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REVIEW

Botulinum toxin A in complex incisional hernia repair: a systematic review

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Abstract

Purpose To evaluate the safety, efficacy, and short and long-term postoperative results of using BTA.

Methods We conducted a systematic review following the recommendations of the PRISMA method. We systematically reviewed the MEDLINE/PubMed and SCOPUS electronic databases for studies published between January 2010 and September 2021. This systematic review was registered in PROSPERO, with registration number CRD42021252445.

Results After applying the selection criteria, 11 relevant articles were selected. The total sample size was 1058 patients. Most studies aimed to assess the rate of fascial closure, followed by the rate of recurrence and reporting of postoperative complications, as well as the need for the components separation technique (CST). None of the studies reported serious complications from using BTA. Regarding fascial closure, all articles had rates above 75%, except for one. Surgical site events ranged between 19% and 29.4%. No recurrence in the group that used BTA was recorded in five studies. The other articles reported recurrence rates ranging from 6.4 to 11.4% in the groups that received BTA. The studies had varying follow-up times ranging from 1 to 49 months, with a mean of 18.6 months (± 11.2).

Conclusion This review described most of the key points about the preoperative use of BTA in hernia repair. It can be concluded that the use of BTA is a safe and effective practice that promotes good short and long-term results. However, the limitations of the current literature prevent more accurate conclusions on the subject.

Keywords Incisional hernia · Botulinum toxins · Type A · Abdominal wall · Systematic review

Introduction

Incisional hernias occur in approximately 10–15% of patients with a previous abdominal incision [1]. They can develop early in the postoperative period or even years after surgery. Patients with this type of hernia usually complain of local discomfort and/or aesthetic damage, and larger hernias may cause chronic local or back pain, postural pain, and other impairments [1–6]. This type of hernia can be clinically diagnosed by considering the patient's history of previous surgery and confirmed by physical examination. In cases of doubt, imaging tests such as ultrasonography or computed tomography may be requested [7].

With the advancement of research, other techniques have been described for the repair of complex incisional hernias, such as the component separation technique (CST) published by Ramirez et al. in 1990, which has been improved over time. Based on this publication, either the anterior component separation technique (ACST) or the posterior component separation technique (PCST) can be employed. The PCST was further improved with the association of the transversus abdominis muscle release technique (TAR) [1, 8].

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Preoperative progressive pneumoperitoneum (PPP) or local injection of botulinum toxin (BTA) are used as adjunct methods to component separation techniques [9].

The PPP technique, using a tissue expander, seeks to slowly and progressively increase the pressure on the abdominal wall so as to stretch the muscles, thereby reducing the tension at the time of surgical occlusion of the hernia defect [10].

Botulinum toxin A causes preoperative paralysis of the lateral abdominal muscles and consequent reduction in intra-abdominal pressure, thus facilitating primary fascial closure and reducing the need for CST [11–13].

Therefore, the objective of this study is to evaluate the administration of botulinum toxin A in the preoperative preparation of patients with complex abdominal incisional hernia in terms of safety, intraoperative efficacy, and short and long term postoperative results.

Methods

This systematic review was conducted according to the PRISMA guidelines [14] and registered in PROSPERO (CRD42021252445). Original articles that involved patients with complex abdominal incisional hernias in which botulinum toxin A was used as an adjunct treatment to hernia repair surgery were included.

Eligibility criteria

Studies carried out with humans, published in English, Portuguese, and Spanish between January 2010 and September 2021 were selected.

Information sources and search strategy

We conducted literature searches in the electronic databases MEDLINE/PubMed and SCOPUS by combining Medical Subject Headings (MeSH) terms. The terms used for the search were "botulinum" AND "hernia" NOT "hiatal" NOT "diaphragmatic" NOT "disc". We manually searched the references cited in the articles identified by the electronic search strategy to add to our work. The drill-down strategy was included in the supplementary material.

Study selection

Two independent pairs of authors read the titles and abstracts of each pre-selected article separately to identify studies that met the inclusion criteria. In addition, four authors read the full-text articles separately to ensure that the systematic review criteria were met. Any disagreements between the authors were resolved by discussion with a third author.

