
Although most individuals with reversible cerebral vasoconstriction syndrome (RCVS) have excellent outcomes, 5% to 14% do poorly (discharge modified Rankin Scale score>3). Singhal et al conducted a single-center retrospective study (1998–2016; n=162) to identify predictors of persistent clinical worsening (development of new persistent focal or cognitive deficits or abrupt worsening of existing deficits), radiological worsening (occurrence of new lesion on any follow-up brain scan), early angiographic progression (worsened overall angiographic appearance on cerebral angiograms performed within 30 days of baseline compared with immediately prior study), and poor discharge outcome (modified Rankin Scale score, 4–6).

The mean age of the cohort was 44±13 years; 78% were women. Persistent clinical worsening occurred in 14% at 6.6±4.1 days after symptom onset, radiological worsening in 27% (mainly new infarcts), and angiographic progression in 15%. Individuals with clinical worsening were mostly women, with higher rates of hypertension, depression, exposure to serotonergic antidepressants, higher rates of treatment with intra-arterial vasodilators, and immunosuppressive agents, such as glucocorticoids and cyclophosphamide. Clinical worsening correlated with angiographic progression, new nonhemorrhagic lesions, longer duration of hospitalization, and worse discharge outcomes.

Glucocorticoids were administered to 46 (28%) patients, of which 33 received glucocorticoids for presumed primary angiitis of the central nervous system or RCVS. Of those 46, 17 (37%) showed persistent clinical worsening; of 116 patients not treated with glucocorticoids, only 6 (5%) showed worsening (P<0.001).

After adjusting for covariates, glucocorticoid treatment was an independent predictor of clinical, imaging, and angiographic worsening and poor outcome. Prior serotonergic antidepressant use predicted clinical and angiographic worsening but not poor outcome. Intra-arterial vasodilator therapy independently predicted clinical worsening and poor discharge outcome but was offered to more severe cases. Age and sex did not independently predict worsening. Infarction on baseline imaging predicted poor outcome.

The study is limited by the retrospective design; there was variability in treatment decisions, imaging modality, and timing of imaging studies and clinical selection bias in obtaining serial imaging. Nevertheless, the study’s strengths include the relatively large sample size and wealth of clinical and imaging data, extracted by chart review. Angiographic categorization was completed without knowledge of treatment to minimize bias.

This study highlights the potential dangers of glucocorticoid use in RCVS and need for clinician education. Because of the low index of suspicion for RCVS, patients with thunderclap headache and vasoconstriction on vascular imaging are often misdiagnosed with primary angiitis of the central nervous system. The authors have previously shown that recurrent thunderclap headaches, or a single thunderclap headache combined with normal neuroimaging, border zone infarcts, or vasogenic edema, has 98% to 100% specificity for RCVS. In such patients, it is prudent to withhold glucocorticoids, which have no proven benefit and potential harm in RCVS.

Poorthuis et al (Female and male-specific risk factors for stroke: a systematic review and meta-analysis. JAMA Neuro. 2017;74:75–81.)

Although epidemiological studies have consistently shown sex differences in stroke incidence, the underlying reasons and influence of sex-specific stroke risk factors on stroke risk remain unclear. Poorthuis et al conducted a systematic review and meta-analysis by searching PubMed, EMBASE, and the bibliographies of articles for observational studies published from January 1, 1985, through January 26, 2015, reporting the associations between sex-specific risk factors and ischemic stroke, hemorrhagic stroke, any stroke, and stroke mortality.
The search identified 78 studies (70 longitudinal and 8 case control) comprising 10187540 persons. For ischemic stroke, female-specific risk factors included any hypertensive disorder in pregnancy (pooled relative risk [RR], 1.8; 95% confidence interval [CI], 1.5–2.2) and gestational hypertension (RR, 1.8; 95% CI, 1.4–2.3). Female-specific characteristics for hemorrhagic stroke included late menopause (RR, 2.2; 95% CI, 1.2–4.2) and gestational hypertension (RR, 5.1; 95% CI, 1.8–14.3). Female-specific characteristics for any stroke were oophorectomy (RR, 1.4; 95% CI, 1.3–1.5), hypertensive disorders in pregnancy (RR, 1.6; 95% CI, 1.5–1.8), preeclampsia or eclampsia (RR, 1.5; 95% CI, 1.4–1.7), gestational hypertension (RR, 1.51; 95% CI, 1.27–1.80), preterm delivery (RR, 1.6; 95% CI, 1.5–1.8), and stillbirth (RR, 1.9; 95% CI, 1.2–3.0). Hysterectomy was protective against any stroke (RR, 0.9; 95% CI, 0.8–0.9). Relative risk of stroke mortality was 1.6 (1.0–2.4) after gestational hypertension.

Male-specific risk factors associated with ischemic stroke included androgen deprivation therapy (RR, 1.2; 95% CI, 1.1–1.3) and orchietomy (RR, 1.2; 95% CI, 1.0–1.5). Erectile dysfunction was associated with increased risk of any stroke (RR, 1.4; 95% CI, 1.2–1.5). The available data did not allow for pooling of estimates for male-specific risk factors for hemorrhagic stroke or stroke mortality. Numerous sex-specific factors could not be pooled but were found to affect stroke risk in individual studies: in women, these included parity, vascular calcifications in breast tissue, reproductive period, and age at menarche for women; in men, they included testosterone therapy, testosterone levels, and estradiol levels.

This systematic review and meta-analysis provides some clues on the association between sex-specific risk factors and stroke risk and mortality; however, it is limited by the intrinsic biases associated with observational studies, including nonrandom allocation of treatment, study heterogeneity, different methods and definitions for outcome measurements, variations in covariates used in adjusted models, limited comparability given the use of different definitions for risk factors, and heterogeneity in reference groups. Because of the variations in definitions, much of the data could not be pooled for meta-analyses. In addition, the authors curiously excluded studies in which stroke occurred during pregnancy or the puerperium, yet they included sex-specific risk factors, such as preeclampsia and hypertensive disorders of pregnancy, known to increase risk of stroke during that period. Nevertheless, this is a comprehensive, systematic overview of female- and male-specific risk factors for stroke and stroke mortality. Further study is needed to develop a more robust understanding of pathophysiologic mechanisms underlying sex differences in stroke.