




Stroke in Male-to-Female Transgenders: A Systematic Review and Meta-Analysis

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ABSTRACT: Background: The effect of hormonal therapy has been extensively studied in women. However, similar data on male-to-female (MTF) transgenders, another important population that receives hormonal therapy is lacking. Existing studies in MTF transgenders are skewed toward mental health and health-harming behaviors while few have focused on chronic health conditions. Our study aims to review the existing data on stroke in MTF transgenders and perform a quantitative analysis on the frequency of this condition in this special population. **Methods:** PubMed, Cochrane, Scopus, Embase, ClinicalTrials.gov, and Web of Science were systematically searched for studies that reported data on the occurrence of cerebrovascular diseases in MTF transgenders. We reported the hormonal regimens, clinical characteristics, and outcomes of stroke in MTF transgenders. A meta-analysis of proportions was performed by the random-effects model to compute for the frequency of cerebrovascular events in MTF transgenders. **Results:** Fourteen studies were included in the qualitative analysis while five studies were included in the quantitative analysis. A total of 109 MTF transgenders (Mean 14; range 1–53) suffered a cerebrovascular event. Random-effect modeling analysis showed an overall estimated frequency of 2% for cerebrovascular events in transgenders with a moderate degree of heterogeneity ($I^2 = 62\%$). **Conclusion:** Hormonal therapy in MTF transgenders may confer cardiovascular risks in this population. However, more population-based studies that include clinical characteristics and outcomes of chronic health diseases in MTF transgenders are warranted. Such studies may be crucial in directing future guidelines on the health care and management of MTF transgenders.

RÉSUMÉ : La fréquence des accidents vasculaires cérébraux chez les femmes transgenres : revue systématique et méta-analyse. **Contexte :** Les effets de l'hormonothérapie ont fait l'objet de nombreuses études chez les femmes. Toutefois, il en va autrement des effets de l'hormonothérapie chez les femmes transgenres, c'est-à-dire déclarées de sexe masculin à la naissance, qui forment une autre tranche importante de la population soumise à ce type de traitement. Les études actuelles sur les femmes transgenres sont principalement orientées vers la santé mentale et les comportements préjudiciables à la santé, mais peu portent particulièrement sur les maladies chroniques. L'étude ici présentée visait donc à examiner les données actuelles sur la survenue des accidents vasculaires cérébraux (AVC) chez les femmes transgenres, et à réaliser une analyse quantitative de la fréquence de ce type d'affection dans cette tranche de la population. **Méthode :** Une recherche systématique a été entreprise dans les bases de données PubMed, Cochrane, Scopus, Embase, ClinicalTrials.gov et Web of Science sur des études faisant état de données sur la fréquence des affections vasculaires cérébrales chez les femmes transgenres. Ont par la suite été consignés les schémas posologiques des traitements hormonaux, les caractéristiques cliniques et les résultats cliniques des AVC chez les femmes transgenres. L'équipe a enfin procédé à une méta-analyse des proportions à l'aide d'un modèle à effets aléatoires afin de calculer la fréquence des événements vasculaires cérébraux chez les femmes transgenres. **Résultats :** Ont été incluses 14 études dans l'analyse qualitative et 5 dans l'analyse quantitative. Au total, 109 femmes transgenres (moyenne : 14; plage : 1-153) ont subi un événement vasculaire cérébral. Ainsi, d'après l'analyse du modèle à effets aléatoires, la fréquence générale des événements vasculaires cérébraux chez les personnes transgenres a été estimée à 2 %, et le degré d'hétérogénéité s'est révélé moyen ($I^2 = 62\%$). **Conclusion :** L'hormonothérapie chez les femmes transgenres peut accroître les risques d'événements cardiovasculaires dans ce groupe particulier de personnes. Toutefois, il faudrait mener d'autres études fondées sur cette population, qui tiennent compte des caractéristiques cliniques et des résultats cliniques des maladies chroniques chez les femmes transgenres. En effet, les résultats pourraient s'avérer d'une importance cruciale dans l'élaboration de lignes directrices sur les soins de santé à donner aux femmes transgenres et sur la prise en charge des affections vasculaires cérébrales.