Data extraction

We used a pre-defined data collection form in Excel® to extract the following variables: title, author(s), study design, country, year, objectives, sample size, gender of participants, age, BMI (kg/m^2), number of previous repairs, location of the hernia, width of the fascial defect, type of surgery performed, use of mesh, rate of fascial closure, separation of components, brand of BTA used, time of administration, units of BTA, method of application, use of ultrasound, effect of BTA administration, surgical site complications, recurrence rate, mortality rate, and follow-up time.

Quality assessment

We evaluated the quality of the studies using the Newcastle–Ottawa Scale (NOS) questionnaire for cohort studies [15].

Presentation of results

We present the data in tables with descriptions of the studies, general data for each article, participant characteristics, interventions, sample characteristics, and outcomes.

Ethical aspects

As this is a systematic review of previously published studies, there was no need to submit it to an Ethics and Research Committee.

Results

After screening a total of 316 studies, only 11 studies were eligible for this systematic review according to the PRISMA diagram (Fig. 1).

Methodological quality and risk of bias

The summary of the methodological quality assessment of the studies included in this review is shown in Table 1.

Characteristics of the selected studies and population samples

Most studies were performed in the United States [11, 16–18], followed by Mexico [19–21]. The number of papers published recently on the subject has increased, with 6 of the 11 articles published in 2020 [11, 16, 17, 22–24]. Retrospective cohorts predominated. Most studies were unicentric, two were bicentric [20, 23] and one was multicentric [17].

