Le risque de TVC chez la femme augmente

- La prédominance féminine (3 femmes/ 1 homme) chez les sujets jeunes et d'âge moyen s'est accrue durant les dernières décennies
  - 55% de femmes avant 1981 et 70% après 2001
- Les causes gynéco-obstétricales représentent environ 20% des cas de TVC
  - Contraception orale ++
  - Grossesse
  - Post-partum (6 semaines suivant l'accouchement)
  - Traitement hormonal substitutif
  - Fécondation in vitro

Bousser et Crassard, *Thrombosis Research* 2012; Zuurbier *et al., Int J Stroke* 2016

Review

International Journal of Stroke WSO

Sex differences in cerebral venous thrombosis: A systematic analysis of a shift over time

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Abstract

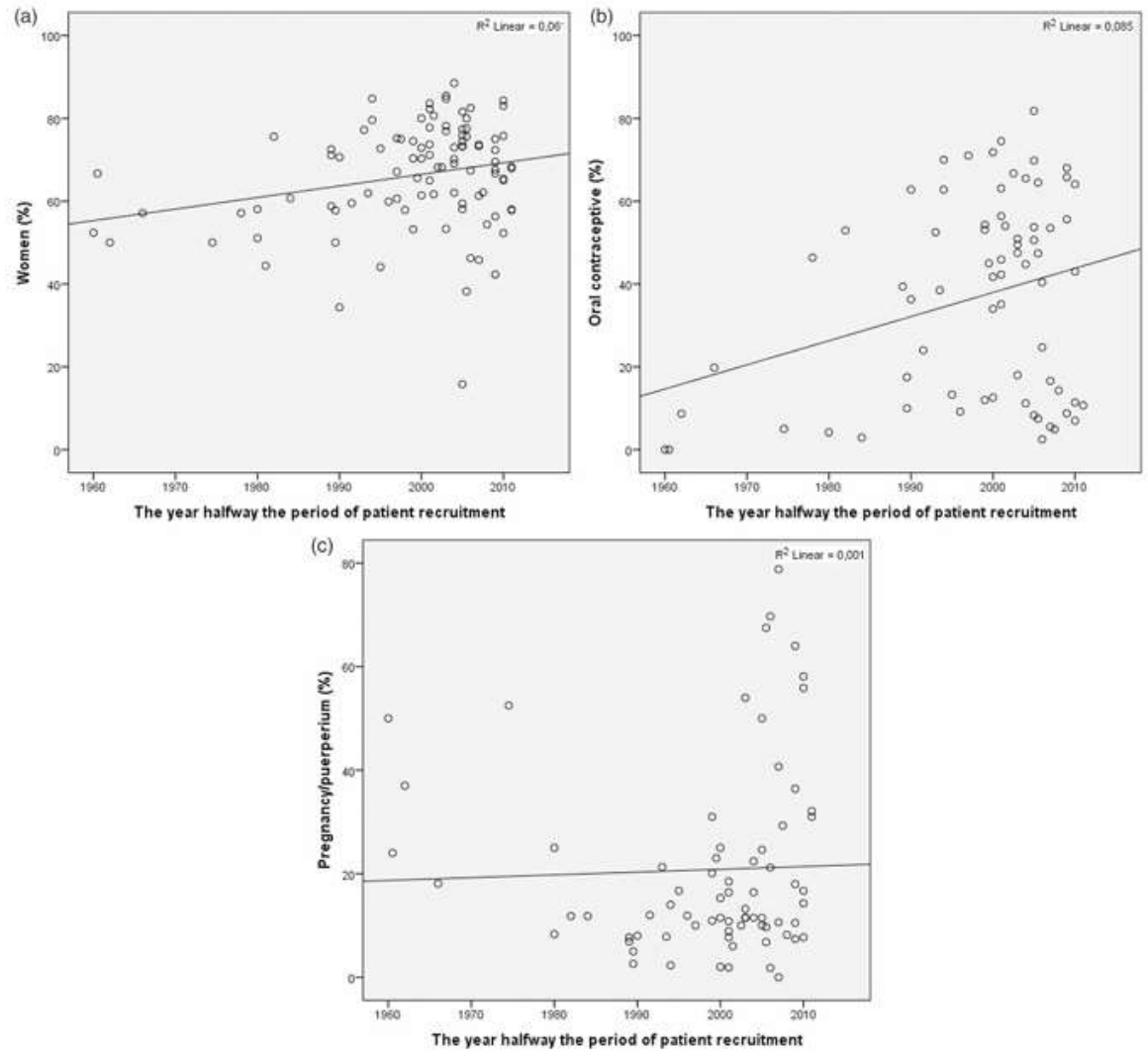
Background: In contemporary studies, cerebral venous thrombosis is three times more common in adult women than in men.

