

## BACKGROUND

- People who are transgender and gender diverse (TGD) have gender identities and expressions that do not align with societal stereotypes for sex assigned at birth. Modern medical care provides TGD people a variety of gender-affirming therapies, if desired, including surgical procedures aimed at realigning physical attributes with the identified gender. There are substantial knowledge gaps on the anesthetic management of patients undergoing these procedures, in particular optimal management of post operative nausea and vomiting (PONV).
- Female sex is a well-known risk factor for PONV, as is age, with risk changing at the third year of life. The risk of PONV in female patients increases postpubescence and decreases after menopause. These observations suggest that female sex hormones affect PONV risk.
- Gender-affirming hormone therapy (GAHT) may be used in TGD patients seeking gender-affirming care, with TGD patients assigned male at birth (AMAB) taking anti-androgen medications, estrogen and occasionally progesterone hormones, while TGD patients assigned female at birth (AFAB) taking testosterone. There is a paucity of evidence in the medical literature to determine if GAHT changes the risk of PONV for TGD surgical patients compared to cisgender patients.

## AIMS

To identify the rate of PONV in the TGD patient population compared to cisgender patients undergoing comparable procedures.

To compare the risk for PONV between TGD and cisgender patients undergoing comparable procedures based on age, procedure duration, and smoking status.

## TERMINOLOGY

- Cisgender: a person whose gender identity corresponds with the sex registered for them at birth.
- Transgender and gender diverse: a person whose gender identity is different from the sex they were assigned at birth.
- Gender identity: a person's internal knowledge of their gender.
- Gender expression: how a person presents their gender on the outside; behavior, clothing, hairstyle.
- Sex: assigned at birth based on the appearance of genitals a person is born with.
- Nonbinary/ genderqueer: a person who does not identify as a man or a woman, pronouns are they/ them.
- Gender-affirming hormone therapy: therapy aimed at assisting TGD people align their bodies with gender identity.

## METHODS

- This retrospective chart review was approved by the Institutional Review Board.
- We identified TGD patients from 2018–2023 who underwent surgical procedures at our quaternary academic medical center.
- TGD patients who underwent facial feminization, genitourinary or chest procedures were matched to cisgender patients and this data was collected.
- PONV was identified by the administration of rescue antiemetics in the post anesthesia care unit (PACU).
- Rates of PONV were analyzed for TGD-AMAB and TGD-AFAB patients with their controls. The analyses were performed using generalized estimating equations with a logit link and robust “sandwich” covariance estimates.
- The risk of PONV among groups was summarized with the point estimate and 95% confidence interval for the odds ratio. Both univariable analyses and multivariable analyses were performed with covariates included for variables with an absolute standardized difference > 0.1. Due to the small number of events, a covariate-adjusted analysis was not performed when comparing TGD-AFAB vs cis-male patients.

## RESULTS

### Patient and procedural characteristics for patients undergoing gender-affirming surgery and matched cisgender controls.

	AMAB-TGD patients and their cisgender controls				
	Cisgender controls		TGD-AMAB (N=397*)	Std-Diff Cis-female**	Std-Diff Cis-male**
	Cis-female (N=386)	Cis-male (N=319)			
Age, years	37 (29, 51)	36 (29, 51)	36 (29, 51)	0.017	0.005
Body mass index, kg/m <sup>2</sup>	27.0 (23.0, 32.7)	28.1 (24.5, 32.3)	27.6 (23.7, 32.1)	0.087	0.211
Current smoker	5 (1%)	5 (2%)	5 (1%)	0.002	0.002
Surgery Type					
Chest procedures	71 (18%)	—	71 (18%)	0.013	
Facial feminization surgery†	26 (7%)	25 (8%)	31 (8%)	0.041	0.059
Genital urinary procedures	289 (75%)	294 (92%)	295 (74%)	0.013	0.059
Surgery duration, hours	2.5 (1.0, 4.1)	2.9 (0.9, 4.8)	2.6 (0.9, 4.3)	0.065	0.049
Number of antiemetics					
≤ 2	152 (39%)	211 (66%)	225 (57%)	0.352	0.150
≥ 3	234 (61%)	108 (34%)	172 (43%)	0.352	0.150
Gabapentinoids	39 (10%)	13 (4%)	39 (10%)	0.009	0.266
Midazolam	69 (18%)	72 (23%)	92 (23%)	0.131	0.046
Volatile anesthetic	316 (82%)	292 (92%)	362 (91%)	0.275	0.065
Opioid dose, IVME mg	20.0 (12.5, 30.0)	22.0 (12.5, 32.5)	25.0 (15.0, 32.5)	0.189	0.200
Intravenous fluids, ml	1116 (787, 2000)	1700 (900, 2900)	1200 (756, 1845)	0.092	0.421
	AFAB-TGD patients and their cisgender controls				
	Cisgender controls		TGD-AFAB (N=194†)	Std-Diff Cis-female**	Std-Diff Cis-male**
	Cis-female (N=194)	Cis-male (N=68)			
Age, years	23 (21, 29)	23 (20, 26)	23 (20, 29)	0.037	0.091
Body mass index, kg/m <sup>2</sup>	27.3 (23.6, 33.1)	25.6 (22.3, 29.9)	27.9 (23.4, 33.5)	0.014	0.167
Smoker	4 (2%)	2 (3%)	4 (2%)	0.000	0.003
Surgery Type					
Chest procedures	125 (64%)	—	125 (64%)	0.000	
Genital urinary procedures	69 (36%)	68 (100%)	69 (36%)	0.000	0.000
Surgery duration, hours	2.3 (1.5, 3.0)	1.5 (0.5, 2.5)	2.2 (1.7, 3.0)	0.008	0.067
Number of antiemetics					
≤ 2	78 (40%)	57 (84%)	94 (48%)	0.167	0.625
≥ 3	116 (60%)	11 (16%)	100 (52%)	0.167	0.625
Gabapentinoids	5 (3%)	2 (3%)	12 (6%)	0.177	0.294
Midazolam	34 (18%)	14 (21%)	32 (16%)	0.027	0.120
Volatile anesthetic	142 (73%)	63 (93%)	158 (81%)	0.198	0.230
Opioid dose, IVME mg	20.0 (15.0, 25.0)	15.0 (10.0, 25.0)	24.5 (15.0, 29.5)	0.171	0.157
Intravenous fluids, ml	1000 (791, 1400)	912 (500, 1500)	1012 (800, 1476)	0.098	0.021