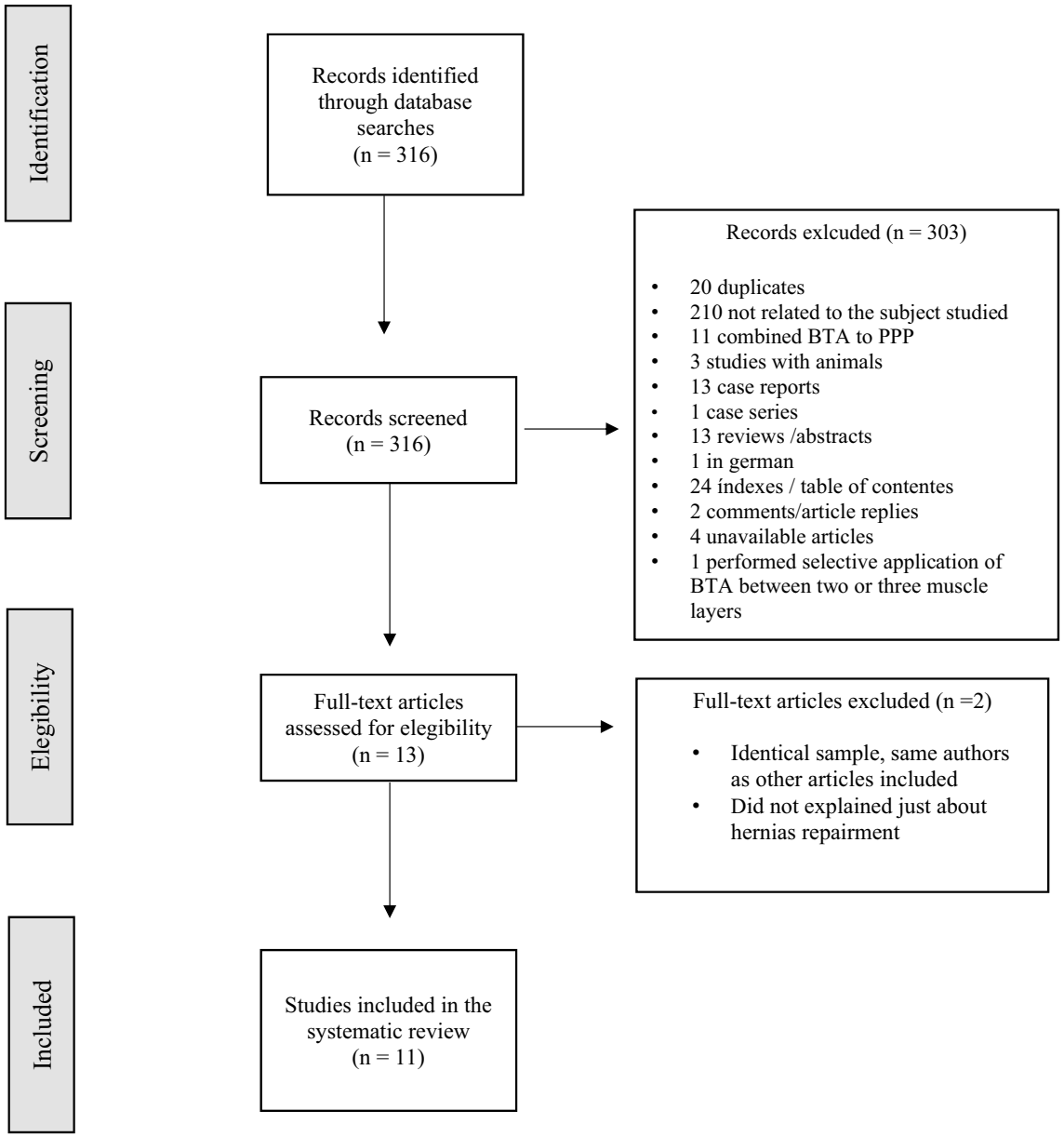

Fig. 1 Flowchart of the articles selection

The different studies presented similar objectives. The most cited objective was the evaluation of the fascial closure rate [11, 16, 17, 20, 22], followed by the recurrence rate [11, 16, 22, 25] and reporting of postoperative complications [11, 16, 22, 23], as well as the need for CST [11, 16, 22]. Two articles focused on the analysis of alterations in the lateral abdominal muscles, such as their thickness and length [19, 21], and two others presented the institutional experience with the preoperative use of BTA [18, 24].

The total sample size was 1058 patients, with a median of 37 (interquartile range-IIQ-32–108) patients per a study, ranging from 14 to 388. All studies had samples composed of males and females, except one in which the sample was composed only of men [21]. Women predominated in the samples. One study did not inform the proportion of men and women [17] (attempts were made to obtain information from the author, without success). The mean age of the participants was greater than 51.5 in all studies, except in one study [21] in which the mean age was 34.8 ± 12.3 years. The median age in the studies was 59.5 years (IQR 54.7–60.8). The mean BMI was greater than 30 kg/m^2 except in two articles [20, 24] and two studies did not bring this data [21, 22]. Baseline characteristics of the included studies are presented in Table 2.

Table 1 Quality assessment of articles according to the Newcastle–Ottawa Scale—NOS questionnaire ($n=8$)

Author	Selection				Comparability	Outcome/Exposure			Ponctuation
	1	2	3	4	5	6	7	8	
Eltsner et al. (2017)	★	–	★	★	★	★	★	★	7/9
Catálan-Garza et al. (2020)	★	–	★	★	★	★	★	★	7/9
López et al. (2016)	★	–	★	★	★	★	★	★	7/9
Nielsen et al. (2020)	★	–	★	★	★	★	–	★	6/9
Elstner et al. (2016)	★	–	★	★	★	★	★	★	7/9
Deerenberg et al. (2020)	★	–	★	★	★	★	★	★	7/9
Horne et al. (2021)	★	★	–	★	★★	★	★	★	8/9
Bueno-Llédo et al. (2020)	★	★	★	★	★★	★	★	★	9/9
Deerenberg et al. (2021)	★	–	★	★	★	★	★	★	7/9
Zendejas et al. (2013)	★	★	★	★	★	★	★	★	8/9
Ibarra-Hurtado (2014)	★	–	★	★	★	★	★	★	7/9

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The cohort that presents the following descriptions receives stars for each criteria: (1) The exposed cohort (with BTA) was truly or poorly representative of the average in the community; (2) Selection of the unexposed cohort (without BTA) from the same community; (3) Information on BTA dose, surgical technique and long-term surgical outcomes; (4) Defect repair outcomes must not be present at baseline; (5) Presence of multivariate analysis that include different sample groups; (6) Independent evaluation of the outcome; (7) Studies that followed the patient for a period of up to 1 year—final defined by the review; 8) At least 80% of the patients were followed up until the end or if the article does not describe any significant losses at follow-up

The control case that presents the following descriptions receives stars for each criteria: (1) Defined cases with independent validation; (2) Series of obviously repetitive or consecutive cases; 3) Selection of control in the community; (4) Outcomes must not be present in the control previously; (5) Presence of multivariate analysis that include different sample groups; (6) Reliable disclosure through secure records or case/control blinding; (7) Same parameters evaluated in cases and controls; (8) Same "non-operable" rate for cases and control. Source: own authorship