Aim: To study the change in sex ratio over time in cerebral venous thrombosis.

Summary of review: We systematically reviewed the literature. Any type of study with at least 40 patients with cerebral venous thrombosis that reported sex ratio was eligible. We ranked studies according to the year halfway the period of patient recruitment. Pediatric studies were analyzed separately. Out of 6068 publications identified by our search, 112 studies (23,638 patients), published between 1966 and 2014, were included. The proportion of women among patients with cerebral venous thrombosis significantly increased over time from a median of 54.8% in studies prior to 1981 to 69.8% after 2001 ($p = 0.002$). There was a significant correlation between time of the study and proportion of women (Pearson's correlation coefficient 0.25, $p = 0.01$). Oral contraceptive use among women with cerebral venous thrombosis also increased over time (Pearson's correlation coefficient 0.29, $p = 0.01$). In contrast, the percentage of pregnancy-related cases remained stable (Pearson's correlation coefficient 0.04, $p = 0.77$). Among 1702 patients from pediatric studies, 39% were female and there was no correlation between sex ratio and time of the study (Pearson's correlation coefficient −0.42, $p = 0.14$).

Conclusions: In adult patients with cerebral venous thrombosis, there is a shift in sex ratio over time with an increase in the proportion of women, whereas this is not observed in pediatric populations. A possible explanation for this phenomenon is an increase over time in the use of oral contraceptives by adult women.

Figure 2. Change in sex ratio and gender-specific risk factors. In each figure, time is plotted on the *x*-axis. Studies were ranked according to the year halfway the period of patient recruitment. On the *y*-axis percentage of women (a), oral contraceptive use (b), and pregnancy-related CVT (c) are plotted. Each dot indicates a single study.



Contraception orale et TVC

- Dans toutes les séries de TVC, les contraceptifs oraux sont le facteur de risque le plus fréquent chez les femmes (47% dans l'étude ISCVT)
- Les CO augmentent significativement le risque de TVC (OR 5,59, IC 95% 3,95 – 7, 91; p < 0,001)

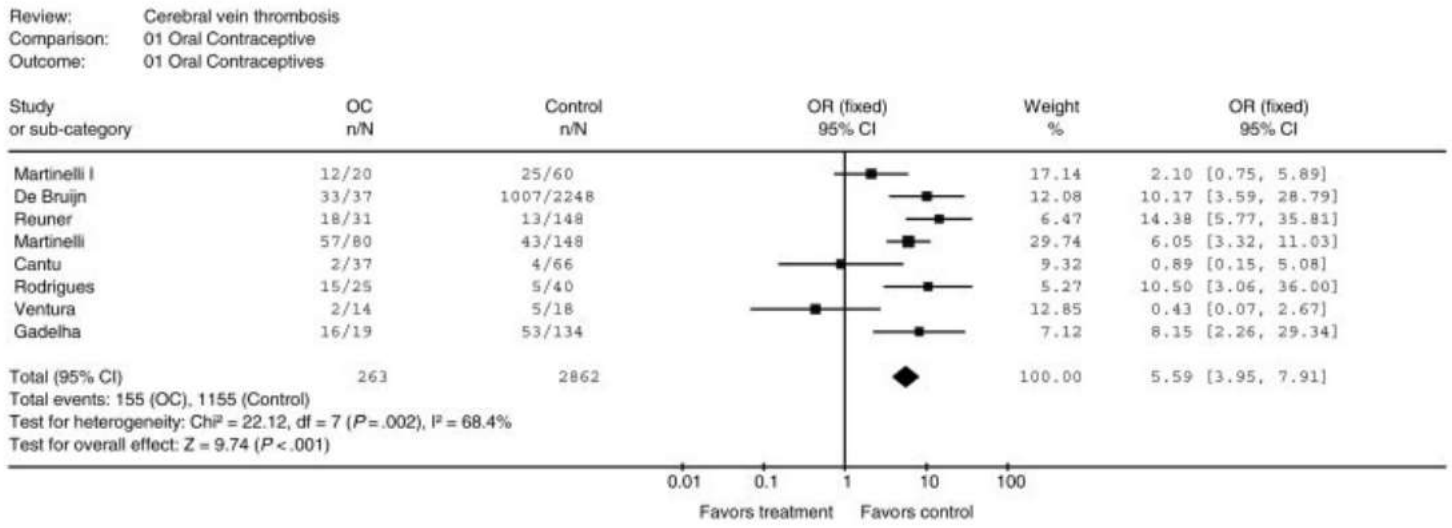


Figure 2. Odds ratio for cerebral vein thrombosis for oral contraceptive users. n indicates the number positive; N, total number.