Keywords: Stroke, Hormonal therapy, Sex steroids, Transwomen, Transgenders

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INTRODUCTION

The term transgender is ascribed to individuals who transcend culturally defined categories of gender. Their gender identity,

expression, or behavior are not congruent with their natal sex.^{1,2} This is in contrast to cisgenders whose gender identity aligns with their sex assigned at birth.³ Male-to-female (MTF) transgenders

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or transwomen are those whose sex was assigned male, but who identify as female.¹ Recent estimates for MTF transgenders are at 6.8 in 100,000 individuals.⁴

Despite increasing gains in rights, there remain enormous gaps in addressing the health needs of transgender individuals.^{2,5} They suffer from stigma and high rates of depression, anxiety, and HIV infection.⁶ Though there have been more studies on the transgender population in recent years, the majority of health research for transgenders has focused on mental health, cross-sex hormone therapy, health-harming behaviors, and HIV/AIDS. Data on chronic health conditions including cerebrovascular diseases is scant.³ There is also a dearth of data and guidelines on the appropriate medical care for transgender patients.²

Though multiple studies have established the adverse outcomes of hormonal therapy in ciswomen, crucial differences in clinical characteristics exist between ciswomen and transwomen. It is, therefore, not apt to extrapolate these findings to transgender individuals.² Research into the epidemiology and characterization of cerebrovascular diseases in this special population is warranted.

Our study aims to systematically review and report on existing data on stroke in MTF transgenders. Where possible, we hope to describe the clinical characteristics, hormone regimen exposures, and outcomes of MTF transgenders who suffered from stroke.

METHODOLOGY

Standard Protocol Approvals, Registrations, and Patient Consents

We performed this meta-analysis in concurrence with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) and Meta-Analyses of Observational Studies in Epidemiology (MOOSE).^{7,8} We registered the protocol of this review in PROSPERO (CRD42021224819).

Criteria for Selection of Studies

We considered cohort studies, case-control studies, case series, and case reports for this review. We included studies that reported information on the occurrence of stroke in transgender MTF. Exposure included hormonal therapy, i.e. estrogen with or without antiandrogens regardless of dosage. The development of stroke in MTF transgenders was considered to be the outcome of interest. There were no restrictions implemented in terms of age, sex, and ethnicity of the population. We included studies written in the English language.

Search Methods for the Identification of Studies and Selection of Studies

We performed a comprehensive systematic search of records in major scientific databases including MEDLINE by PubMed, CENTRAL by Cochrane, Scopus, Embase, ClinicalTrials.gov, Web of Science, and HERDIN from inception until November 2020. Search strategies (detailed in Appendix) were developed using Medical Subject Headings (MeSH) and text words related to transgender persons and sex steroids or hormone therapy. The outcome of interest included terms pertaining to stroke or cerebrovascular disease. To ensure literature saturation, hand searching of additional studies was done by going through the reference section

of included studies and relevant reviews. Personal contacts to authors who published articles were made to obtain further data.

Two investigators (KHDI and JDBD) searched independently to identify relevant articles using the search term strategies developed. After deduplication, the titles and abstracts of the remaining studies were assessed by two authors using predetermined screening criteria. Full-text articles of studies that fulfilled the screening criteria were retrieved and evaluated using predetermined eligibility criteria. Disagreements were solved with the contribution of a third reviewer (AIE) and via consensus. Finally, studies that satisfied the eligibility criteria were included in the quantitative analyses.

Methodological Quality Assessment of the Included Studies

We used the Newcastle–Ottawa Scale (NOS) to evaluate the quality of observational studies included in the review (see Supplementary Material).⁹ The risk of bias was independently assessed by two investigators (KHDI and JDBD) while disagreements were resolved with the contribution of two other reviewers (AIE and MCPF) and by consensus. For the present review, factors that would make a study have a low risk for bias included clearly defined selection criteria, representativeness of the sample of transgender patients, and appropriate ascertainment of outcomes.