General characteristics of defect and hernia repair using BTA

In the analysis of the studies, most of the hernias were of the primary incisional type, and among the recurrences, there was a variation of one to five previous repair attempts. In addition, the majority of operated hernias were located in the midline, with significant percentages of lateral hernias, as well as repair of a parastomal hernia [19]. All types of midline hernias from M1 to M5 and lateral hernias from L1 to L4 (according to European Hernia Society—EHS) [26] were operated. The average width of the defect was between 10 and 16 cm in the studies. Only three studies [19, 21, 25] described the mean difference in defect width observed after using BTA, but one of them [19] was not significant. The main characteristics related to the hernia defect and repair are described in Table 3.

Regarding the type of surgery, most cases opted for open surgery, with Rives-Stoppa being the most used technique. Only two studies addressed laparoscopic surgery, one varied between laparoscopic and assisted laparoscopic surgery [25], and the other used both open and laparoscopic approaches [18]. All articles used mesh in more than 90% of patients, except for one that used it in 23.5% of repairs [21]. However, there was one study that did not present data on mesh placement [24].

All articles reported success in fascial defect closure above 75% when using BTA, except for one that presented 40.9% of fascial closure [18]. In three articles, fascial closure was reported in 100% of repairs using BTA [21–23]. In cases in which primary fascial closure was not possible, bridge closure was chosen in some studies [22, 24], and programmed closure in another study [11]. The need to use component separation techniques (CST) ranged from 0 to 73% of cases in the groups that used BTA. One study did not require CST [22], and one of the articles performed this technique in 73% of cases in the group that used BTA and 75.9% in the control group [17].

General characteristics of preoperative use of BTA

The main characteristics related to the preoperative use of BTA are shown in Tables 4 and 5. Most studies used BTA from the Botox® brand. The recommended administration time before surgery in most articles was 4 weeks [11, 16, 19, 20, 22–24], but some adopted a longer time: 40.1 days

Table 2 General characteristics of the selected studies, sorted by year of publication. May–June 2021. Salvador, Bahia

Author	Country, Year	Study type	Objective
Deerenberg et al.	United States, 2021	Single center non-randomized clinical trial	To compare the rate of fascial closure during abdominal wall reconstructions between patients treated with and without preoperative BTA. In addition, the necessity for component separation techniques, postoperative complications and recurrence rates were studied
Horne et al.	United States, 2021	Multicenter Case–Control	To evaluate the role of chemical component separation in enabling primary fascial closure in patients with ventral hernias measuring 15 cm or more in their greatest dimension
Bueno-Llédo et al.	Spain, 2020	Single-center retrospective cohort	To compare the results of 2 groups of patients with LMIHs using only ACST versus pre-surgical BTA plus subsequent RSR. This was done by focusing on SSOs, primary fascial closure possibility, time of hospital stay and recurrence rate
Deerenberg et al.	United States, 2020	Single-center prospective cohort	To examine the effects of preoperative BTA injections in abdominal wall reconstruction on fascial closure rates, necessity for CST, postoperative complications, and rate of relapses
Nielsen et al.	Denmark, 2020	Bicenter retrospective cohort	To report the short-term complications of preoperative administration of BTA before abdominal wall reconstruction for large ventral hernias with loss of domain or anticipated difficulty in achieving midline closure
Catálan-Garza et al.	Spain, 2020	Single-center retrospective cohort	To present the experience with 32 patients using BTA on the lateral abdominal oblique muscles in the preoperative preparation of patients before elective complex ventral hernia repair
Elstner et al.	Australia, 2016	Single-center prospective cohort	To analyze whether the administration of BTA before elective surgery in patients with large ventral hernia defects can decrease recurrence rates
López et al.	Mexico, 2016	Bicenter retrospective cross-sectional cohort	To evaluate the results of the preoperative application of BTA (Botox®) as an alternative for closing the abdominal wall in incisional hernias with defects of 10 cm and up to 15 cm
Chavez-Tostado et al.	Mexico, 2014	Bicenter retrospective cohort	To evaluate the results of transitory muscle relaxation secondary to flaccid paralysis after BTA injection
Ibarra-Hurtado	Mexico, 2014	Single center non-randomized clinical trial	To evaluate whether the application of BTA on the lateral abdominal wall musculature of patients with incisional hernia secondary to open abdomen management modifies its thickness and length
Zendejas et al.	United States, 2013	Single center non-randomized clinical trial	To review the institutional experience to compare patients who underwent incisional hernia repair with and without BTA-induced paralysis of the abdominal wall musculature

