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ORIGINAL ARTICLE

# Implementing preoperative Botulinum toxin A and progressive pneumoperitoneum through the use of an algorithm in giant ventral hernia repair

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## Abstract

**Background** Repair of large ventral hernias with loss of domain can be facilitated by preoperative Botulinum toxin A (BTA) injections and preoperative progressive pneumoperitoneum (PPP). The aim of this study is to evaluate the outcomes of ventral hernioplasty using a standardized algorithm, including component separation techniques, preoperative BTA and PPP.

**Methods** All patients between June 2014 and August 2018 with giant hernias (either primary or incisional) of more than 12 cm width were treated according to a previously developed standardized algorithm. Retrospective data analysis from a prospectively collected dataset was performed. The primary outcome was closure of the anterior fascia. Secondary outcomes included complications related to the preoperative treatment, postoperative complications, and recurrences.

**Results** Twenty-three patients were included. Median age was 65 years (range 28–77) and median BMI was 31.4 (range 22.7–38.0 kg/m$^2$). The median loss of domain was 29% (range 12–226%). For the primary and secondary endpoints, 22 patients were analyzed. Primary closure of the anterior fascia was possible in 82% of all patients. After a median follow-up of 19.5 months (range 10–60 months), 3 patients (14%) developed a hernia recurrence and 16 patients (73%) developed 23 surgical site occurrences, most of which were surgical site infections (54.5%).

**Conclusion** Our algorithm using both anterior or posterior component separation, together with preoperative BTA injections and PPP, achieved an acceptable fascial closure rate. Further studies are needed to explore the individual potential of BTA injections and PPP, and to research whether these methods can prevent the need for component separation, as postoperative wound morbidity remains high in our study.

**Keywords** Ventral hernia · Loss of domain · Component separation techniques · Botulinum A · Progressive pneumoperitoneum

## Introduction

One of the most prevalent complications after midline laparotomy is an incisional hernia [1]. Incisional hernias often require surgical repair as they may cause discomfort and pain [2]. Giant hernias, which are more than 10 cm in width, or hernias with loss of domain (LOD) of more than 20%, in which the abdominal cavity is unable to fully

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accommodate the abdominal contents within its fascial boundaries, pose additional difficulties [3, 4]. In these hernias, closure of the fascia is impossible or will cause high pressure with a substantial risk of complications, such as abdominal compartment syndrome and pulmonary dysfunction [4]. Despite the risk of complications, surgical closure of a hernia with LOD might be indicated when quality of life is low. LOD can cause long-term disability, loss of core muscles, back pain, paradoxical respiratory motion, mesenteric edema, poor bowel function, skin necrosis, enterocutaneous fistula, and cosmetic issues [4]. For the repair of a giant hernia (with or without loss of domain), additional medialization of the rectus abdominis muscles might be required to achieve tension-free closure. Anterior or posterior component separation techniques (i.e. (modified) Ramirez [5] or transverse abdominis release (TAR)) can be used to obtain additional medialization of the rectus abdominis muscles [6]. In addition to component separation techniques, a progressive preoperative pneumoperitoneum (PPP) has shown to be a safe way to facilitate closure in hernias with LOD [7–10]. The use of PPP was first described by Goñi Moreno in 1947 [11]. PPP causes gradual expansion of the abdominal muscles and pneumatic lysis of adhesions in the abdominal cavity or hernia sac.

A more recent finding is that Botulinum toxin A (BTA) can be used to facilitate closure too, as it lowers the tension on the lateral abdominal muscles [12–14]. The combination of BTA and PPP, however, has been little described; the few studies that have been done suggest positive results [15]. This combination, however, is not always necessary for adequate repair. Additionally, PPP is rather expensive because it might require preoperative hospital stay [16].

A standardized preoperative strategy is required for patients with a giant hernia, as preoperative BTA and/or PPP can aid fascial closure, but their effects cannot be adjusted intra-operatively.

This preoperative strategy would ideally distinguish between patients with a giant hernia that [1] could be treated without preoperative aids, [2] patients in whom BTA alone would suffice, and [3] patients that would need the combination of BTA and PPP. As current literature is void of recommendations for use of these preoperative aides, an empirical algorithm was developed based on clinical experience. This retrospective analysis aimed to determine the closure rate of the anterior fascia aided by Botulinum toxin A and/or preoperative progressive pneumoperitoneum by the use of the algorithm, and could also serve as an evaluation of whether the algorithm is valuable in determining the need for these preoperative tools in specific patient groups. Secondary outcomes included complications related to the preoperative treatment, postoperative complications, and recurrences.

