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Published in:
Journal of Plastic, Reconstructive & Aesthetic Surgery

DOI (link to publication from Publisher):
10.1016/j.bjps.2023.10.126

Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

Journal of Plastic, Reconstructive & Aesthetic Surgery 88 (2024) 235–242

Intra-abdominal pressure increases peri-operatively in patients undergoing deep inferior epigastric perforator flap reconstruction: A prospective study linking high intra-abdominal pressure to non-fatal lung embolism within one patient☆

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Received 8 July 2023; Accepted 23 October 2023

KEYWORDS
DIEP reconstruction;
Autologous breast reconstruction;
Intra-abdominal pressure;
Thromboembolic events

Summary *Background:* The deep inferior epigastric perforator (DIEP) flap is the gold standard for autologous breast reconstruction. The procedure and peri-operative period are associated with the risk of severe post-operative complications, like venous thromboembolic events (VTE) and lung embolism. Whether the intra-abdominal pressure (IAP) increases after the closure of the abdominal defect, thereby potentially affecting the venous backflow and the risk of VTE, is currently not known.
Aim: The primary aim is to test if the closure of the abdominal donor site increases the IAP in women undergoing secondary DIEP flap breast reconstruction.
Materials and method: By using a Unometer, we measured the intravesical pressure as a surrogate marker for the IAP, at baseline, immediately after, and 24 h after abdominal skin closure, for 13 patients.
Results: The mean IAP increased from 6.1 mmHg (95% CI 4.6–7.7) at baseline to 9.0 mmHg (95% CI 8.0–10.0) immediately after skin closure [mean diff. 2.9 (95% CI 1.0–4.8) ($p = 0.007$)] and

☆ Clinical trial registration: The clinical trial is registered with ID number 2021-082 in the Danish Data Protection Agency.

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https://doi.org/10.1016/j.bjps.2023.10.126

further up to 11.7 mmHg (95% CI 9.0–14.5) 24 h after closure [mean diff. 5.3 (95% CI 1.4–9.1) (p = 0.012)]. We found that IAP varies among the patients, regardless of the tightness of abdominal closure or rectus plication (n = 3). Immediately after closure, none of the isolated patients showed abnormal levels of IAP (> 12 mmHg), while eight out of 12 isolated patients (67%) showed IAP levels above the normal range after 24 h. One patient developed a non-fatal lung embolism.

Conclusion: The mean IAP increases significantly over the post-operative period after DIEP flap reconstruction, although abnormal IAP values are only seen 24 h after the closure of the skin.

Breast cancer is one of the most common malignant diseases diagnosed among women worldwide.[1] The prognosis has improved significantly, because of the implementation of screening and adjuvant therapy, leaving an increasing number of patients eligible for the reconstruction of the breast following a mastectomy.[1,2]

The deep inferior epigastric perforator (DIEP) flap is known as the gold standard in autologous breast reconstruction since it was first described in 1989 and 1994.[3,4] On the basis of perforators from the deep inferior epigastric artery, a new breast is formed from the abdominal skin and subcutaneous tissue, leaving the underlying rectus muscle intact.[3,4] However, the procedure and peri-operative period are associated with the risk of severe post-operative complications, like venous thromboembolic events (VTE) and fatal lung embolism, reported in between 0% and 6% of the patients.[5-8] Several risk factors for VTE in relation to surgery are known. Studies and meta-analyses investigating VTE-related prognostic factors including 14 studies and 151,714 patients, found that age > 60 years, Body mass index (BMI) > 30, immobilisation, major surgery, and malignancy were risk factors for developing VTE.[9]

Theoretically, increased intra-abdominal pressure (IAP) leads to increased intrathoracic pressure because of the cephalic deviation of the diaphragm, subsequently obstructing the deep venous blood flow.[10] These changes in pressure within the abdomen lead to decreased venous return from the lower extremities and blood stasis in the deep venous system with a potential risk of developing VTE and pulmonary embolisms.[10] While blood is circulating through the vascular system, the endothelial cells' surface components trigger different anticoagulant pathways. The efficacy of natural anticoagulants, determined by the ratio of endothelial cell surface to blood volume, increases drastically as the blood moves from large vessels into microcirculation. Presumably because of the prolonged residence time in large veins, impairing the natural mechanism of coagulation, the risk of thrombus formation increases.[11]

Whether the closure of the rectus sheath and abdominal skin after DIEP flap reconstruction is affecting IAP is currently not known.