Martinelli *et al., N Engl J Med* 1998; Dentali *et al*., *Blood* 2006

Contraception orale et TVC

- Le risque augmente avec l'âge et la dose d'oestrogène, et de façon très importante en cas de thrombophilie génétique associée (facteur V Leiden, mutation G20210A)
- Des cas de TVC ont aussi été rapportés avec les patches transdermiques, les anneaux vaginaux, et les CO de troisième génération
- **Les CO à base d'oestrogènes sont définitivement contre-indiqués après une TVC survenue sous CO, pendant la grossesse ou le post-partum**

TABLE 3. RISK OF CEREBRAL-VEIN THROMBOSIS IN WOMEN ACCORDING TO WHETHER THEY HAD THE G20210A PROTHROMBIN-GENE MUTATION OR THE G1691A FACTOR V MUTATION AND USED ORAL CONTRACEPTIVES.*

COMBINATION†	PATIENTS WITH CEREBRAL-VEIN THROMBOSIS (N=27)	HEALTHY CONTROLS (N=93)	ODDS RATIO (95% CONFIDENCE INTERVAL)
	no. (%)		
No G20210A, no OC	3 (11)	64 (69)	1 (reference group)
No G20210A, OC	17 (63)	27 (29)	13.4 (3.5–51.3)
G20210A, no OC	0	1 (1)	—
G20210A, OC	7 (26)	1 (1)	149.3 (31.0–711.0)
No G1691A, no OC	3 (11)	63 (68)	1 (reference group)
No G1691A, OC	21 (78)	28 (30)	15.8 (4.3–57.2)
G1691A, no OC	0	1 (1)	—
G1691A, OC	3 (11)	0	—

Martinelli *et al., N Engl J Med* 1998 ; Durmus *et al., Ther Adv Neurol Disord* 2020

Original Investigation

Risk of Cerebral Venous Thrombosis in Obese Women

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JAMA Neurol. 2016;73(5):579-584.

IMPORTANCE Obesity is a risk factor for deep vein thrombosis of the leg and pulmonary embolism. To date, however, whether obesity is associated with adult cerebral venous thrombosis (CVT) has not been assessed.

OBJECTIVE To assess whether obesity is a risk factor for CVT.

DESIGN, SETTING, AND PARTICIPANTS A case-control study was performed in consecutive adult patients with CVT admitted from July 1, 2006 (Amsterdam), and October 1, 2009 (Berne), through December 31, 2014, to the Academic Medical Center in Amsterdam, the Netherlands, or Inselspital University Hospital in Berne, Switzerland. The control group was composed of individuals from the control population of the Multiple Environmental and Genetic Assessment of Risk Factors for Venous Thrombosis study, which was a large Dutch case-control study performed from March 1, 1999, to September 31, 2004, and in which risk factors for deep vein thrombosis and pulmonary embolism were assessed. Data analysis was performed from January 2 to July 12, 2015.

MAIN OUTCOMES AND MEASURES Obesity was determined by body mass index (BMI). A BMI of 30 or greater was considered to indicate obesity, and a BMI of 25 to 29.99 was considered to indicate overweight. A multiple imputation procedure was used for missing data. We adjusted for sex, age, history of cancer, ethnicity, smoking status, and oral contraceptive use. Individuals with normal weight (BMI <25) were the reference category.

Original Investigation

Risk of Cerebral Venous Thrombosis in Obese Women

JAMA Neurol. 2016;73(5):579-584.

RESULTS The study included 186 cases and 6134 controls. Cases were younger (median age, 40 vs 48 years), more often female (133 [71.5%] vs 3220 [52.5%]), more often used oral contraceptives (97 [72.9%] vs 758 [23.5%] of women), and more frequently had a history of cancer (17 [9.1%] vs 235 [3.8%]) compared with controls. Obesity (BMI ≥30) was associated with an increased risk of CVT (adjusted odds ratio [OR], 2.63; 95% CI, 1.53-4.54). Stratification by sex revealed a strong association between CVT and obesity in women (adjusted OR, 3.50; 95% CI, 2.00-6.14) but not in men (adjusted OR, 1.16; 95% CI, 0.25-5.30). Further stratification revealed that, in women who used oral contraceptives, overweight and obesity were associated with an increased risk of CVT in a dose-dependent manner (BMI 25.0-29.9: adjusted OR, 11.87; 95% CI, 5.94-23.74; BMI ≥30: adjusted OR, 29.26; 95% CI, 13.47-63.60). No association was found in women who did not use oral contraceptives.

