INTERVENTIONAL RADIOLOGY
Official journal of the Japanese Society of Interventional Radiology and Asia Pacific Society of Cardiovascular and Interventional Radiology

ORIGINAL RESEARCH

Preoperative Image-guided Botulinum Toxin A Injection in Complex Abdominal Wall Hernia Repair

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Abstract:
Purpose: This study aimed to examine the effectiveness of preoperative image guided botulinum toxin A injection in achieving fascial closure and reducing recurrence rates after repair of complex incisional abdominal wall hernias.
Material and Methods: A total of 32 patients, consisting of 14 males and 18 females, with complex incisional hernias who underwent image guided botulinum toxin A injection at a median 33 [28-38.3] days before surgery were included in this retrospective study. Their mean age was 59.4 ± 11.2 years. Abdominal computed tomography imaging was obtained prior to botulinum toxin A administration to characterize the hernia defects of 26 patients (81.3%, 26/32). The transverse and vertical abdominal wall defects were measured and recorded. Three-dimensional objects of the hernia sac and peritoneal cavity were created based on the delineated borders, and volumes were calculated. The loss of domain was determined using the following formula:

$$LOD = \frac{x}{x+y},$$

where x represents the hernia sac volume and y represents the peritoneal volume. Under ultrasound guidance, the abdominal wall musculature was injected with 300 units of botulinum toxin A across six sites. The fascial closure rate and rate of hernia recurrence were the principal outcomes investigated.
Results: Fascial closure was achieved in 29 patients (90.6%, 29/32). Recurrence was observed in two patients (6.3%, 2/32) over an average followup of 2.5 ± 1.5 years (maximum 6.5). Fascial closure was obtained in 12 out of 14 patients with previous hernia repairs (85.7%, 12/14). One botulinum toxin A related complication was observed—a weakened cough that resolved without further treatment.
Conclusions: Botulinum toxin A is safe and effective in improving rates of fascial closure and reducing instances of reoccurrence in patients with complex incisional hernias.

Keywords:
hernia, incisional hernia, loss of domain, botox, botulinum

Interventional Radiology 2025; 10: e2023-0044
https://doi.org/10.22575/interventionalradiology.2023-0044
https://ir-journal.jp/

Introduction

Postoperative incisional hernias occur as a complication in up to 30% of all abdominal surgeries performed in the United States [1-3]. Necessitating approximately 500,000 repairs annually, abdominal hernia repair is one of the most commonly performed surgery [1, 4, 5]. The repair of incisional hernias is associated with significant rates of recurrence reportedly reaching high as 43% with mesh repair and 60% without mesh reinforcement [3, 5-7]. This high recurrence rate can be primarily attributed to the challenge of minimizing tension during the reapproximation of the ab-

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Received: December 9, 2023, Accepted: May 2, 2024, Advance Publication by J-STAGE: November 22, 2024

dominal fascia [2, 4, 5, 7, 8]. Large long-standing hernias or hernias with significant loss of domain (LOD) can result in large defects or chronically retracted abdominal musculature that increase the complexity of repair, making it difficult to achieve fascial closure without using mesh to bridge the defect [2, 4]. In addition to the dimensions of the hernia itself, many patient factors can negatively impact repair outcomes such as obesity (body mass index (BMI) ≥ 30 kg/m^2), diabetes mellitus, smoking, steroid or immunosuppression usage, poor nutritional status, and old age [7, 9]. In an effort to stratify patients based on risk of recurrence and challenge in obtaining fascial closure, the term "complex hernia" has been standardized, delineating patients into three groups: minor, moderate, and major [2, 9]. Broadly, complex hernias are characterized by one or more of the following features: large size, soft tissue infection or abnormality, patient's history that increases risk of poor outcome, and the clinical context of the repair [9].