Intravesical pressure is an accepted surrogate marker for IAP, with a normal range between 5 and 7 mmHg, defined by The World Society of Abdominal Compartment Syndrome (WSACS).[12] The elevated IAP is a result of the elevated intra-abdominal volume or because of the extrinsic compression of the abdominal content, and defined as sustained or repeated pathologic elevations of IAP ≥ 12 mmHg.[12] Pathological IAP values are seen as a continuum ranging from mild IAP elevations/Intra-abdominal hypertension to severe abdominal compartment syndrome.[13]

Objective

The primary aim of this study is to test whether IAP increases after the closure of the rectus abdominis rectus sheath and abdominal skin in women undergoing secondary DIEP flap breast reconstruction.

Materials and method

Study design

Prospective uncontrolled longitudinal study

Patients

The study is based on 13 women undergoing secondary, unilateral DIEP flap reconstruction of the breast at the Department of Plastic- and Breast Surgery, Aalborg University Hospital, Denmark, consecutively included from April 2021 to November 2021.

Primary end point

Bladder pressure, as a surrogate marker for IAP, measured at baseline, immediately after the closure of the abdominal sheath and abdominal skin, and 24 h after closure.

Power

To be able to detect an increase in mean IAP from 6 to 15 mmHg (SD 6), with a power of 0.8 and an alpha at 0.05, a total number of 12 patients are needed.

Measurements

The intravesicular pressure is measured according to standard guidelines from the WSACS,[12] as a surrogate marker of the IAP. IAP is measured through a standard Foleys catheter

in the bladder, with attached UnoMeter™ Abdo-Pressure™, IAP monitoring system, Stand-alone (Unomedical).

The system is primed with a 20-mL sterile saline solution before measuring, and a zero-reference point is marked at the mid-axillary line on the iliac crest. The Unometer is raised vertically from the reference point, the tube clamp for the bio-filter is opened, and the pressure is measured after stabilisation of the meniscus. The tube clamp for the bio-filter is hereafter closed and the Unometer is placed on the operation table before the next measurement.

Timepoint definitions and related peri-operative patient conditions

For each patient, we standardise relevant patient conditions and measure the IAP at:

1. Baseline: Defined as the timepoint before surgery, with the patient being under general anaesthesia, in a supine position, without the use of relaxants.
2. Immediately after surgery: Defined as the timepoint immediately after the surgery ended, with the patient being under general anaesthesia, in a supine position, and without the use of relaxants.
3. 24 h after surgery: Defined as the timepoint 24 h after the surgery ended, with the patient being awake at the ward, in bed with the hip flexed 30°, non-fasting, and without a compression belt at the time of measurement.

Blinded for the IAP measures, the same two microsurgeons performing the surgery, subjectively, but consensually, categorise the patients on the basis of the skin closure tightness. The closure is noted as either loose, moderate, or tight skin closure, with or without having performed rectus plication.