BTA Botulinun Toxin A, *CST* Component separation technique, *LMIHs* Large Midline Incisional Hernia, *ACST* Anterior component separation technique, *SSO* surgical sites ocurrences, *RSR* Rives-Stoppa retromuscular

on average (standard deviation not shown) [19]. One study used a shorter time interval, with a median of 6 days [18] (IQR 1–19). The time adopted in other articles ranged from 1 to 4 weeks [25], with an average of 31.6 days and a standard deviation of ten [23]. The amount of BTA administered in most articles was 300 units, ranging from 100 to 500 units. The application method varied. Six application points were used in five articles [11, 16, 18, 24, 25] 10 application points in three articles [19, 21, 22], and in 6 to 10 points in one article BTA was applied [23]. Most teams used ultrasound-guided BTA injection. Ultrasound was not used in two studies [19, 20], but in one of these studies, computed tomography guidance was used [19]. In one study, both ultrasound and computed tomography were used [16]. One study did not present a protocol or detailed information on how BTA was administered [17].

Table 3 Characteristics of the defects and hernia surgeries

Author	Previous repair	Hernia location	Defect width (cm)	Defect. width mean after BTA (cm)	Mean difference in defect. width after BTA (cm)	Type of surgery	Use of mesh	Fascial closure	Components separation
Deerenberg et al. (2021)	–	–	14.1 ± 5.1 14.1 ± 4.7 (p.886)	–	–	Open	96% 97% (p.585)	81% 92% (p.036	47% 61% (p.042)
Horne et al.	59.1% 55% (p.502)	M: 72.8% 82% L: 27.2% 18% (p.440)[a]	15 (10–23) 16 (10–22) (p.556)	–	–	Open	90.7% 94% (p.344)	85.2% 86% (p.934)	75.9% 73% (p.587)
Bueno-Llédo et al.	30% 27.5%	M: 100%	15.7 15.5 p(.344)	–	–	Open	100% 100%	95% 100% p(.878)	100% 0
Deerenberg et al. (2020)	50%	M Laterais[b]	15.3 ± 5.5	–	–	Open	98%	91%	57%
Nielsen et al.	10.8%	M: 94.4% L: 8.3%[c]	12.1 ± 3.4	–	–	Open	100%	100%	40.5%
Catálan-Garza et al.	–	–	–	–	–	Varied by the size of the defect, does not describe which	–	77.8%	75%
Elstner et al.	78,1%	M: 23 71.8% L: 28.1%	12.3	–	Up to 7.54[d]	LOL	100%	–	18,7%
López et al.	–	–	10–15	–	–	Open	100%	75%	25%
Chavez-Tostado et al.	28%	M: 62% L: 28%	14.6	14.3	0.3[e]	Open	100%	78%	21%
Ibarra-hurtado et al.	100%	M: 100%	14.6 ± 2.2	9.68	4.79	Open	23,5%	100%	52,9%
Zendejas et al.	100%	M: 90% 95.4% L: 10% 4.6%	–	–	–	Open/Laparoscopic	100% 100%	36.4% 40.9% p(.3)	7.6% 18,2% p(.2)

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M midline hernias, *L* lateral hernias, *LOL* Laparoscopic-open-laparoscopic;

[a]Data obtained considering all hernias with a lateral component as lateral hernias, and the rest as midline hernias

[b]Only flank hernias

[c]Considering the terminology "transverse hernia" as lateral hernia

[d]Data was described as up to 58%, but we reported in centimeters to make the table homogeneous

[e]Not significant

Two studies [21, 25] described the length of the lateral abdominal muscles before and after BTA application. The mean gain in muscular length after using BTA was between 2.44 and 4.5 cm in these studies.

