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Association of current Estradiol use with carotid intimal media thickness among transgender women: a cross-sectional study.

Rodrigo de Carvalho Moreira, MD, MsC, PhD

Evandro Chagas National Institute of Infectious Diseases,
Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil

Background

-> Epidemiologic studies suggest that transgender population has higher burden of cardiovascular (CV) risk factors and CV disease

Individual CV risk factors:
HIV infection (Aschhmean,2011)
Smoking
Hormone use
Injection of liquid silicon and inflammation (ÁLVAREZ, 2016)
Sex-reassignment surgery (CICCONE et al., 2017)

-> It is uncertain whether the use of feminizing hormone such as estradiol (E2) or ethinylestradiol (EE) affects CV risk.

Objectives

- Assess CV risk and investigate the relationship between current use of E2, EE or both and carotid intima-media thickness (cIMT) in transgender women (transwomen).

Study population

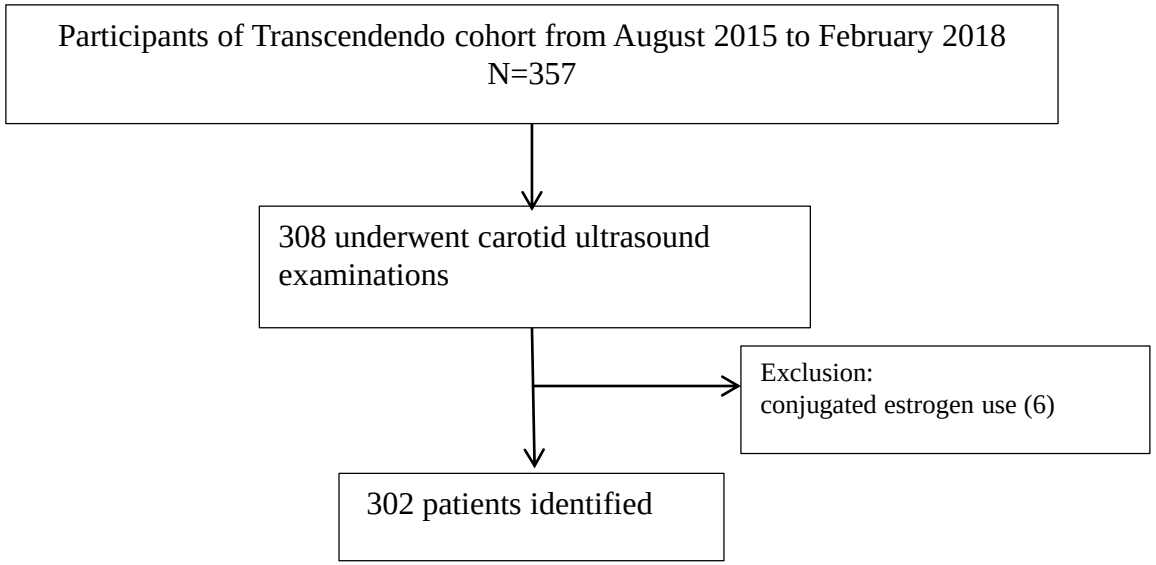
Study participants of Transcendendo cohort:

(1) Transcender, a respondent-driven sampling (RDS) study conducted at Fiocruz, (Grinsztejn B, et all 2017)
(2) transwomen who reached the site seeking for HIV prevention or care, HIV and other sexual transmitted infection testing or participation in other studies
(3) from the Fiocruz HIV Clinical Cohort

