Cardiovascular and Metabolic Science www.ancam.org.mx

Chapter 23

Vol. 33 Supplement 5
October-December2022

doi: 10.35366/108064

Cerebrovascular disease in women

Enfermedad cerebrovascular en la mujer

Dulce Bonifacio-Delgadillo*

INTRODUCTION

The cerebrovascular event or stroke definition is based on the sudden onset of focal neurological dysfunction due to infarction or hemorrhage in the brain, retina, or spinal cord. It is currently defined as an acute episode of the brain, retina, or spinal cord dysfunction lasting more than 24 hours or of any duration if it demonstrates infarction or hemorrhage on imaging studies or autopsy.[1] Of them, 87% are ischemic, and 10% are hemorrhagic.[2] In the ResISSSTE brain stroke network, the percentages were 80.8% ischemic, 14.0% hemorrhagic, and 5.2% transient ischemic attacks.

In 2010, an estimated 16.9 million strokes occurred, and 102 million disability-adjusted life years were lost.[1,2]

GENDER DIFFERENCES IN THE EPIDEMIOLOGY OF STROKE

Incidence, prevalence, and mortality due to CVD are higher in men in almost all the world, except in Arab countries in the Middle East, North Africa, Israel, and Western Europe, where mortality is higher in women.[3] In Mexico, PREMIER registered 55.2% of women, with a mean age of 63 years (IQR 48.5-75).[4]

NON-MODIFIABLE GENDER-INDEPENDENT RISK FACTORS

In ResISSSTE brain, 55.7% were women, with a mean age of 71 years versus 66 years in men. At the time of the stroke, women are older, and the higher prevalence is attributable to the fact that women live longer and confer a higher risk (17% versus 15% after 50 years).[5] Survival of low-income patients is reduced by 30% (relative risk, 0.70, 95% confidence interval, 0.65-0.74) *(Table 1)*.[6]

MODIFIABLE GENDER-INDEPENDENT RISK FACTORS

INTERSTROKE described the impact of modifiable risk factors for cerebral infarction that are summarized in *Table 2*.[7]

RISK FACTORS ATTRIBUTABLE TO THE FEMALE GENDER

Early menarche

There are controversial data, but it has been found that early and late menarche (< 10 or > 17) have a higher cardiovascular risk, but the association to a stroke is weak.

The risk of stroke is 1.7 times higher with oral contraceptives that contain estrogens; it varies depending on the dose of estradiol. In the risk of a stroke, it is recommended to avoid hormonal contraception with estrogens. Contraception with progestogens does not confer a more significant risk.

Pregnancy

In pregnancy and postpartum, the risk of stroke is three times higher than in other young adults. The crude incidence is 30.0 per 100,000 pregnancies, including ischemic, venous thrombosis, and hemorrhage. Hypertensive

* Specialist in radiology and imaging, subspecialist in neuroradiology, and neurological endovascular therapy. Master in Medical Sciences, Full Professor in the specialty of Neurological Endovascular Therapy, Coordinator of the ResISSSTE Cerebro (Brain) program. Act Secretary of the Sociedad Mexicana de Neurorradiología and Vocal of the Sociedad Iberoamericana de Enfermedad Vascular Cerebral.

How to cite: Bonifacio-Delgadillo D. Cerebrovascular disease in women. Cardiovasc Metab Sci. 2022; 33 (s5): s497-s501. https://dx.doi.org/10.35366/108064

disorders of pregnancy (preeclampsia, eclampsia, and gestational hypertension) confer a fivefold increased risk of stroke. It also increases if congenital heart disease, atrial fibrillation, primary thrombocytopenia, or migraine occurs. Risk factors for a specific type of stroke as arteriovenous malformations and aneurysms, predispose to brain hemorrhage, while other factors predispose to both hemorrhage and thrombosis. *Table 3* lists the risk factors for ischemic and those associated with both.[3]

Diagnosis

Neuroimaging should be performed before any reperfusion therapy.[8] Computed tomography without contrast is acceptable during all trimesters because the risk of delaying the diagnosis of a time-dependent disease outweighs the risk of radiation, contrasting with iodine for angio-tomography and perfusion is acceptable if they are essential to decide treatment. Magnetic resonance does not produce radiation; therefore, it is the choice for pregnant women if it does not delay the time to diagnosis.

Alteplase intravenous is reasonable in pregnant women with disabling ischemic stroke who meet the criteria for thrombolysis, do not cross the placenta, and are not expected to increase the risk of bleeding in the fetus; the decision is based on the risk of maternal bleeding, especially early postpartum.

