groups were the external oblique (EO), internal oblique (IO), and transversus abdominis (TA), as reported by all studies [16, 24–27]. While ultrasound guidance was frequently employed, not all studies explicitly stated its use.

The surgical techniques also differed. Eva Barbara et al. [27] reported more frequent use of component separation in the BTX group, often with biological mesh, whereas José Bueno et al. [24] applied a Rives-Stoppa retromuscular repair with synthetic mesh. Zendejas et al. [16] differentiated between ventral and incisional hernia repairs, and Fair et al. [26] described the use of abdominal wall reconstruction (AWR) with or without component separation. Myofascial coaptation was used in both groups in the study by Soo Hyun et al. [25].

The type of mesh varied between synthetic and biological, depending on the study and group allocation. Most studies used synthetic mesh, although some, such as Eva Barbara et al. [27], reported a preference for biological mesh in patients receiving BTX-A. Follow-up periods were inconsistently reported; however, Bueno et al. [24] documented a median follow-up of 19.6 months, and Zendejas et al. [16] reported 18 months. Others did not explicitly mention follow-up duration (Supplementary material).

Characteristics of excluded studies

After assessing full texts, five studies were excluded for the following reasons: two articles had incorrect variables, two were non-comparative studies, and one had insufficient data. In total, seven articles were included in the final analysis.

