



Risk Factors for Acute Intraoperative Bradycardia in Patients Undergoing Gender-affirming Mastectomy

Les facteurs de risque de bradycardie intraopératoire aiguë lors de la mastectomie d'affirmation de genre

Sarah M. Thornton, BA¹, Ellen C. Shaffrey, MD¹ ,
Caroline C. Bay, BA¹ , Joshua C. Verhagen, BS¹, Peter J. Wirth, MD¹,
Armin Edalatpour, MD¹ , Jacqueline S. Israel, MD¹,
Katherine M. Gast, MD¹, and Venkat K. Rao, MD, MBA¹ 

Abstract

Purpose: Gender-affirming mastectomy surgery is highly desired within both transmasculine and nonbinary patient populations. The development of cardiac arrhythmias has been reported within this population. Acute intraoperative bradycardia in patients undergoing gender-affirming mastectomy has not been well described previously. This study aimed to describe the frequency of acute intraoperative relative bradycardia in patients undergoing gender-affirming mastectomies and identify potential risk factors that contribute to its occurrence. **Methods:** A retrospective review was performed for all patients who underwent gender-affirming mastectomy at a single institution. Data regarding patient demographics, comorbidities, and perioperative course were collected. Patients were separated into those who did and did not develop acute intraoperative bradycardia. The definition of relative intraoperative bradycardia was a heart rate below sixty beats per minute. Logistic regression was performed to determine which variables were predictive of bradycardia. **Results:** A total of 337 patients underwent gender-affirming mastectomy between January 2018 and January 2023. Of these patients, 144 (42.7%) experienced acute intraoperative relative bradycardia, with 97 (67.4%) requiring anesthetic intervention and 5 (3.5%) requiring halting or abortion of surgery. Two patients (1.4%) required compressions for asystole. Fluoxetine as an outpatient medication (OR: 2.63, $P = .002$) and harvest of a nipple graft (OR: 2.77, $P = .018$) were associated with a significantly increased risk of developing acute intraoperative bradycardia. **Conclusion:** Acute intraoperative relative bradycardia may be a unique phenomenon in patients undergoing gender-affirming mastectomies due to variables specific to this patient population. A future study comparing patients undergoing gender-affirming mastectomy to those undergoing elective breast surgeries is forthcoming to assess further risk factors.

Résumé

Introduction: La mastectomie d'affirmation de genre est hautement désirée dans les populations d'hommes trans et de patients non binaires. Des cas d'arythmie cardiaque ont été observés dans ces populations. La bradycardie intraopératoire aiguë chez les patients qui subissent une mastectomie d'affirmation de genre n'est pas bien décrite. La présente étude visait à décrire la fréquence de bradycardie relative intraopératoire aiguë chez les patients qui subissent une mastectomie d'affirmation de genre et à déterminer les facteurs de risque de cette occurrence. **Méthodologie:** Les chercheurs ont réalisé une étude

¹ Division of Plastic and Reconstructive Surgery, University of Wisconsin School of Medicine and Public Health. Madison, WI, USA

Received April 7, 2024. Revised July 14, 2024. Accepted July 24, 2024.

Corresponding Author:

Venkat Rao, Division of Plastic and Reconstructive Surgery, University of Wisconsin Health University Hospital, 600 Highland Avenue, Box 3236, Clinical Science Center, Madison, WI 53792, USA.

Email: rao@surgery.wisc.edu

rétrospective auprès de tous les patients qui avaient subi une mastectomie d'affirmation de genre dans un seul établissement. Ils ont recueilli les données relatives aux caractéristiques démographiques, aux autres maladies et à la trajectoire périopératoire des patients, qui ont été répartis entre ceux qui avaient présenté et ceux qui n'avaient pas présenté de bradycardie intraopératoire aiguë. La bradycardie intraopératoire relative était définie comme une fréquence cardiaque inférieure à soixante battements à la minute. Les chercheurs ont procédé à une régression logistique pour établir quelles variables étaient prédictives d'une bradycardie. **Résultats:** Au total, 337 patients ont subi une mastectomie d'affirmation de genre entre janvier 2018 et janvier 2023. De ce nombre, 144 (42,7 %) ont présenté une bradycardie relative intraopératoire aiguë, dont 97 (67,4 %) ont eu besoin d'une intervention anesthésique. Dans cinq de ces cas (3,5 %), la chirurgie a dû être interrompue ou abandonnée. Deux patients (1,4 %) ont dû subir des compressions à cause d'une asystole. La fluoxétine administrée en contexte ambulatoire (RC: 2.63, $P=0.002$) et le prélèvement d'une greffe du mamelon (RC: 2.77, $P=0.018$) étaient associés à un risque considérablement plus élevé de bradycardie intraopératoire. **Conclusion:** La bradycardie relative intraopératoire aiguë peut être un phénomène unique chez les patients qui subissent une mastectomie d'affirmation de genre en raison de variables propres à cette population. Une prochaine étude qui comparera les patients subissant une mastectomie d'affirmation de genre à ceux qui subissent une chirurgie mammaire non urgente est annoncée pour évaluer les autres facteurs de risque.