We used the Murad tool to evaluate the risk of bias in noncomparative cohorts and case series/reports. We considered “poor,” “moderate,” or “good” quality when 3 or fewer, 4, or 5 of the criteria were fulfilled, respectively.¹⁰ Three investigators (KHDI, AIE, and JDBD) evaluated the methodological quality of the included studies; discrepancies were resolved by consensus and discussion with a fourth reviewer (MCPF).

Data Collection

Data from the included studies were extracted by two investigators (KHDI and JDBD) using standardized forms, which included the following information regarding the study: title, citation, setting, design and duration, the total population of patients in the study, the number of patients in the population of interest, comorbidities, hormonal regimens taken, clinical characteristics, and outcomes.

Statistical Analyses

To summarize data, we used frequencies and proportions for categorical variables while means (standard deviation) or medians (range) were used for continuous variables. We expressed the data in 95% confidence intervals. We considered the individual patient as the unit of analysis. We performed the meta-analysis of proportions by utilizing the following R (Version 3.6.3) packages: metafor, meta, and weightr. We included studies with > 5 included patients in the meta-analysis. The proportions were pooled by the random-effects model measured using the restricted maximum likelihood estimator. The data for computed proportions that fell in the range of < 0.20 or > 0.80 were converted using logit transformation. This was done to improve their statistical properties. We performed leave-one-out sensitivity analyses as well as a set of case deletion diagnostics based on linear regression analyses to assess the robustness of summary estimates on the effect of outliers. In addition, we constructed a Baujat plot to mark studies largely influencing the summary statistics. To evaluate the heterogeneity of pooled estimates, we employed