Safety and short and long-term results

Table 6 summarizes the main information regarding the safety and efficacy of BTA in hernia repair. Four articles reported no side effects of BTA administration [16, 18, 22, 24], while one study noted pain in 2.7% of patients [23]. Another study reported that all patients experienced

Table 4 Characteristics related to the preoperative use of BTA

Author	BTA brand	Time of administration	BTA units	Application methods	Use of ultrasound
Deerenberg et al. (2021)	Botox® (Allergan Pharmaceuticals)	4 weeks	200–300 U	Six points of the internal and external oblique: 3 sites on each side near the midaxillary line at three equidistant points between the rib cage and the iliac crest	Yes
Horne et al.	–	–	–	–	–
Bueno-Llédo et al.	Dysport® (Ipsen Pharma)	4 weeks	500 U	Ten points: two on the midaxillary line between the costal margin and the iliac crest and three between the anterior axillary line and the midclavicular line between the costal margin and the iliac crest with similar sites on the opposite side	Yes[a]
Deerenberg et al. (2020)	Botox® (Allergan Pharmaceuticals)	4 weeks	200–300 U	Six points, on all three muscle layers, or on the two outermost layers only: 3 sites on each side near the mid-axillary line at three equidistant points (5 cm) between the rib cage and the iliac crest	Yes[b]
Nielsen et al.	Botox® (Allergan Pharmaceuticals	31.6 days	300 U	Six to ten points: three to five points of injection on each side of the patient in each of the three muscle layers	Yes
Catálan-Garza et al.	Botox® (Allergan Pharmaceuticals)	4 weeks	300 U	Six points on the abdominal wall, one on each side of the subcostal midclavicular line, the anterior axillary line, and the superior anterior superior iliac spine	Yes
Elstner et al.	Botox® (Allergan Pharmaceuticals) or Equivalent dose Dysport® (Ipsen Pharma)[c]	1–4 weeks	300 U	Six points: 3 on each side along the anterior axillary line equidistant and between the costal margin at the level of the ninth rib and the anterior superior iliac spine	Yes
López et al.	Botox®(Allergan Pharmaceuticals)	4 weeks	100 U	Ten points: 5 on each side of the abdomen[d]	No
Chavez-Tostado et al.	Botox®(Allergan Pharmaceuticals)	40.1 days	100 U	Ten points: 2 on the midaxillary line between the costal edge and the external iliac crest and 3 on the edge of the external oblique muscle	No
Ibarra-hurtado et al.	Dysport® (Ipsen Pharma)	–	500 U	Ten points: two on the midaxillary line between the costal margin and the level of the iliac crest and three between the anterior axillary line and the midclavicular line between the costal margin and the level of the iliac crest, with similar sites on the opposite side	Yes
Zendejas et al.	Botox® (Allergan Pharmaceuticals)	6 (1–19) days[e]	300 U	Six injection sites on the patient's abdominal wall: right/left subcostal; anterior axillary right/left; right/left lower quadrants	Yes

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[a]Used ultrasound and electroneuromyography;

[b]Ultrasound was used, but most injections were guided by computed tomography;

[c]The Dysport equivalent dose is 2–3 times the Botox dose;

[d]Used an image to demonstrate the injection sites, but without the precise description;

[e]Used median and not mean

Table 5 Differences in lateral abdominal wall (cm) before and after BTA application

Author	Left muscular lenght mean before BTA	Left muscular lenght mean after BTA	Mean gain in left muscular lenght after BTA	Right muscular lenght mean before BTA	Right muscular lenght mean after BTA	Mean gain in right muscular lenght after BTA
Deerenberg et al. (2021)	–	–	–	–	–	–
Horne et al.	–	–	–	–	–	–
Bueno-Llédo et al.	–	–	–	–	–	–
Deerenberg et al. (2020)	–	–	–	–	–	–
Nielsen et al.	–	–	–	–	–	–
Catálan-Garza et al.	–	–	–	–	–	–
Elstner et al.	16.8	21.3	4.5	16.8	21.3	4.5
López et al.	–	–	–	–	–	–
Chavez-Tostado et al.	–	–	–	–	–	–
Ibarra-hurtado et al.	10.85	13.29	2.44	10.73	13.32	2.59
Zendejas et al.	–	–	–	–	–	–