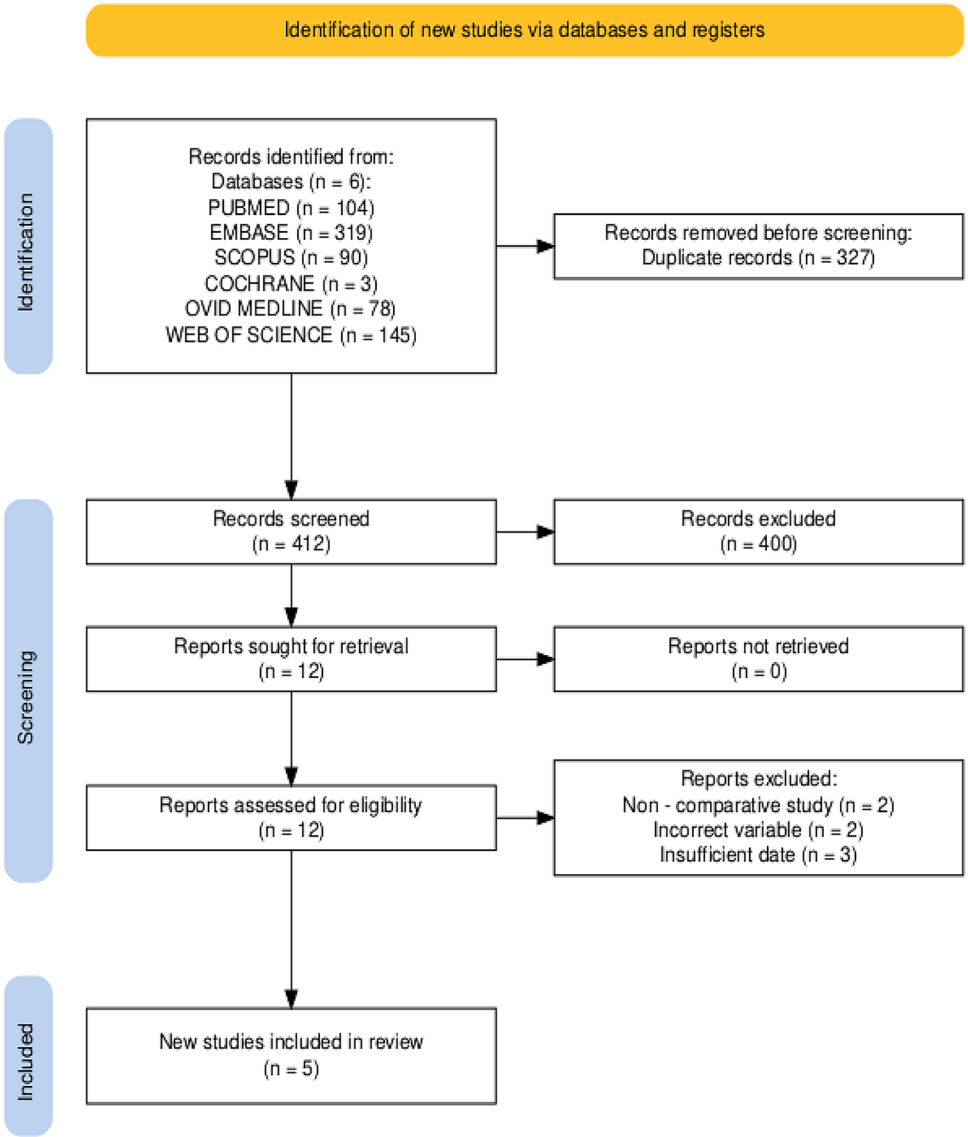

Fig. 1 PRISMA flow diagram of the included studies

Risk of bias in included studies

The risk of bias for the randomized controlled trial included in this review was classified as "Moderate" and evaluated using the ROB-2 tool (Fig. 2). For non-randomized studies, including one propensity score-matched study, two cohort studies, and one case-control study, the risk of bias was assessed using the ROBINS-I tool, also resulting in a "Moderate" risk classification for all studies (Fig. 3).

Data synthesis

Fascial closure

Five studies were included to assess fascial closure outcomes. Benjamin Zendejas reported a relative risk (RR) of 0.89 (95% CI: 0.49–1.61), indicating no significant difference. Eva Barbara showed an RR of 0.88 (95% CI: 0.80–0.98), demonstrating a significant benefit in the experimental group. José Bueno presented an RR of 0.95 (95% CI: 0.87–1.02), without statistical significance. Lucas Fair, contributing the highest weight in the global analysis, reported an RR of 1.02 (95% CI: 0.94–1.10), with no significant difference. Soo Hyun reported an RR of 1.00 (95% CI: 0.83–1.20), also without differences. Overall, the group without preoperative BTX-A injection included 611 patients, of whom 513 achieved fascial closure. The group that received preoperative injections included 258 patients, with 232 achieving fascial closure. The combined analysis showed an RR of 0.95 (95% CI: 0.90–1.01; $p=0.10$), with

Table 1 Summary of studies on preoperative botulinum toxin injection in giant incisional hernia repair

Author	Country	Study Type	Total Patients	Patients	Hernia Characteristics	Botulinum Toxin	Surgical Technique	Mesh	Follow-up Time
Eva Barbara et al. (2021)	United States	Propensity Score Matched Study	220	No BTX: 145 (60/72 M: F); With BTX: 75 (62/35 M: F)	Hernia width: 14.1 cm (avg.); Hernia volume: 1405 cm^3 (avg.)	Muscles: EO, IO, TA; Dose: 200–300 UI; 1 month before surgery	No BTX: Less frequent component separation; With BTX: More frequent component separation	No BTX: Mainly synthetic mesh; With BTX: Mainly biological mesh	Not explicitly mentioned
José Bueno et al. (2020)	Spain	Prospective Cohort Study	80	No BTX: 40 (57.5 ± 13.6); With BTX: 40 (51.5 ± 13.9)	Hernia width: 15.7 cm (No BTX); 15.5 cm (With BTX)	Muscles: EO, IO, TA; Dose: 500 UI; 4 weeks before surgery	No BTX: Component Separation Technique (CST); With BTX: Rives-Stoppa retromuscular repair (RSR)	No BTX: Occasionally biological mesh; With BTX: Mostly synthetic mesh	Median: 19.6 months (range: 11–35 months)
Soo Hyun et al. (2024)	South Korea	Prospective Study	10	No BTX: 10 (62.2 ± 3.71); With BTX: 10 (62.2 ± 3.71)	Hernia width: 4–8 cm (both groups)	Muscles: EO, IO, TA; Dose: 150 UI; 4 weeks before surgery	No BTX: Myofascial coaptation; With BTX: Myofascial coaptation	Mainly synthetic mesh (only)	Not explicitly mentioned
Benjamin Zendejas et al. (2013)	United States	Case-Control Study	88	No BTX: 66 (60.7 ± 11.5); With BTX: 22 (61.8 ± 11.4)	Hernia width: 117.5 cm^2 (No BTX); 59.7 cm^2 (With BTX)	Muscles: TA, EO; Dose: 300 UI; 41% pre-op, 59% day before surgery	No BTX: Ventral Hernia Repair (VHR); With BTX: Incisional Hernia Repair (IHR)	Mostly synthetic mesh with some biological mesh	18 months
Lucas Fair et al. (2024)	United States	Retrospective Cohort Study	426	No BTX: 350 (57.5 ± 14.9); With BTX: 76 (59.3 ± 12.7)	Hernia size: 90 cm^2 (range: 45.0–164.1 cm^2); With BTX: 9 cm^2 (range: 2.0–31.5 cm^2)	Muscles: EO, IO, TA; Dose: 300 UI; 3–6 weeks before surgery	No BTX: Component separation; With BTX: AWR with CST in some cases	Mesh used, type not specified	Not explicitly mentioned