Keywords

gender-affirming surgery, bradycardia, top surgery, anesthesia, plastic surgery, asystole, mastectomy

Mots-clés

chirurgie d'affirmation de genre, bradycardie, chirurgie du haut, anesthésie, chirurgie plastique, asystole, mastectomie

Introduction

There are estimated to be approximately 1.3 million adults identifying as transgender or nonbinary living in the United States.¹ For these individuals, gender-affirming surgery (GAS) has been demonstrated to increase self-confidence, improve quality of life, and decrease gender dysphoria.²⁻⁴ The incidence of GAS continues to rise with increased social acceptance and access to care, with a majority of patients undergoing breast and chest surgery.^{5,6} The 2015 US Transgender Survey noted that 97% of transmasculine respondents either desired or had undergone chest masculinization surgery.⁷ Gender-affirming mastectomy (GM) involves excision of the glandular breast tissue and excess skin and repositioning and reshaping of the nipple-areolar complex for patients who desire to retain nipples to create a more masculine or nonbinary chest phenotype.^{8,9} This is often the first surgical intervention pursued by transgender men, as testosterone treatment can only achieve partial breast regression.¹⁰

A 2019 review of the American College of Surgeons National Surgical Quality Improvement Program database demonstrated that GM has a similar risk profile to mastectomy in the cisgender population, with a 4.7% rate of all-cause complications.¹¹ However, at our institution, patients undergoing gender-affirming mastectomies frequently develop acute intraoperative relative bradycardia. Both plastic and reconstructive (PRS) surgeons and anesthesiologists have reported cases requiring anesthetic intervention, halting of surgery, and rarely chest compressions. Intraoperative bradycardia can be indicative of cardiovascular stress and may increase patient's risk of 30-day postoperative mortality and stroke.¹² The development of intraoperative cardiac arrhythmias during GM has been reported in the literature; however, the etiology of these arrhythmias has yet to be elucidated.¹³

Identifying, treating, and ideally preventing intraoperative bradycardia during GM is paramount for patient safety. Our study aims to describe the frequency of acute intraoperative relative bradycardia in patients undergoing gender-affirming mastectomies at our institution and identify potential risk factors that could be contributing to its occurrence.

Methods

A retrospective review was performed for all patients who underwent gender-affirming mastectomy by two senior authors (VKR, KMG) at a single institution from 2018 to 2023. Patient demographic and comorbidity data were collected, including anesthesia-relevant health conditions, such as hypertension and sleep apnea, and outpatient medications. Intraoperative data included both anesthetic and surgical interventions. Anesthetic variables of interest included which induction agents were used and if regional blocks were performed. Heart rate and blood pressure were assessed by using intraoperative anesthesia data. Surgical intervention data included the type of top surgery, either periareolar or double incision mastectomy with or without free nipple grafting, and if liposuction and fat grafting were performed. Patients were subsequently separated into those who did and did not experience acute intraoperative bradycardia. Data regarding the incidence of hypotension during bradycardia, whether surgery was halted, if atropine or glycopyrrolate were administered, and whether chest compressions were started were also recorded. Intraoperative relative bradycardia was defined as any patient who experienced an acute change in heart rate that dropped below 60 beats per minute (BPM). Hypotension was defined as either a systolic pressure below 90 mmHg or a diastolic pressure below 50 mmHg. Heart rate and blood pressure were determined by examining the intraoperative anesthesia record.

Statistical Analysis

Statistical analyses were conducted with R (version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). Data distributions were checked using the Shapiro-Wilk test of normality. All variables tested were found to be nonparametric. Univariate analysis of nonparametric variables with bradycardia as a binary, dependent variable was assessed using the Mann-Whitney *U* test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. Variables found to have *P* values $\leq .2$ in univariate analysis were included in multivariable analyses. A *P* value of .20 was chosen to minimize excluding potentially significant predictors in multivariable analysis. For multivariable analysis, a logistic regression model with bradycardia as the dependent variable was built to explore the relationship between bradycardia and the selected variables. The model was refined to include only significant predictors. The linearity assumption was assessed, and the model was checked and addressed for separation, collinearity, and outliers. The omnibus test was used to verify the model fit the data well.

