

Preoperative Botulinum toxin A enabling defect closure and laparoscopic repair of complex ventral hernia

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Abstract

Introduction Operative management of complex ventral hernia still remains a significant challenge for surgeons. Closure of large defects in the unprepared abdomen has serious pathophysiological consequences due to chronic contraction and retraction of the lateral abdominal wall muscles. We report outcomes of 56 consecutive patients who had preoperative Botulinum toxin A (BTA) abdominal wall relaxation facilitating closure and repair.

Methods This was a prospective observational study of 56 patients who underwent ultrasound-guided BTA into the lateral abdominal oblique muscles prior to elective ventral hernia repair between November 2012 and January 2017. Serial non-contrast abdominal CT imaging was performed to evaluate changes in lateral oblique muscle length and thickness. All hernias were repaired laparoscopically, or laparoscopic-open-laparoscopic (LOL) using intraperitoneal onlay mesh.

Results 56 patients received BTA injections at predetermined sites to the lateral oblique muscles, which were well

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tolerated. Mean patient age was 59.7 years, and mean BMI was 30.9 kg/m² (range 21.8–54.0). Maximum defect size was 24 × 27 cm. A subset of 18 patients underwent preoperative pneumoperitoneum as an adjunct procedure. A comparison of pre-BTA to post-BTA imaging demonstrated an increase in mean lateral abdominal wall length from 16.1 cm to 20.1 cm per side, a mean gain of 4.0 cm/ side (range 1.0–11.7 cm/side) (p < 0.0001). This corresponds to an *unstretched* mean length gain of 8.0 cm of the lateral abdominal wall. Laparoscopic/LOL primary closure was achieved in all cases, with no clinical evidence of raised intra-abdominal pressures. One patient presented with a new fascial defect 26 months post-operative.

Conclusion Preoperative BTA to the lateral abdominal wall muscles is a safe and effective technique for the preparation of patients prior to operative management of complex ventral hernias. BTA temporary flaccid paralysis relaxes, elongates and thins the chronically contracted abdominal musculature. This in turn reduces lateral traction forces facilitating laparoscopic repair and fascial closure of large defects under minimal tension.

Keywords Complex ventral hernia · Botulinum toxin A · Preoperative progressive pneumoperitonealisation · Component separation · Laparoscopic repair

Complex ventral hernia repair remains a challenging procedure for surgeons. Large defect size, fascial disruption, scarring, mesh from previous repairs, obesity, diabetes and other comorbidities all combine to produce a scenario which is complex, demanding and has an inherently high risks of failure. The risk of recurrence following open repair of incisional ventral hernia is as high as 63% for suture repair and 32% for prosthetic repair at 10 years [1]. The advent of laparoscopic ventral hernia repair and primary closure of the midline has been shown to reduce recurrence rates when compared to standard bridging mesh repair techniques. Recent studies have reported recurrence rates between 4.8 and 33% for bridging mesh repair compared with 0-7.7% for hernia defect closure and mesh repair [2–5].

Several techniques have been previously described with the purpose of expanding the abdominal wall, including pneumoperitonisation [6] and myocutaneous fascial expanders [7, 8]. However, these have largely fallen out of favour due to high risk profiles and poor results. Today the mainstay of myofascial lengthening still remains operative, with the evolution of numerous component separation techniques, since first described by Ramirez in 1990 [9].

Recently, a novel technique for preoperative abdominal wall relaxation and lengthening has been described using *Botulinum toxin A* (BTA). BTA is a neuromodulating agent, which when injected preoperatively into lateral abdominal wall muscles, has been shown to result in temporary flaccid paralysis and lengthening of the targeted muscles [10–17]. We report our outcomes of 56 consecutive patients who were administered preoperative Botulinum toxin A (BTA) to provide flaccid paralysis of the abdominal wall muscles, facilitating surgical closure and repair.

Materials and methods

This is a single-centre prospective cohort study of patients who have presented with complex ventral hernias (CVH) from November 2012 until January 2017 (and ongoing). Patients underwent a comprehensive multidisciplinary preoperative management process which included preoperative abdominal wall preparation using BTA injections to the lateral oblique muscles prior to surgery. A complex ventral hernia was defined as (i) a recurrent, multi-recurrent or traumatic hernia in the midline or lateral abdominal wall with a minimum fascial defect of 6 cm as either one dominant defect or an accumulation of multiple smaller Swiss-cheese type defects and/or (ii) a loss of domain >20%. The multidisciplinary preoperative management protocol includes detailed abdominal wall imaging, preoperative optimisation of comorbidities and abdominal wall preparation with BTA, with or without preoperative progressive pneumoperitoneum (PPP) [Personal communications Jacombs 2017 Comprehensive Multidisciplinary Preoperative Management Programme for Patients with Complex Ventral Hernia (submitted)].