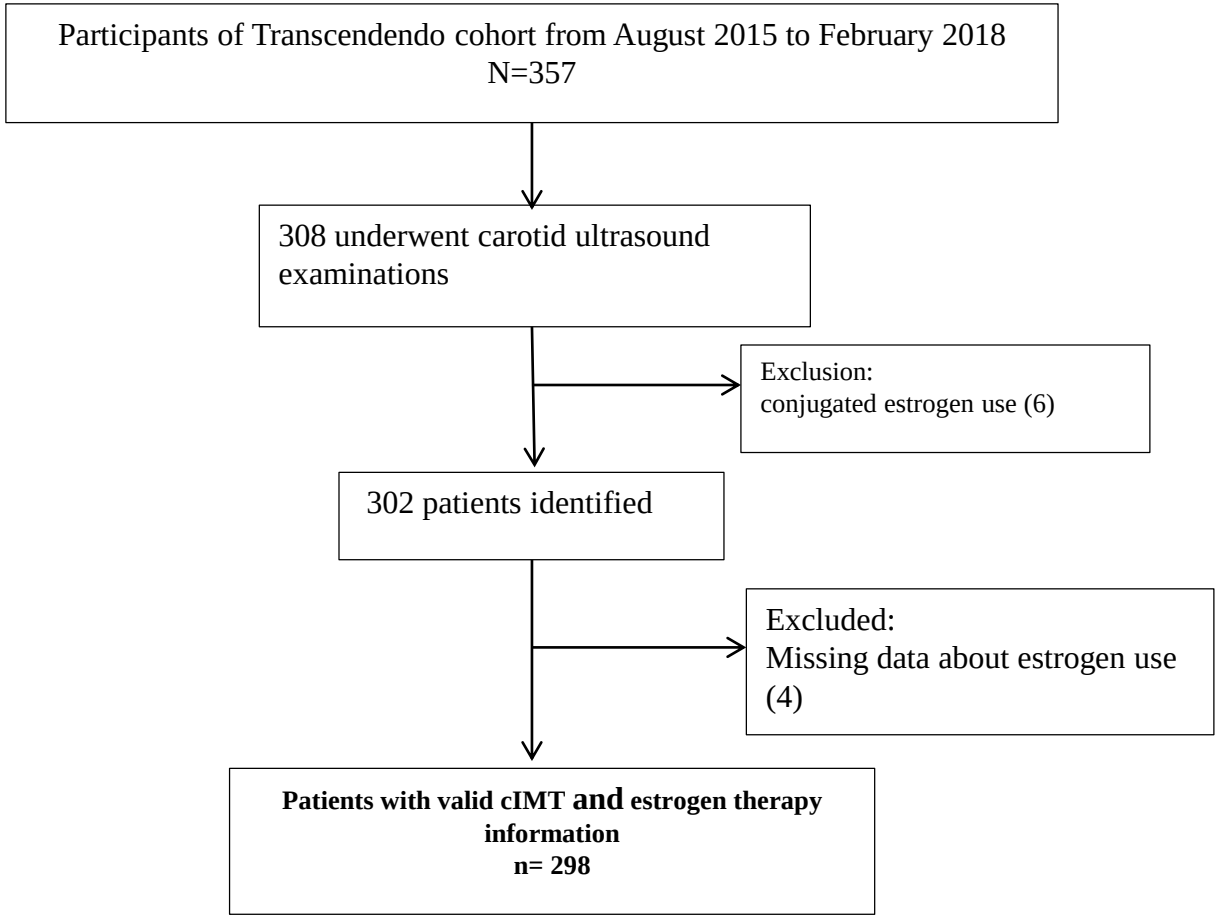
Study population : Patient Identification Flowchart

Participants of Transcendendo cohort from August 2015 to February 2018
N=357

Study population : Patient Identification Flowchart



Study population : Patient Identification Flowchart



Methods

Main outcome: Carotid artery intima-media thickness (cIMT), measured with a linear transducer (10-MHz linear transducer, VIVID 7, GE) and calculated automatically by Medical Imaging Applications software (MIA, Coralville, Iowa) following the Mannheim consensus.

Main predictor: Hormonal therapy, we computed currently (30 days) reported hormonal medication use and classified them as “etinilestradiol”, “estradiol” or “both”

Methods

"Ethinylestradiol"-Use of ethinylestradiol excluding those which also used estradiol plus progestogen injectable or estradiol plus progestogen oral or estradiol oral isolated or estradiol transdermal

"Estradiol"- estradiol plus progestogen injectable or estradiol plus oral progestogen or oral estradiol isolated or transdermal estradiol excluding those also using ethinylestradiol

"Mixed" – estradiol plus progestogen injectable or estradiol plus oral progestagen or oral estradiol isolated or transdermal estradiol plus ethinylestradiol

Methods

Descriptive characteristics of participants are given as absolute counts, percentages, medians and interquartile ranges and compared according to 75th percentile cut-off on cIMT.

To assess CV risk, ASCVD and Framingham scores were calculated.

We used multiple logistic regression models to investigate the relationship between current hormone use and cIMT adjusting for demographic, clinical, laboratory variables. The best model was chosen automatically by a genetic algorithm based on the AIC.

Results

Hormone use

	Above 75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
Age median (IQR)	29 (24,36)	38 (31,50.5)	31 (25,38)	<0.001
Current use of hormones				0.0046
None	119 (54.84)	55 (77.46)	174 (60.42)	
Estradiol	60 (27.65)	13 (18.31)	73 (25.35)	
Ethinylestradiol	13 (5.99)	1 (1.41)	14 (4.86)	
Both	25 (11.52)	2 (2.82)	27 (9.38)	
Hormones: route of administration				0.0061
Intramuscular	74 (32.89)	13 (17.81)	87 (29.19)	0.0138
Oral	71 (31.56)	12 (16.44)	83 (27.85)	0.0123
Transdermal	24 (10.67)	9 (12.33)	33 (11.07)	0.6942