Subgroup analysis was conducted among cases that experienced intraoperative bradycardia. A logistic regression model was utilized to examine the effects of the selected patient variables on developing intraoperative hypotension. For all tests of normality and regressions, the level of statistical significance was set at *P* = .05.

Results

Three-hundred and thirty-seven patients who underwent gender-affirming mastectomy between January 2018 and January 2023 met inclusion criteria. Thirty-four cases were excluded from the analysis due to incomplete data. See Table 1 for patient characteristics. Patients had a median age of 25 (IQR 16-34), and 310 (92%) were classified as ASA 1 or 2. Two-hundred and forty-three (72.1%) patients had no relevant comorbidities, and 318 (94.4%) patients had no prior difficulty with anesthesia. Of note, 125 (37.9%) patients were taking a selective serotonin reuptake inhibitor (SSRI) (11.6% fluoxetine, 1.2% citalopram, 0.003% fluvoxamine, 24% other). Additionally, 257 (76.3%) patients were on some form of hormone therapy, including, but not limited to, testosterone patches, gels, and injectables.

One hundred and forty-four (42.7%) patients experienced acute intraoperative relative bradycardia, with 97 (67.4%) requiring anesthetic intervention and 5 (3.5%) requiring halting of surgery. Two patients (1.4%) underwent compressions due to progression to asystole, and both had return of spontaneous circulation. There were no mortalities and, to our knowledge, no subsequent cardiac events within 30 days.

In univariate analysis, several patient factors were found to be significant (*P* < .2): age, SSRI use, prior difficulty with anesthesia, ASA status, nipple graft involvement, cardiac arrhythmia history, hyperlipidemia, and etomidate use. These variables were included as predictors for multivariable logistic regression analysis; however, cardiac arrhythmia, hyperlipidemia, and etomidate use were not found to be significant (*P* > .05). Hormone therapy (*P* = .682), use of a regional pectoralis

block (*P* = .574), and BMI (*P* = .799) were not correlated with increased risk of intraoperative bradycardia (Table 2).

The final multivariable logistic regression model included age (*P* < .001), SSRI use (*P* < .001), prior difficulty with anesthesia (*P* = .017), and free nipple grafting (*P* = .019) as significant, independent predictors of increased risk of intraoperative bradycardia. ASA statuses 2 or 3 were associated with a lower probability of bradycardia (*P* = .009, *P* = .004) (Table 3).

The variables significant for predicting intraoperative bradycardia were then used to assess their effects on bradycardic patients developing hypotension (Table 4). Only SSRI use was found to significantly increase the probability of intraoperative bradycardic patients developing hypotension (*P* < .023).

Discussion

At our institution, both plastic surgeons and anesthesiologists have noted a pattern of the development of acute intraoperative relative bradycardia in patients undergoing gender-affirming mastectomies, with 42.7% of 337 patients experiencing a bradycardic event. Our analysis identified several patient-specific factors that significantly correlated with intraoperative bradycardia, specifically SSRI use (*P* < .001), and free nipple grafting (*P* = .019). Bivariate analysis also demonstrated that increased age (*P* < .001) was independently associated with the risk of intraoperative bradycardia.

Free nipple grafting was significantly correlated with the development of intraoperative relative bradycardia (OR: 2.77, *P* = .019). During free nipple grafting, the nipple-areolar complex (NAC) is harvested as a full-thickness skin graft and transferred to a new location on the chest.¹⁴ To our knowledge, there is no established connection between free nipple grafting and bradycardia in the literature but given that the nipple-areolar complex receives autonomic innervation from T1 to T5 sympathetic postganglionic fibers, we speculate that it is possible that disruption of this innervation could contribute to bradycardia.¹⁵ Stimulation of NAC sympathetic nerves during the nipple harvest part of the procedure could lead to reflex bradycardia via the baroreflex mechanism. This potential explanation is hindered by the young age of the included patients. Older age is associated with blunting of the baroreflex, meaning patients require a larger stimulus to fully activate adrenergic vasoconstriction.¹⁶ Therefore, older patients, not young patients, would be likely to demonstrate a more severe failure to maintain vascular tone and subsequent bradycardia and hypotension.¹⁷