Abdominal wall imaging

A baseline non-contrast axial abdominal computed tomography (CT) scan was performed in both resting and functional phases. The functional CT scan required the patient to produce a "ballooning" and "crunching" manoeuvre whilst lying supine on the CT machine table. Three-dimensional volume-rendered (3DVR) images were generated from baseline CT data using a widely available computer-based post-processing techniques to generate photo-realistic panoramic images of the abdominal wall. 3DVR imaging confers the ability to peel away layers of the abdominal wall as required to reveal points of interest. Functional abdominal CT imaging was repeated approximately 10 days after preoperative abdominal wall preparation (BTA \pm PPP) and post-operatively at 1–2 months and at 6 months. Additional imaging was performed as required.

Measurements of axial muscle length were taken along the deep surface of the abdominal wall muscle complex from the lateral border of the quadratus lumborum to the medial edge of the rectus abdominis on each side. Muscle thickness was measured at mid-axillary line from the deep surface of transversus abdominis (TA) to the superficial surface of external oblique (EO).

All of the imaging performed in this cohort was performed by a single radiologist (JR) and critically reviewed by both surgeon (NI) and radiologist (JR) to identify, measure and assess the abdominal wall and its function. This included assessing the hernia, its contents and any complicating features such occult hernias, areas of muscle atrophy, mesh location and complications and associated abnormalities which may compromise the stability of the abdominal wall and may potentially be the cause of previous repair failures.

Abdominal wall preparation

BTA injections were performed 7–14 days prior to the planned date of surgery. Using aseptic technique and under ultrasound guidance, patients received either 300 or 200 units of BTA (onabotulinumtoxinA as either BOTOX[®] or equivalent amount of Dysport[®]) into all three muscle layers of interest: external oblique, internal oblique and transversus abdominis, using a technique previously described [10, 15].

PPP was performed on a subset of patients as an adjunct to BTA. Indications for PPP were a fascial defect ≥ 15 cm, or infra-umbilical defect ≥ 9 cm or a loss of domain $\geq 20\%$. PPP therapy was performed 3–7 days prior to surgery using a 22-gauge spinal needle and under ultrasound guidance, away from previous or planned incision sites. 300 ml of air was insufflated using a technique previously described [11]. An 8 Fr pigtail catheter was then inserted into the largest pocket of intraperitoneal air and insufflation of up to 1000 ml of air was performed, depending on patient tolerance. Patients were monitored overnight and discharged home the following day.

Surgical management

All patients underwent total laparoscopic (TL) or laparoscopic-open-laparoscopic (LOL) mesh repair as previously described [10, 11, 18]. After general anaesthesia and endotracheal intubation, indwelling urinary catheter and nasogastric tube were inserted. Abdominal insufflation was performed using Veress needle and multiple 5, 12 and 15 mm laparoscopic ports were inserted bilaterally as required, under vision.

Fascial closure was obtained in TL operations with approximation of fascial edges using transcutaneous nonabsorbable No 5 Ti-CronTM sutures in a transverse shoelace fashion along the length of the defect. When required, a laparoscopic-assisted LOL technique utilised a 7 cm gel access port to enable repeated entry into the peritoneal cavity to facilitate mesh resection and bowel inspection after adhesiolysis, and occasionally to enable fascial closure under direct vision. After primary closure, the repair was reinforced with a composite-polypropylene mesh (Bard SeprameshTMST, Bard VentralightTMST or Bard VentralightTMST EchoTM) measured and tailored to the length of the defect with appropriate overlap. The mesh was anchored at 6 and 12 o'clock using transfascial nonabsorbable sutures, and at four key positions using mesh tails which were pulled transfascially. Remaining fixation was performed using absorbable fixation tacks. The preferred mesh placement was intraperitoneal onlay mesh (IPOM). However, three patients required a hybrid procedure with modified Rives-Stoppa pre-peritoneal mesh placement. The transverse length of the mesh was measured to the transverse diameter of the fascial defect plus 7 cm overlap on each side. When required, two adjoining pieces of mesh are used and shaped to provide adequate mesh coverage.