Abbreviations: BTX – Botulinum Toxin; RR – Relative Risk; CI – Confidence Interval; CST – Component Separation Technique; RSR – Rives-Stoppa Repair; AWR – Abdominal Wall Reconstruction; VHR – Ventral Hernia Repair; IHR – Incisional Hernia Repair; UI – International Units; MD – Mean Difference; I^2 – I-squared (Measure of Heterogeneity); PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

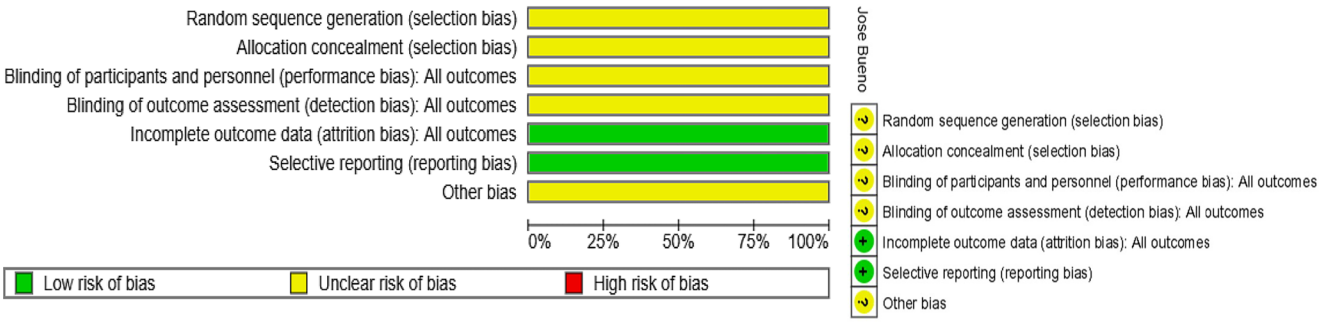

Fig. 2 Risk of Bias Assessment in Randomized Controlled Trials Using the ROB-2 Tool