SSRI use also correlated with intraoperative relative bradycardia and hypotension (*P* = .002, *P* = .023). The use of an SSRI was also associated with the development of hypotension during bradycardia (OR: 3.33, *P* = .015). This is particularly relevant in the context of GAS, as transgender patients experience minority stress, have a high incidence of depressive disorder, and receive 3.4 to 3.9 times more prescriptions for antidepressants and anxiolytics than the cisgender population.¹⁸ Previous work has provided evidence that antidepressants are associated with decreased vagal tone and reductions in baseline heart rates.¹⁹ These findings suggest that SSRIs may affect patient

Table 1. Patient Characteristics. FNG, Free Nipple Grafting.

Characteristics	n (%)
Total patients	337
BMI	Median 28.65; IQR 10.3
Age	Median 25; IQR 9
Anesthesia difficulty	
No prior difficulty with anesthesia	318 (94.4)
Prior difficulty with anesthesia	19 (5.6)
ASA status	
ASA I	99 (29.4)
ASA II	211 (62.6)
ASA III	27 (8)
Comorbidities	
None	243 (72.1)
Hypertension	19 (5.6)
Ischemic heart disease	1 (0.3)
Cardiomyopathy	1 (0.3)
Cardiac arrhythmias	0 (0)
Stroke	2 (1.0)
Diabetes	9 (2.7)
Hyperlipidemia	20 (5.9)
Kidney disease	2 (1.0)
Sleep apnea	18 (4.7)
Asthma	56 (16.6)
Number of comorbidities	
0	243 (72.1)
1	72 (21.4)
2	14 (4.2)
3	4 (1.2)
4	4 (1.2)
Anesthetic agents used	
Morphine	2 (0.6)
Propofol	328 (97.3)
Dexamethasone	87 (25.8)
Midazolam	300 (89.0)
Fentanyl	303 (90.0)
Lidocaine	324 (96.1)
Succinylcholine	13 (3.9)
Rocuronium	66 (19.6)
Hydromorphone	26 (7.7)
Etomidate	4 (1.2)
Hormone therapy	
Yes	257 (76.3)
No	80 (23.7)
SSRI use	
No	212 (62.9)
Fluoxetine	39 (11.6)
Citalopram	4 (1.2)
Paroxetine	0 (0.0)
Other ^a	82 (24.3)
Mallampati class	
Mallampati Class 1	130 (38.6)
Mallampati Class 2	155 (46.0)
Mallampati Class 3	25 (7.4)
Mallampati Class 4	2 (0.6)

(continued)

Table 1. (continued)

Characteristics	n (%)
Mallampati Class 5	25 (7.4)
Pecs I block performed	
Yes	184 (54.6)
No	153 (45.4)
Duration of anesthesia	Median 115 min; IQR: 35
Surgical technique	
Double incision mastectomy with FNG	295 (87.5)
Double incision mastectomy w/o FNG	42 (12.5)
Liposuction performed	
Yes	228 (67.7)
No	109 (32.3)
Surgery halted	
Yes	5 (3.5)
No	139 (96.5)
Anesthesia intervention	
Yes	97 (67.4)
No	47 (32.6)

^aFluvoxamine, citalopram, escitalopram, sertraline, duloxetine, bupropion, or venlafaxine.

hemodynamics intraoperatively. Nevertheless, evidence-based guidelines currently state that SSRIs should not be held prior to surgery, as the risk of withdrawal justifies continuation.²⁰ Further research should be pursued to investigate a potential causal relationship between SSRI use and intraoperative bradycardia. Unfortunately, there were not enough patients taking SSRIs to separately analyze their effect on the risk of intraoperative bradycardia.

The authors were surprised by the odds ratio of ASA 2 which suggests this classification may act as a protective factor against relative bradycardia during gender-affirming mastectomy. This may be attributable to a sizable representation of patients with ASA level 2 and coincidence. Future studies are needed to fully uncover the relationship between ASA status and bradycardia gender-affirming mastectomy.

It is unlikely that the anesthetic regimen itself is the sole cause of increased rates of bradycardia in patients undergoing gender-affirming mastectomies at our institution. The anesthesia personnel for these cases vary greatly, and no single provider is responsible for the majority of gender-affirming mastectomy cases. Further, there have been no anecdotal reports of relative bradycardia in other plastic surgery cases or in other surgical subspecialty operating rooms. Additionally, there were no significant associations between bradycardia and anesthetic agents used.