Post-operatively, patients were fitted with an abdominal binder which was worn until 3 months post-repair. Select patients with comorbidities requiring close observation were sent to intensive care as a preventative risk mitigation strategy. Deep vein thromboembolic prophylaxis including enoxaparin 40 mg daily and T.E.D.TM anti-embolism stockings continued throughout the admission. Additionally, sequential calf compression devices were used for a minimum 48 h and continued until the patient was mobilising. Antibiotic prophylaxis was commenced at anaesthetic induction and continued for 72 h. Patients with confirmed or suspected mesh infections were managed

perioperatively on intravenous antibiotics under the advice of a microbiologist.

Statistical analyses were performed using XLSTAT for Microsoft Excel[®] with a p < 0.05 significance. Descriptive statistics included means and range and standard deviation for the variables

Results

From November 2012 until January 2017 (and ongoing), a total of 56 patients (29 males and 27 females) underwent preoperative BTA preparation of the abdominal wall muscles, followed by elective ventral hernia repair. The patients mean age was 59.7 ± 12.8 years (range 20–84) with a mean BMI 30.9 kg/m² (range 21.8–54). Forty-five patients (80%) presented with midline defects, 11 patients (20%) presented with lateral defects and 18 (32%) demonstrated loss of domain \geq 20% (Table 1). The mean transverse fascial defect was 11.6 cm \pm 5.2 cm (range 5.0–28.0 cm). The smallest hernia defect was 5 × 9 cm and the largest 28 × 19 cm.

Forty patients (73%) had undergone at least one previous repair with 27 (48%) of these repairs utilising mesh. The mean number of prior hernia repairs was 2.4 (range 1–7).Thirty-six patients (46%) had at least one comorbidity (Table 1), including diabetes (20%), cardiovascular (16%) and respiratory (9%) disease. Twenty-nine (52%) of patient were overweight, obese or morbidly obese (Table 1). There were 21 (38%) ex-smokers, five of who had ceased smoking between 3 and 12 months prior to surgery. There were no active smokers at the time of surgery.

BTA injections were generally well tolerated, with none of the patients experiencing any complications requiring intervention. Several patients experienced superficial bruising after injection. A common side effect from the abdominal wall paralysis was a sensation of bloating, beginning at approximately the third day post-injection and only resolving after the hernia repair was performed. Most patients reported a weak cough, and four reported back pain following BTA injection. When these symptoms occurred, an abdominal binder was used to alleviate their symptoms, with some effect. Of the 18 patients who underwent adjunct PPP, eight patients (44%) experienced pneumoperitoneum-related complications. These included subcutaneous emphysema in 4 (22%) patients, pneumomediastinum in 4 (22%) patients, pneumothorax in 3 (17%) patients (none requiring insertion of chest drain), pneumocardium in 1 (6%) patient and metabolic acidosis in 1 (6%) patient. These complications were all managed conservatively and required no intervention.

All patients received BTA administration prior to surgery, 31 patients received 300 units of BTA (Fig. 1) and Table 1 Demographic and
characteristics of patients with
complex ventral hernias
undergoing assessment and
management with a
comprehensive
multidisciplinary preoperative
management protocol

Characteristic	СVН
Age (range)	59.7 ± 12.8 years
	(20-84 years)
Gender	
Female (%)	27 (48%)
Male (%)	29 (52%)
Complex ventral hernia	
Mean maximal transverse dimension (range)	11.6 cm \pm 5.5 cm (5.0–28.0 cm)
Number of midline defects (%)	45 (80%)
Number of lateral defects (%)	11 (20%)
Patients loss of domain ≥ 20	18 (32%)
BMI (kg/m ²)	
Obese (BMI 30–39)	14 (25%)
Morbidly obese (BMI ≥ 40)	4 (7%)
Overall mean (range)	$30.9 \pm 6.4 \ (21.8-54.0)$
Smokers	
Ex-smokers	21 (38%)
Ex-smoker (cease <12 m prior to consultation)	5 (9%)
Other comorbidities	
Diabetes	11 (20%)
Cardiovascular	9 (16%)
Respiratory	5 (9%)
Malignancy	5 (9%)
Immunosuppression	4 (7%)
Connective tissue disorder	1 (2%)
Complex ventral hernia	
Mean maximal transverse dimension (range)	11.6 cm + 5.5 cm (5.0-28.0 cm)
Number of midline defects (%)	45 (80%)
Number of lateral defects (%)	11 (20%)
Patients loss of domain >20	18 (32%)