The peri- and post-operative regime regarding women undergoing the DIEP flap procedure at Aalborg University Hospital

Thrombosis prophylaxis	- 2500 IE low-molecular-weight heparin (LMWH) administered subcutaneously in the morning, same day as the surgery. 2500 IE LMWH more 6–12 h post-operatively. - 5000 IE LMWH injected once a day from the first to the 28th post-operative day. - During surgery the patient's lower extremities are connected to an Intermittent Pneumatic Compression Device and surgical staff performs intermittent mobilisation of both legs. - IPC socks are worn until discharge.
Antibiotics	- Cloxacillin is administered intravenously, a single dose pre-operatively (2 g), and a single dose repeated after 3-4 h of surgery (1 g.).
Mobilisation	- Patients are mobilised as early as possible, usually within the first post-operative day, with adequate use of pain medication. The patients are mobilised with a supporting bra and compression belt. When in bed, the headboard is elevated with a minimum of 30 degrees. - A physiotherapist instructs the patients to perform relevant exercises with good quality.
Other initiative	- The patients are instructed to use a compression belt around the abdominal cicatrice for a total of 12 weeks.

Statistical methods

The differences in mean IAP are tested by paired t-test, with prior testing of normally distributed data. Regression analyses are performed to evaluate changes in mean IAP over time. Data is presented with mean, SD, and p-values < 0.05 are considered statistically significant. The statistical analysis and illustrations are performed using Stata software, Stata/MP 17.0 for Mac (StataCorp).

Approvals

An informed written and signed consent is obtained before inclusion, and any measurements or patient characteristics are obtained. The study was approved by the Health Ethics Committee of Northern Jutland, Denmark, and the Danish Data Protection Agency before initiation.

Results

Patient characteristics

Patient characteristics are presented in Table 1. Because of the miscommunication, IAP failed to be measured for one patient, at 24 h after closure. Otherwise, the dataset was complete.

The mean age is 51 years (SD 5.1), mean BMI 26.1 (SD 2.2), and mean duration of surgery at 6.65 h (SD 0.56) (Table 1). Seven patients are categorised as having loose skin closure, five patients as moderately tight closure, and one patient as tight closure. Three patients had an additional rectus plication done. All patients followed the same peri-operative regime and procedure of anaesthesia. The patients were evaluated as performance status ASA 1–2, with no untreated hypertension or atrial fibrillation present. They were all mobilised within 24 h after surgery and wore an abdominal compression belt at all times.

Post-operative complications and thromboembolic events

One patient (Table 1 **) experienced post-operative bleeding from the donor site and was re-operated 3 h after the end of the primary surgery. Apart from the re-operation, this patient followed a normal post-operative regime, was mobilised the next day, and discharged after 4 days. The IAP was 5 mmHg at baseline 9 mmHg immediately after surgery and 16 mmHg 24 h after surgery.

One patient (Table 1 ***) was diagnosed with deep venous thrombosis and lung embolism 2 months after the DIEP flap reconstruction. Before the reconstruction, this patient was evaluated as ASA 2, with known comorbidity including asthma and neuropathic pain. Because of the recurrent invasive breast cancer, she was treated with a mastectomy 2 years before the current reconstruction. While receiving chemotherapy treatment, she was diagnosed with lung embolism and treated with LMWH. After the antithrombotic treatment, the patient did not have any symptoms and was not further examined for underlying or unrecognised

Table 1 Patient characteristics. Patients marked with * show decreasing IAP after 24 h. Patient 4 is missing 24 h measurement. ** Patient with post-operative bleeding and re-operation. *** Patient that developed post-operative non-fatal lung emboli.

Patient	Age (years)	BMI	Duration of surgery (hours)	Rectus plication	Closure tightness	ASA performance group
*1**	46	27.6	5.88	Yes	Loose	1
*2**	44	25.5	6.58	Yes	Moderate	1
*3**	43	26.4	6	No	Loose	1
4	55	25.4	7	No	Loose	1
5	58	24.5	7	No	Moderate	2
6	56	29.8	7.42	No	Loose	1
7	50	20.8	6.53	No	Tight	1
*8**	54	25.1	6.48	No	Moderate	1
9	51	28.4	5.52	No	Loose	2
10	47	26.3	7.30	Yes	Loose	2
*11***	56	27.3	7.13	No	Loose	2
*12****	57	27.4	6.45	No	Moderate	2
13	50	25.2	7.13	No	Moderate	1
Mean	51 (SD 5.1)	26.1 (SD 2.2)	6.65 (SD 0.56)			

thromboembolic disease, as the lung emboli developed under active chemotherapy.