Endovascular thrombectomy with abdominal protection and limited use of X-rays is reasonable in pregnant women with large vessel occlusions (LVO). Thrombectomy may not be associated with thrombolysis in LVO because it can increase the risk of bleeding.[9]

Menopause

Due to the protective effect of estrogens on the vessels, the age of onset of menopause is a risk factor for stroke (relative risk of 1.25 in those under 40 versus 0.99 in those under 45). Vasomotor symptoms are interrelated with anxiety, depression, panic attacks, and lack of sleep which could increase the risk associated with hypertension and hyperlipidemia.

Late introduction of estrogen hormone replacement (> 10 years) increases the risk

Table 1: Comparison of risk factors between men and women treated for stroke in the ResISSSTE brain network.

Risk factors	Men (N = 102) n (%)	Women (N = 134) n (%)
Arterial hypertension	74 (72.6)	100 (74.6)
Diabetes mellitus	38 (37.3)	43 (32.1)
Smoking	9 (8.8)	4 (3.0)
Obesity	19 (18.6)	22 (16.4)
Chronic kidney disease	5 (4.9)	8 (6.0)
Epilepsy	2 (2.0)	2 (1.5)
Heart failure	4 (3.9)	4 (3.0)
Dyslipidemia	7 (6.9)	3 (2.2)
Cancer	6 (5.9)	13 (9.7)
Myocardial infarction	13 (12.7)	4 (3.0)
Valvulopathy	6 (5.9)	8 (6.0)
Arrhythmia	8 (7.8)	16 (11.9)
Previous heart attack	8 (7.8)	21 (15.7)

Source: personal communication, Bonifacio Delgadillo D.

Table 2: Magnitude of the impact of modifiable risk factors for cerebral infarction.

Risk factor	OR	Population attributable risk (RAP)
Arterial hypertension	2.98, IC 99% (2.72-3.28)	47.9%, IC 99%, 45.1-50.6%
Regular physical activity	0.60, 0.52-0.70	35.8%, 27.7-44.7%
Waist-hip ratio	1.44, 1.27-1.64	18.6%, 13.3-25.3%
Diabetes mellitus	1.16, 1.05-1.30	3.9%, 1.9-7.6%

Table 3: Risk factors for stroke during pregnancy.

Predisposing of ischemic stroke	Predisposing of ischemic and hemorrhagic stroke
Amniotic fluid embolism	Chronic kidney disease
Antiphospholipid antibody syndrome	Reversible cerebral vasoconstriction syndrome
Atrial fibrillation	Hypertensive disorders of pregnancy
Cardioembolism	Migraine
Cervical artery dissection	Older
Choriocarcinoma	Peripartum infection
Congestive heart failure	Primary thrombocytopenia
Diabetes mellitus	Coagulopathy
Congenital heart disease	
HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count)	Posterior Reversible Encephalopathy Syndrome (PRES)
Peripartum cardiomyopathy	
Systemic lupus erythematosus	

of thromboembolic events; early introduction confers little or no risk.[3]

Thrombosis of veins or cerebral venous sinuses

It represents 0.5 to 1 of all strokes; in women, it is three times more frequent than in men. Predisposing factors are genetic (thrombophilia) and acquired, which can be transitory (pregnancy, puerperium, surgery, trauma, or exogenous hormones) or permanent (cancer or antiphospholipid syndrome). The most common presentation is a headache. Treatment includes parenteral anticoagulation, regardless of bleeding, low molecular weight heparin, and oral anticoagulation with vitamin K antagonists or dabigatran. In pregnancy, therapeutic doses of low molecular weight heparin.[10]

Symptoms and simulators of infarction

Presenting symptoms are similar in women and men; however, women are less likely to be diagnosed with CVD (67.8 versus 76.8) and less likely to investigate etiology but have a similar risk of recurrence (2.3 versus 2.6), which may be due to characterization bias.[11] In the ResISSSTE brain, 22.6 of stroke mimics were presented in men and 29.9 in women.

TREATMENT AND PROGNOSIS OF ISCHEMIC STROKE IN WOMEN

Women may benefit from intravenous thrombolysis even more than men but are less likely to receive it.[12] There is no gender difference in the benefit of mechanical thrombectomy.[13] *Figure 1* shows the cases of a 95-year-old woman in whom successful