25 patients received 200 units of BTA. This was performed in an attempt to delineate the optimal dosage of BTA. A further subset of 18 patients received PPP (Fig. 2) The effects of the different treatments were analysed individually. Initial analysis demonstrated that BTA therapy resulted in a significant increase in lateral abdominal length in all sub groups (Table 2). The mean length gain per side in the 300 unit BTA group was 4.4 ± 2.2 cm (p < 0.0001), and in the 200 unit BTA group the mean length gain per side was 3.6 ± 0.9 cm (p < 0.0001). In the BTA only group, the mean length gain per side was 4.2 ± 2.5 cm (p < 0.0001), and the BTA with PPP group demonstrated a mean length gain per side 3.7 ± 1.9 cm (p < 0.0001). When all results were pooled, the mean overall length gain per side was 4.0 ± 2.3 cm (p < 0.0001) (Table 2).

Further statistical analysis compared the difference between dosages of 300 units BTA and 200 units BTA. Even though the mean length gain of 200U-BTA $(3.6 \pm 0.9 \text{ cm})$ was lower than 300U-BTA $(4.4 \pm 2.2 \text{ cm})$ this difference was not statistically significant [*z*-score = 1.16, *p* = 0.12 (NS)]. Similarly the BTA only treatment (mean length gain 4.2 ± 2.5 cm) was compared to the BTA + PPP treatment (mean length gain 3.7 ± 1.9 cm); there was no statistical difference between the groups [*z*-score 1.30, *p* = 0.09 (NS)].

Surgical outcomes

Of the 56 patients undergoing preoperative BTA abdominal wall preparation, seven patients had their operative repair performed by other surgeons. The remaining 49 patients were all operated on by two surgeons (NI and PC). In all cases, the hernia defect(s) were closed by either a total laparoscopic-mesh repair (41 patients 73%) or laparoscopic-open-laparoscopic (15 patients 27%). Eight (16%) required the addition of endoscopic single port component separation to achieve fascial closure [Personal



Fig. 1 Functional CT imaging of the effect of Botulinum toxin A on the anterior abdominal wall in complex ventral hernia. Pre-BTA and Post-BTA functional 2D axial images at the same lumbar level, in resting and crunching phases, of a 59-year-old male with a 15.8×21.5 cm midline defect. He had a loss of domain of 22% and had one failed hernia repair. These images illustrate the dynamic changes to the anterior abdominal wall seen in CVH patients after BTA injections. (1) The pre-BTA resting phase image demonstrates the chronically contracted and thickened lateral abdominal wall muscles (baseline-resting). (2) The pre-BTA crunching phase image demonstrates the minimal ability of the chronically contracted lateral abdominal wall to contain the abdominal viscera during an action that required contraction of the lateral abdominal wall. This resulted in the increased evisceration of the intraabdominal organs (baseline-functional). (3) The post-BTA resting phase image demonstrates the thinning and elongation of the lateral abdominal wall that is observable clinically and radiographically after 2-3 days after BTA injection. (4) The post-BTA crunching phase image demonstrates the functional change in the anterior abdominal wall with active decrease of hernia size and contents. After BTA during a functional phase when the abdominal wall is activated the abdominal wall works to contain the intraabdominal contents within the abdominal cavity

communication Elstner 2017 Single Port Component Separation: endoscopic external oblique release for complex ventral hernia repair (Submitted)]. No patient required conversion to laparotomy to complete the operation, and there was one unplanned return to operating theatre due to small bowel anastomotic leak. The mean operative time was 414 ± 155 min (range 147–695 min).

A SeprameshTM-polypropylene composite-barrier mesh, or its equivalent was placed in the IPOM position in 53 patients (94%), with the remaining three patients having Rives-Stoppa retro-rectus mesh placement due to scarring from previous surgery. Two (3.6%) patients underwent staged repairs. One patient with giant ventral hernia presented with a history of six previous failed repairs and an incarcerated hernia. On reduction of the hernia, a cluster of small bowel was found to be adherent to polypropylene mesh, with separation not feasible without serosal damage or enterotomy. A small bowel resection was carried out, excising a 25 cm piece of polypropylene mesh en bloc. The procedure was then staged by 4 days. The patient subsequently developed a small bowel anastomotic leak on day 8. The mesh was explanted and the procedure was completed 10 months later. The second-staged procedure was due to a large bowel enterotomy, which was immediately noted and repaired endoscopically. The peritoneal cavity was washed out, intravenous antibiotics were continued and the surgery was staged 72 h later. Definitive mesh repair took place during the second procedure, with no further complications.