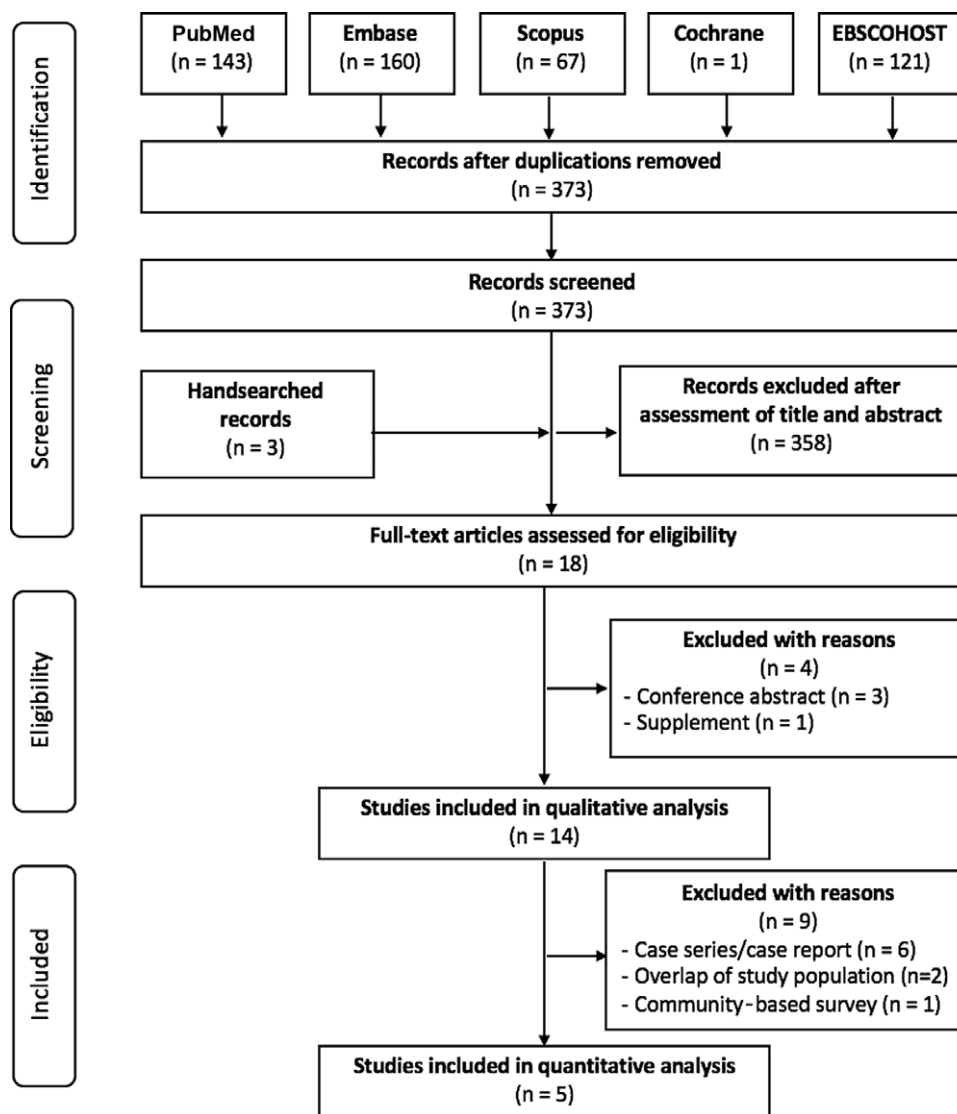


Figure 1: PRISMA flow diagram for study selection.

the chi-squared test (χ^2 ; p-value < 0.10 to detect significant heterogeneity) and I^2 tests with >25%, >50%, and >75% considered as low, moderate, or high degree of heterogeneity, respectively.

RESULTS

Included Studies

We identified a total of 492 studies from the electronic database search. No relevant studies were identified from Clinicaltrials.gov and from HERDIN. A total of 373 articles remained after excluding duplicates. After assessing the titles and abstracts, we excluded 358 due to non-relevance. The full texts of 18 articles were subjected to eligibility criteria. Fourteen studies were included in the qualitative analyses while 5 of these studies were included in the quantitative analyses (Figure 1). The studies by Asscheman et al. 1989 and 2011 were not included in the quantitative analysis due to an overlap with the population of van Kesteren et al. 1997 (same but expanded cohort).¹¹⁻¹³ Asscheman et al. 2011 was also excluded since they reported on stroke as a

cause of mortality instead of morbidity¹³. Nokoff et al. 2018 was excluded from the quantitative analysis since it was a community-based study where data were taken from self-reported surveys.¹⁴

Assessment of Risk of Bias

We appraised three comparative cohort studies using the NOS, which revealed Wierckx et al., 2013 and Getahun 2018 et al., 2018 to be of good quality while the study of Nokoff et al. 2019 was of poor quality. Evaluation of the remaining observational studies was performed using the Murad tool.¹⁰ Five studies were assessed to be of good quality while the rest were of moderate quality (see Supplementary Material).

Population, Exposure and Outcome Characteristics in the Included Studies

A total of 14 studies reported MTF transgenders who developed stroke. There were 8 retrospective cohort studies, 5 case reports, 1 cross-sectional survey, and 1 case series (Table 1).

Table 1: Table of included studies

First author (year)	Type of study	Study setting	Inclusive years
Asschemann 1989	Noncomparative cohort	Free University Hospital Amsterdam, the Netherlands	1972–1986 (14)
Van Kesteren 1997*	Noncomparative cohort	Free University Hospital Amsterdam, the Netherlands	1975–1994 (19)
Asschemann 2011	Noncomparative cohort	VU University Medical Center Amsterdam, the Netherlands	1975–2007 (32)
Wierckx 2013*	Comparative cohort	Ghent University Hospital, Belgium	1986–2012 (26)
Getahun 2018*	Comparative cohort	Kaiser permanente sites, USA	2006–2014 (8)
Nota 2019*	Noncomparative cohort	Gender clinic, Amsterdam	1972–2015 (43)
James 2020*	Noncomparative cohort	Outpatient clinics or hospitals in Minnesota, USA	1974–2015 (41)
Nokoff 2018	Cross-sectional survey	Noninstitutionalized adults in the USA	NA
LaHue 2019	Case series	San Francisco General Hospital, USA	2010–2017 (7)
deMarinis 1978	Case report	Johns Hopkins Hospital, Maryland, USA	NA
Biller 1995	Case report	Indiana University, USA	NA
Egan 2002	Case report	Oregon Stroke Center, USA	NA
Mullins 2008	Case report	Cork University Hospital, Ireland	NA
Kwan 2019	Case report	University of Toronto, Canada	NA