## Methods

First, a preoperative strategy or algorithm for the treatment of complicated giant ventral hernias was developed in a large tertiary care university hospital in Ghent, Belgium. The algorithm was based on both hernia width and the presence or absence of loss of domain (Fig. 1). The rationale behind the algorithm was based on the primary goal of achieving

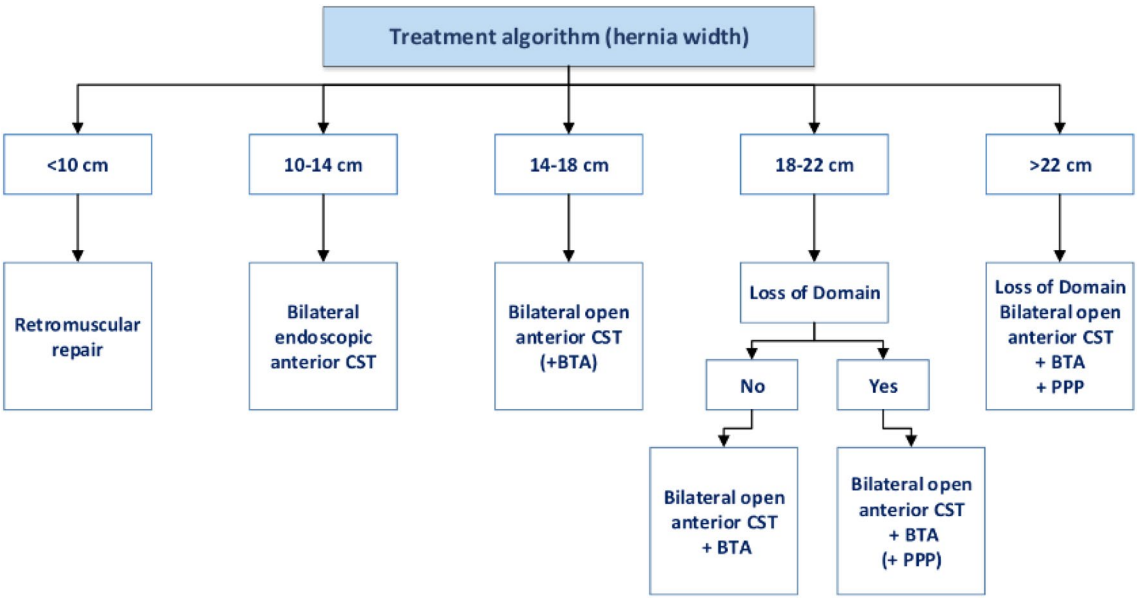


**Fig. 1** Treatment algorithm

anterior fascial closure after hernia repair. With this in mind, the interventions used in sequential fashion were (1) the gold standard retromuscular repair (Rives–Stoppa [17, 18]); (2) anterior component separation technique; (3) BTA injections; and (4) PPP. In hernias with a width of up to 10 cm, retromuscular repair was performed. The size of the defect at which the additional tool of anterior CST was added was set as 14 cm. BTA can be considered when the surgeon believes anterior fascia closure might still not be achievable despite the use of anterior CST, and from 18 cm hernia width, PPP can be considered to implement some "reserve" to prevent the surgeon from being unable to close the fascia intraoperatively. In large hernias over 22 cm of width, volume reduction and maximal medial advancement of the rectus muscles are desired; all tools are hypothesized to be needed in this specific complicated subset of patients.

Approval of the Medical Ethics Committee was obtained prior to this study. Adult patients with an elective repair of a giant hernia, either primary or incisional, who presented between June 2014 and August 2018 were treated accordingly.

As illustrated in Fig. 1, BTA injections (Botulinum toxin A, Allergan, Inc., Irvine, California) and PPP were administered to patients with a clinically estimated hernia width of more than 18 cm, thickened oblique muscles based on computed tomography (CT) examinations and/or a LOD ≥ 20% based on volumetric measures on CT [19]. BTA injections were administered according to the protocol written by Zielinksi et al. [20]. BTA injections of 300 units dissolved in 150 cc 0.9% sodium chloride solution were given at three levels bilaterally. The injections were performed under ultrasound guidance by an experienced radiologist, using a Philips iU22 device equipped with a 3–9 MHz linear transducer and a biopsy guide. The injections were given into the transverse abdominal muscle, internal oblique, and external oblique muscle.