Post-procedure, 29 patients (52%) were admitted to the intensive care unit (ICU) for ongoing monitoring and support. All were planned ICU admissions aside from a 62-year-old male, with known paroxysmal atrial fibrillation, who went into rapid atrial fibrillation and early



Fig. 2 2D axial and Coronal CT images Pre-BTA + PPP and Post-BTA + PPP. 2D CT scan Pre-BTA+PPP (**A**) and post-BTA and PPP (**B**, **C**) showing reduction in hernia contents and pneumatic adhesiolysis of most, but no all visceral adhesions. Surgically important mesenteric adhesions (**B**) and small bowel adhesions (**C**) were clearly

identified and the anatomical locations could be determined. These imaging results enable the surgeon to preoperatively determine anatomical safe areas for laparoscopic entry and port placement as well as pre-empt areas of visceral adhesion that requires surgical adhesiolysis and/or resection

Table 2 Ana	dysis of Pre-BTA and Post-BTA	elongation for patients undergoing p	reoperative BTA abdominal wall pre	paration		
Treatment	Mean transverse defect size (cm) (range)	Mean Pre-BTA length of lateral abdominal wall muscles (per side) (cm)	Mean Post-BTA length of lateral abdominal wall muscles (per side) (cm)	Mean gain in lateral abdominal wall muscles (per side) (cm) (range)	<i>p</i> value	95% confidence intervals
All patients $n-56$	$11.7 \pm 5.2 \text{ cm} (5.0-28.0 \text{ cm})$	$16.1 \pm 3.9 \text{ cm}$	$20.1 \pm 4.0 \text{ cm}$	$4.0 \pm 2.3 \text{ cm} (0.111.7 \text{ cm})$	p < 0.0001 (z- score = -7.34)	3.55–4.45 cm
300 units BTA	$12.6 \pm 5.3 \text{ cm} (5.024.0 \text{ cm})$	$16.0 \pm 4.0 \text{ cm}$	$20.4 \pm 4.1 \text{ cm}$	$4.4 \text{ cm} \pm 2.2 \text{ cm} (0.111.7 \text{ cm})$	p < 0.0001 (z- score = -5.79)	3.82-4.98 cm
n = 31						
200 units BTA	$10.5 \pm 5.1 \text{ cm} (5.8-25.0 \text{ cm})$	$15.9 \pm 3.9 \text{ cm}$	$19.5 \pm 4.0 \text{ cm}$	3.6 ± 0.9 cm (1.0–5.4 cm)	p < 0.0001 (z- score = -4.56)	3.34–3.86 cm
n = 25						
BTA only $n = 38$	$9.8 \pm 4.3 \text{ cm} (5.028.0 \text{ cm})$	16.7 ± 4.1 cm	$20.9 \pm 4.0 \text{ cm}$	$4.2 \pm 2.5 \text{ cm} (0.211.7 \text{ cm})$	p < 0.0001 (z-score = -6.27)	3.62 – 4.78 cm
BTA + PPP n = 18	$15.6 \pm 4.8 \text{ cm} (8.0-24.0 \text{ cm})$	$14.7 \pm 3.0 \text{ cm}$	$18.4 \pm 3.6 \text{ cm}$	$3.7 \pm 1.9 \text{ cm} (0.1-7.2 \text{ cm})$	p < 0.0001 (z-score = -4.44)	3.05-4.35 cm

respiratory failure post-operatively in recovery. His symptoms resolved with ICU homeostatic support without further sequelae. There were no unexpected returns to ICU once the patient had been discharged to the ward. The mean length of hospital admission was 12.3 ± 11.4 days (range 2–57 days). In this group, there were two patients who required prolonged hospitalisations of 55 and 57 days, predominantly for social

and rehabilitation reasons.