One potential mechanism of intraoperative relative bradycardia and hypotension during breast surgery is a vasovagal response. Capsular stretch, caused by hematoma and other intraoperative techniques, may trigger a vasovagal response, similar to the autonomic effect of insufflation during abdominal laparoscopic surgery.^{21–23} Multiple case studies have described instances of vasovagal responses to mechanical disruption during breast surgery.^{24–26} Patients undergoing breast augmentation and breast

Table 2. Univariate Analysis. FNG, Free Nipple Grafting.

Variable	Percentage without intraoperative bradycardia n (%)	Percentage intraoperative bradycardia n (%)	P value
Total patients	193 (57.3)	144 (42.7)	
Age	Median 25; IQR 8	Median 27; IQR 9	.012
BMI			.623
BMI <18.5	6 (3.1)	2 (1.4)	
BMI 18.5-24.9	52 (26.9)	42 (29.2)	
BMI 25-29.9	48 (24.9)	41 (28.5)	
BMI >30	87 (45.1)	59 (41.0)	
Prior difficulty with anesthesia	7 (3.6)	12 (8.3)	.093
ASA status			.054
ASA I	47 (24.4)	52 (36.1)	
ASA II	128 (66.3)	83 (57.6)	
ASA III	18 (9.33)	9 (6.25)	
Comorbidities			
Hypertension	13 (6.74)	6 (4.17)	.440
Ischemic heart disease	0 (0.0)	1 (0.7)	.883
Cardiomyopathy	1 (0.5)	0 (0.0)	>.999
Cardiac arrhythmias	0 (0.0)	0 (0.0)	.008
Stroke	0 (0.0)	2 (1.4)	.3548
Diabetes	7 (3.6)	2 (1.4)	.358
Hyperlipidemia	8 (4.1)	12 (8.3)	.1686
Kidney disease	1 (0.5)	1 (0.7)	>.999
Sleep apnea	11 (5.7)	7 (4.86)	.9253
Asthma	34 (17.6)	22 (15.3)	.6725
Anesthetic agents used			
Morphine	1 (0.5)	1 (0.7)	.999
Propofol	187 (96.9)	141 (97.9)	.8133
Dexamethasone	51 (26.4)	36 (25.0)	.8651
Midazolam	173 (89.9)	127 (88.2)	.808
Fentanyl	175 (90.7)	128 (88.9)	.7224
Lidocaine	185 (95.9)	139 (96.5)	.975
Succinylcholine	7 (3.63)	6 (4.17)	>.999
Rocuronium	41 (21.2)	25 (17.4)	.4534
Hydromorphone	14 (7.25)	12 (8.33)	.8721
Etomidate	4 (2.07)	0 (0.0)	.139
Hormone therapy	144 (74.6)	113 (78.5)	.487
SSRI use	54 (28.0)	71 (49.3)	<.001
Mallampati class			.309
Mallampati Class 1	69 (35.8)	61 (42.4)	
Mallampati Class 2	88 (45.6)	67 (46.5)	
Mallampati Class 3	18 (9.3)	7 (4.9)	
Mallampati Class 4	1 (0.5)	1 (0.7)	
Mallampati Class 5	17 (8.8)	8 (5.6)	
Pecs I block performed	104 (53.9)	80 (55.6)	.846
Duration of anesthesia (mins)	115	115	.933

(continued)

Table 2. (continued)

Variable	Percentage without intraoperative bradycardia n (%)	Percentage intraoperative bradycardia n (%)	P value
Surgical technique			
Double incision mastectomy with FNG	161 (83.4)	134 (93.1)	.013
Double incision mastectomy w/o FNG	32 (16.6)	10 (6.94)	.013
Liposuction performed	130 (67.4)	98 (68.1)	.913

reconstruction using deep inferior epigastric perforator flaps were noted to experience bradycardia, hypotension, and even asystole, soon after placement of self-retaining retractors.²⁶ The authors suggest that this autonomic instability could be due to vagal afferent signaling.²⁴ Afferent stretch receptor fibers from the vagus nerve are present in the visceral pleura. Excessive sympathetic stimulation of these fibers intraoperatively can cause overstimulation of cardiac mechanoreceptors, resulting in a compensatory parasympathetic response.²⁴ Another case report noted severe intraoperative bradycardia in a patient undergoing modified radical mastectomy immediately after irrigating the wounds with normal saline.²⁷ This was hypothesized to be due to stretch receptor activation versus the diving reflex, a protective reflex to conserve oxygen during diving in the water, which is triggered by the application of cold water to areas of the face supplied by the trigeminal nerve.²⁷

Of note, although 76.3% of patients included in our study were on testosterone therapy, the use of hormone therapy was not associated with an increased risk of intraoperative bradycardia ($P = .682$). Testosterone has a controversial risk profile, with some evidence that it may increase venous thromboembolism risk in the testosterone-treated transgender population.²⁸ Further, testosterone therapy has been shown to compromise endothelial function, increasing cardiovascular risk.²⁹ However, our results do not support holding testosterone preoperatively to prevent bradycardia.