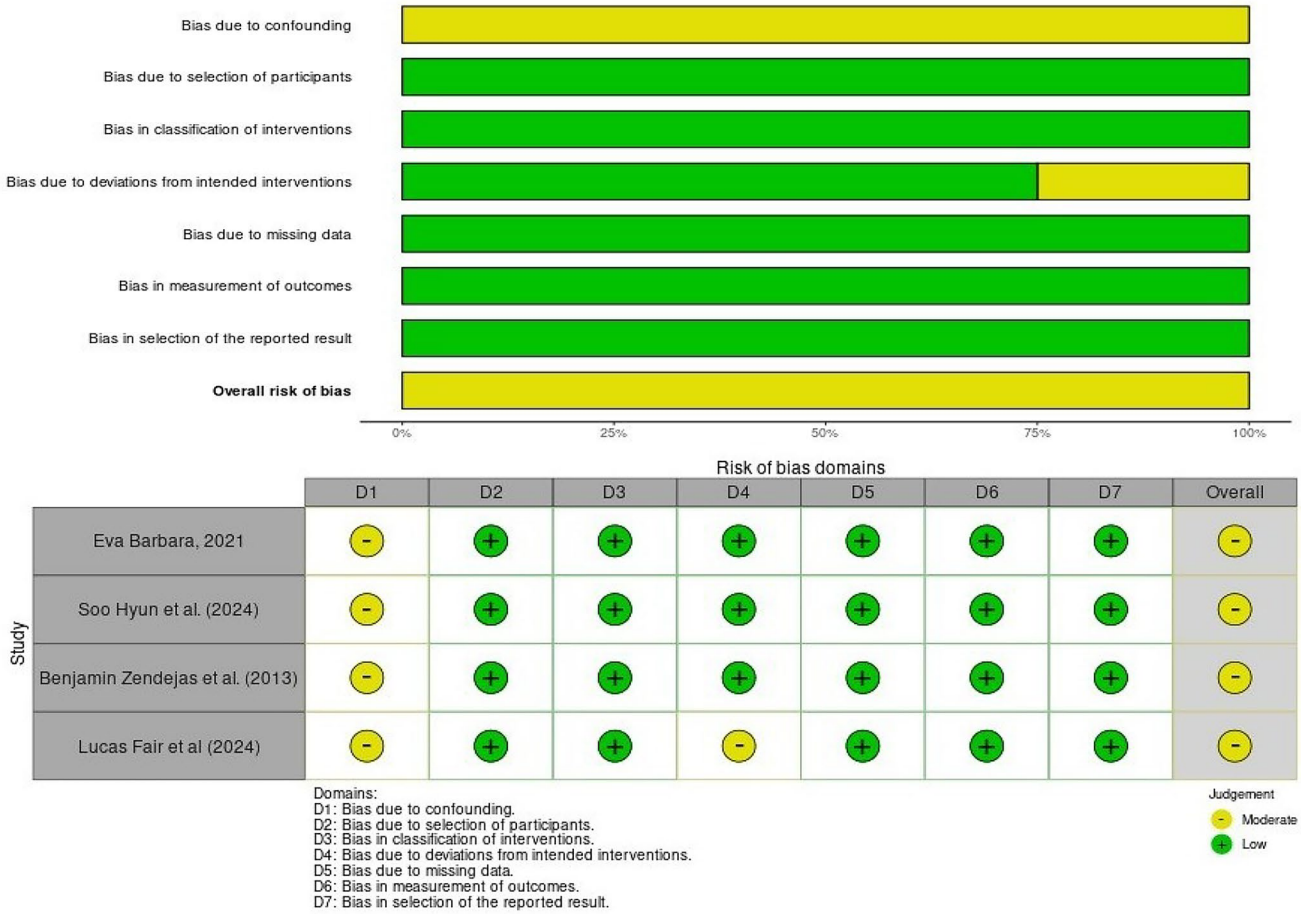

Fig. 3 Risk of Bias Assessment in Non-Randomized Intervention Studies Using the ROBINS-I Tool

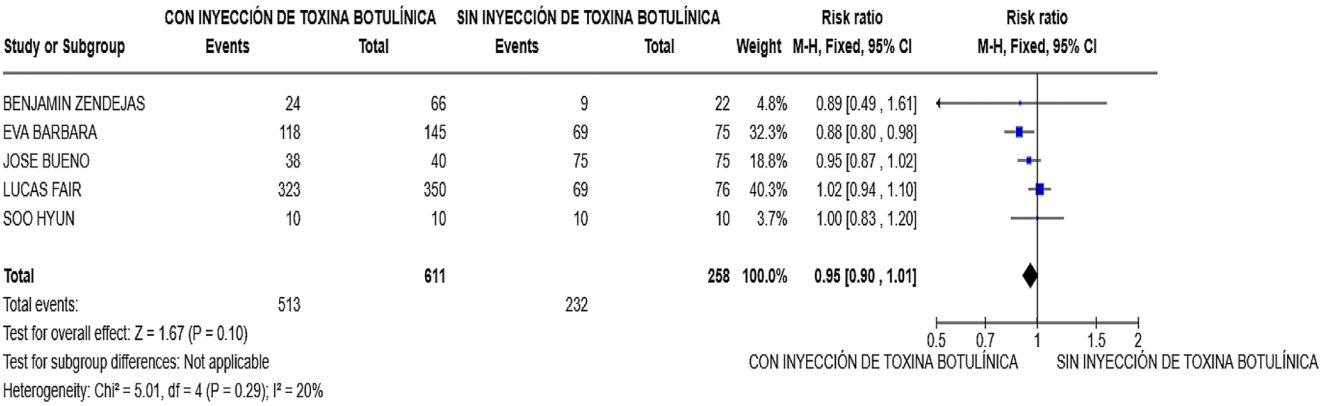

Fig. 4 Forest Plot of Fascial Closure Rates in Patients with Giant Incisional Hernias

no significant differences between studies. The low heterogeneity ($I^2 = 20\%$) indicates minimal variability across the studies (Fig. 4).

Hernia recurrence

Four studies were analyzed to assess hernia recurrence following preoperative BTX-A injection. Benjamin Zendejas reported an RR of 1.00 (95% CI: 0.22–4.60), with no significant difference. Eva Barbara showed an RR of 0.80 (95% CI: 0.35–1.83), also without significant differences. José Bueno presented a notably low RR of 0.02 (95% CI: 0.00–0.44), though this narrow confidence interval reflects uncertainty due to the small sample size. Lucas Fair, contributing 44.6% of the global analysis weight, reported an RR of 1.39 (95% CI: 0.79–2.46), with no statistical significance. In total, the

