Surgery Open Science 10 (2022) 7–11

Contents lists available at ScienceDirect

Surgery Open Science

journal homepage: https://www.journals.elsevier.com/surgery-open-science

Dysautonomia following breast surgery: Disproportionate response to postoperative hematoma

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ARTICLE INFO

Article history:
Received 23 March 2022
Received in revised form 11 May 2022
Accepted 18 May 2022
Available online 25 May 2022

ABSTRACT

Background: Up to 10% of patients undergoing breast surgery suffer from bleeding complications. Some experience severe hypotension and bradycardia of unclear etiology. Similar to the vasovagal hyperstimulation provoked by abdominal insufflation during laparoscopic surgery, we hypothesize that chest wall stretch from postoperative breast hematoma may mechanically stretch the vagus nerve, triggering dysautonomia disproportionate to the degree of blood loss.

Methods: A single-institution retrospective review of patients requiring reoperation for hematoma evacuation following breast surgery between 2011 and 2021 was performed. The relationship between hematoma volume and hemodynamic instability, as well as hematoma volume and vasovagal symptoms, was measured.

Results: Sixteen patients were identified. Average hematoma volume was 353 mL, and average minimum mean arterial pressure was 64 mm Hg (range: 34–102 mm Hg). Fifty-six percent of patients reported symptoms including dizziness, somnolence, and/or syncope. Accounting for body surface area, patients with larger hematomas had similar minimum mean arterial pressures compared to those with smaller hematomas, 55 and 73 mm Hg, respectively (P = .0943). However, patients in the large hematoma group experienced over 3 times as many vasovagal symptoms, 88% and 25%, respectively (P = .0095).

Conclusion: Patients with large hematomas reported significantly more vagal symptoms compared to those with small hematomas despite similar mean arterial pressures. In addition, the trend of lower mean arterial pressures and heart rates more closely resembles vagal hyperstimulation than hypovolemic shock. Early hematoma evacuation to relieve vagal nerve stretch and parasympatholytics to reverse dysautonomia are targeted interventions to consider in this patient population rather than fluids, vasopressors, and blood products that are used in cases of hemodynamic instability due to hypovolemia alone.

INTRODUCTION

Up to 10% of patients [1] undergoing breast surgery will suffer from a bleeding complication. Of these patients, some experience bradycardia and hypotension that are disproportionate to their volume of blood loss. Hypotension and bradycardia, rather than the expected tachycardic response to hypovolemia, are more consistent with a vasovagal response due to a hematoma causing capsular stretch and mirror the well-described autonomic effect of abdominal insufflation during laparoscopic surgery [2,3]. Progression to shock and asystole is a rare but highly morbid consequence of an extreme vagal reaction. Thus, understanding the physiology of patients with postoperative breast hematomas is critical for providing definitive care.

Prior work has described physiology of the vasovagal Bezold–Jarisch reflex [4]. Massive efferent signaling along the vagus nerve inhibits signal generation at the cardiac sinoatrial and atrioventricular nodes and promotes systemic vasodilation, which overwhelms the balance between sympathetic and parasympathetic tone [5]. As a result, pooled venous blood does not provide adequate preload to the heart, and the reduced heart rate cannot compensate for this underfilling [6]. If untreated, the brain is not sufficiently perfused and the patient syncopates. This autonomic reflex occurs in response to a variety of situations: pain, fear, blood loss, anesthesia administration, orthostasis, cytokine release, and others [5–8].

This potentially dangerous hypotension is a well-known risk of laparoscopic surgery, particularly during abdominal insufflation imposing mechanical compression on abdominal viscera and mechanical stretch

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https://doi.org/10.1016/j.sopen.2022.05.011

along the abdominal wall [3]. Paradoxical bradycardia, rather than the expected reflex tachycardia, observed in these situations supports this theory. Moreover, this response worsens with rapid insufflation and high intra-abdominal pressures and improves with slower insufflation and lower pressures, suggesting that the degree and speed of abdominal and peritoneal stretch are important mediators of vagal activity [9]. One case report specifically noted that the bradyarrhythmia began when an abdominal retractor was placed, citing the direct stretching of the vagus nerve as the culprit [10]. This phenomenon is thus clinically relevant, with multiple reports of bradycardia progressing to cardiac arrest [11].