Following the DIEP flap reconstruction, the patient was mobilised on the first post-operative day, did not experience any immediate post-operative problems, and was discharged 3 days after surgery. Fourteen days post-surgery the patient was diagnosed with the infection of the abdominal scar and treated with antibiotics for a total of 7 weeks while being clinically examined at the Department of Breast Surgery. Seventy days post-surgery the patient suddenly experienced shortness of breath and was hospitalised and diagnosed with deep venous thrombosis and lung embolies, by ultrasound and spiral CT scan. She was treated with therapeutic doses of anticoagulant, Eliquis, and continues to use anticoagulant for the rest of her life. She was further examined for thromboembolic disease, which ruled out thrombophilia.

The IAP for this patient was 5.5 mmHg at baseline, 12 mmHg immediate post-operative, and 15 mmHg 24 h post-operatively. The length of her surgery was 6.45 h just below the mean length of surgery (6.65).

Descriptive changes in IAP and its association to patient characteristics

Changes in IAP vary among the included patients, regardless of the tightness of abdominal closure or performed rectus plication (Figure 1A and B). From baseline to the timepoint

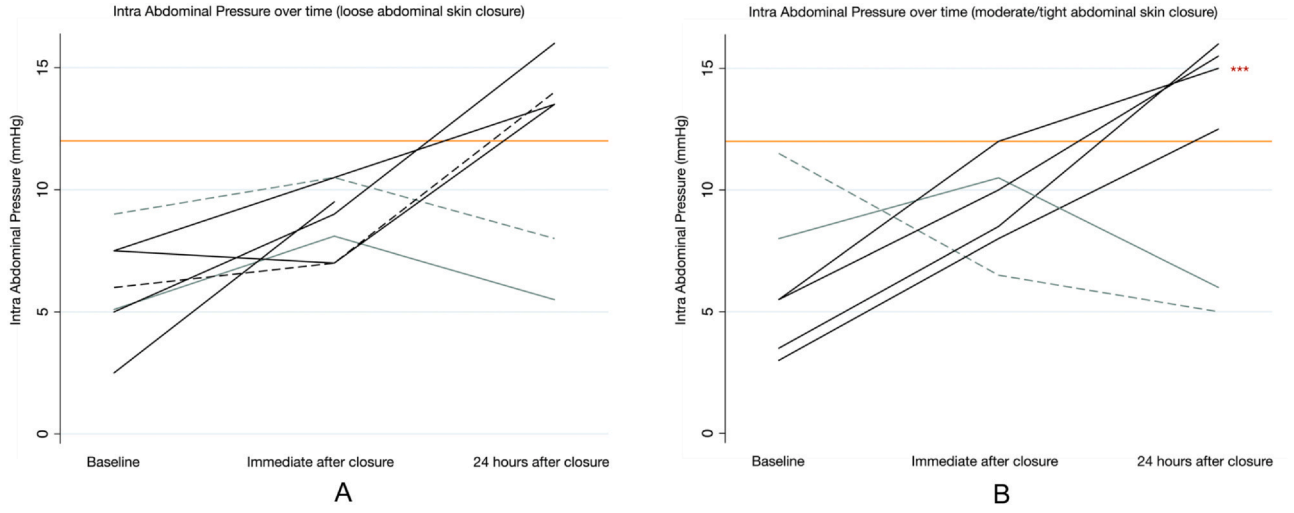

Figure 1 A: Longitudinal illustration of IAP over time for patients with loose skin closure, market at baseline, immediately after and 24 h after the closure of the rectus muscle facia and abdominal skin. The abnormal referral line of IAP > 12 mmHg is illustrated in orange, and patients having additional rectus plication are illustrated with dotted lines. B: Longitudinal illustration of IAP over time for patients with moderate to tight skin closure, market at baseline, immediately after, and 24 h after the closure of the rectus muscle facia and abdominal skin. The abnormal referral line of IAP > 12 mmHg is illustrated in orange, and patients having additional rectus plication are illustrated with dotted lines. *** Patient that developed post-operative non-fatal lung emboli.