The clinical significance of hemodynamic instability during surgery cannot be overstated, as it may lead to adverse outcomes such as increased postoperative cardiovascular and cerebrovascular events and, potentially, increased postoperative morbidity.^{30,31} This risk is compounded by the fact that the majority of gender mastectomy operations (95.5%) are performed in the outpatient setting.¹¹ Intraoperative bradycardia may be associated with poor cardiac output and severe hypotension requiring aggressive anesthetic intervention.³² There is not an established severity or duration of bradycardia which increases the risk of postoperative complications. Intraoperative hypotension, with mean arterial pressure of <80 mm g for ≥ 10 min, is associated with end-organ injury, postoperative cardiac and renal morbidity, and mortality.^{33,34} A 2011 study demonstrated that intraoperative hypotension was one of seven perioperative variables that

Table 3. Multivariable Logistic Regression Results for Intraoperative Bradycardia Versus Select Risk Factors

Variable	Adjusted Odds Ratio		
	OR	95% CI	P value*
Age (years)			<.001
<20	-	-	-
20-29	3.995	1.750, 10.100	.002
30-39	3.691	1.464, 10.110	.008
>40	17.157	5.025, 65.138	<.001
SSRI use			<.001
None	-	-	-
Fluoxetine	2.654	1.261, 5.706	.011
Other ^a	2.608	1.516, 4.536	<.001
Prior difficulty with anesthesia			.017
No	-	-	-
Yes	3.729	1.294, 11.612	.017
ASA status			.003
I	-	-	-
II	0.483	0.283, 0.817	.007
III	0.196	0.064, 0.551	.003
Nipple graft involvement			.019
No	-	-	-
Yes	2.675	1.216, 6.398	.019

*Where $P < 0.05$ is significant. OR, odds ratio; CI, confidence interval.

^aFluvoxamine, citalopram, escitalopram, sertraline, duloxetine, bupropion, or venlafaxine.

were predictive of cardiac and cerebrovascular complications in noncardiac surgery.³⁰ Of note, there is a sparsity of literature describing the sequelae of the impact of intraoperative bradycardia and hypotension on wound healing.

Based on the results of this study, it is appropriate to consider taking measures of precaution prior to gender-affirming mastectomy. This could include incorporating the risk of relative bradycardia into a presurgical timeout or a preoperative multidisciplinary discussion between plastic surgeons and anesthesiologists.

This study is limited by its retrospective nature and relatively small cohort size. Further, our choice to define relative bradycardia as any heart rate under 60 bpm could incorrectly result in the inclusion of patients with low heart rates at baseline into our bradycardic group. Future studies could instead define bradycardia as a certain percentage below each patient's baseline heart rate. Our methods could also have resulted in an artificially high rate of bradycardia, as we considered patients with any bradycardia during any point in the operation as part of the bradycardic group. Therefore, patients did not need to experience sustained or clinically significant bradycardia and could instead simply have one reading of <60 bpm and be considered part of the bradycardic group. Future studies could instead only include patients with sustained bradycardic episodes. Additionally, our study lacks a control group. Future research will compare this patient population to patients undergoing breast reduction, augmentation mammoplasty, and gender-affirming breast augmentation at our

Table 4. Multivariable Logistic Regression Results for Intraoperative Hypotension of Bradycardic Patients Versus Select Risk Factors.

Variable	Adjusted odds ratio		
	OR	95% CI	P-Value*
Age (years)			.415
<20	-	-	-
20-29	0.356	0.018, 2.360	.361
30-39	0.212	0.010, 1.547	.184
>40	0.197	0.008, 1.906	.205
Hormone therapy use			.089
No	-	-	-
Yes	0.392	0.122, 1.090	.089
SSRI use			.023
None	-	-	-
Fluoxetine, fluvoxamine	2.563	0.875, 8.694	.102
Citalopram	0.213	0.009, 1.956	.212
Other ^a	3.328	1.313, 9.369	.015
Prior difficulty with anesthesia			.810
No	-	-	-
Yes	1.205	0.285, 6.510	.810
ASA status			.358
I	-	-	-
II	1.709	0.756, 3.888	.197
III	0.863	0.175, 4.529	.856
Nipple graft involvement			.928
No	-	-	-
Yes	0.927	0.153, 4.572	.928

*Where $P < .05$ is significant. OR, odds ratio; CI, confidence interval.