In our practice, a portion of patients with a hematoma following breast surgery experiences bradycardia and hypotension, and symptoms of dizziness and syncope to a degree which appears disproportionate to the volume of blood loss. This is inconsistent with the expectation of hemorrhagic shock. A literature review identified 2 studies that describe vasovagal reactions secondary to mechanical disruption during chest wall or breast surgery. Schusterman et al described progression from bradycardia to asystole secondary to vagal stretch during breast augmentation [12]. In this case series, 3 patients were successfully treated with the antimuscarinic glycopyrrolate, although 1 patient required chest compressions before returning to normal sinus rhythm [12]. Fan et al followed a woman undergoing unilateral deep inferior epigastric perforator artery reconstruction immediately after mastectomy with intraoperative hypotension and bradycardia [13]. The episode began after Wheatlander self-retaining retractors were placed against the second and fourth ribs and resolved immediately following retractor release [13]. The authors attributed this autonomic instability to vagal afferent signaling along the patient's visceral pleura [13].

No study to date describes the mechanism of vagal afferent stretch among patients with postoperative hematoma after breast surgery. The objective of this study is to characterize the relationship between blood loss and clinical symptoms in patients who undergo breast surgery complicated by hematoma. We hypothesize that the chest wall stretch from hematoma formation following breast surgery may trigger vasovagal hyperstimulation.

METHODS

A retrospective review of clinical records was performed, analyzing patients who returned to the operating room for hematoma evacuation following partial mastectomy or mastectomy without reconstruction at a single, tertiary-care, academic medical center between 2011 and 2021. The data extracted from the electronic medical record included patient age, height, weight, medications including vagolytics and β-blockers, postoperative symptoms, and perioperative vital signs. Systolic and diastolic blood pressures, heart rate, and mean arterial pressures (MAPs) were collected. Blood pressure and MAP were noted in 2 ways: the first measurement was recorded in the operating room immediately before anesthesia administration; the second was the single minimum systolic and diastolic pressure recorded during overall perioperative period, which included before, during, and after surgery. The presence or absence of vasovagal symptoms included dizziness, somnolence, lightheadedness, chest pain, syncope, and near-syncope. Complaints of breast pain or localized surgical site pain were not included in the data extraction.

We aimed to determine the relationship between volume of the hematoma and presence of hemodynamic instability measured by preoperative and minimum perioperative MAP. In addition, the relationship between volume of the hematoma and vagal response symptoms was analyzed. To differentiate large versus small hematomas, the cohort was divided into 2 groups with the cutoff being median hematoma volume (300 mL). The preoperative and the minimum perioperative MAPs were averaged among groups. A *t* test was used to compare the average MAPs and the percentage of symptomatic patients between the 2 groups. Further analysis was used to control for the varying impact of body surface area (BSA) on hematoma volume calculations. As previously mentioned, the cohort was divided with the cutoff being median hematoma volume per BSA (144.9 mL/m^2) to differentiate large versus small hematomas, and a *t* test was used to compare the average MAPs and percentage of symptomatic patients. A Student 2-tailed *t* test was used with a p-value of less than 0.05 determined as significant. All statistical analyses were performed using Microsoft Excel software (Version 16.57). Given the minimal risk and retrospective nature of the study originally designed as part of a quality improvement project, it was deemed exempt from Institutional Review Board review.

RESULTS

We identified 16 patients who required reoperation for hematoma evacuation during the study period (Table 1). All patients were female with a median age of 62 (range: 46–76). Nineteen percent of patients were taking preoperative β-blockers. No patients received atropine or other vagolytic medications; rather, the intraoperative hypotension was managed with fluids and vasopressors as needed. In the preoperative setting, the average heart rate was 75 beats/min (range: 59–93 beats/min), the average blood pressure was 126/67 mm Hg (range: 55–185/36–130 mm Hg), and the average MAP was 87 mm Hg (range: 48–137 mm Hg). The average hematoma volume was 353 mL (range: 50-1000 mL). Perioperatively, the average minimum heart rate was 65 beats/min (range: 53-84 beats/min), the average minimum blood pressure was 96/48 mm Hg (range: 41–147/30-92 mm Hg), and the average minimum MAP was 64 mm Hg (range: 32-102 mm Hg). Fifty-six percent of patients reported symptoms including dizziness, somnolence, and/or syncope.