*Included in quantitative analysis.

Inclusive years of cohort studies ranged from 8 to 43 years (Mean 26 years).

Table 2 presents data on the MTF cohorts as a whole. Details regarding the age, hormonal therapy regimens, and baseline cardiovascular risk factors indicated therein refer to the entire MTF cohort of each study.^{11–18} The sizes of the MTF populations ranged from 49 to 2842 (Mean 1002) while the number of patients who suffered a cerebrovascular event ranged from 1 to 53 (Total 109, Mean 14). Only three studies reported types of stroke.^{11,12,16} Only a handful of studies were able to specify details regarding hormonal therapy and cardiovascular risk factors in these patients. MTF transgenders received varied preparations of estrogen either orally, transdermally, or via injection with or without antiandrogens. Only two cohort studies reported the duration of hormone therapy in the MTF cohort: 19.4 years \pm 7.7 in Asschemann et al., 2011 and 6.0 years (3–11 years) in Wierckx et al., 2013. Getahun et al. 2018 was the sole study that reported the average maximum daily dosage of estradiol in MTF transgenders who suffered from either VTE or ischemic stroke (4.1 mg; range 1–10mg).

Table 3 summarizes data from case series, case reports, and cohort studies that reported details regarding MTF individuals who suffered from stroke.^{2,13,15,19–23} Of the 23 patients reported, only 13 patients had data regarding stroke type.^{2,19–23} The majority of the strokes were ischemic in nature (10 out of 14) with varying locations. One patient suffered from concurrent ischemic stroke and subarachnoid hemorrhage.² Hormone use in these individuals was relatively high and ranged from 2 to 32 years. The patients were notably young with 19 individuals being under 60 years of age. Risk factors such as prior stroke, hypertension, diabetes, and smoking were identified in 16 patients, whereas 2 case reports reported no known risk factors in their patients.^{19,20}

Frequency of Cerebrovascular Events in MTF Transgenders

Institution-based cohort studies that reported the development of cerebrovascular events in MTF transgenders' ongoing hormonal therapy were included in the quantitative analysis. The term cerebrovascular events refer to any stroke type, i.e. transient ischemic attack, ischemic stroke, hemorrhagic stroke, or subarachnoid hemorrhage. Random-effect modeling analysis for the frequency of cerebrovascular events in MTF transgenders showed an overall estimate of 2% (Figure 2). The analysis detected a moderate degree of heterogeneity ($I^2 = 62\%$). This could be due to the heterogeneity of stroke types included in the meta-analysis. Subgroup analysis was not done since only five studies were included.

DISCUSSION

Random-effect modeling revealed an overall frequency of 2% for cerebrovascular events among MTF transgenders. However, epidemiological data on the incidence and clinical characteristics of cerebrovascular disorders in MTF transgenders is still lacking. Details, albeit limited, regarding the clinical characteristics of these patients were also reported in the present study. The majority were under 60 years of age. Hormonal therapy regimens varied and included estrogens with or without antiandrogens taken for a duration of 2–32 years. Ischemic stroke was the most commonly reported cerebrovascular event.