For PPP, after cardiopulmonary evaluation, a catheter (Medionics' Swan Neck Coil 2 cuff peritoneal dialysis, inner diameter of 2.6 mm and outer diameter of 5 mm) was placed through open surgery, under general anesthesia, subcostally in the right or left hypochondriac region at the day of admission. Up to 2 L of ambient air were insufflated into the abdominal cavity at day zero. On daily basis and until hernia repair, a variable amount of ambient air was insufflated into the abdominal cavity through a microporous filter, up until the point where the patient was no longer comfortable. All patients were hospitalized during insufflation. Thromboprophylaxis (low molecular weight heparin, LMWH) at therapeutic dose was administered daily.

Mesh was used for all hernia repairs, which was fixated with continuous suture of Prolene 2-0.

Anterior fascial closure after hernia repair surgery took place with a running long-term absorbable polydioxanone suture 0, in a small step fashion with a small bite configuration. Suture length to wound length ratio was not measured.

### Data collection

Retrospective data extraction from this prospectively collected data was performed. The following data were extracted from medical records: achievement of primary anterior fascial closure, baseline characteristics (age, gender, body mass index (BMI), smoking, medical history, and previous hernia surgery), hernia characteristics based on the EHS classification [21], data on the surgical procedure (ASA classification, surgery duration, type of repair, antibiotic prophylaxis, type and location of mesh), and follow-up time. Postoperative data in the form of postoperative complications, the surgical site occurrences (SSO), hernia recurrences, and reoperations were collected. A surgical site occurrence was defined as a surgical site infection (superficial, deep, mesh infection), seroma, hematoma, wound and fascia dehiscence, or enterocutaneous fistula formation. Information about BTA and PPP (side of the catheter (right or left), number of days for insufflation, amount of insufflated air) was collected. Additionally, the size of the hernia defect and volume of the hernia sac were measured from CT examinations before and after BTA and/or PPP, when available. The pre- and post-BTA abdominal muscle length was measured at the level of the mid-third lumbar vertebra and the inside of the abdominal wall. Measurements started at the paravertebral muscles and ended in the midline (or hernia) using post-processing analyses with SyngoVia Version VB20A (Siemens). All data were analyzed using SPSS ® Statistics for Windows, version 24.0.0.1, IBM corp. Armonk, NY.

## Results

A total of 23 patients (12 males and 11 females), with a median age of 65 years (range 28–77 years) were treated between June 2014 and August 2018. Median BMI was 31.4 kg/m$^2$ (range 22.7–43.3 kg/m$^2$). Three patients (13%) were current smokers, 10 (43.5%) were ex-smokers, and 10 (43.5%) were non-smokers. Seven patients (30.4%) had diabetes mellitus. All patient characteristics are listed in Table 1.

### Hernia characteristics

Fourteen patients (60.9%) had a recurrent hernia and nine patients (39.1%) had a primary hernia. CT scans to evaluate preoperative loss of domain were available for 17 patients (73.9%). The median LOD was 29% (range 12–226%), based on hernia sac volume to abdominal cavity volume ratio.

**Table 1** Patient characteristics

| Patient characteristics | Overall $N=23$ |
|---|---|
| Age, years, median (range) | 65 (28–77) |
| Male (%) | 12 (52.2) |
| BMI, kg/m$^2$ (range) | 31.4 (22.7–43.3) |
| Smoking (%) | 3 (13.0) |
| ASA classification (%) | |
| II | 14 (60.9) |
| III | 9 (39.1) |
| Diabetes mellitus (%) | 7 (30.4) |
| Hypertension (%) | 16 (69.6) |
| Cardiac disease (%) | 9 (39.1) |
| Pulmonary disease (%) | 8 (34.8) |
| Hepatic disease (%) | 3 (13.0) |
| Renal disease (%) | 0 (0) |
| History of malignant disease (%) | 8 (34.8) |
| Corticosteroids use (%) | 1 (4.3) |
| Primary hernia (%) | 9 (39.1) |
| Recurrent hernia (%) | 14 (60.9) |
| Number of previous herniotomies | |
| 1 | 9 (39.1) |
| 2 | 3 (13.0) |
| 4 | 2 (8.7) |