In recent years, the use of preoperative botulinum toxin A (BTA) in hernia repairs has gained attention [4, 8, 10, 11]. BTA is a neurotoxin produced by the bacteria *Clostridium botulinum*, with various uses ranging from cosmetic procedures to treatment of dystonia, hyperhidrosis, and various other conditions [3]. Mechanistically, BTA functions at the presynaptic terminal of the neuromuscular junction by impairing the release of acetylcholine resulting in a flaccid paralysis of the targeted muscle [2, 3, 7, 10, 11]. This paralysis has a rapid onset of 2-3 days, reaching maximal effect around 4 weeks and persisting for up to 6 months [2, 3, 7, 10]. The benefits conferred by BTA are believed to be multifaceted—the initial paralysis results in lengthening of the abdominal musculature, decreasing the defect size and significantly reducing the intraoperative difficulty of achieving fascial closure [2-5, 7, 8, 12]. The persistent effects drastically reduce the tension imposed on the fascia during closure and the subsequent healing process [5, 7, 8, 11, 12]. This diminished tension is believed to reduce the risk of complications such as abdominal compartment syndrome, reduced pulmonary capacity, or fascial dehiscence and subsequent hernia recurrence [5, 7, 8, 11, 12]. This study aims to report on fascial closure outcomes, recurrence rates, and complications associated with preoperative ultrasound guided BTA administration by interventional radiologists prior to surgical repair of complex incisional hernias.

Material and Methods

This retrospective study was approved by the institutional review board, and the need to obtain informed consent from the patients was waived. A total of 33 patients, ages 18-75 years, who underwent an image guided BTA injection into the abdominal muscles prior to hernia repair between May 2017 and April 2023 were identified by a imaging database search (mPower Nuance Communications, Burlington, MA). The observation period for followup was until February 2024. Patients who had nonincisional hernias, para-stomal hernia, and emergent cases or who failed to meet complex hernia criteria were excluded. **Table 1** shows patient demographics. Of those identified, one did not undergo hernia repair. The remaining 32 patients were included in this study. The followup period was calculated from the date of hernia repair surgery.

Table 1. Patient Characteristics.

Characteristic	n = 32
Age (years)*	59.4 ± 11.2
Sex	
Male	14 (43.8%)
Female	18 (56.3%)
Body mass index (kg/m^2)**	31.3 [28.1–34]
Diabetes mellitus	9 (28.1%)
Current smoker	5 (15.6%)
Chronic obstructive pulmonary disease	3 (9.4%)
Immunocompromised	4 (12.5%)
Previous repair	14 (43.8%)
Hernia	
Vertical defect (cm)**	13 [9.8–15.8]
Transverse defect (cm)**	10 [8–16.3]
Loss of domain**	7.9 [1.8–21]
Classification	
Minor	1 (3.1%)
Moderate	22 (68.8%)
Major	9 (28.1%)

Data reported as n (%) unless indicated otherwise
*Data reported as mean ± standard deviation
**Data reported as median [interquartile range]

BTA injection

Ultrasound guided (Zenari Z.One Pro, Mahwah, NJ) BTA injections were performed at a median 33 [28-38.3] days before the scheduled surgeries. The BTA injection procedure was performed in the interventional radiology suite using intravenous midazolam (Fresenius Kabi, Bad Homburg, Germany) and fentanyl (Hospira, Lake Forest, IL, USA) for moderate sedation and in conjunction with local anesthetic. Patients were positioned supine or in lateral decubitus based on body habitus and access direction. Ultrasound was used to identify the muscle bellies of the transversus abdominis (TA), internal oblique (IO), and external oblique (EO) at three sites along the midaxillary line bilaterally (**Fig. 1A**). Lidocaine 1% (Hospira, Lake Forest, IL) was percutaneously administered to each of these six sites. A solution of 300 units of BTA (Botoxâ, Allergan, Chicago, IL) diluted in 150 mL of 0.9% saline (2 units/mL) was prepared. Under ultrasound guidance, a 21-gauge echotip needle (Cook Medical, Percutaneous Entry Thinwall Needle, Bloomington, IN) was advanced into the muscle belly of TA (**Fig. 1B**), and 1-2 mL of 0.9% saline was injected to confirm correct needle placement. Ultrasound demonstrated a ballooning hypoechoic density as the saline hydrodissected between the muscle fibers, allowing for visual confirmation of appropriate needle placement (**Fig. 1C**). Then, 50 units of BTA were injected among the three muscle bellies, as the needle was withdrawn (**Fig. 1D**). The procedure was repeated at the five re-