Results

- Clinical characteristics

	Above 75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
Race				0.8912
White	58 (26.01)	17 (23.61)	75 (25.42)	
Black	51 (22.87)	16 (22.22)	67 (22.71)	
Brown/mixed	114 (51.12)	39 (54.17)	153 (51.86)	
Hypertension	29 (13)	24 (33.33)	53 (17.97)	<0.001
Dislipidemia	31 (14.03)	16 (22.22)	47 (16.04)	0.0998
Smoking				0.2359
Current	106 (47.53)	30 (41.67)	136 (46.1)	
Former	26 (11.66)	14 (19.44)	40 (13.56)	
Never	91 (40.81)	28 (38.89)	119 (40.34)	
Diabetes	2 (0.9)	5 (6.94)	7 (2.37)	0.0107

Results

Clinical and laboratory characteristics

	Above 75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
Creatinine median (IQR)	0.86 (0.76,0.96)	0.91 (0.8,1.02)	0.87 (0.76,0.97)	0.0339
Glucose median (IQR)	88 (79,96)	95 (85,102)	89 (79,98)	0.0105
CRP median (IQR)	0.2 (0.1,0.6)	0.3 (0.15,0.85)	0.2 (0.1,0.6)	0.3994
Total cholesterol median (IQR)	159 (137,180)	173.5 (149.75,192.5)	162 (141,182)	0.0037
HDL median (IQR)	41 (34,50)	40.5 (31.75,48)	41 (34,50)	0.3691
Systolic BP median (IQR)	110 (100,120)	120 (110,125)	110 (100,120)	< 0.001
Diastolic BP median (IQR)	70 (65,80)	80 (70,85)	75 (65,80)	< 0.001

Results

	Above 75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
Waist median (IQR)	81 (76,89)	89 (83,96)	83 (77,91)	< 0.001
BMI median (IQR)	24.04 (21.46,26.66)	26.7 (23.6,28.93)	24.45 (21.6,27.65)	< 0.001
Physical or sexual violence	141 (63.23)	48 (66.67)	189 (64.07)	0.5971
Hormones ever	212 (95.5)	66 (91.67)	278 (94.56)	0.2343

Results

Clinical characteristics

	Above 75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
History of cardiovascular disease	8 (3.59)	7 (9.72)	15 (5.08)	0.0592
Familiar history of cardiovascular disease	38 (17.04)	19 (26.39)	57 (19.32)	0.0807
Plastic surgery	69 (30.94)	20 (27.78)	89 (30.17)	0.6111
Industrial silicone	101 (45.29)	46 (63.89)	147 (49.83)	0.0061
HIV infection	117 (52.47)	43 (59.72)	160 (54.24)	0.2826

Results

Transgender characteristics

	75th percentile cIMT			
	No	Yes	Total	P value
Total	225	73	298	
Age at hormone initiation median (IQR)	17 (15,20)	17 (15,20.75)	17 (15,20)	0.8675
Medical guided hormones				0.4338
Never	169 (75.78)	53 (73.61)	222 (75.25)	
Age at perception median (IQR)	9 (7,12)	8 (7,11)	9 (7,12)	0.5244
Age at transformation median (IQR)	16 (14,19)	16 (13,18)	16 (14,18)	0.3865
Gender related surgery*	97 (43.5)	29 (40.28)	126 (42.71)	0.6185

* mammoplasty, orchiectomy, facial surgery, vaginoplasty among others.