*BMI* body mass index, *ASA* American Society of Anesthesiologists

**Table 2** BTA and preoperative progressive pneumoperitoneum

| Treatment | Overall $N=23$ |
|---|---|
| BTA, number (%) | 20 (87.0) |
| Days before surgery | 45 (8–120) |
| Δ muscle length pre- and post-BTA, right (cm) | 3.6 (0.4–7.6) |
| Δ muscle length pre- and post-BTA, left (cm) | 2.7 (0.7–7.9) |
| PPP, number (%) | 17 (73.9) |
| Side drain, right (%) | 16 (94.1) |
| Total air (liters) | 10.2 (6.4–19.1) |
| Total days of air insufflation | 12 (7–21) |
| Days before surgery | 14 (5–43) |
| HSV/ACV ratio before BTA and/or PPP | 0.31 (0.12–2.26) |
| HSV/ACV ratio after BTA and/or PPP | 0.33 (0.08–2.00) |
| BTA + PPP combination, number (%) | 14 (60.7%) |
| Days before surgery, BTA | 43 (8–120) |
| Δ muscle length pre- and post-BTA, right (cm) | 4.3 (0.4–7.6) |
| Δ muscle length pre- and post-BTA, left (cm) | 4.2 (1.3–7.9) |
| Days before surgery, PPP | 14 (5–37) |
| Side drain, right (%) | 13 (92.9) |
| Total air (L) | 10.4 (6.4–19.1) |
| Total days of air insufflation | 11 (7–21) |

All values are median (range) or *n* (%)

*PPP* preoperative progressive pneumoperitoneum, *HSV* hernia sac volume, *ACV* abdominal cavity volume, Δ difference in muscle length

## BTA and PPP

Twenty patients (87%) received BTA injections with a median of 45 days before surgery (range 28–119 days). The median difference in muscle length on the right side pre- and post-BTA injections was 3.6 cm (cm) (range 0.4–7.6 cm) and on the left side 2.7 cm (0.7–7.9 cm). Seventeen patients (73.9%) underwent PPP. A median of 10.2 L of air, with a range of 6.4–19.1 L, was insufflated over a median period of 12 days (range 7–21 days). The insufflation of the abdominal cavity was initiated 14 days before surgery (median, range 5–43). The hernia sac volume (HSV) to abdominal cavity volume (ACV) ratio was 0.29 before BTA and/or PPP (median, range 0.12–2.26, 6 CT scans missing) and 0.33 after BTA and/or PPP (range 0.09–2.00, 6 CT scans missing). Fourteen patients (60.9%) received the combination of BTA injections and PPP. Data regarding patients having both BTA and PPP are summarized in Table 2. Several patients did not require both BTA and PPP based on their clinical presentation and our algorithm. For example, in case LOD was present without thickened lateral abdominal wall musculature, only PPP was administered preoperatively. When we evaluate the practical usefulness of our algorithm, in the hernia group with widths between 14 and 18 cm, the actually performed pre- and intra-operative treatment differed in seven out of nine patients (77.8%) from what was suggested according to the algorithm. In contrast, in all patients from both groups with hernias over 18 cm, the proposed surgical technique from the algorithm was used. Only three out of 14 patients in those two groups (21.4%) received different preoperative management than suggested by the algorithm. Details on the pre- and intraoperative operative treatment per treatment group from the algorithm are summarized in Table 3. Additionally, the hernia characteristics using the EHS classification are presented in Table 3 [21].

## Complications of PPP and BTA

The administration of BTA injections did not result in complications. The use of PPP, however, resulted in complications in five patients. One patient had a cardiac arrest at day 5 of PPP and cardiopulmonary resuscitation was performed successfully. Post hoc evaluation showed an AV block grade II, with no signs of pulmonary or air embolisms. A PPP catheter was replaced approximately 2 weeks after the cardiac arrest. Consequently, the patient developed a liver hematoma, which was drained surgically. Another patient had a hematoma retro rectus at the site of the catheter during PPP, confirmed with a CT scan, which