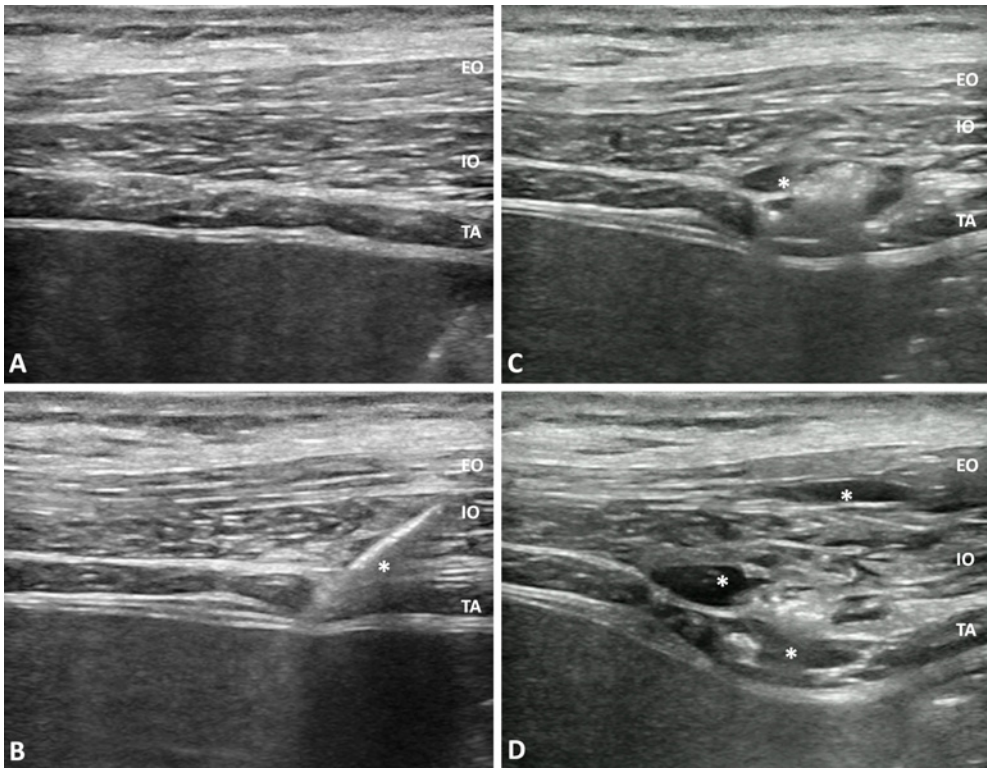

Figure 1. A. Ultrasound image of the anterior abdominal musculature before needle insertion for BTA injection. The layers of the EO, IO, and TA are marked respectively. B. Demonstration of the echogenic needle (*) being guided into the abdominal musculature. C. Saline hydrodissection (*) of the fascial planes of the IO and TA. D. Post-BTA injection displaying BTA fluid depot in the layers of the EO, IO, and TA (*).

maining sites. Complications relating to BTA injections were graded according to the Society of Interventional Radiology adverse event classification [13].