Table 2 Patient characteristics on the basis of the groups with normal IAP at all times and high IAP at 24 h after the closure of the abdominal rectus sheath and abdominal skin. The groups were tested with t-test of the mean, reporting the difference of the mean, with 95% CI and p-value.

	Patients with high IAP (> 12 mmHg)	Patients with normal IAP (< 12 mmHg)	t-test of the mean diff. (95% CI)	p-value
Number of patients	n = 8	n = 4		
Age (years)	53.1 (49.7:56.5)	46.8 (38.8:54.7)	6.4 (0.4:12.3)	**0.039***
BMI	26.2 (23.9:28.5)	26.1 (24.4:27.9)	0.1 (−3.2:3.3)	0.97
Time of surgery (Hours)	6.8 (6.3:7.3)	6.2 (5.7:6.8)	0.6 (−1.2:1.3)	0.12
Baseline IAP (mmHg)	5.4 (4.1:6.8)	8.4 (4.2:12.6)	−3.0 (−5.7:−0.2)	**0.036***
IAP immediately after closure (mmHg)	9.0 (7.5:10.5)	8.9 (5.8:12.0)	0.1 (−2.4:2.6)	0.93
IAP 24 h after closure (mmHg)	14.5 (13.4:15.6)	6.1 (4.0:8.2)	8.4 (6.6:10.2)	**< 0.0001***

* Significant p-values.

immediately after closure, the IAP increases in 12 out of 13 patients, although none above normal levels (IAP > 12 mmHg). From baseline and up to 24 h after closure, the IAP increases further in eight out of 12 patients (67%), for all eight patients above the normal IAP level (12.5–16 mmHg). In total, four patients show an IAP within the normal range at all peri-operative times. Patients with high IAP are generally older [6.4 (95% CI: 0.4:12.3) (p = 0.0387)] and show a lower baseline IAP value [−3.0 (95% CI: −5.7:−0.2) p = 0.0356)] (Table 2). No significant difference between the groups is found concerning BMI or length of surgery.

Changes in mean IAP between different per operative timepoints and over time

The mean IAP increases from 6.1 mmHg (95% CI: 4.6–7.7) at baseline to 9.0 mmHg (95% CI: 8.0–10.0) immediately after skin closure [mean diff. 2.9 (95% CI: 1.0–4.8) (p = 0.007)] and further up to 11.7 mmHg (95% CI: 9.0–14.5) 24 h after skin closure [mean diff. 5.3 (95% CI: 1.4–9.1) (p = 0.012)] (Figure 2). In regression models, the mean IAP increases significantly over time (p < 0.0001) with regression coefficients from baseline to immediate after closure of 2.9 (95% CI: 0.7–5.1), to 24 h after closure [coef. 5.6 (95% CI: 3.3–7.7)] (Figure 2).

Discussion

By this prospective study, we investigate whether IAP increases over the peri-operative time after DIEP flap reconstruction, and theoretically contributes to the risk of VTE. Interestingly, we show that the IAP increases significantly from baseline to immediately after the closure of the abdominal rectus sheath and abdominal skin, although not above normal IAP levels.

No studies have previously addressed this issue in relation to DIEP flap reconstruction. However, two studies investigated changes in IAP for patients undergoing abdominoplasty, with additional correction of rectus abdominal