Salvador, Bahia

Table 6 Safety and short and long term results May–Jun, 2021

Author	Side effects of BTA administration	Surgical site events	Recurrence	Mortality	Follow-up time (months)
Deerenberg et al. (2021)	–	28% 21% (p.312)	12% 9% (p.589)	–	29 14 (p.589)[a]
Horne et al.	–	–	–	–	12
Bueno-Llédo et al.	None	–	5% 0 p(.087)	–	19.6 (11–35)
Deerenberg et al. (2020)	None	19%	6.4%	1.8%	14
Nielsen et al.	2.7% with pain	24.3%	10.8%	0	1
Catálan-Garza et al.	None	27.8%	11.4%	0	24
Esltner et al.	100% feeling bloated or distended	–	0	0	19 (5–39)
López et al.	100% with perception of a flaccid abdomen with less tension and a marked decrease in the intensity of previous pain	25%	0	0	12
Chavez-Tostado et al.	–	28%	0	0	15
Ibarra-hurtado et al.	–	29.4%	0	0	49 (37–61)
Zendejas et al.	None	13.6% 9.1% p(.72)	9.1% 9.1% p(1)	–	18.4 ± 11.7 15.6 ± 13.1 p(.39)

Salvador, Bahia

[a]Follow-up data were not presented separately, but together with recurrence rate

a feeling of swelling and distension [25], while a third study described a perception of a more flaccid abdomen, with less tension and a decrease in previous pain intensity in all patients [20]. The remaining studies did not report on these outcomes.

Surgical site events ranged from 19 to 29.4%, with surgical site infections being the most prevalent finding, followed by seromas. Five studies did not report recurrence rates in the group that received BTA [19–22, 25], while the other studies reported rates ranging from 6.4 to 11.4% in

the groups that received BTA, and one study did not report this information [17]. One study recorded a mortality rate of 1.8% [16].

The follow-up time across the various studies ranged from 1 to 49 months, with a mean of 18.6 ± 11.2 months. However, one study had a shorter follow-up, with an average of 1 month [23].

Discussion

The relaxing effect of BTA on the musculature and its antinociceptive effect has already been established [27]. Studies that investigated this effect demonstrated that patients in the BTA group reported less postoperative pain and used fewer opioids during hospitalization than control groups [18, 25]. Studies have also shown a significant decrease in the thickness and an increase in the length of the muscles of the lateral abdominal wall through comparisons with computed tomography of patients before and after the use of BTA, resulting in a significant reduction in hernia defect size and increasing defect closure rates [21, 22, 25, 28–30].

In 2021, Timmer et al. published a systematic review with a meta-analysis of 23 studies to present an overview of the indications, technical aspects, and treatment regimens of BTA injections regardless of the clinical scenario [31]. From data from four studies, they reported that BTA significantly increases the lateral abdominal wall muscle length by 3.2 cm on each side. A meta-analysis from the other three studies showed that BTA pretreatment increases the fascial closure rate. In another systematic review with meta-analysis published in 2017 [32], Weissler et al. described an increase of 1.03 cm in right-sided abdominal wall muscle and 0.95 cm in left-sided abdominal wall muscle length after Botox injection, which confirms the data summarized in this review that BTA is feasible and important to treat complex hernias. Distinctively from these previous studies, in this present review, we specified our purpose to use BTA just in incisional hernias, with no animal models and we described with more detail the safety and surgery results to summarize evidence in this important topic.

However, findings in imaging exams do not necessarily imply clinical and surgical benefits, but motivate further investigation. In this sense, there are divergences, and among the included articles, ten of them proved the benefit and advocated the use of BTA as an adjunct in surgery for difficult-to-repair hernias [11, 16, 19–21, 23, 25, 33]. The article with the largest sample size showed no operative or postoperative benefits with the use of BTA, but it did not provide information about how BTA was used, and it was the result of a retrospective analysis of a database [17].

The inclusion criteria for the group in which BTA was used varied greatly, generating a selection bias among patients. Most articles considered only the size of the defect [16, 17, 20, 22, 23]. Other studies used the defect size and loss of domain as inclusion criteria [19, 33, 34], and one of them also used BMI [11]. Another article adopted the concept of a complex hernia [33] as an inclusion criterion but did not specify which complexity criteria should be taken into account [25]. One of the studies used the preference of the surgeon as inclusion in the BTA group [18]. Most studies did not describe the inclusion of consecutive patients, which may have generated a confirmation bias of "good results from a promising technique".