Key Points

Question: Is obesity a risk factor for cerebral venous thrombosis?

Findings: In this case-control study that included 186 cases and 6134 controls, obesity was associated with a statistically significant 3-fold increased risk of cerebral venous thrombosis. Stratification by sex revealed that in women who used oral contraceptives, the risk was increased 30-fold. In contrast, we found no association in men or women who did not use oral contraceptives.

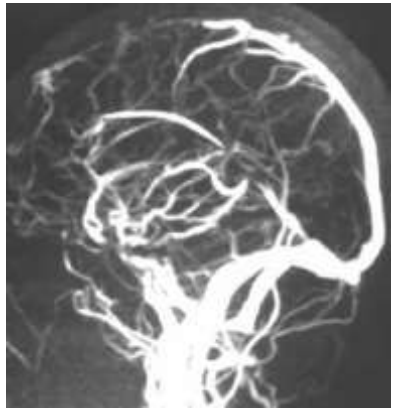
Meaning: Obesity is a strong risk factor for cerebral venous thrombosis in women who use oral contraceptives.

Table 5. Stratification by Oral Contraceptive Use in Women

BMI	No. (%) of Study Participants[a]		Adjusted OR (95% CI)[b]
	Cases (n = 129)	Controls (n = 3148)	
No OC use			
<25	17 (13.2)	1190 (37.8)	1 [Reference][c]
25-29.99	11 (8.5)	843 (26.8)	0.85 (0.30-2.41)
≥30	7 (5.4)	384 (3.1)	1.29 (0.46-3.66)
OC use			
<25	36 (27.9)	486 (15.4)	5.09 (2.58-10.02)
25-29.99	31 (24.0)	186 (5.9)	11.87 (5.94-23.74)
≥30	27 (20.9)	59 (1.9)	29.26 (13.47-63.60)

Procréation médicalement assistée et TVC

- De rares cas de TVC et de thrombose jugulaire ont été décrits après stimulation ovarienne
- Risque de thrombose veineuse x 5-10 durant le premier trimestre de grossesse par FIV
- Mécanismes favorisant la thrombose
  - Stimulation ovarienne elle-même favorisant élévation du fibrinogène, des facteurs II, V, VII, VIII et IX et diminution de la concentration de l'AT III
  - Syndrome d'HSO causant déplétion intravasculaire, hémoconcentration, augmentation de la viscosité sanguine favorisant la thrombose (risque x 100)



Cerebral venous thrombosis secondary to ovarian hyperstimulation syndrome

We report a case of a woman who underwent in-vitro fertilisation embryo transfer treatment for infertility and developed an acute stroke (left hemiparesis and headache). The stroke was caused by cerebral venous thrombosis due to ovarian hyperstimulation syndrome. We review the current background about this uncommon disorder.

Man et Hui, *Hong Kong Med J 2011*
Farooqui *et al., Stroke* 2021

AOGS
Acta Obstetricia et Gynecologica Scandinavica

AOGS SYSTEMATIC REVIEW

Thromboembolism and in vitro fertilization – a systematic review

MARIA SENNSTRÖM[1], KARIN ROVA[2], MARGARETA HELLGREN[3], RAGNHILD HJERTBERG[4], EVA NORD[1], LARS THURN[2,5] & PELLE G. LINDQVIST[2,6]

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Key Message

There is a very high risk of thromboembolism in in vitro fertilization complicated by ovarian hyperstimulation syndrome. Thromboprophylaxis is warranted in the first trimester when ovarian hyperstimulation syndrome occurs.

	IVF		Control group			Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Rova, 2012	32	19194	160	935338	34.9%	9.76 [6.68, 14.27]	2012	
Henriksson, 2013	36	23498	38	116960	31.6%	4.72 [2.99, 7.45]	2013	
Hansen, 2014	36	16191	61	149893	33.5%	5.47 [3.62, 8.27]	2014	
Total (95% CI)		**58883**		**1202191**	**100.0%**	**6.39 [4.03, 10.05]**		
Total events	104		259					

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 7.45$, df = 2 ($p = 0.02$); $I^2 = 73\%$
Test for overall effect Z = 7.86 ($p < 0.00001$)

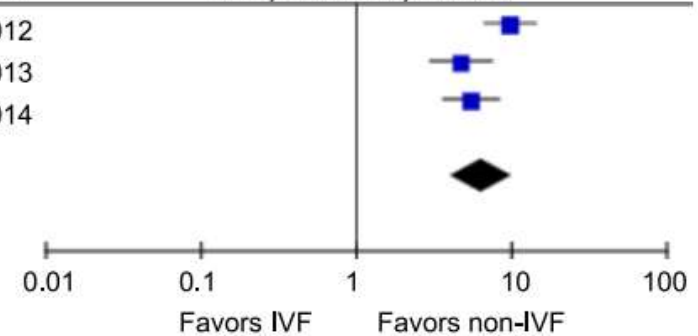

Figure 3. Meta-analysis of risk of first trimester VTE in IVF pregnancies. [Color figure can be viewed at wileyonlinelibrary.com].