^aEscitalopram, sertraline, duloxetine, bupropion, or venlafaxine.

institution and will assess whether these risk factors should be considered in all patients undergoing breast surgery. This will also help elucidate whether the proposed mechanism of bradycardia should be specific to the transgender population or among all patients having breast surgery.

Conclusions

Acute intraoperative relative bradycardia is a common phenomenon in patients undergoing gender-affirming mastectomies. Our study demonstrates that age, antidepressant use, prior difficulty with anesthesia, and free nipple grafting are independently associated with increased risk of intraoperative bradycardia. We recommend heightened awareness of the possibility of intraoperative relative bradycardia while performing gender-affirming mastectomies and nipple grafting procedures and preoperative discussion between surgery and anesthesia teams.

Author Contributions

SMT and ECS did data collection and manuscript writing. CCB did data analysis, data interpretation. AE did data interpretation. JCV did data collection. PJW did manuscript writing. JSI, KMG, and VKR did manuscript revision.


Declaration of Conflicting Interests


The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.


Funding


The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Ellen C. Shaffrey  <https://orcid.org/0000-0001-8751-7309>

Caroline C. Bay  <https://orcid.org/0000-0003-1059-9961>

Armin Edalatpour  <https://orcid.org/0000-0001-6283-6581>

Venkat K. Rao  <https://orcid.org/0009-0007-3377-7405>

References

- Herman A, Flores JL, O'Neill KR. UCLA Other Recent Work Title How Many Adults and Youth Identify as Transgender in the United States? Publication Date Data Availability. Accessed November 6, 2023. <https://escholarship.org/uc/item/4xs990ws>
- Dhejne C, Van Vlerken R, Heylens G, Arcelus J. Mental health and gender dysphoria: a review of the literature. *Int Rev Psychiatry*. 2016;28(1):44-57.
- Agarwal CA, Scheefer MF, Wright LN, Walzer NK, Rivera A. Quality of life improvement after chest wall masculinization in female-to-male transgender patients: a prospective study using the BREAST-Q and body uneasiness test. *J Plast Reconstr Aesthet Surg*. 2018;71(5):651-657.
- Olson-Kennedy J, Warus J, Okonta V, Belzer M, Clark LF. Chest reconstruction and chest dysphoria in transmasculine minors and young adults: comparisons of nonsurgical and postsurgical cohorts. *JAMA Pediatr*. 2018;172(5):431-436.
- Chaya BF, Berman ZP, Boczar D, et al. Gender affirmation surgery on the rise: analysis of trends and outcomes. *LGBT Health*. 2022;9(8):582-588.
- Wright JD, Chen L, Suzuki Y, Matsuo K, Hershman DL. National estimates of gender-affirming surgery in the US. *JAMA Netw Open*. 2023;6(8):e2330348-e2330348.
- Cuccolo NG, Kang CO, Boskey ER, et al. Masculinizing chest reconstruction in transgender and nonbinary individuals: an analysis of epidemiology, surgical technique, and postoperative outcomes. *Aesthetic Plast Surg*. 2019;43(6):1575-1585.
- Bluebond-Langner R, Berli JU, Sabino J, Chopra K, Singh D, Fischer B. Top surgery in transgender men: how far can you push the envelope? *Plast Reconstr Surg*. 2017;139(4):873e-882e.
- Wilson SC, Morrison SD, Anzai L, et al. Masculinizing top surgery: a systematic review of techniques and outcomes. *Ann Plast Surg*. 2018;80(6):679-683.
- McEvenue G, Xu FZ, Cai R, McLean H. Female-to-male gender affirming top surgery: a single surgeon's 15-year retrospective review and treatment algorithm. *Aesthet Surg J*. 2018;38(1):49-57.
- Cuccolo NG, Kang CO, Boskey ER, et al. Mastectomy in transgender and cisgender patients: a comparative analysis of epidemiology and postoperative outcomes. *Plast Reconstr Surg Glob Open*. 2019;7(6):E2316.
- Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371(9627):1839-1847.