The studies differed in terms of characteristics of the defect and hernia repair and samples, as only two studies focused on midline hernias [21, 22]. Most studies addressed midline and lateral hernias as well as midline hernias with a lateral component, ranging from M1 to M5 and from L1 to L4 (according to the European Hernia Society -EHS) [26]. These hernias have different characteristics. Midline hernias with a lateral component, for example, have a significantly increased risk of surgical site events when compared with midline and pure lateral hernias [36]. Some studies demonstrated that patients with midline hernias obtained the greatest benefits with BTA [25]. Others were even more precise and stated that midline hernias M3 to M5 benefit more from the use of BTA than midline hernias M1 [16].

The presentation of only defect width data predominated in the studies. However, it is important to understand that width is not the only parameter that matters for hernia repair, but also the length and area of the defect. In this sense, the samples of some studies varied greatly, from small defects with an area of 45 cm^2 to large defects of 648 cm^2 [25]. Regarding the type of surgery, most cases opted for open surgery, with the most commonly used technique being the Rives-Stoppa [37]. However, in some cases, more than 5 different techniques were used [19, 20], which generates a large amount of confusion.

Regarding the use of BTA, the lack of standardization in the existing literature has led to no consensus regarding the ideal dose, concentration, injection site, number of layers, or administration time before surgery. While most studies used 300 units, those that administered 100 units also observed an effect and obtained fascial closure in more than 75% of cases [19, 20]. One study compared groups that received 200 and 300 units of BTA and found that those that received 200 units gained an average of 3.6 cm in length on each side of the abdominal wall, while those that received 300 units gained an average of 4.4 cm in length. However, this difference was not statistically significant ($P = 0.12$) [27]. Regarding the number of muscle layers, there were no statistically significant differences in fascial closure, CST, or postoperative complication rates when injection techniques were compared, including all three muscle layers or just the two outer layers [12].

The costs of BTA administration are rarely reported but are estimated at 400–600 euros more per patient [22, 38]. While this cost initially seems high, it becomes lower when compared to the costs of reoperations due to recurrences, as well as the management of serious postoperative complications generated by more invasive techniques to obtain fascia closure that can be avoided with the use of BTA.

Fascial closure is an important factor in reducing postoperative complications such as surgical site events and recurrence rates [39–41] and it was the main objective of most of the articles included in this study [11, 16, 17, 20, 22]. Fascial closure was achieved in 100% of cases using BTA in some studies [21–23, 28, 29]. However, only one of these studies achieved such an effect without using the CST, the Rives-Stoppa technique, in all patients in the group that used BTA [22].

CST involves dissection of tissue planes and distortion of the abdominal wall anatomy [12, 42–44]. Therefore, any type of CST used in the repair of large ventral hernias is associated with an increased risk of postoperative complications and recurrence rates [45]. One study used CST in 73% of the cases in the BTA group, without describing the indication for such a technique. This was the only study in the sample that failed to demonstrate an increase in fascial closure rates or a decrease in the need for CST or an improvement in outcomes reported by patients after 1 year [17].

No recurrence in the group that used BTA was recorded in five studies [19–22, 25]. However, these data become unreliable considering that the average follow-up time was a little over 1 year and a half. A study using 3-year follow-up data from the ISAAC and INSECT trials (elective exploratory laparotomy) determined that a minimum follow-up of 3 years is required to accurately assess the incidence of post-repair incisional hernia recurrence. The authors demonstrated that 31.5% of all incisional hernias develop within the first 6 months after surgery, 54.4% within 12 months, and 88.9% within 5 years. The fact that more than 50% of all incisional hernias develop more than 12 months after laparotomy supports the need for adequate follow-up [46].

Despite the promising results of this review, some limitations must be considered. Firstly, all articles included were observational and retrospective studies, especially because preoperative use of BTA in large ventral and incisional hernias is off-label in many countries, which makes it difficult to perform randomized clinical trials. Secondly, the studies presented a heterogeneous sample ranging from 14 to 388, with most articles conducted with a small population sample. Six of them had less than 40 patients [19, 21, 25, 31]. Lastly, some studies did not report basic data such as sex, average age, or even characteristics about the administration of BTA [17] and the mean gain in the lateral abdominal wall after BTA application [11, 16–20, 22–24].

In conclusion, this review describes most of the key points about the preoperative use of BTA in hernia repair. It can be concluded that the use of botulinum toxin is a safe practice as no serious complications were attributed to the use of BTA in any of the studies. Some studies have also demonstrated that this is an effective practice that promotes good results in the short and long term, but we need more clinical trials on this to increase the evidence of this practice.

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Declarations

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