Two groups were divided by blood loss, with the cutoff being the median hematoma volume of 300 mL (Table 2). The large hematoma group had an average blood loss of 489 mL, and the small hematoma group had an average blood loss of 179 mL ($P = .0036$). The 2 groups had similar average preoperative MAPs, 78 and 99 mm Hg, respectively ($P = .0792$) and similar average perioperative minimum MAPs, 57 and 73 mm Hg, respectively ($P = .1596$). Although more patients in the large hematoma group displayed symptoms compared to the small hematoma group, 67% and 43%, respectively, this difference was not significant ($P = .1902$).

Further analysis stratified groups by volume of blood loss with respect to patient BSA to control for individual patient weight, height, and body habitus that could change the impact of a set hematoma volume. Again, the cohort was divided with the cutoff being median hematoma volume per BSA (144.9 mL/m^2), with the large blood-per-BSA group having an average hematoma volume of 506 mL compared to the small group volume of 200 mL ($P = .0087$). There was no significant difference between the 2 groups in average preoperative MAP (79 and 95 mm Hg, respectively, $P = .1698$) or average minimum MAP (55 and 73 mm Hg, respectively, $P = .0943$). However, 88% of patients in the large blood-per-BSA group reported symptoms compared to 25% in the small blood-per-BSA group ($P = .0095$).

CASE REPORTS

Two representative patient hospital courses are described in detail below.

The first patient was a 59-year-old woman with ER-positive, HER2-negative invasive ductal carcinoma. She was otherwise healthy with no known history of hematologic or autonomic dysfunction, nor was she taking any vasoactive medications. She presented for bilateral mastectomy and sentinel lymph node biopsy. After an uncomplicated procedure, she was brought to the recovery area. Estimated blood loss was 180 mL in the index operation. She had some sanguineous drainage from her right-sided Blake drain and a small, soft swelling concerning for a hematoma. Seven minutes later, she displayed reduced respiratory effort and down-trending blood pressures (Fig 1). An Ambu bag was applied, and she received single dose administration of 5 mg IV ephedrine

Table 1
Characteristics of 16 patients included in this case series

Patient	*Age*	*Height (cm)*	*Weight (kg)*	*BSA (m^2)*	*Hematoma size (mL)*	*Hematoma per BSA (mL/m^2)*	*Systolic BP (mm Hg)*	*Diastolic BP (mm Hg)*	*MAP (mm Hg)*	*Heart rate (beats/min)*	*Minimum systolic BP (mm Hg)*	*Minimum diastolic BP (mm Hg)*	*Minimum MAP (mm Hg)*	*Minimum heart rate (beats/min)*	*Atropine*	*Symptoms*	*Preop β-blocker*
1	74	158.5	58.0	1.60	200	125	185	80	115	72	147	68	94	62			
2	55	157.0	81.2	1.88	1000	532	150	40	77	75	66	30	42	61		✓	✓
3	76	160.5	70.2	1.77	500	282	155	75	102	93	117	45	69	65		✓	✓
4	58	162.6	84.4	1.95	300	154	89	60	70	68	70	31	44	59		✓	
5	53	167.6	79.8	1.93	500	259	130	80	97	74	92	40	57	64		✓	✓
6	48	165.1	71.2	1.81	50	28	129	69	89	70	119	68	85	67			
7	70	162.0	88.8	2.00	600	300	89	36	54	70	89	36	54	63		✓	
8	58	160.0	76.4	1.84	250	136	150	130	137	86	75	37	50	62		✓	
9	55	156.5	79.0	1.85	600	324	135	73	94	85	94	42	59	62			
10	72	161.3	72.1	1.80	250	139	160	60	93	61	129	61	84	54			
11	46	167.6	92.1	2.07	300	145	55	45	48	74	55	45	48	74			
12	54	170.2	90.7	2.07	300	145	80	65	70	59	80	41	54	57		✓	
13	74	173.0	102.8	2.22	300	135	150	60	90	84	140	62	88	72			
14	62	155.3	58.2	1.58	100	63	149	88	108	90	121	92	102	84			
15	58	160.0	93.3	2.04	150	74	108	65	79	64	41	31	34	53		✓	
16	75	158.8	55.8	1.57	250	159	105	52	70	79	102	45	64	83		✓	
Average	62	162.3	78.4	1.87	353	188	126	67	87	75	96	48	64	65	0%	56%	19%