**Table 3** Surgical characteristics per subgroup from the algorithm

| Hernia width | Width 14–18 cm *N* = 9 | Width 18–22 cm *N* = 6 | Width > 22 cm *N* = 8 |
|---|---|---|---|
| Treatment algorithm | Bilateral anterior CS (+BTA) | Bilateral anterior CS +BTA (+PPP) | Bilateral anterior CS +BTA +PPP |
| Age, years, median (range) | 67 (46–74) | 68 (63–77) | 63 (28–69) |
| BMI, kg/m$^2$ (range) | 31.4 (24.7–43.0) | 29.8 (22.7–36.8) | 36.3 (25.5–43.3) |
| Recurrent hernia (%) | 5 (55.6) | 3 (50.0) | 6 (75.0) |
| EHS classification | | | |
| M1-M4W3 | 1 (11.1) | 2 (33.3) | 2 (25.0) |
| M1-M5W3 | 0 (0) | 2 (33.3) | 1 (12.5) |
| M2-M4L2W3 | 1 (11.1) | 0 (0) | 0 (0) |
| M2-M5W3 | 0 (0) | 1 (16.7) | 4 (50.0) |
| M2-M5W2 | 1 (11.1) | 0 (0) | 0 (0) |
| M2-M5L2W3 | 0 (0) | 0 (0) | 1 (12.5) |
| M3-M4W3 | 1 (11.1) | 0 (0) | 0 (0) |
| M3-M5W3 | 4 (44.4) | 0 (0) | 0 (0) |
| L2-W3 | 1 (11.1) | 0 (0) | 0 (0) |
| Missing | 0 (0) | 1 (16.7) | 0 (0) |
| BTA only (%) | 3 (33.3) | 2 (33.3) | 1 (12.5) |
| PPP only (%) | 1 (11.1) | 0 (0) | 2 (25.0) |
| PPP + BTA (%) | 5 (55.6) | 4 (66.7) | 5 (62.5) |
| Surgery (%) | 9 (100.0) | 5 (83.3) | 8 (100.0) |
| Surgery time, minutes (range) | 265 (150–399) | 260 (220–370) | 323 (215–396) |
| Type of surgery | | | |
| Anterior CS, bilateral (%) | 2 (22.2) | 5 (83.3) | 8 (100.0) |
| TAR, bilateral (%) | 1 (11.1) | 0 (0) | 0 (0) |
| Anterior CS, unilateral (%) | 1 (11.1) | 0 (0) | 0 (0) |
| TAR, unilateral (%) | 1 (11.1) | 0 (0) | 0 (0) |
| Comb. anterior CS and TAR (contralateral sides) (%) | 3 (33.3) | 0 (0) | 0 (0) |
| No CS (%) | 1 (11.1) | 0 (0) | 0 (0) |
| No repair (%) | 0 (0) | 1 (16.7) | 0 (0) |
| Mesh location | | | |
| Intraperitoneal | 4 (44.4) | 5 (83.3) | 8 (100.0) |
| Retromuscular | 5 (55.6) | 0 (0) | 0 (0) |
| Mesh type | | | |
| Synthetic | 9 (100) | 5 (83.3) | 7 (87.5) |
| Biologic | 0 (0) | 0 (0) | 1 (12.5) |

*BMI* body mass index, *EHS* European Hernia Society, *BTA* botulinum Toxin A, *PPP* progressive preoperative pneumoperitoneum, *CS* component separation, *TAR* transverse abdominal release, *Comb.* combination

was drained during hernia repair. One patient was admitted to the intensive care unit due to hemorrhagic shock based on an extensive hematoma after placement of the PPP catheter at day 5. This hematoma was drained surgically. One patient developed an enterocutaneous fistula during PPP. The fifth patient died preoperatively due to hemorrhage at the site of the bursa omentalis and multiorgan failure after 5 days of PPP, and was, therefore, not evaluated in further analyses (Fig. 2).

## Surgical characteristics

All abdominal hernia repairs ($N = 22$) were elective laparotomies. Hernia repair was performed by either anterior component separation or transversus abdominis release, except in one patient. This patient did not need component separation and could be repaired without this technique. Intra-operatively, the median length of the hernia was 20 cm (range 8–30 cm) and the median width was 21 cm (range 12–30 cm). Mesh localization was either

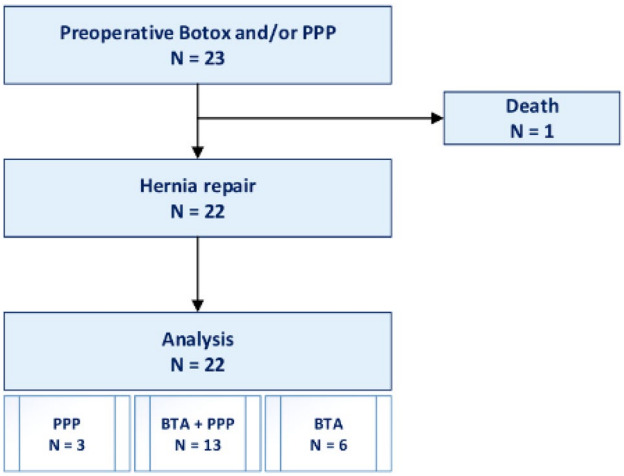


**Fig. 2** Flowchart data analysis

intraperitoneal ($N=17$, 77.3%) or retromuscular ($N=5$, 22.7%). Median length of the meshes used was 42 cm (range 28–50 cm) and median width was 32 cm (range 26–38 cm). Median mesh surface (length × width) was 1344 $cm^2$ (range 572–1850 $cm^2$). All patients were clinically re-evaluated in July 2019. The follow-up period, therefore, ranged from 10 to 60 months, with a median follow-up of 19.5 months. All surgical characteristics can be found in Table 3.