Three-dimensional (3D) hernia volume measurement

Abdominal computed tomography (CT) imaging (GE Healthcare, Boston, MA), pre-BTA and postoperatively, of 26 patients (81.3%, 26/32) was obtained. A slice thickness of 5 mm was used during image acquisition. The transverse and vertical abdominal wall defects were measured using the measurement tool in the picture archiving and communication system (Change Healthcare, Nashville, TN), with values rounded to the nearest whole centimeter. The vectors were drawn as a line that connected the edges of healthy abdominal wall musculature in axial and sagittal views (**Fig. 2**). The volume of the hernia sac was measured using General Electric-Amazon Web Services (Boston, MA). For volume measurement, the most inferior aspect of the hernia sac was identified in the axial plane, and an outline was drawn to delineate the extent of the sac protruding beyond the healthy abdominal wall. The peritoneal cavity borders were defined by the diaphragm superiorly, retroperitoneum posteriorly, abdominal musculature anteriorly and laterally, and the level of the pubic symphysis inferiorly. The radiograph was incrementally advanced, with outlines of the hernia sac and peritoneal cavity drawn at each slice. 3D objects of the sac and peritoneal cavity were created based on the delineated borders, and their volumes were calculated to the nearest tenth cubic centimeter. The *LOD* was determined using the following formula:

$$LOD = \frac{x}{x+y},$$

where x represents the hernia sac volume and y represents the peritoneal volume [14]. **Table 1** summarizes the characteristics of hernia.

Statistical analysis

The continuous variables are summarized with means and standard deviations, if normally distributed. Continuous variables with a nonnormal distribution are reported as medians and interquartile ranges. A Shapiro-Wilk test was used to determine normality. Discrete variables are presented as proportion or percentage of occurrence.

Results

Fascial closure was achieved in 29 out of 32 patients (90.6%) who underwent hernia repair surgery. Component separation technique was used in 28 cases (87.5%) and mesh reinforcement in 29 (90.06%). **Table 2** shows the concurrent procedures. The average followup time was 2.5 ± 1.5 years, with a maximum followup time of 6.5 years. Hernia recurrence was observed in two patients (6.3%) at 7.2 months and 1.5 years after hernia repair, respectively. Fascial closure was obtained in 12 of 14 patients (85.7%) who had previously undergone hernia repairs. In this subset of