There were seven patients (14%) with post-operative complications. The most significant complications were in one patient with rapid atrial fibrillation and type II respiratory failure (as detailed above) and one patient with a transient ischaemic attack on post-operative day 4 that was managed conservatively with neurological consultation. The same patient developed a seroma that required repeated aspiration. Other wound complications included a minor wound infection requiring conservative wound management only (one patient), minor bleeding from a drain exit site that occurred post discharge and resolved with conservative management (one patient), port-site hernia requiring surgical repair (four patients), persistent pain from transfascial mesh anchor suture (one patient) which required removal of the suture and a post-operative collection and infection most likely from disruption of a patent urachus (one patient) not evident at the time of surgery, requiring aspiration and intravenous antibiotics. Recently, one patient (2%) presented at 26 months post-repair, with a single-midline hernia defect evident beyond the region of mesh coverage. Whether this represents a failure to identify the defect at time of surgery, mesh shrinkage or a de novo occurrence, remains under investigation.

Discussion

The repair of complex ventral hernias is particularly challenging for surgeons, and despite new techniques and approaches, recurrence rates remain alarmingly high. BTA is a new technique with great potential for the preoperative preparation of the abdominal wall prior to surgical repair [12]. Previous studies have demonstrated that BTA therapy is generally well tolerated [10, 13–15, 17–20], and in conjunction with other methods such as PPP, facilitates primary closure without the extensive disruption of tissues which is created by traditional component separation [11, 20]. To date, there has been multiple studies supporting the developing hypothesis that BTA facilitates primary closure at the time of surgery, but its extended duration of action also protects the repair line during the critical initial 3 months of wound healing. It does so by prolonged

minimisation of lateral traction forces, which physiologically serve to pull the wound apart [10, 15, 17, 20, 21].

In 2009, Ibarra-Hurtado et al. reported in a prospective study of 12 patients with abdominal wall hernia occurring after open abdomen management, a mean hernia defect reduction of 5.25 ± 2.32 cm following BTA application under electromyography guidance of the abdominal wall. In six patients, primary fascial closure was achieved; the remaining six patients required component separation. No recurrences were reported at 9 months [13]. Subsequently, in 2014 in a trial of 17 patients with similar characteristics, they reported abdominal wall muscle thickness reduction and length increase after injection of 250 IU of BTA. Measurements were taken using CT assessment post-BTA injection [17]. Farooque et al. [15] also demonstrated that BTA induced thinning and lengthening of the lateral abdominal wall musculature, comparable to the increase in abdominal wall length after surgical component separation.

Zielinski et al. [19] reported the use of 300 IU BTA in 18 patients with open abdomen 12–24 h after the initial laparotomy once patient was hemodynamically stable. Primary closure was achieved in 83% of cases. Mortality rate was 11% however unrelated to BTA. There were no complications related to the use of BTA.

Conversely, Chevez et al. [16] reported a series of 14 patients undergoing large incisional hernia repair who were injected 50 IU of BTA on each side of the abdominal wall under EMG guidance. Pre-BTA and 4 weeks post-BTA images were analysed with no significant change in size of hernia defect following administration of 100 IU of BTA. However, primary closure was achieved in 78% of their cases.

Fifty-six patients with complex ventral hernia were treated in our centre from November 2012 to January 2017, and underwent either total laparoscopic or laparoscopic-open-laparoscopic (LOL) repair. 53 patients underwent intraperitoneal (IPOM) mesh repair and 3 underwent laparoscopic adhesiolysis and assessment of fascial defect followed by modified Rives-Stoppa pre-peritoneal mesh placement. This alternative technique was performed due to the absence of adequate domain for laparoscopic closure of defect and mesh placement, following administration of either 300 or 200 IU. Our experience over the course of this study demonstrated that both dosages of BTA-300 and 200 units result in significant axial muscle elongation, but when outcomes were analysed there was no statistically significant difference between the two BTA doses. This suggests that the lower dose may be as efficacious as the higher dose, or as demonstrated by Chavez et al. the lesser dose despite less measurable gain on imaging can still have a positive impact on achieving primary closure. In our series, we reduced our dose of BTA from 300 IU with the first 31 patients, to 200 IU for the second 25 patients, and when compared, these two groups demonstrated a slight reduction in the gain achieved from the BTA, however the difference was not statistically significative.