## Intra- and postoperative complications

With regard to the primary outcome, in four patients (18.1%), the anterior fascia could not be closed during the initial operation. One patient had a small bowel perforation during adhesiolysis, which was repaired immediately during the first operation, but a second stage repair a few days later was required. In three other patients (13.6%) the anterior layer could only be closed using a small part of the hernia sac to cover the intraperitoneal mesh. With regard to the secondary endpoints, 16 patients (72.7%) developed 23 surgical site occurrences (SSOs) postoperatively (summarized in Table 4). Twelve patients (54.5%) had a surgical site infection (SSI), of which six patients (26.1%) had a deep infection. One deep infection was managed by antibiotic treatment alone, two deep infections required (partly) surgical mesh removal, and the remaining three were treated with negative pressure therapy. Other SSOs included seromas ($N=4$, 18.2%), hematomas ($N=4$, 18.2%), postoperative fascia dehiscence ($N=3$, 13.6%). None of these SSOs required additional therapy, except for one seroma, which was drained by ultrasound guidance and subsequently drained during surgery. No postoperative enterocutaneous fistulas were seen. Other complications included pneumonias in three patients, of whom two needed admission to the intensive care unit. A total of three patients (13.6%) experienced a hernia recurrence, of which one received surgical repair. Hernia recurrence repair was performed and a synthetic mesh was placed intraperitoneally. Cumulatively, five surgical interventions took place: one for hernia recurrence

**Table 4** Recurrences and surgical site occurrences (SSOs) per subgroup from the algorithm

| Hernia width | Width 14–18 cm<br>$N=9$ | Width 18–22 cm<br>$N=5$[a] | Width > 22 cm<br>$N=8$ |
|---|---|---|---|
| Treatment algorithm | Bilateral anterior CS (+BTA) | Bilateral anterior CS +BTA (+PPP) | Bilateral anterior CS +BTA +PPP |
| Direct fascial closure achieved (%) | 9 (100) | 4 (80.0) | 5 (62.5) |
| Recurrence (%) | 0 (0) | 1 (20.0) | 2 (25.0) |
| Reoperation for either recurrence or complication (%) | 0 (0) | 2 (40.0) | 3 (37.5) |
| Patients with ≥ 1 SSO | 5 (55.5) | 3 (60.0) | 8 (100.0) |
| Total SSO | 7 | 4 | 13 |
| Surgical site infection (%) | 4 (44.4) | 3 (60.0) | 6 (75.0) |
| Superficial or wound dehiscence | 4 (44.4) | 1 (20.0) | 2 (25.0) |
| Deep | 0 (0) | 2 (40.0) | 4 (50.0) |
| Seroma (%) | 1 (11.1) | 0 (0) | 3 (37.5) |
| Hematoma (%) | 2 (22.2) | 0 (0) | 2 (25.0) |
| Fascia dehiscence (%) | 0 (0) | 1 (20.0) | 2 (25.0) |
| Enterocutaneous fistula formation (%) | 0 (0) | 0 (0) | 0 (0) |
| Follow-up, months (median, range) | 17 (10–40) | 13 (12–31) | 32.5 (19–60) |

[a]5 as one patient did not receive repair

and a deep SSI (4.5%) and four (18.2%) for other postoperative complications.

## Discussion

Preoperative preparation of patients with giant ventral and incisional hernias is essential to obtain the best possible outcomes in terms of fascial closure rate. However, the effects of preoperative aids cannot be enhanced intraoperatively; the needed effect size has to be determined beforehand. Therefore, a standardized preoperative strategy based on clinical and radiological parameters would be useful to estimate the needed effect size, informing on whether there is need for the use of BTA, PPP, or both. This cohort of 23 patients, treated according to a standardized algorithm for a giant ventral hernia with or without LOD, shows that BTA and PPP facilitate closure in ventral hernia repair. The primary fascial closure rate is 82%.

### Component separation technique

Component separation techniques were used as the first tool in our algorithm to facilitate medialization of the rectus muscles and closure of the anterior fascia. Surgeons that refrain from using component separation techniques might not achieve anterior fascial closure in all patients, as illustrated by Renard et al. (primary closure in 42 out of 45 patients, 94%) [7]. In our study, anterior CST and TAR were applied in all but one patient; anterior CST was planned in addition to BTA for this patient, but BTA alone made anterior fascial closure possible. Despite being associated with more wound complications than TAR [22], anterior CST renders nearly 6 cm of medialization of the rectus sheath (in postmortem human specimens), which can contribute to tension-free fascial closure [6]. In three patients in our study, to avoid intraperitoneal mesh placement and obtain anterior fascia closure, a unilateral TAR was done on one side to facilitate the closure of the posterior layer, and a unilateral anterior CST was done on the other side to ensure anterior fascial closure. In none of the patients both anterior CST and TAR were performed at the same side. Another component separation method could be represented by the endoscopic external oblique release as described by Rosen et al. [23], but as the achieved fascial advancement is limited to approximately 80% of what can be achieved by an open technique, the latter was used in our study.