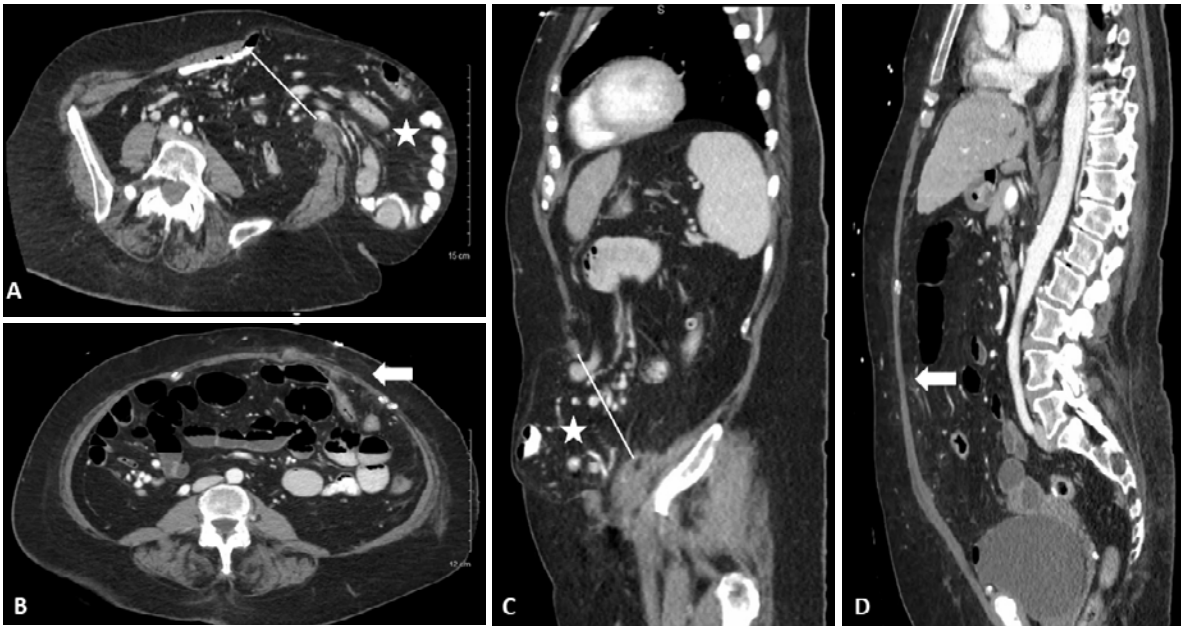

Figure 2. A. Preoperative axial view CT demonstrating transverse dimensions of hernia defect (white line) and hernia pouch (white star). B. Postoperative axial view CT showing complete resolution of hernia defect and reduction of hernia pouch contents into the peritoneal cavity (white arrow). C. Preoperative sagittal view CT demonstrating vertical dimensions of hernia defect (white line) and hernia pouch (white star). D. Postoperative sagittal view CT showing complete resolution of hernia defect and reduction of hernia pouch contents into the peritoneal cavity (white arrow).

Table 2. Surgical Repair Outcomes and Characteristics.

Item	n (%)
Fascial closure	29 (90.6%)
Component separation technique	28 (87.5%)
Mesh reinforcement	29 (90.6%)
Concurrent procedure	9 (28.1%)
Colectomy	3 (9.4%)
Ileocolic anastomosis	2 (6.3%)
Cholecystectomy	1 (3.1%)
Ileorectal anastomosis	1 (3.1%)
Ileostomy closure	5 (15.6%)
Small bowel resection	1 (3.1%)
Gastrocutaneous fistula repair	1 (3.1%)
Umbilical reconstruction	2 (6.3%)

Table 3. Adverse Events.

Event	n (%)
BTA	
Weakened cough*	1 (3.1%)
Surgical	
Abdominal muscle spasm	1 (3.1%)
Hematoma	2 (6.3%)
Ileus	2 (6.3%)
Seroma	3 (9.4%)
Serosal injury	5 (15.6%)
Infection	3 (9.4%)
Deep vein thrombosis	1 (3.1%)

*Grade 1: mild adverse event according to Society of Interventional Radiology Adverse Event Classification [13]
BTA, botulinum toxin A

patients, no instances of recurrence were observed over an average followup period of 2.8 ± 1.6 years (maximum of 6.5 years).

One patient (3.1%, 1/32) experienced a persistently weakened cough as a result of BTA administration, classified as mild according to the new adverse event classification by the Society of Interventional Radiology [13]. Surgical complications were observed in 14 patients (43.8%, 14/32), **Table 3** reports the details.

Discussion

In this study, fascial closure was achieved in 29 patients (90.6%, 29/32), aligning with previous BTA studies reporting the rates between 81 and 94% [2-4, 8, 10]. Meanwhile, rates of fascial closure in complex hernias without BTA pre-treatment have been reported between 77 and 81% [3, 15]. There were two instances of hernia reoccurrence (6.3%, 2/32), which falls within the reported range of 3-9% among previous studies investigating BTA in hernia repair [3, 4, 8]. It is important to view these results in the context of the patients' clinical backgrounds, as 22 patients (68.8%, 22/32) were classified as "moderate" complexity and 9 (28.1%, 9/32) as "major" [9]. Patient BMI is one factor recognized as a significant risk during hernia repair [6]. In this study, 18 patients (56.3%, 18/32) were classified as obese (BMI ≥ 30 kg/m^2) and 7 (21.9%, 7/32) as morbidly obese (BMI ≥ 35 kg/m^2). Rates of recurrence have been shown to increase with each subsequent hernia repair procedure [7]. In this study, 12 patients (37.5%, 12/32) had previously under-

gone a single hernia repair procedure, 2 (6.3%, 2/32) had undergone three repair procedures, and 1 (3.1%, 1/32) had undergone two previous repairs. All patients with previous repairs remained free of recurrence at the end of this study, with an average followup of 2.8 ± 1.6 years. Moreover, nine patients (28.1%, 9/32) underwent concurrent procedures in addition to the hernia repair. Despite all these challenging factors, this study demonstrated high fascial closure rates and low rates of reoccurrence over an impressive followup period up to 6.5 years (mean: 2.5 ± 1.5 years).

