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Migraine as a cardiovascular risk factor for women

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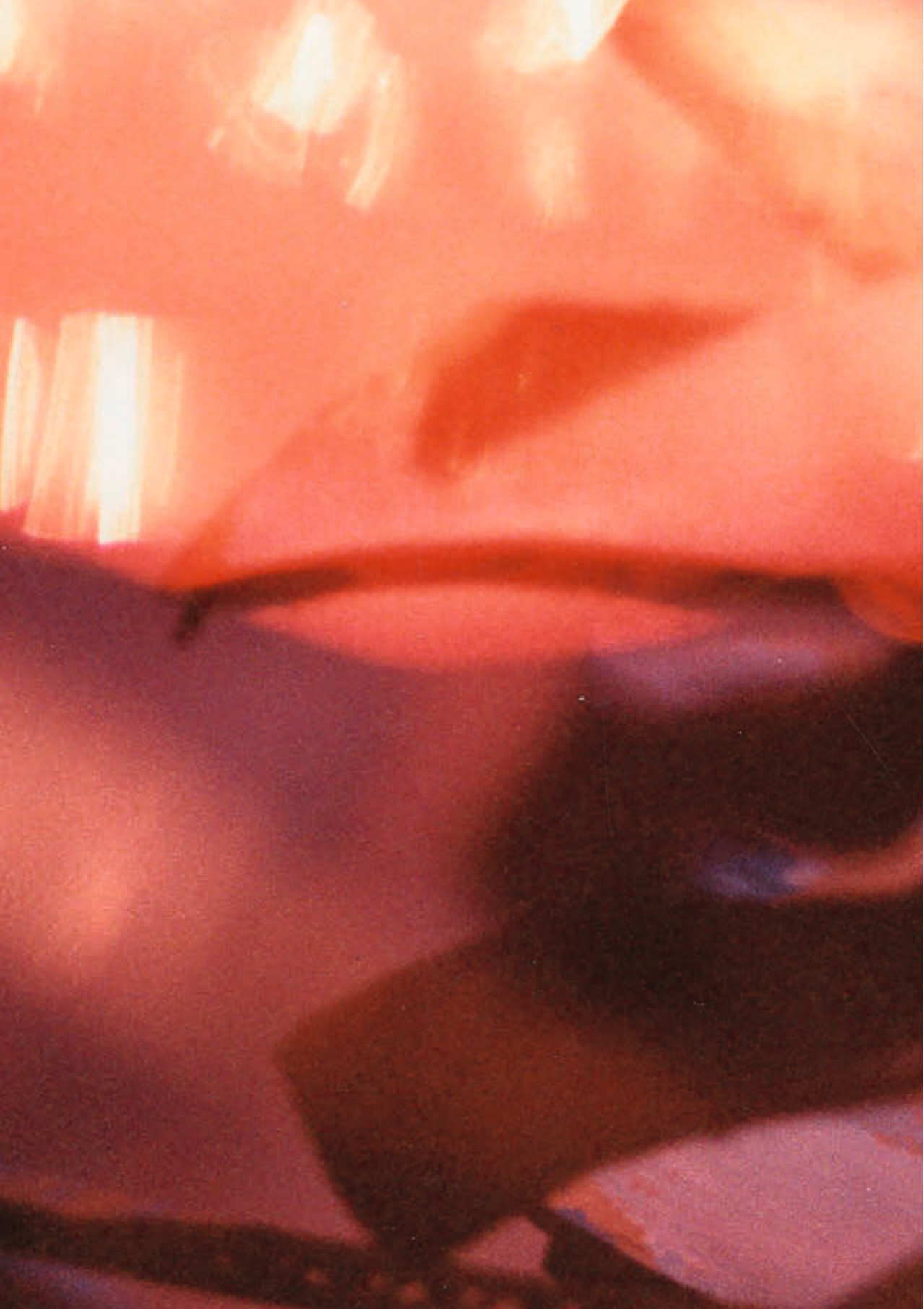
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CHAPTER 6

| Stroke after pregnancy disorders

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Dear Editor,

Women with hypertensive pregnancy disorders are at risk of developing stroke, possibly mediated by female-specific risk factors. Pregnancy is considered to be a stress test for cardiovascular health later in life.¹ In the current study we assessed the occurrence of pregnancy disorders, among women with a history of ischemic stroke who participated in the Dutch acute stroke study (DUST) and related these risk factors to migraine, age of stroke onset, stroke subtype, radiological characteristics and clinical outcome. Details and results of the prospective, multicenter DUST study have previously been published elsewhere.² Out of the 429 living female participants in DUST with ischemic stroke and clinical outcome at 3 months follow-up, 166 women consented to participate in the current questionnaire follow-up study, assessing female-specific risk factors for cardiovascular disease.