Table 2
The relationship between hematoma size, average preoperative MAP, average minimum MAP, and patient symptoms

Comparison by hematoma volume[*]			
	Large	*Small*	*Significance*
Average volume (mL)	489	179	$P = .0036$
Average preoperative MAP (mm Hg)	78	99	$P = .0792$
Average minimum MAP (mm Hg)	57	73	$P = .1596$
Symptoms (%)	67	43	$P = .1902$
Comparison by hematoma volume as percent BSA[†]			
	Large	*Small*	*Significance*
Average volume (mL)	506	200	$P = .0087$
Average preoperative MAP (mm Hg)	79	95	$P = .1698$
Average minimum MAP (mm Hg)	55	73	$P = .0943$
Symptoms (%)	88	25	$P = .0095$

[*] Cutoff set to median hematoma volume, 300 mL.
[†] Cutoff set to median hematoma volume-per-BSA, 144.9 mL/m^2.

and 1000 mL fluid bolus. Five minutes later, she became bradycardic to 53 beats/min and hypotensive to 41/31 mm Hg. Clinically, she was pale and minimally responsive. She returned to the operating room for evacuation and removal of 150 mL of hematoma. Upon opening the prior incision and evacuating the clot, she immediately stabilized and required no additional pressor support or fluid resuscitation. She was admitted overnight and remained stable for the remainder of her course. Hemoglobin was 10.6 g/dL the following morning, down from 12.9 g/dL preoperatively. She was discharged the following morning without issue.

The second patient was a 75-year-old woman with ER-positive, HER2-negative invasive lobular carcinoma. Her medical history was significant for severe back pain secondary to L4–L5 spondylolisthesis managed with lumbar spinal fusion. She had no known history of hematologic or autonomic dysfunction. She took a stable dose of amlodipine for 9 years prior to her right partial mastectomy and sentinel lymph node biopsy. She was discharged the day of surgery without apparent complication. That evening, she fainted in her home before presenting to an outside hospital emergency department, and vasovagal syncope was the suspected etiology. She was given 400 mL of fluid, and her blood pressure stabilized. She planned to return to same-day surgery the next morning for operative evacuation of the hematoma. Her blood pressure on admission was 114/45 mm Hg with a heart rate of 83 beats/min. In the preoperative area, she developed a widened pulse pressure with a blood pressure of 150/40 mm Hg. Anesthesia was then administered, and her blood pressure dropped to 80–100/40–50 mm Hg. She received IV fluid, and 250 mL of clot was evacuated. Her blood pressure was 100/60 mm Hg at the remainder of the case, and she subsequently remained stable for the remainder of her admission. She was discharged later that day and had no further complications.

DISCUSSION

In this case series, 16 patients with breast surgery had their postoperative courses complicated by hematoma. Those with large and small hematomas have similar preoperative MAPs (78 and 99 mm Hg, respectively) as well as similar minimum perioperative MAPs (57 and 73 mm Hg, respectively). Although those with larger hematomas displayed more symptoms (67% and 43%), this finding was not significant. After controlling for variations in patient height, weight, and body habitus using BSA calculations, patients with large and small hematomas for BSA still had similar preoperative MAPs (79 and 95 mm Hg, respectively) and minimum perioperative MAPs (55 and 73 mm Hg, respectively); however, those in the large blood loss-per-BSA group reported more than 3 times as many symptoms as those in the small blood loss-per-BSA group (88% and 25%, respectively), a finding that was statistically significant. Neither of these findings is consistent with the presentation of hemorrhagic shock; rather, these observations more closely resemble a vasovagal response.