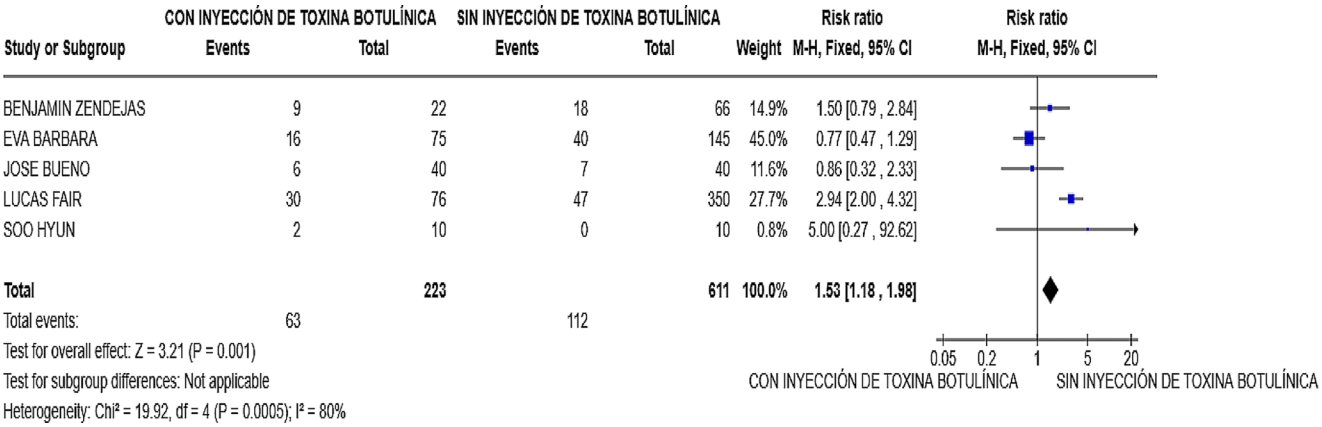

Fig. 5 Forest Plot of Hernia Recurrence in Patients with Giant Incisional Hernias

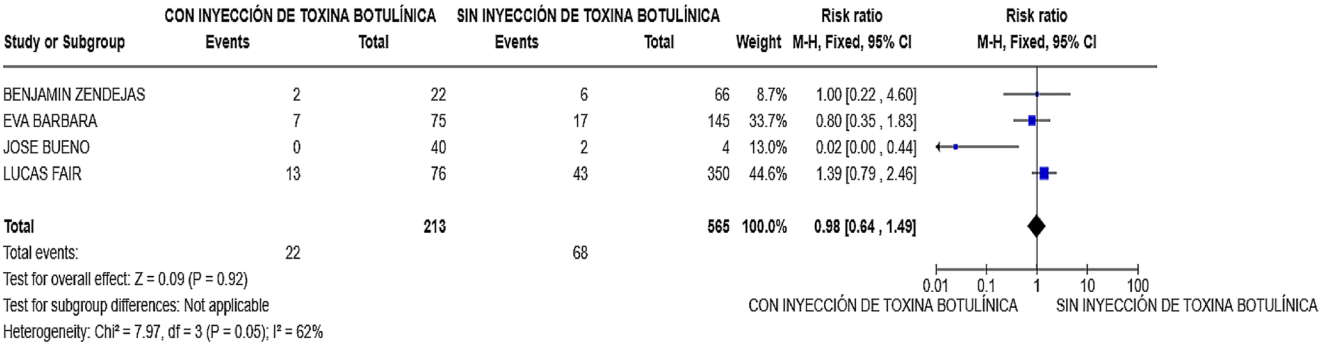

Fig. 6 Forest Plot of Postoperative Complications in Patients with Giant Incisional Hernias

non-BTX group included 565 patients, with 68 experiencing hernia recurrence, while the BTX group included 213 patients, with 22 recurrences. The combined analysis produced an RR of 0.98 (95% CI: 0.64–1.49; $p = 0.92$), showing no significant differences between groups. Moderate heterogeneity ($I^2 = 62\%$) suggests some variability, possibly due to methodological differences and sample sizes (Fig. 5).