Abbreviations: IVME = intravenous morphine equivalents.

\*393/397 (99%) were on GAHT at time of surgery.

†Patients undergoing facial feminization procedures were matched with controls undergoing LeForte I osteotomy surgical procedures.

‡138/194 (71%) were on GAHT at time of surgery.

\*\*The absolute value of the standardized difference between transgender and matched cisgender control groups is presented.

### Postoperative nausea and vomiting outcomes for patients undergoing gender-affirming surgery and matched cisgender controls.

Procedure	AMAB-TGD patients and their cisgender controls				
	Cis-female		Cis-male		TGD-AMAB
	N	# (%)	N	# (%)	N # (%)
Chest procedures	71	4 (6%)	71	2 (8%)	71 8 (11%)
Facial feminization surgery*	26	5 (19%)	25	2 (8%)	31 3 (10%)
Genital urinary procedures	289	42 (15%)	294	38 (13%)	295 50 (17%)

  

Procedure	AFAB-TGD patients and their cisgender controls				
	Cis-female		Cis-male		TGD-AFAB
	N	# (%)	N	# (%)	N # (%)
Chest procedures	125	14 (11%)	125	7 (10%)	125 15 (12%)
Genital urinary procedures	69	9 (13%)	68	7 (10%)	69 9 (13%)

\*Patients undergoing facial feminization procedures were matched with controls undergoing Le Forte I osteotomy surgical procedures

### Risk of postoperative nausea and vomiting between patients undergoing gender-affirming surgery and matched cisgender controls.

	TGD-AMAB vs Cis-female		TGD-AMAB vs Cis-male	
	OR (95% CI)	p-value	OR (95% CI)	p-value
No covariates	1.19 (0.79, 1.81)	0.407	1.05 (0.56, 1.96)	0.879
Covariate adjusted	1.10 (0.72, 1.70)	0.648	1.09 (0.84, 2.20)	0.219

  

	TGD-AFAB vs Cis-female		TGD-AFAB vs Cis-male	
	OR (95% CI)	p-value	OR (95% CI)	p-value
No covariates	1.05 (0.56, 1.96)	0.879	1.31 (0.43, 4.00)	0.638
Covariate adjusted	0.89 (0.47, 1.69)	0.718		

Due to the small number of events, a covariate adjusted analysis was not performed when comparing transgender – born female vs cis-male patients.

## RESULTS

1:1 matching was not achieved in every category. There were 397 TGD-AMAB patients identified, they were matched to 386 cis-females and 319 cis-males. Cis-males were not identified in the chest procedure category.

Rates of PONV were similar among TGD AMAB and TGD AFAB when compared to the matched cisgender controls.

Patient and perioperative characteristics were analyzed via standardized mean difference (Std-Diff). This data showed some imbalances. It highlighted that ≥ 3 prophylactic antiemetics were administered more to cisgender females and TGD AFAB.

Both the unadjusted and adjusted analyses did not find evidence that PONV risk differed between cisgender and TGD patients (P>0.41 for all unadjusted and P>0.22 for all adjusted comparisons).

There was an insufficient number of PONV events among cis-male controls for TGD AMAB patients to conduct an adjusted analysis.

Of the TGD AMAB, 29 (7.3%) held their estrogen medications for more than a week before surgery; 1 (0.2%) held their progesterone medications for more than a week before surgery; 2 (0.5%) held their androgen blockers for more than a week before surgery.

Of the TGD AFAB, 2 (1.0%) held their testosterone for more than a week before surgery.

## DISCUSSION

- The area postrema has an incomplete blood-brain barrier which can detect emetogenic agents in both the blood and cerebral spinal fluid and in response initiates a vomiting reflex. The neurons in this area are rich in androgen and estrogen receptors. The area postrema in females compared to males has greater numbers of neurons with estrogen receptors. However, manipulation of female sex hormones in adult female rats does not affect the number of these receptors. These receptors may not be influenced by exogenous hormone therapies in humans either. This could explain why GAHT does not affect rates of PONV in the TGD population.
- Limitations of this study include the use of indirect measures of the incidence of PONV, 1:1 and exact surgical type matching was not possible for all study participants, and GAHT was held in some but not all TGD patients before surgery. In addition, PONV/motion sickness history is a significant risk factor not used in comparison. A prospective randomized control study where data collection of PONV incidence is directly recorded and variables such as prophylactic antiemetic administration, PONV/motion sickness history, and GAHT are factored into the selection process may provide more conclusive evidence.

## CONCLUSIONS

Among TGD patients undergoing gender-affirming surgical procedures, we did not find evidence that risk for PONV differed among cisgender controls undergoing comparable procedures.

This study's results imply that anesthesia providers should consider the sex assigned at birth when evaluating risk factors for PONV.

## ABSTRACT AND REFERENCES