Results

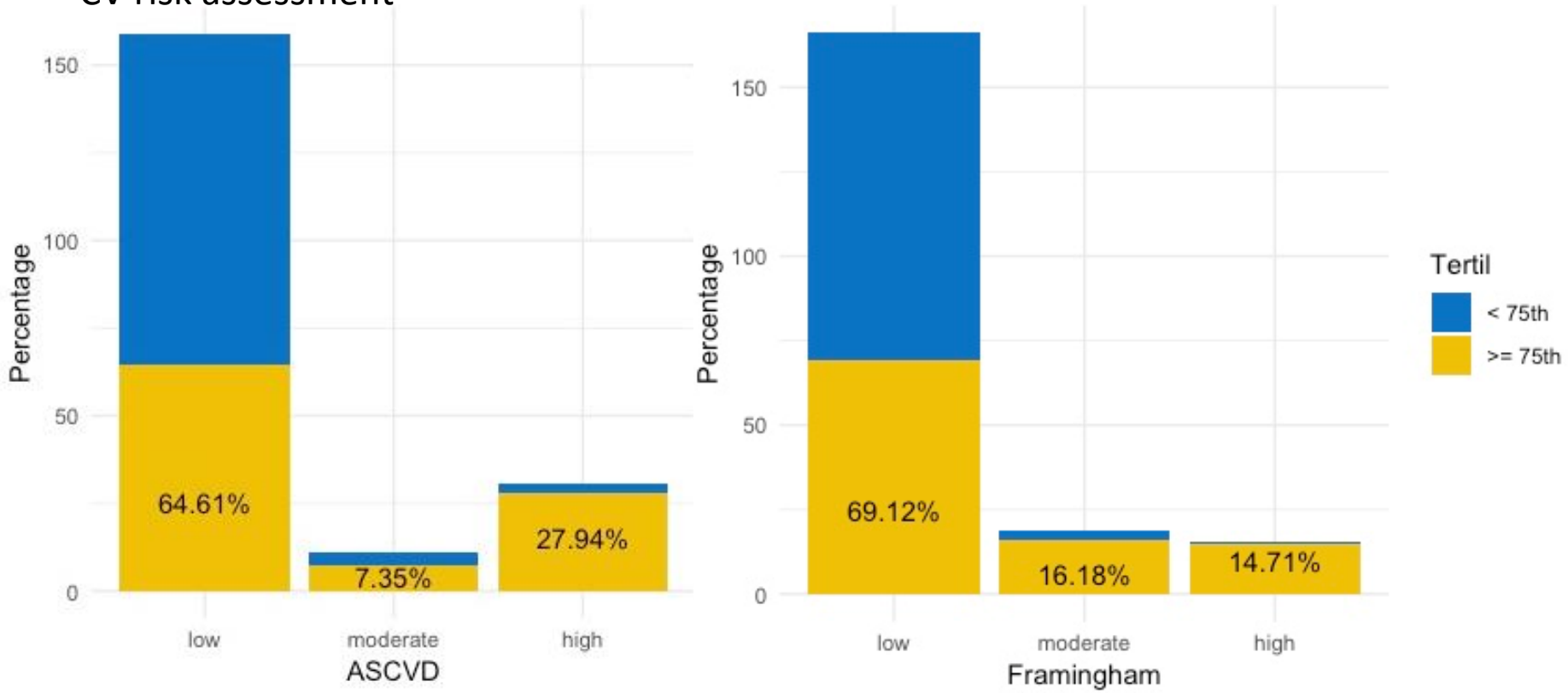
CV risk assessment

	Above 75th percentile cIMT			
	No	Yes		p-value
Framingham 10 years				<0.001
High	1 (0.5)	10 (14.71)	11 (4.1)	
Moderate	5 (2.5)	11 (16.18)	16 (5.97)	
Low	194 (97)	47 (69.12)	241 (89.93)	
ASCVD* 10 years				<0.001
High	5 (2.5)	19 (27.94)	24 (8.96)	
Moderate	7 (3.5)	5 (7.35)	12 (4.48)	
Low	188 (94)	44 (64.71)	232 (86.57)	

*Atherosclerotic cardiovascular disease risk score

Results

CV risk assessment



Results

Final logistic regression model with predictors of cIMT

Variables	OR (95%CI)	p-value
Physical activity	0.13 (0.01-0.66	0.0239
Familiar history	9.81 (2.60-45.16)	0,0015
Race		
Black	0.41(0.05-2.64)	0,3507
Brown	2.49(0.55-13.07)	0,2513
Any drug at 12 months	0.12(0.02-0.47)	0,0053
Dislipidemia	0.13(0.02-0.66)	0,0209
Smoking		
Former	4.07(0.74-25.82)	0,1164
Current	8.97(1.74-58.99)	0,0138
Current use of Hormones		
Estradiol	0.10(0.02-0.42)	0,0031
Ethinylestradiol	2.73(0.10-33.74)	0,4607
Mixed	0.29(0.04-1.62)	0,1804

Compared with transwomen with no current use of hormones, current use of E2 was associated with 90% less odds of increased cIMT.

Variables	OR (95%CI)	p-value
Age at hormone start	0.96(0.88-1.04)	0,3371
Age	1.13(1.06-1.22)	>0.001
Income	1.00(0.99-1.00	0,469
Age at perception	1,24(1.07-1.46)	0,0045
Onset of sex	0,91(0.82-0.99)	0,0546
Glucose	1,02(1.00-1.04)	0,0471
PCR	1,20(0.91-1.54)	0,1219
Systolic pressure	1,23(1.12-1.39)	>0.001
Diastolic pressure	0,80(0.69-0.90	0,0014
Waist	1,17(1.03-1.33)	0,0124
BMI	0,77(0.57-1.00	0,0588

Results

Conclusion

- A negative association between cIMT and current estradiol use was found in transgender women.
- The ASCVD equation identified more participants as high risk among those with increased cIMT.
- While conflicting results exist about estrogen replacement therapy in women, these data suggest cardioprotective effects of estradiol use without medical supervision in younger transwomen.
- Follow up studies are needed to confirm its safety and it might be reinforced as a choice of hormone therapy for transwomen.

Results

Thank you

rodrigo.moreira@ini.fiocruz.br