### BTA

If anterior CST was estimated not to be enough for achieving anterior closure of the fascia, BTA was applied 4–6 weeks preoperatively. Only two protocols for BTA injections have so far been described: a three-point and five-point technique, respectively [20, 24]. Either one of these does not seem preferable over the other. BTA alone has been reported to give a 0.5–1.5 cm extra muscle length on each side of the abdominal wall on average. Other authors, however, found 1–5 cm of myofascial advancement with the use of BTA [12, 13, 25–27]. In this study, the addition of BTA injections resulted in an extra increase in length of 2.0–3.0 cm of the lateral abdominal wall muscles, without causing additional complications. This finding is in line with the current literature; no complications of BTA use as a preoperative aid have been recorded, only minor inconveniences such as bruising after injection or a sensation of bloating [12]. One study even found an additional analgesic effect postoperatively of BTA [28].

### PPP

In case a significant loss of domain of more than 20% was calculated preoperatively, the use of PPP was indicated, as shown in our algorithm (Fig. 1). PPP insufflations were performed daily with ambient air, until the patient experienced scapular pain, abdominal pain, or dyspnoea. The use of ambient air has been advocated, because nitrous oxide, carbon dioxide, and oxygen are absorbed four times faster in the peritoneal space than ambient air [10, 29]. This causes the necessity to top up the volume often and with large quantities, while the use of ambient air results in easier maintenance of the pneumoperitoneum. No current consensus has been reached with regard to the amount of air to be injected, the frequency of the insufflations, and the length of the period the pneumoperitoneum should be maintained. Therefore, we used 2 L at the time of catheter placement intra-operatively and 1 L daily. It is suggested that PPP does not cause further benefit after 6–10 days [29]. However, CT scans at 7 days after starting PPP showed only partial reduction of the hernia content in most of our patients, with limited air accumulation in the abdominal cavity itself. Therefore, we continued PPP for a maximum of 21 days. The average LOD was 53% before admission (median 29%). PPP caused a mean increase in HSV/ACV ratio of 4%. This increase is understandable from the law of Laplace, and was also found by Sabbagh et al. [8] reporting a 1%-increase in the ratio incisional hernia volume to total peritoneal content. Other authors, however, report a significant decrease in this ratio, from 5 to 22% [7, 15, 30]. Their findings could justify the use of an abdominal binder between PPP sessions, to restrict air going to the hernia sac. However, air inside the hernia can cause lysis of possible adhesions and facilitate fascial closure [31]. Complications related to PPP in our study are predominantly hematomas, and one patient died because of an extensive bleeding and hemodynamic shock (however,

probably also related to his frail preoperative state). We treated all our patients with a therapeutic dosage of low molecular weight heparins from the start of PPP to prevent pulmonary embolisms. This serious complication has been described using laparoscopy [32] and is probably caused by increasing pressure at the level of the caval vein. However, in the light of our current findings—showing a high incidence of hematomas and bleeding complications—it might be better to use prophylactic dosage LMWH during PPP. Other authors describe subcutaneous emphysema, shoulder pain, abdominal pain, nausea, anxiety, intestinal perforation, and even mortality [7, 10, 15, 29, 31, 33]. Therefore, PPP asks for deliberate use in specific patient groups only. An evidence-based cut-off for LOD should be established to help surgeons decide on when to use PPP as a preoperative aid for hernia repair. As the primary goal is to close the anterior fascia, lenient cut-off for LOD should be utilized.

## Complications

Surgical repair of these giant hernia defects was accompanied by several complications. Twelve patients (54.5%) experienced a surgical site infection (superficial or deep) and 3 patients (13.6%) had a recurrence. Five patients (22.7%) had to have a reoperation for either a recurrence or postoperative complication. These complications could not have entirely been avoided, as this is a very complex patient group. More than 90% of the patients were overweight (BMI > 25 kg/m$^2$) and many had comorbidities (as shown in Table 1). When compared to the literature on ventral hernias with LOD, our SSI rate of 54.5% seems high. This might be partially be explained by the fact that we included wound dehiscence without proof of positive cultures in the superficial SSI rate. Other authors describe infection rates between 5 and 26% [7, 19, 34–38]. Also, the number of patients receiving a reoperation seems relatively high with 22.7%, compared to a 10–15% reoperation rate [35, 38]. A possible explanation might be that we considered negative pressure wound therapy, as initiated with wound debridement in the OR, as a reoperation. Only one other study—more in line with our data—finds that one-third of the patients had to be reoperated [36]. These relatively high numbers could be due to the rather extreme width of the hernias researched in this study. Patient selection may have differed from the abovementioned studies. Additionally, the large number of comorbidities present in the researched group hinders the direct comparison of outcomes with findings from other authors. The number of patients having a recurrence (13.6%) is within line of expectations for these complicated hernias. Other authors report 4–16% recurrences [7, 19, 34–38].