- Wu SS, Raymer CA, Kaufman BR, Isakov R, Ferrando CA. The effect of preoperative gender-affirming hormone therapy use on perioperative adverse events in transmasculine individuals undergoing masculinizing chest surgery for gender affirmation. *Aesthet Surg J*. 2022;42(9):1009-1016.
- Bustos SS, Kuruoglu D, Yan M, et al. Nipple-areola complex reconstruction in transgender patients undergoing mastectomy with free nipple grafts: a systematic review of techniques and outcomes. *Ann Transl Med*. 2021;9(7):612-612.
- Liu N, Krassioukov AV. Postpartum hypogalactia in a woman with Brown-Séquard-plus syndrome: a case report. *Spinal Cord*. 2013;51(10):794-796.
- Huang CC, Sandroni P, Sletten DM, Weigand SD, Low PA. Effect of age on adrenergic and vagal baroreflex sensitivity in normal subjects. *Muscle Nerve*. 2007;36(5):637-642.
- Goyal P, Maurer MS. Syncope in older adults. *J Geriatr Cardiol*. 2016;13(5):380.
- Mueller SC. Mental health treatment utilization in transgender persons: what we know and what we don't know. *Am J Psychiatry*. 2020;177(8):657-658.
- Licht CMM, De Geus EJC, Van Dyck R, Penninx BWJH. Longitudinal evidence for unfavorable effects of antidepressants on heart rate variability. *Biol Psychiatry*. 2010;68(9):861-868.
- Huysse FJ, Touw DJ, Van Schijndel RS, De Lange JJ, Slaets JPI. Psychotropic drugs and the perioperative period: a proposal for a guideline in elective surgery. *Psychosomatics*. 2006;47(1):8-22.
- Leech MM, Herrick MD, Parnell KE, Rosenkranz KM. Dysautonomia following breast surgery: disproportionate response to postoperative hematoma. *Surg Open Sci*. 2022;10:7-11.
- Gutt CN, Oniu T, Mehrabi A, et al. Circulatory and respiratory complications of carbon dioxide insufflation. *Dig Surg*. 2004;21(2):95-105.
- Atkinson TM, Giraud GD, Togioka BM, Jones DB, Cigarroa JE. Cardiovascular and ventilatory consequences of laparoscopic surgery. *Circulation*. 2017;135(7):700-710.
- Fan KL, Tilt A, Abbate OA, Masden DL. Vagal stimulation as result of pleural stretch secondary to retraction during internal mammary anastomosis. *Plast Reconstr Surg Glob Open*. 2018;6(9):1-2.
- Schusterman A, Schusterman M. Asystole in young athletic women during breast augmentation: a report of three cases. *Aesthetic Plast Surg*. 2012;36(5):1160-1163.
- Vingan NR, Teitelbaum S, Moorman R, Kenkel JM. Asystolic cardiac arrest associated with unstable bradycardia during augmentation mammoplasty: a case report. *Aesthet Surg J Open Forum*. 2022;4.
- Karthik A, Narayanan A, Vasudevan A. Sudden bradycardia during saline wash of the chest wall in a patient undergoing modified radical mastectomy – a case study. *Indian J Anaesth*. 2023;67(9):837-838.
- Moravek MB. *Gender-Affirming Hormone Therapy for Transgender Men.*; 2018. <http://journals.lww.com/clinicalobgyn>
- Gulanski BI, Flannery CA, Peter PR, Leone CA, Stachenfeld NS. Compromised endothelial function in transgender men taking testosterone. *Clin Endocrinol (Oxf)*. 2020;92(2):138-144.

30. Sabaté S, Mases A, Guilera N, et al. Incidence and predictors of major perioperative adverse cardiac and cerebrovascular events in non-cardiac surgery. *BJA: British Journal of Anaesthesia*. 2011;107(6):879-890.
31. Cheung CC, Martyn A, Campbell N, et al. Predictors of intraoperative hypotension and bradycardia. *Am J Med*. 2015;128(5):532-538.
32. Solomon SC, Saxena RC, Neradilek MB, et al. Forecasting a crisis: machine-learning models predict occurrence of intraoperative bradycardia associated with hypotension. *Anesth Analg*. 2020;130(5):1201-1210.
33. Wesselink EM, Kappen TH, Torn HM, Slooter AJC, van Klei WA. Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. *Br J Anaesth*. 2018;121(4):706-721.
34. Wijnberge M, Schenk J, Bulle E, et al. Association of intraoperative hypotension with postoperative morbidity and mortality: systematic review and meta-analysis. *BJS Open*. 2021;5(1):1-8.