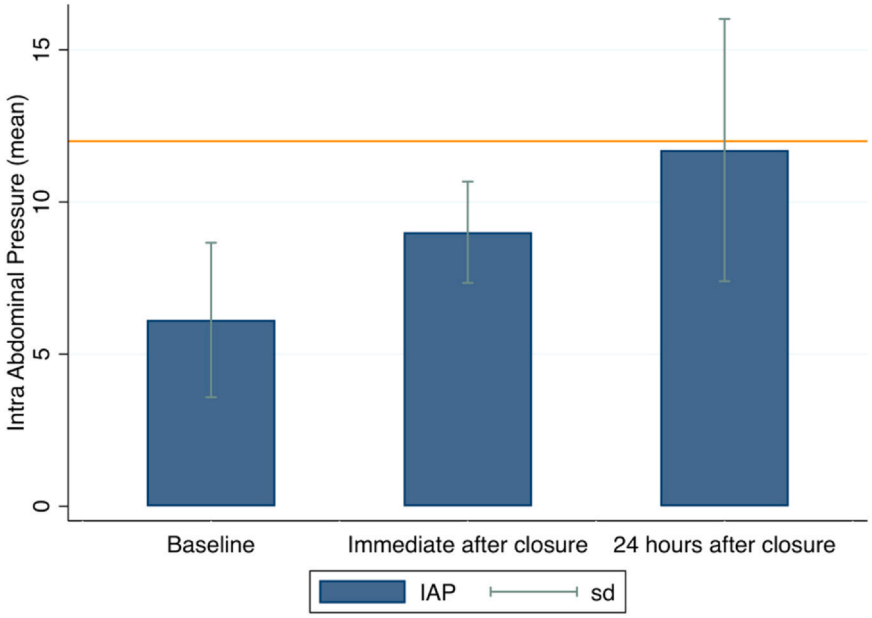

Figure 2 Illustration of the mean IAP and SD, at baseline, immediately after, and 24 h after the closure of the rectus muscle facia and abdominal skin. The abnormal referral line of IAP > 12 mmHg is illustrated in orange.

diastases.[14,15] Both studies show increasing IAP comparing mean IAP values before surgery and after surgery, although proper clarification of IAP measurement and method were not reported in these papers. For measurements of IAP, we use the WSACS guidelines from 2013, pathologically defining values above 12 mmHg.[12] In line with our measure method and results, Pereira et al. found that the IAP for patients undergoing abdominoplasty and additional rectus plication increases significantly from 6.6 mmHg pre-plicature to 9.3 mmHg post-plicature.[16] The authors in this latter study do not report IAP levels at 24 h post-surgery.

In contrast to our results, the current literature reports an average decrease in IAP, comparing baseline levels with levels after 24 h after surgery,[14,15] although approximately 50% of the patients had IAP levels above 12 mmHg in one of the studies.[14] Still, we find that mean IAP continues to increase up until 24 h after skin closure, with levels above the normal range for the majority of the patients. This is regardless of the tension of skin closure or whether rectus plication is performed.

Interestingly, four patients showed a decreasing IAP after 24 h, and in addition, only IAP values within the normal range at all peri-operative timepoints. These patients are generally younger and show higher baseline IAP levels. Because our study was not designed to address this issue, these results need to be reported with caution and can only be regarded as explorative. Yet, our results are in accordance with the current literature, reporting that the increasing age is a predictive marker of IAP above 12 mmHg in patients undergoing heart surgery.[17] Furthermore, low baseline levels of IAP (OR 0.7) and untreated hypertension (OR = 6.8) have been independently associated with high IAP in multivariate analyses.[17] We found no significant association between BMI or comorbidity and IAP in our data.

Understanding the abdomen as a hydraulic system, the IAP is determined by the volume of organs contained within the abdomen and the compliance of the abdominal walls, some flexible (abdominal wall and diaphragm), and some rigid (costal arch, spine, and pelvis).[10,13] Thus, during the peri-operative time, several factors may theoretically impact the IAP, that is, the use of suppressors and muscle relaxations, duration of surgery, immobilisation, gastropareses, paralytic ileus, bleeding and oedema around the abdominal wall and skin, pain and positive end-expiratory pressure, and external compression (abdominal compression belt). In our study, we endeavoured to standardise the setup and found no major differences in the abovementioned factors. One factor that might impact the 24-hour estimates though, is body positioning and our current post-operative regime, with patients lying in bed with 30 degrees elevated headboard. This factor was consistent for all included patients; nevertheless, elevation from a supine position is known to be associated with increased IAP for critically ill patients.[18,19] A strength of our study is that the included patients were all women who underwent the same unilateral breast reconstruction, performed by the same two microsurgeons, and were treated according to the same overall anaesthetic and post-operative principles and instructions.