Postoperative complications

Five studies evaluated postoperative complications such as hematoma, seroma, surgical site infection, and mesh infection following preoperative BTX-A injection. Benjamin Zendejas reported an RR of 1.50 (95% CI: 0.79–2.84), with no significant difference. Eva Barbara showed an RR of 0.77 (95% CI: 0.47–1.29), also without significant differences. José Bueno presented an RR of 0.86 (95% CI: 0.32–2.33), without statistical significance. Lucas Fair, contributing 27.7% of the global analysis weight, reported an RR of 2.94 (95% CI: 2.00–4.32), indicating a significant increase in complications. Soo Hyun reported an RR of 5.00 (95% CI: 0.27–92.62), though the small sample size limited its relevance. Overall, 611 patients in the non-BTX group experienced 112 complications, while 223 patients in the BTX group had 63 complications. The combined analysis yielded an RR of 1.53 (95% CI: 1.18–1.98; $p = 0.001$), indicating a significant increase in postoperative complications associated with BTX-A injections. The heterogeneity was high ($I^2 = 80\%$), reflecting substantial variability between studies (Fig. 6).

Hospital stay duration

Three studies assessed the effect of BTX-A on hospital stay duration. Benjamin Zendejas reported a mean difference (MD) of 1.10 days (95% CI: -4.38 to 6.58), with no significant difference. Eva Barbara showed an MD of 0.80 days (95% CI: -1.21 to 2.81), also without significance. Soo Hyun reported no variation between groups, with an MD of 0.00 days (95% CI: -1.93 to 1.93). The combined analysis indicated a mean difference of 0.43 days (95% CI: -0.92 to 1.78; $p = 0.53$), suggesting no significant differences in hospital stay duration between the groups. The heterogeneity was zero ($I^2 = 0\%$), indicating high consistency across the included studies (Fig. 7).

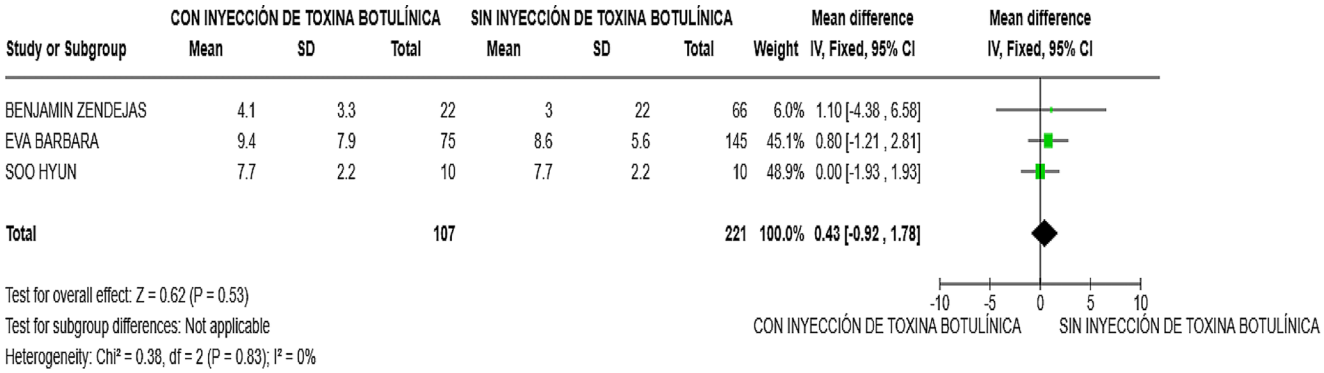

Fig. 7 Forest Plot of Hospital Stay Duration in Patients with Giant Incisional Hernias

Discussion

This systematic review and meta-analysis aimed to evaluate the effect of preoperative botulinum toxin A (BTX-A) injections compared to conventional management in the treatment of giant incisional hernias. The analyzed outcomes included fascial closure, hernia recurrence, postoperative complications, and hospital stay duration.

The global analysis showed that preoperative BTX-A injection did not result in significant differences in fascial closure compared to conventional management (combined RR: 0.95; 95% CI: 0.90–1.01; $p=0.10$), with low heterogeneity (I^2 = 20%), indicating consistent results across the included studies. These findings suggest that, overall, BTX-A does not offer a clear benefit for fascial closure. However, a positive trend was observed in Eva Barbara's study, which demonstrated a significant benefit in facilitating fascial closure (RR: 0.88; 95% CI: 0.80–0.98) [27]. In contrast, other individual studies by Benjamin Zendejas [16], José Bueno [24], Lucas Fair [26], and Soo Hyun [25] did not report significant differences, reinforcing the lack of a conclusive global impact.