Although there is mounting evidence of the efficacy of BTA in the realm of hernia repair, there is a lack of consensus regarding the optimal dosage of preoperative BTA. The literature reports doses ranging from 100 to 500 units, with 300 units being the most commonly used [2, 7, 8, 11, 12]. Higher dosages do not seem to be associated with more adverse events, but one study using only 100 units reported a fascial closure rate of 77%, far below the rates of other studies [3, 7, 10]. In this study, 29 patients (90.6%, 29/32) received 300 units, and 3 (9.4%, 3/32) received 600 units. Two patients received 600 units, due to BMI > 50.0 kg/m^2, and the third received 600 units at the operators' discretion. All instances of recurrence received 300 units. The literature and these results indicate a minimal dosage threshold to achieve full paralysis and a ceiling effect in which escalating doses provide no further benefit. One patient received BTA but was not a candidate for hernia repair due to the inability to achieve tobacco cessation for the prescribed interval.

Although BTA has been repeatedly demonstrated as safe, it may still have risks. The delivery of BTA requires exacting precision, especially in patients with long-standing hernias who have reduced thickness of their abdominal musculature. Thinning of the abdominal wall muscle bellies decreases the size of an already small target and increases the risk of off-target delivery [2-4]. Utilization of ultrasound guided BTA injection can significantly mitigate these risks via direct visualization of needle placement [3, 12]. Appropriate needle placement can be readily demonstrated through hydrodissection of the muscle fibers in conjunction with use of an echogenic needle. Here, the interventional radiologist has a role to play, as there is significant technical skill required to properly visualize and delineate these thin muscle bellies, especially in patients with a large body habitus or adiposity [1, 12]. The most common adverse events that have been reported in BTA administration are weak cough/sneeze, back pain, and bruising at the site of injection [3, 5, 10, 12]. These are reported to occur in less than 5% of patients, with minimal to no treatment required [3]. Some centers have avoided injection of the TA in patients with a history of back pain, and another center has incorporated abdominal binders for these patients that have reportedly provided sufficient relief of symptoms [3, 10]. In this study, one (3.1%, 1/32) adverse event occurred in a patient who received 300 units. The patient reported a persistent weak cough for 2 months after BTA administration that resolved without additional treatment.

Limitations of this study are as follows: possible sources of selection bias in patient selection, lack of standardized followup, procedure variability, and lack of a comparison arm. During the patient selection process, all potential cases with complex hernia were not identified and only the patients referred to the interventional radiologist by the surgeons for BTA injection were included. The retrospective nature of this study precluded a standardized followup protocol to obtain established metrics at predetermined timepoints. Several patients were lost to followup or were deceased by the end of the study diminishing the reported followup time. Due to the retrospective methodology of this study, there was variability in the BTA administration doses as there were not predefined criteria for the choice of 600 units vs 300 units. One patient received 600 units due to operators' clinical judgment. In addition, this study lacks a comparison arm of patients who underwent hernia repair, without BTA, at the same institution to provide context for the efficacy of BTA. Measurement of wall thickness pre-BTA and at designated intervals post-BTA would have provided illuminating data regarding the mechanism by which BTA confers its benefit.

In summary, preoperative image guided BTA administration is safe and effective in improving rates of fascial closure and reducing instances of reoccurrence in patients with complex incisional hernias, particularly in those who have failed previous repairs. Although preoperative BTA administration is currently used off-label, there is a strong rationale for integrating it into the standard of care for incisional hernias repair, emphasizing the need for further adoption.

Acknowledgement: We would like to thank Terri Smith for her help with 3D volume measurements. The material presented in this manuscript was presented at the SIR Annual Scientific Meeting 2021 (abstract no. 430).

Conflict of Interest: None

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contribution: SC conceptualized the study. SC and AK designed the study. JB, AK, MT, NK, YK, MG, and SC collected the data. AK, JB, and SC interpreted the image. JB and AK performed the statistical analysis. JB drafted the manuscript. AK and SC edited the drafted manuscript. JB, AK, MT, NK, YK, MG, and SC critically reviewed the study. JB, AK, MT, NK, YK, MG, and SC was responsible for the final approval the study.

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