Goni Moreno's PPP technique has been available for many years, nonetheless, it fell in disuse due to limited indications and complication rates, despite many positive reports in the literature [6, 22]. It has gained traction again over the last 5 years thanks to recent studies that have shown renewed potential as adjuvant preoperative technique for the management of CVH. The main advantage of PPP is that it allows the return of the hernia contents to the abdominal cavity. It also improves patient tolerance to the increased abdominal volume following the hernia repair by multiple mechanisms [22]. Based on the premise that a tension-free repair is the gold standard [23], the use of concomitant multiple techniques is warranted in the complex hernia. Elstner et al. [18] reported on the use of PPP as an adjuvant preoperative technique to BTA. Sixteen patients with a mean loss of domain of 28% were included in the study, and received both PPP and BTA prior to surgery, and demonstrated a mean gain of 5.6% in abdominal circumference, compared with a mean gain of 8.3% in hernia sac circumference. Primary closure was achieved in all patients with no instances of post-operative abdominal compartment syndrome, wound dehiscence or prolonged ventilatory support. Similarly, Bueno-Lledo et al. [20] also used concomitant PPP and BTA for management of large incisional hernias, achieving a significant increase in hernia volume and abdominal cavity volume with no significative changes in the hernia/abdominal cavity volume ratio. On the other hand, both of these studies reported a considerable increase in PPP-related complications such as shoulder tip pain, subcutaneous emphysema, pneumothorax and pneumopericardium.

In this series, the subset of patients who underwent BTA + PPP showed no further elongation of the abdominal wall muscle when compared to BTA alone. The reasons for this result most likely arise from the very short duration of PPP therapy used here, compared with the much longer duration of PPP which most previous studies observed. However, our results did indicate that there was an increase in abdominal cavity volume *prior to surgery* which allowed an understanding of the independent benefits of BTA and PPP. BTA appears to be the main contributor to elongation and thinning of the abdominal wall musculature, whereas PPP appears to facilitate adhesiolysis (pneumatic adhesiolysis), and identifies areas of adhesions to the anterior abdominal wall, demonstrating safe areas for port placement.

Conclusion

Preoperative BTA injection to the lateral obliques is a safe, effective and reproducible technique in patient preparation for operative management of complex ventral hernias. The flaccid paralysis delivered by BTA resulted in the relaxation, elongation and thinning of the chronically contracted abdominal lateral wall musculature. This infers reduction of the physiological lateral traction forces of the abdominal wall, and consequently facilitates laparoscopic repair and primary closure of large defects under minimal tension. We have shown that there was no statistically significant difference in the length gain achieved from 200 and 300 IU of total BTA dose. Likewise, despite PPP not demonstrating a major influence on elongation and thinning of abdominal wall muscle, it does play an advantageous role in selected patients at time of surgery by facilitating hernia reduction, adhesiolysis and elucidation of safe site for abdominal access both endoscopic and open as could be seen in post-PPP CT scan. On the other hand, a limitation of the study is the small sample and the short mean follow-up duration. Further long-term follow-up of these cases is required in order to identify possible delayed recurrence of ventral hernia.

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Compliance with ethical standards

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References

- Burger JWA, Luijendijk RW, Hop WCJ, Halm JA, Verdaasdonk EGG, Jeekel J (2004) Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg: 176–183
- Zeichen MS, Lujan HJ, Mata WN, Maciel VH, Lee D, Jorge I et al (2013) Closure versus non-closure of hernia defect during laparoscopic ventral hernia repair with mesh. Hernia 17(5):589–596
- Giordano S, Garvey PB, Baumann DP, Liu J, Butler CE (2017) Primary fascial closure with biologic mesh reinforcement results in lesser complication and recurrence rates than bridged biologic mesh repair for abdominal wall reconstruction: a propensity score analysis. Surgery 161(2):499–508
- 4. Suwa K, Okamoto T, Yanaga K (2016) Closure versus non-closure of fascial defects in laparoscopic ventral and incisional