The Global Burden of Disease Lifetime Risk of Stroke Collaborators in 2016 reported a 24.5% global lifetime risk of stroke in 2016. The risk among men was 24.7% almost similar to the risk among women at 25.1%. Ischemic stroke risk was higher compared to hemorrhagic stroke risk.²⁴ Meanwhile, the risk of stroke for people aged 18–50 has been estimated at 10%–15%.²⁵

Table 2: Population characteristics of MTF transgenders identified in cohort studies

Author (year published)	Total MTF cohort (N)	MTF who suffered from stroke (n)	Type of stroke (n)	Age	Hormonal therapy regimens	Baseline data available on cardiovascular risk factors
Asscheman 1989	303	1	TIA (1)	Median 32 years (range 16–67 years)	- PO: Cyproterone acetate, ethinyl estradiol, diethylstilbestrol - IM: Estradiol-17-undecanoate	NR
vanKesteren 1997	816	6	TIA (5) ICH (1)	Mean 41 years (range 18–86 years)	- PO: Cyproterone acetate, ethinyl estradiol - Transdermal estradiol	NR
Asscheman 2011	966	5 (as cause of death)	NR	Mean 31.4 years \pm 11.4 years (range 16–76 years)	- PO: Conjugated estrogens, ethinyl estradiol, estradiol valerate - Estrogen injections - Transdermal estrogen - Antiandrogens: cyproterone acetate and spironolactone	Current smoking 38.6%
Wierckx 2013	214	5	NR	43.7 years \pm 12.6 years	- PO: Ethinyl estradiol, estradiol valerate, estriol - Transdermal estradiol: 17 β -estradiol gel or estradiol patch	NR
Getahun 2018	2,842	53	Ischemic stroke (1)	4.0 years (SD, 3.0)	- PO: estradiol valerate - Transdermal estradiol gel or estradiol patches	Current smoker 15% Overweight 29%; Obese 23% High total blood cholesterol 6% Elevated blood pressure 16% Prior acute cardiovascular event 1.9%
Nota 2019	2,517	29	NR	NR	- Estrogens with or without antiandrogens	NR
James 2020	49	2	NR	Median 24years (range 5–74)*	- Estrogen: 31 (63.3%), Spironolactone: 28 (57.1%), Progestin: 9 (18.4%), Finasteride: 2 (4.1%), GnRH agonist: 1 (2%)	Smoking 44% Alcohol abuse/dependence: 16.3% Illicit drug use 32.7%
Nokoff 2018	307	8	NR	NR	NR	Current smoker 19.4% Binge drinking 21% Does not meet physical activity aerobic recommendations 54.7%

ICH = Intracerebral hemorrhage; IM = Intramuscular; GnRH = Gonadotropin-releasing hormone; MTF = Male-to-female; NR = Not reported; PO = Per orem; TIA = Transient ischemic attack.

* Data refers to the entire transgender cohort.

Similar to global data, the present study revealed more reports of ischemic stroke compared to hemorrhagic stroke. However, the estimated frequency arrived at in the present study is much smaller compared to the aforementioned lifetime stroke risk worldwide (2% vs. 24.5%) as well as compared to the risk of stroke in the young (2% vs. 10%–15%). Issues that relate to the precise definition of transgender status, the predominance of hospital-based data, which may bias toward those individuals with better health-seeking behavior, and the gap in healthcare access of transgender individuals may account for this lower prevalence of cerebrovascular disease in the MTF population.

Formal epidemiologic studies on the incidence and prevalence of transgenderism are faced with methodological issues

such as in ascertainment of transgender status.²⁶ A higher prevalence is yielded with self-identification as opposed to utilizing precise diagnostic criteria for gender dysphoria.²⁷ This is reflected in the present study in which some studies used the criteria for gender dysphoria,^{11,12} others used DSM-III-3, DSM-IV, and ICD codes^{15,16} while other studies defined transgender status as individuals referred to specialist or gender clinics.^{13,17,18} These methodological issues could have affected the precision of the estimates of frequency in the present study.