We did not address the possible correlation between IAP and central venous pressure, which theoretically can increase the risk of VTE because of impaired venous backflow.[10] However, Kılıç et al. found a significant correlation between increasing IAP and increasing central venous pressure for patients undergoing heart surgery.[17] Furthermore, Berjeaut et al. found a post-operative correlation between the use of abdominal compression garments and increased venous stasis in patients undergoing abdominoplasty.[20] A study by Momeni et al. examined the lower extremity stasis within patients undergoing reconstructive breast surgery with a free abdominal flap. They found that the lower extremity venous stasis persisted post-operative and through the day of discharge.[21]

Although thromboembolic events were not defined as study endpoints in our study, one patient developed deep venous thrombosis and lung emboli 70 days after the DIEP reconstruction. Interestingly, this patient had a relatively low baseline IAP, showed a significant rise in IAP immediately after surgery, and showed IAP above the normal range and among the highest measured IAP in our cohort after 24 h (15 mmHg). In addition, this patient was 57 years old at the time of surgery, had a BMI of 27.4, and was evaluated as ASA 2 with known cardiovascular comorbidity. Two years before the reconstruction, the patient was diagnosed and treated for a deep venous thrombosis and lung emboli, while undergoing chemotherapy. In addition, the abdominal skin closure for this patient was reported as subjectively moderate tight closure, although no rectus plication was performed.

The association between high IAP and reduced venous backflow and our current finding of increasing IAP for women undergoing DIEP reconstruction emphasises the importance of implementing the principles of enhanced recovery after surgery (ERAS), limiting external factors that theoretically may impact the IAP and the risk of VTE, that is, immobilisation, compression belt, pain, and subsequent impaired deep respiration.

Moreover, the rare and thus unexpected thromboembolic event occurring for one of the 13 patients included in the study, emphasises the importance of careful patient selection, aiming to limit risk factors, that is, age, previous thromboembolic events, and cardiovascular comorbidity, for safer autologous breast reconstructions.

This study has some mentionable limitations. The study was powered on the basis of the current literature and assumptions of described IAP cut-off values aiming to show an increase from 6 to 15 mmHg. Thus, the study was not powered for performing subgroup analysis or subdividing the population further.

The closure of the rectus sheath and the abdominal closure were performed by different residents and the tightness of the abdominal closure was consistently evaluated by the same two supervising. However, the evaluation of tightness may therefore be regarded as subjective and associated with both inter- and intraobserver variations. Several factors may impact the IAP, including previous abdominal surgery. Before performing the DIEP reconstruction, included patients were evaluated on the basis of the previous abdominal surgery, and DIEP reconstruction was not performed if the blood supply was compromised. For the study purpose, no other information regarding previous surgery was obtained, which could bias the results.

Conclusion

We find that the mean IAP increases significantly over the peri-operative time for women undergoing unilateral DIEP flap reconstruction of the breast. Abnormal IAP levels are only seen 24 h after the closure of the skin, regardless of the tightness of skin closure or rectus plication performed. One patient developed deep venous thrombosis and lung emboli post-operatively, which is associated with high and abnormal IAP levels 24 h post-surgery. Overall, our results emphasise the importance of careful patient selection and for applying principles of ERAS, limiting the effect on IAP and the potential risk of thromboembolic events.

Funding

No external funding.

Ethical approval

The study was approved by the Health Ethics Committee of Northern Jutland, Denmark, and the Danish Data Protection Agency before initiation.

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according to the written informed consent.

Data availability

The data used to support the findings in this study is included in the article.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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