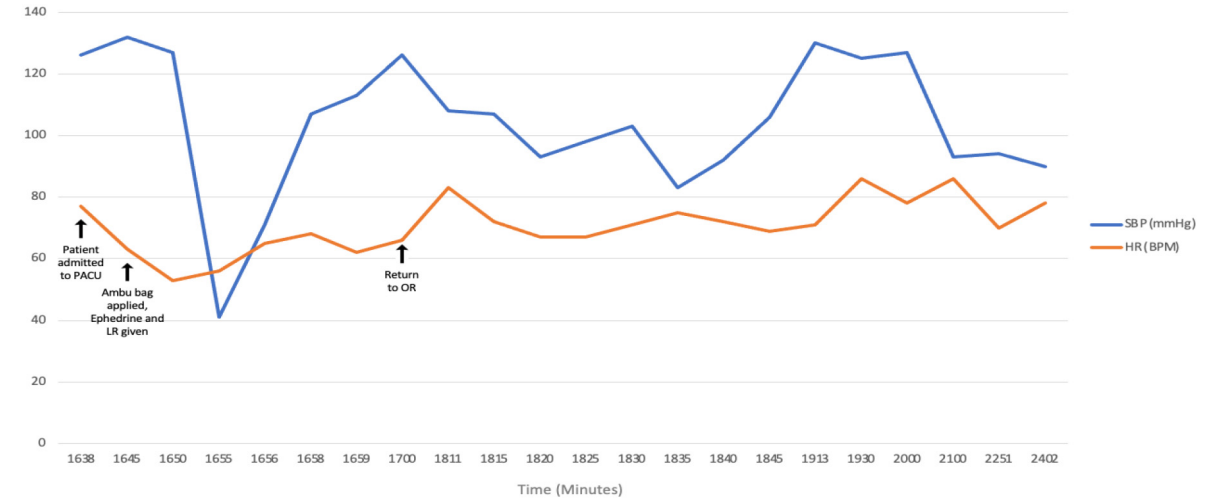

Fig 1. Postoperative course of representative patient in series (patient 16) demonstrating changes in systolic blood pressure and heart rate.

Overall, this relationship suggests that blood loss does not appear to correlate directly with the presence, absence, or degree of hemodynamic stability. The similar MAPs between groups support the hypothesis that the hemodynamic changes observed in this series are not linearly related to the degree of hypovolemia or blood loss. In addition, the chronology of blood pressure recovery in the cases described here demonstrates rapid stabilization of vital signs following opening of the incision, release of the stretch, and hematoma evacuation. Patients required minimal support thereafter. This is a further deviation from the expected need for prolonged resuscitative efforts typically required in the setting of hemorrhagic shock.

However, the significant finding of patients experiencing more vasovagal symptoms with larger hematomas was independent of hemodynamic status. Based on this result, we suspect that stretch secondary to hematoma expansion—similar to the mechanical effects of surgical retractors or breast implants—stimulates the vagus nerve, driving the signs and symptoms of vasovagal hyperstimulation observed in this series. The consequent trend toward hypotension and often observed bradycardia is thus likely a product of autonomic dysregulation rather than hypovolemic shock.

Patients in this series lost between 50 and 1,000 mL of blood. Therefore, their observed symptoms should reflect Class I or II shock, characterized by normal blood pressure and possible tachycardia [14]. However, the average minimum MAP of 64 mm Hg and heart rate of 65 beats/min are on the lower end of normal and more closely resemble the classic hypotension and bradycardia seen with a vagal response.