These findings partially align with previous literature on the use of BTX-A in abdominal wall reconstruction. Timmer et al. [28], highlight that BTX-A can reduce abdominal wall tension and lengthen lateral muscles, facilitating fascial closure in large or complex hernia defects. Some studies have documented an average elongation of up to 6.3 cm in lateral muscles, improving surgical conditions [9, 10]. However, these effects were not consistently observed in all analyzed cases, limiting their generalizability. Additionally, Weissler et al. [29] noted that BTX-A could increase fascial closure rates up to 100% in selected patients with large and complex defects, potentially reducing the need for invasive surgical techniques such as component separation. However, the findings from this review show inconsistent benefits across studies, likely due to variations in patient characteristics and surgical protocols. The heterogeneity in surgical techniques and patient populations could have contributed to these mixed results.

The global results of this review did not show a statistically significant benefit of BTX-A in reducing hernia recurrence rates (combined RR: 0.98; 95% CI: 0.64–1.49; $p=0.92$). The analysis also indicated moderate heterogeneity (I^2 = 62%), which could be influenced by differences in study populations, surgical protocols, and follow-up durations. Among individual studies, José Bueno reported a notably low recurrence rate (RR: 0.02; 95% CI: 0.00–0.44) [24], suggesting a significant benefit of BTX-A. However, the wide confidence interval reflects the uncertainty due to the small sample size. In contrast, Lucas Fair [26], contributing the most weight to the global analysis (44.6%), reported a non-significant RR of 1.39 (95% CI: 0.79–2.46), indicating a possible trend toward higher recurrence rates in the BTX group.

These results differ from prior reviews such as Timmer et al. [28], which reported recurrence rates of 0% in BTX-treated patients over a mean follow-up period of 19 months, particularly in complex defects. Similarly, Weissler et al. [29] found recurrence rates of 0% over a follow-up period of 24.7 months. A possible explanation for the discrepancy between this meta-analysis and previous findings is the shorter follow-up duration in the included studies. Studies showing reduced recurrence with BTX-A had longer follow-up periods (19–24.7 months), allowing for better detection of late recurrences. In contrast, the studies included in this meta-analysis may have had shorter follow-up periods, limiting the ability to detect later-stage recurrences.

The global results of this review showed a statistically significant increase in postoperative complications in the BTX-treated group (combined RR: 1.53; 95% CI: 1.18–1.98; $p=0.001$). However, it is important to note that the evaluated complications—seromas, hematomas, surgical site infections, and mesh infections—are primarily related to the surgical procedure itself rather than directly to the use of BTX-A. The high heterogeneity (I^2 = 80%) suggests considerable variability among the studies, likely influenced

by differences in patient populations, surgical protocols, and sample sizes. Among individual studies, Lucas Fair [26], with the highest weight in the global analysis (27.7%), reported an increased incidence of complications (RR: 2.94; 95% CI: 2.00–4.32). Similarly, Benjamin Zendejas [16] (RR: 1.50) and Soo Hyun [25] (RR: 5.00) also reported higher complication rates in the BTX group, although without reaching statistical significance. Conversely, Eva Barbara [27] (RR: 0.77) and José Bueno [24] (RR: 0.86) found no significant differences between the groups, contributing to the overall variability.

These findings differ from previous reviews like that of Timmer et al. [28], which suggested that BTX-A could facilitate surgical management by reducing abdominal wall tension and the need for invasive procedures. However, the data in this review suggest that BTX-A does not directly influence postoperative complications, as these events are more likely related to surgical factors rather than preoperative BTX-A injections. In this review, the most frequent complications were hematomas, seromas, surgical site infections, and mesh infections, all associated with the surgical act itself. Although previous reviews have reported a favorable safety profile for BTX-A [29], this meta-analysis did not observe a reduction in postoperative complications. The variability in surgical techniques, patient characteristics, and BTX-A injection protocols in the included studies could explain these discrepancies.

Given the high degree of heterogeneity ($I^2 = 80\%$), these findings should be interpreted with caution. Variability in surgical protocols and patient characteristics could have influenced the outcomes. Therefore, additional randomized controlled trials with greater methodological uniformity are necessary to validate these findings and determine whether certain patient subgroups might benefit from BTX-A without increasing postoperative complication rates.

The results of this review found no significant differences between BTX-treated groups and controls regarding hospital stay duration (combined mean difference: 0.43 days; 95% CI: -0.92 to 1.78; $p = 0.53$), with zero heterogeneity ($I^2 = 0\%$), indicating high consistency among the included studies. Analyzing the individual results, Benjamin Zendejas [16] reported a mean difference of 1.10 days favoring the non-BTX group (95% CI: -4.38 to 6.58), while Eva Barbara [27] reported a difference of 0.80 days (95% CI: -1.21 to 2.81), also favoring the control group. Soo Hyun [25] found no difference in hospital stay duration (MD: 0.00 days; 95% CI: -1.93 to 1.93). None of these results reached statistical significance, reinforcing the absence of a clinically relevant impact of BTX-A on this outcome.