hernia repairs: a review of the literature. Surg Today 46(7):764–773

- Mitura K, Skolimowska-Rzewuska M, Garnysz K (2017) Outcomes of bridging versus mesh augmentation in laparoscopic repair of small and medium midline ventral hernias. Surg Endosc 31(1):382–388
- Goni Moreno I (1971) Pneumoperitoneum applied to the surgical preparation of large chronic eventrations. Prensa medica argentina 58(21):1037–1041
- Admire AA, Dolich MO, Sisley AC, Samimi KJ (2002) Massive ventral hernias: role of tissue expansion in abdominal wall restoration following abdominal compartment syndrome. Am Surg 68(5):491–496
- Jacobsen WM, Petty PM, Bite U, Johnson CH (1997) Massive abdominal-wall hernia reconstruction with expanded external/ internal oblique and transversalis musculofascia. Plast Reconstr Surg 100(2):326–335
- Ramirez OM, Ruas E, Dellon AL (1990) "Components separation" method for closure of abdominal-wall defects: an anatomic and clinical study. Plast Reconstr Surg 86(3):519–526
- Elstner KE, Jacombs AS, Read JW, Rodriguez O, Edye M, Cosman PH et al (2016) Laparoscopic repair of complex ventral hernia facilitated by pre-operative chemical component relaxation using Botulinum Toxin A. Hernia 20(2):209–219
- Elstner KE, Read JW, Rodriguez-Acevedo O, Cosman PH, Dardano AN, Jacombs AS et al (2017) Preoperative chemical component relaxation using Botulinum toxin A: enabling laparoscopic repair of complex ventral hernia. Surg Endosc 31(2):761–768
- Weissler JM, Lanni MA, Tecce MG, Carney MJ, Shubinets V, Fischer JP (2017) Chemical component separation: a systematic review and meta-analysis of botulinum toxin for management of ventral hernia. J Plast Surg Hand Surg:1–9
- Ibarra-Hurtado TR, Nuno-Guzman CM, Echeagaray-Herrera JE, Robles-Velez E, de Jesus Gonzalez-Jaime J (2009) Use of botulinum toxin type a before abdominal wall hernia reconstruction. World J Surg 33(12):2553–2556
- Ibarra Hurtado TR (2014) Toxina botulínica A: su importancia en pacientes con grandes hernias abdominales. Revista Hispanoamericana de Hernia. 2(4):131–132
- 15. Farooque F, Jacombs AS, Roussos E, Read JW, Dardano AN, Edye M et al (2016) Preoperative abdominal muscle elongation with botulinum toxin A for complex incisional ventral hernia repair. ANZ J Surg 86(1–2):79–83
- Chávez-Tostado KV, Cárdenas-Lailson LE, Pérez-Trigos H (2014) Resultado de la aplicación preoperatoria de toxina botulínica A en el tratamiento de hernias incisionales gigantes. Revista Hispanoamericana de Hernia. 2(4):145–151
- 17. Ibarra-Hurtado TR, Nuno-Guzman CM, Miranda-Diaz AG, Troyo-Sanroman R, Navarro-Ibarra R, Bravo-Cuellar L (2014) Effect of botulinum toxin type A in lateral abdominal wall muscles thickness and length of patients with midline incisional hernia secondary to open abdomen management. Hernia 18(5):647–652
- Elstner KE, Read JW, Rodriguez-Acevedo O, Ho-Shon K, Magnussen J, Ibrahim N. Preoperative progressive pneumoperitoneum complementing chemical component relaxation in complex ventral hernia repair. Surg Endosc. 2016
- Zielinski MD, Goussous N, Schiller HJ, Jenkins D (2013) Chemical components separation with botulinum toxin A: a novel technique to improve primary fascial closure rates of the open abdomen. Hernia 17(1):101–107
- Bueno-Lledo J, Torregrosa A, Ballester N, Carreno O, Carbonell F, Pastor PG et al (2017) Preoperative progressive pneumoperitoneum and botulinum toxin type A in patients with large incisional hernia. Hernia 21(2):233–243

- Zendejas B, Khasawneh MA, Srvantstyan B, Jenkins DH, Schiller HJ, Zielinski MD (2013) Outcomes of chemical component paralysis using botulinum toxin for incisional hernia repairs. World J Surg 37(12):2830–2837
- Sabbagh C, Dumont F, Fuks D, Yzet T, Verhaeghe P, Regimbeau JM (2012) Progressive preoperative pneumoperitoneum preparation (the Goni Moreno protocol) prior to large incisional hernia

surgery: volumetric, respiratory and clinical impacts. A prospective study. Hernia 16(1):33-40

23. Booth JH, Garvey PB, Baumann DP, Selber JC, Nguyen AT, Clemens MW et al (2013) Primary fascial closure with mesh reinforcement is superior to bridged mesh repair for abdominal wall reconstruction. J Am Coll Surg 217(6):999–1009