This study has significant implications for perioperative teams managing patients with hematoma following breast surgery. The data suggest that in the appropriate patient population, therapeutic options should include rapid hematoma evacuation and consideration of medications like atropine or glycopyrrolate given their parasympatholytic properties which have been used as prophylaxis against or reversal of signs and symptoms of vasovagal hyperstimulation [15,16]. These interventions, rather than the standard high-volume fluid resuscitation or blood transfusions, would more specifically and definitively target the underlying problem. Most importantly, appropriate and expeditious management may avoid additional morbidity in patients with this relatively common complication.

This study has 2 significant limitations. First, it is a single-institution case series and is therefore limited by small sample size. A larger, multi-institutional study would help to further elucidate the pathophysiology observed. The retrospective nature of this study limits the ability to determine whether or not vagal hyperstimulation is the cause of the trend toward hypotension and bradycardia in these patients. We instead hope to alert the surgical and anesthesia communities about this alternative physiologic explanation and offer suggestions for management. More cases and additional research are needed to more definitively tie this phenomenon to the vasovagal reflex.

The tertiary academic center where this case series originated performs approximately 300 partial and complete mastectomies yearly. During the 10-year study period, 16 patients were identified as having postoperative hematoma requiring return to the operating room. Most patients leave the same-day surgery center with instructions to wear a compressive wrap, apply ice, and take nonsteroidal anti-inflammatories or acetaminophen as needed for pain. Of those who suffer a complication, the most common is delayed seroma followed by cellulitis and hematoma. The authors recognize the rarity of this presentation. However, the severity can be extreme; the first patient who rapidly decompensated in the PACU demonstrated a blood pressure of 41/31 mm Hg, which is a particularly striking example. Therefore, the low incidence does not preclude a thoughtful, thorough understanding of the possible underlying process to facilitate a swift, conclusive solution.

To that end, clinical implications first include a recognition of this clinical change and recollection of this possible cause in addition to acute blood loss alone. Second, perioperative teams caring for patients following complications in breast surgery may consider protocols to watch for unexpected hypotension and bradycardia. Such protocols might include additional return precautions added to standard discharge paperwork or members of the care team calling patients who were discharged with postoperative hematoma within 24 hours to evaluate for vasovagal symptoms. Although most patients with hematoma do not develop this clinical presentation, the possible severity of vital sign derangements warrants additional caution for patients who do have a hematoma. Recommendations to avoid driving and operating heavy machinery, as well as staying with friends or family for the first postoperative day, could improve identification of decompensation and hasten return to care.

In conclusion, stretching of the chest wall during surgical retraction can lead to a vagal response with symptoms of vasovagal hyperstimulation and trends in vital signs toward hypotension and bradycardia. These data show that although MAPs were no different between patients with large and small hematomas per BSA, symptoms were significantly more common in the large blood loss-per-BSA group. Therefore, we conclude that it is the degree of mechanical stretch, rather than the degree of blood loss, that is driving this change in postoperative status. Furthermore, vital signs trended toward hypotension and bradycardia disproportionate to and unexpected for the degree of hypovolemia. The dearth of information surrounding this topic and the potential risk

of an overwhelming parasympathetic response progressing to asystole warrant further education and research. A better understanding of the underlying mechanism and the applicable patient population would avoid unnecessary pressor administration, fluid boluses, or blood transfusions and offer definitive treatment such as prompt hematoma evacuation and administration of vagolytic medications.

Author Contributions

KMR contributed to study design, data analysis, interpretation of the data, initial writing of manuscript, and revision of final manuscript. MML contributed to study design, interpretation of the data, initial writing of manuscript, and revision of final manuscript. MDH contributed to interpretation of data and revision of final manuscript. KEP contributed to study background and context, as well as revision of final manuscript.

Conflict of Interest

The authors report no financial or personal relationships with other people or organizations related to this work and its conclusions.

Funding Source

This work was supported by Dartmouth-Hitchcock Medical Center, Department of General Surgery.

Ethics Approval

This project was conceived for quality improvement following an acute event. Given the use of retrospective, deidentified data under a quality improvement process, it therefore was not subjected to Institutional Review Board review.

Meeting Presentation

Abstract presented as a quick shot presentation at the 2022 Academic Surgical Congress Annual Meeting (Abstract ID: ASC20220408).

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