## Limitations

This is a retrospective cohort study, which is sensitive to bias. Also, only 23 patients were analyzed. The results must, therefore, be interpreted with caution, as these numbers are insufficient to provide sound statistical comparisons. Additionally, some patients had a relatively short follow-up period, and CT scans were not always available to confirm that indication for PPP (as through our algorithm) was indeed present; these both are the drawbacks of the presented study. However, LOD is most of the time obvious at clinical examination, so bias on this point would be relatively low. Despite these limitations, the data of these patients add to the current body of knowledge about the combined use of BTA and PPP, what it can offer in hernia defect closure and the potential risks.

## Implications

The combination of anterior CST and BTA seems safe and effective, leading to an anterior fascial closure rate of 82% in our study. PPP use might require more critical deliberation whether it is worth the risk as it resulted in a high complication rate of 29%. The standardized treatment algorithm prevented the surgeon from facing unforeseen intraoperative difficulties in closing the anterior fascia. However, the issue we came across during the usage of proposed algorithm in clinical practice is that it cannot always be successfully applied, as it is not a validated instrument. LOD was only measured when the estimated hernia width was > 18 cm, but had implications for the preoperative treatment, while LOD can also be present in hernias of less than 18 cm width. Meaning, undertreatment might have taken place: patients with LOD, but with an estimated effect width of < 18 cm, could possibly also have benefited from the additional PPP treatment.

On the other hand, overtreatment might also have been present, as the exact benefits and limitations of BTA treatment remain unclear; in some patients, fascial closure might have been achieved without the use of BTA or PPP. Using BTA is expensive and, as BTA is not reimbursed by the insurance companies in Belgium, it poses an additional cost of approximately 500–600 euros for the patient.

PPP is described to cause a decrease in the LOD of the hernia, facilitating tension-free closure of the fascia during repair. An additional advantage of PPP is the lysis of adhesions caused by the insufflated air [31]. A drawback of PPP is that it is even more expensive, as it required preoperative hospital stay in our study. As reported by Renard et al. [7], admission is not mandatory, but safety was considered of utmost importance in our study (as was observed with the patient suffering an AV-block during insufflation). Moreover, PPP showed a high complication rate of 29% which included

severe complications, PPP can cause pain, and PPP is generally experienced as unpleasant by patients, possibly resulting in a lower quality of life. An evidence-based protocol might be of help with indications for its use, and with regard to the amount of air to be insufflated and the number of days the pneumoperitoneum should be maintained. However, as it involves a very heterogeneous and relatively small group of patients with many variables influencing the final outcome, this might be elusive. The individual value of BTA, PPP, and CST cannot be determined based on the results from this study, nor has their value been elucidated in other studies, which only suggest optimistic results of the combined use of these methods [35]. The value of a specific preoperative aid is difficult to determine as the number of patients treated in the current study is too small and overtreatment might have taken place to be certain to achieve fascial closure. Because BTA is associated with fewer complications, it would be useful to distinguish between patients with a hernia with LOD that could be treated with BTA alone, CST alone, and patients that would need the combination of BTA and PPP, and possibly additional CST. This analysis clearly demonstrates, however, that a standardized algorithm may be considered as a guidance during the pre- and intra-operative surgical decision-making, but both preoperative CT assessment and clinical examination remain mandatory to determine the best approach for each individual patient. Larger studies and pooling of data would be required to give recommendations with regard to optimal selection of preoperative preparation methods.

## Conclusions

This study is a description of 23 patients with complex ventral hernia repair facilitated by Botulinum toxin A and preoperative progressive pneumoperitoneum. BTA seems safe to aid closure, whereas PPP requires critical consideration for its use. Further research should be conducted to determine both indications and outcome parameters for each of these preoperative tools in abdominal wall reconstruction.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The authors confirm that the study was approved by the local institutional ethics committee of Ghent University Hospital and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Human and animal rights** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** For this type of study, formal consent is not required.

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