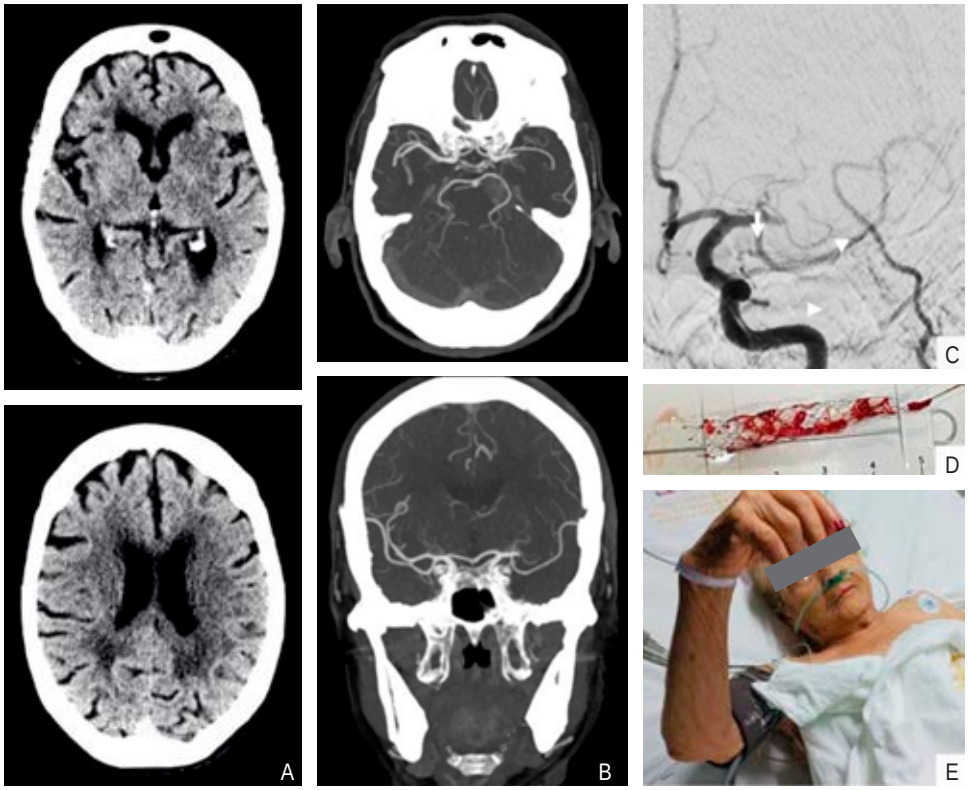

Figure 1:

See text.

recanalization was achieved with mechanical thrombectomy 6 hours after the onset of symptoms. Women have a worse prognosis due to age, functional status before the event, and comorbidities.[8]

CONCLUSION

There are significant differences in epidemiological characteristics, risk factors, and access to treatment in women; strategies are needed to avoid gender disparities in terms of access to prevention, treatment, and research of cerebrovascular disease in women.

REFERENCES

1. Hankey GJ. Stroke. Lancet. 2017; 389: 641-654.
2. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP et al. American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. Circulation. 2020; 141: e139-e596.
3. Christensen H, Bushnell C. Stroke in women. Continuum. 2020; 26: 363-385.
4. Cantú-Brito C, Ruiz-Sandoval JL, Chiquete E, Arauz A, León-Jiménez C, Murillo-Bonilla LM et al. Factores de riesgo, causas y pronóstico de los tipos de enfermedad vascular cerebral en México: Estudio RENAMEVASC. Rev Mex Neuroci. 2011; 12: 224-234.
5. GBD 2016 Lifetime Risk of Stroke Collaborators, Feigin VL, Nguyen G, Cercy K, Johnson CO, Alam T et al. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. N Engl J Med. 2018; 379: 2429-2437.
6. Andersen KK, Dalton SO, Steding-Jessen M, Olsen TS. Socioeconomic position and survival after stroke in Denmark 2003 to 2012: nationwide hospital-based study. Stroke. 2014; 45: 3556-3560.
7. Zeng X, Deng A, Ding Y. The INTERSTROKE study on risk factors for stroke. Lancet. 2017; 389: 35.
8. Powers WJ, Rabinstein AA, Ackerson T, Ackerson T, Adeoye OM, Bambakidis NC et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke. 2019; 50: e344-e418.
9. Ladhani NNN, Swartz RH, Foley N, Nerenberg K, Smith EE, Gubitz G et al. Canadian stroke best practice consensus statement: acute stroke management during pregnancy. Int J Stroke. 2018; 13: 743-758.

10. Coutinho JM, Ferro JM, Canhao P, Barinagarrementeria F, Cantú C, Bousser MG et al. Cerebral venous and sinus thrombosis in women. Stroke. 2009; 40: 2356-2361.
11. Kapral MK, Bushnell C. Stroke in women. Stroke. 2021; 52: 726-728.
12. Reeves MJ, Wilkins T, Lisabeth LD, Schwamm LH. Thrombolysis treatment for acute stroke: issues of efficacy and utilization in women. Womens Health (Lond). 2011; 7: 383-390.
13. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomized trials. Lancet. 2016; 387: 1723-1731.

Correspondence:
Dulce Bonifacio-Delgadillo
E-mail: drabonifacio@yahoo.com.mx