Comparing these findings to prior literature, Timmer et al. [28] suggested that BTX-A could simplify surgical management by facilitating fascial closure, indirectly reducing hospitalization duration. However, specific data on this outcome were not reported in their review. Similarly, Weissler et al. [29] found no significant differences in hospital stay duration between BTX and control groups, aligning with the findings of this review. The studies included in this review may have analyzed patients with varying clinical characteristics and postoperative protocols, influencing hospital stay durations. Although the combined mean difference was positive (0.43 days), the wide confidence interval suggests considerable variability in hospitalization times between patients, limiting the ability to draw definitive conclusions.

Another important consideration emerging from this analysis is the role of patient-centered outcomes beyond traditional clinical measures. While fascial closure rates, hernia recurrence, postoperative complications, and hospital stay were the primary outcomes evaluated, recent studies such as that by Karlsson et al. [30] have emphasized the significance of long-term patient-reported outcomes and quality of life measures following hernia repair. Their findings suggest that even in cases with technically successful repairs, factors like pain, mobility, and psychological well-being strongly influence patient satisfaction and perceived success.

Regarding safety, although none of the included studies reported severe adverse events related to BTX-A administration, it is important to highlight that botulinum toxin type A carries a black box warning issued by the U.S. Food and Drug Administration (FDA) due to the risk of systemic toxin spread. This warning alerts clinicians to potential adverse effects such as dysphagia, generalized muscle weakness, or respiratory compromise, which may occur even in the absence of underlying neuromuscular disorders. These events are rare but serious, and their occurrence underscores the need for strict patient selection, appropriate dosing, and image-guided administration. In the context of abdominal wall reconstruction, the included studies did not report any such complications; however, this risk must still be acknowledged in clinical decision-making and future trials evaluating BTX-A in this setting [31].

Therefore, it is recommended to develop standardized protocols for BTX-A administration, including consistent dosage, optimal timing of injection (typically 2–4 weeks before surgery), injection technique (preferably under ultrasound guidance), and clear clinical indications based on preoperative radiological and anatomical assessments [9, 10, 15, 16]. Furthermore, RCTs with larger sample sizes and low risk of bias are necessary to more accurately assess the impact of BTX-A on primary outcomes such as fascial closure and postoperative complications, as well as secondary outcomes including hernia recurrence and hospital stay duration. These trials should include long-term follow-up periods, as previous studies that reported lower recurrence

rates with BTX-A (e.g., 0% over 19–24.7 months) had longer follow-up durations than those included in this meta-analysis [28, 29]. In addition, patient-reported outcomes—such as pain, physical function, and quality of life—should be incorporated in future research, as proposed by Karlsson et al. [30], to determine whether the theoretical biomechanical benefits of BTX-A translate into tangible improvements in patients' post-surgical experiences and satisfaction. Lastly, it is essential to tailor the use of BTX-A according to individual patient characteristics, including defect size, abdominal wall compliance, prior surgical history, comorbidities, and risk of abdominal compartment syndrome, to maximize its potential benefits and minimize unnecessary exposure in low-risk cases.

These recommendations, grounded in the findings of this review and supported by select individual studies, aim to optimize the use of botulinum toxin A in the surgical repair of giant incisional hernias—improving operative planning, reducing procedural invasiveness when appropriate, and enhancing overall patient outcomes.

Conclusion

Preoperative botulinum toxin type A injection is a safe adjunct in the repair of giant incisional hernias; however, current evidence has not demonstrated a significant clinical benefit. No significant improvements were observed in fascial closure rates, hernia recurrence, or hospital stay duration, and the reduction in postoperative complications was limited. Therefore, the use of BTX-A cannot be routinely recommended in this context. Further high-quality randomized controlled trials are necessary to clarify its potential role and identify which patients, if any, may benefit from its use.

Limitations

This systematic review and meta-analysis has several limitations. First, the small number of included studies, their heterogeneity and design limit the generalizability of the findings. Second, variability in BTX-A administration protocols (dose, timing, technique) and surgical techniques across studies may have influenced outcomes. Third, the follow-up periods in most studies were short, limiting the ability to detect long-term recurrence or chronic complications. Additionally, the risk of bias was moderate in all included studies, and the lack of patient-reported outcomes prevented evaluation of functional recovery and quality of life.

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Declarations

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