In total, 144 participants reported one or more pregnancies (86.7%). The most common reported pregnancy disorders were miscarriage (31 participants, 22.5%) and hypertensive pregnancy disorders (49 participants, 35.3%). No differences were observed for age of stroke onset, stroke subtype, or clinical outcome when comparing the separate groups of patients with a history of miscarriage, preterm delivery, hypertensive pregnancy disorders or placental abruption with patients without these disorders. However, a difference was observed for age of stroke onset (mean difference 10.2 years, 95% CI 2.6–17.8 years, see Table 1) when comparing participants with and without a history of pregnancy complications associated with vascular disease (preeclampsia, HELLP syndrome and placental abruption). Six (50%) of these participants with a history of these pregnancy complications had a stroke before the age of 50 years. Logistic regression resulted in an odds-ratio for having stroke onset <50 years of 4.71 (95% CI 1.38–16.06) for women with a history of pregnancy complications associated with vascular disease compared with women without a history of such pregnancy complications. Moreover, the median age of stroke onset was also earlier in women with migraine compared to women without migraine with a median of 9 years. (Unpublished data: see supplements) No differences were observed for age of stroke onset, stroke subtype, radiological characteristics or clinical outcome when comparing the separate groups of patients with a history of miscarriage, preterm delivery, hypertensive pregnancy disorders, placental abruption or migraine with patients without these disorders.

■ **Table 1.** Stroke characteristics in patients with and without pregnancy complications.

	Pregnancy complications (n = 12)^a	No pregnancy complications (n = 119)^a	p-value
Age at stroke, mean (SD)	53.9 (13.4)	64.1 (12.8)	0.009
BMI at stroke, mean (SD)	29.8 (9.1)	26.0 (4.3)	0.057
Migraine*	4 (36.4)	17 (14.9)	NS
Stroke classification (TOAST)			0.795
Large-artery atherosclerosis	3 (25.0 %)	29 (24.4 %)	
Cardioembolism	1 (8.3 %)	18 (15.1%)	
Small-vessel occlusion	3 (25.0 %)	22 (18.5%)	
Stroke of other determined etiology	2 (16.7%)	9 (7.6%)	
Stroke of undetermined etiology	3 (25.0%)	41 (34.5%)	
Stroke classification (Oxfordshire)			0.497
PACI	5 (41.7%)	48 (40.3%)	
TACI	0 (0.0%)	11 (9.2%)	
LACI	3 (25.0%)	25 (21.0%)	
POCI	2 (16.7%)	23 (19.3%)	
Unclear	1 (8.3%)	12 (10.0%)	
Pre-stroke disability			
mRS ≥ 2	0 (0.0%)	9 (7.6%)	0.602
NIHSS score admission ≥ 5	6 (50.0%)	60 (50.4%)	1.000
Follow up at 3 months			
mRS ≥ 2	4 (33.3%)	53 (44.5%)	0.549
EQ5D ≥ 6	6 (50.0%)	75 (63.0%)	0.681
Barthel index ≤ 17	0 (0.0%)	11 (9.2%)	0.594

BMI, body-mass index; PACI, partial anterior circulation infarcts; TACI, total anterior circulation infarcts; LACI, lacunar infarcts; POCI, posterior circulation infarcts; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Severity Scale, EQ5D, EuroQol five dimensions questionnaire. *Unpublished data

^a Total number of women, not all variables were available for each participant.

An increased risk of ischemic stroke in women with a history of pregnancy complications has been described in large retrospective and prospective cohort studies.^{3,4} The relation of age at stroke onset and history of pregnancy disorders has not been previously reported. The 10 years earlier age of stroke onset in participants with a history of pregnancy complications is consistent with our previous observations of an earlier onset of hypertension and type 2 diabetes mellitus in women with adverse pregnancy outcome.⁵ Pregnancy complications and ischemic stroke share common risk factors, such as obesity and hypertension. This might explain the accelerated stroke development after pregnancy complications. Our finding of a younger age at stroke onset for women with migraine is in line with existing literature.^{6,7}

Some limitations of our study need to be addressed. Firstly, our conclusions are based on relatively few women who experienced pregnancy complications within the cohort and information on pregnancy complications was based on self-reporting and could not be checked in medical records. Therefore, our findings need to be confirmed in a larger study sample. Secondly, selection bias may have occurred due to the retrospective nature of our sub-study and the use of self-reporting.

In conclusion, pregnancy disorders are common among women who experience ischemic stroke. We found that the mean age of stroke onset was about 10 years earlier in participants with a history of pregnancy complications associated with vascular disease (preeclampsia, HELLP syndrome and placental abruption) and 9 years earlier in women with migraine compared with women without such a history. Whether a combination of pregnancy complications and migraine leads to an even further increased risk of younger age at stroke onset should be addressed by future research.

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