Recent studies also suggest that the prevalence rates of self-reported transgender identity are higher compared to prevalence rates based on samples of clinic-referred adults.²⁷ In the present study, the reported populations were all clinic or

Table 3: Clinical characteristics of MTF transgenders who suffered from stroke

Author (year)	N	Type of stroke, location (n)	Age	Hormonal therapy regimen and or duration	Risk factors for stroke
LaHue 2019	8	TIA (1) Ischemic stroke (5) ICH (2) SAH (1)	(average age, 50 ± 9 years; range, 38–61 years)	Six patients (75%) used estradiol (oral or injection) or conjugated estrogen as part of gender-affirming treatment at the time of stroke; one patient used estrogen remotely	Prior stroke or TIA 2 out of 8 HTN 7 out of 8 DM 2 out of 8 Dyslipidemia 1 out of 8 Overweight or obese 2 out of 8 Smoking 5 out of 7 Stimulant use 5 out of 8 Alcohol use 1 out of 8
deMarinis 1978	1	Ischemic stroke, right middle cerebral artery occlusion	40	10 mg of norethynodrel and 0.15 mg of mestranol daily for 5 years	None
Biller 1995	1	Ischemic stroke, bilateral basal ganglia, and subcortical white matter	27	Conjugated estrogens 2.5 mg daily, medroxyprogesterone 10 mg daily, spironolactone 200 mg daily, and estradiol 10 mg injections monthly Duration not reported	None
Egan 2002	1	Ischemic stroke, right frontoparietal	46	Conjugated estrogens 2.5 mg twice daily, estradiol 4 mg twice daily, and medroxy progesterone 20 mg twice daily	History of deep venous thrombosis
Mullins 2008	1	Ischemic stroke, both frontoparietal and left parieto-occipital regions	48	Depot estrogen (estradiol valerate 30 mg every 2 weeks) and progesterone (medroxyprogesterone acetate 150 mg every 2 weeks for 32 years)	Smoking
Asscheman 2011	5	NR, fatal stroke	<60 years: 2 60 years, 62 years, and 75 years	Use of ethinyl estradiol in all In one with previous TIA, treatment changed to transdermal estrogen.	Previous TIA in 2
Wierckx 2013	5	NR	33	2 years; hormonal therapy regimen NR	Smoking, hypercholesterolemia, HTN
			53	2 years; hormonal therapy regimen NR	Smoking, hypercholesterolemia, HTN, T2DM
			56	10 years; hormonal therapy regimen NR	HTN and mechanical heart valve
			58	20 years; hormonal therapy regimen NR	Smoking, hypercholesterolemia
			56	2 years; hormonal therapy regimen NR	Smoking
Kwan 2019	1	Ischemic stroke (left cerebellum)	57	Spironolactone and 17-beta estradiol for 10 years	Hypertension, hypercholesterolemia, insulin resistance, smoking

DM = diabetes mellitus; HTN = Hypertension; ICH = Intracerebral hemorrhage; NR = Not reported; SAH = Subarachnoid hemorrhage; T2DM = Type 2 diabetes mellitus; TIA = Transient ischemic attack.

hospital-based save for one study that used a self-reported survey.¹⁴ Study settings were mostly in European countries or the USA. In addition to the gap in medical knowledge for transgender care, financial, health systems, and socioeconomic barriers exist. It is evident that more population-based studies across the globe that rely on samples taken outside the clinic or hospital setting are needed²⁷. These studies could help close the health equity gap affecting transgenders more so if they proposed potential solutions to address identified healthcare barriers.⁶

In men, estrogen has a questionable role. Some studies suggest that there may be a particular physiologic threshold of circulating androgen levels that protect against ischemic brain injury.²⁸ In women, estrogen administration and the effects of hormonal therapy are more established.¹² Low estrogen levels increase the risk of cardiovascular disease and accelerate atherothrombosis in women below 40 years of age. Hormonal therapy meanwhile in postmenopausal women may increase the risk of cardiovascular

disease.²⁹ The same may be true for cross-sex hormone therapy in transwomen.¹⁵

Recent long-term follow-up studies have shown that estrogen and antiandrogen therapy may negatively impact cardiovascular health in transwomen.¹⁵ A higher cardiovascular mortality rate has been reported in transwomen as opposed to the general population.¹² A handful of studies have also suggested that estrogen use in MTF transgenders confers increased risks of venous thromboembolism and pulmonary embolism¹⁵. However, the mechanisms by which sex steroids may alter vascular physiology and hormone receptor status in transgenders remain to be elucidated.

Two cohort studies identified in the present study compared transgender populations to control cismales and cisfemales. MTF transgenders were reported to have a higher prevalence of cerebrovascular diseases compared to their cis male and cis female counterparts.¹⁶ Getahun et. al.'s findings also suggested that prolonged hormone intake increased the risk for ischemic stroke events

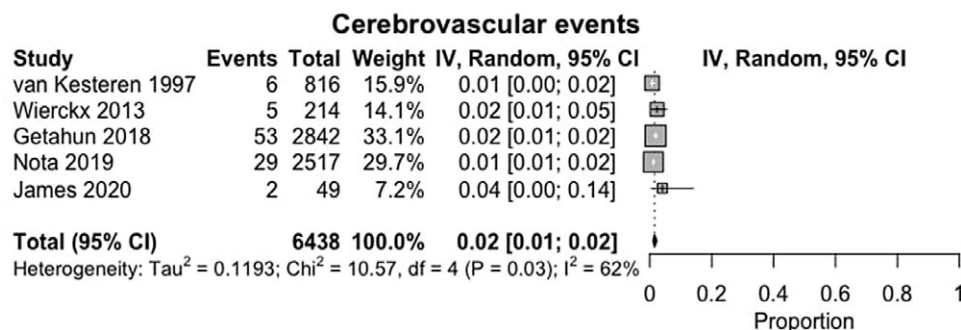


Figure 2: Random-effect modeling analysis for frequency of cerebrovascular events in MTF transgenders.

with the risk becoming substantially higher in those taking estrogen after 6 years or more of follow-up (10-fold higher risk vs. cisgender males and 4-fold higher risk vs. cisgender females).¹⁶

Limitations of the present review include the paucity of studies available on cerebrovascular diseases in transgenders, the small sample sizes of the included studies, and convenience-based sampling methods used in the studies. An association between hormonal therapy use and stroke cannot be made based on this study. Furthermore, the relationship between cross-sex hormone treatment and cardiovascular risk profile in MTF transgenders is complex. The varied preparations, routes of administration, and dosages of hormonal therapy, which were not given in a standardized manner may all have an effect.¹⁵

It is clear that further research is needed to determine how hormonal therapy may influence stroke risk within the transgender population, especially among MTF transgenders. Hormonal therapy for cis-gendered populations is not a guide for cross-sex hormone treatment for transgenders who have a unique physiology and distinct risk factors.

CONCLUSION

There are limited studies in the existing literature that have reported on cerebrovascular diseases in the transgender population. Even fewer studies have described the clinical characteristics and outcomes of stroke in this particular population subset. Though we estimated the frequency of cerebrovascular events in MTF transgenders in our quantitative analysis, our results may have been subject to selection bias, insufficient exposure ascertainment, and issues on the true causality of stroke in these patients. Healthcare issues of transgender individuals have slowly come to light in recent years, but more studies on the epidemiology and clinical profile of cerebrovascular diseases in this special population are warranted. These studies will aid us in coming up with better treatment guidelines for preventive health care and management of cerebrovascular diseases to address the specific needs of MTF transgenders.

DISCLOSURES

The authors have nothing to disclose.

STATEMENT OF AUTHORSHIP

KHDI: Conceptualization, data curation, formal analysis, interpretation of data, writing – original draft, writing – review and editing.

JDBD: Conceptualization, data curation, formal analysis, interpretation of data, writing – original draft, writing – review and editing.

AIE: Conceptualization, data curation, formal analysis, interpretation of data, writing – original draft, writing – review and editing.

MCPF: Conceptualization, data curation, formal analysis, interpretation of data, writing – original draft, writing – review and editing.

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit <https://doi.org/10.1017/cjn.2021.54>.

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