Fécondation in vitro et TVC

Cerebral Venous Thrombosis and Hypercoagulability Associated With In Vitro Fertilization

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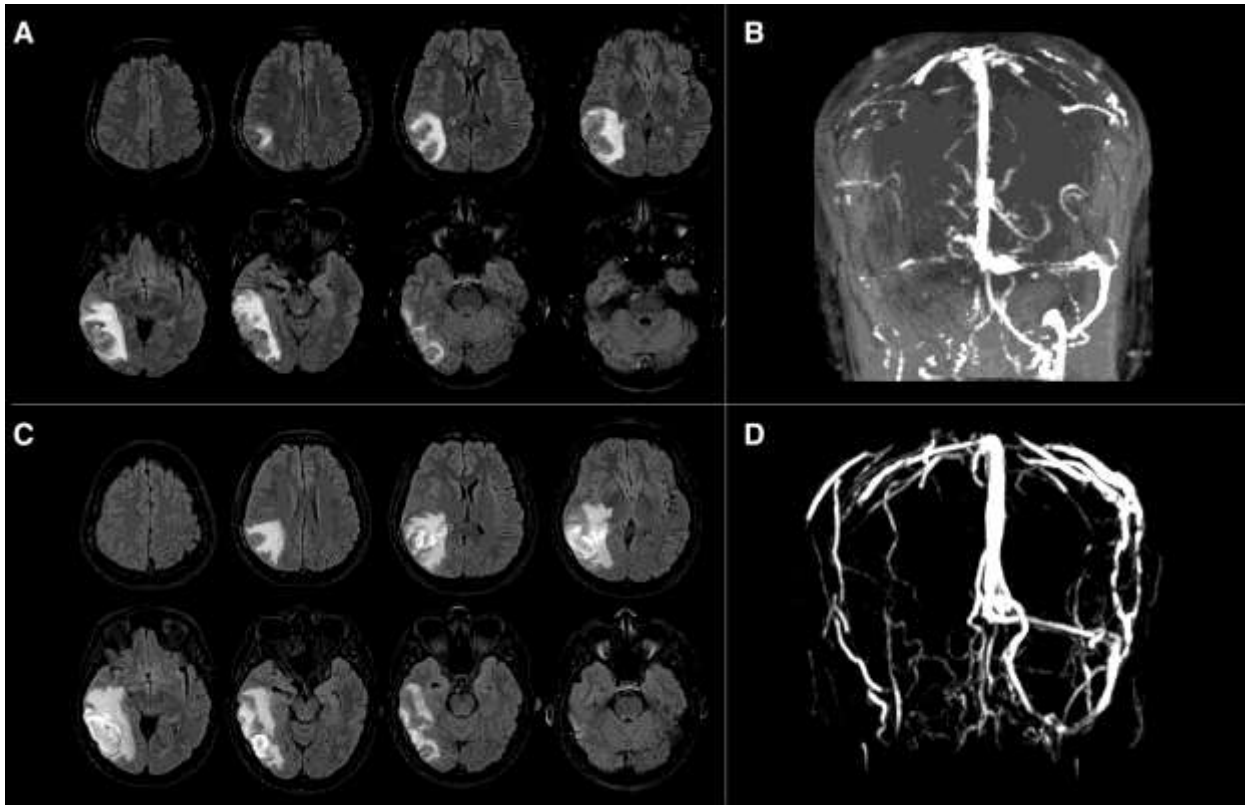

CASE DESCRIPTION

A 38-year-old woman with a history of mild headaches presented to an outside facility at 14 weeks of gestation with worsening headaches. The patient's first pregnancy was terminated due to fetal genetic anomalies not compatible with life, and her current pregnancy was achieved by in vitro fertilization (IVF). Her IVF protocol consisted of a period of combined estrogen and progesterone oral contraceptive pills followed by 12 days of follitropin alfa and menotropin injections for ovarian stimulation. After that, she received injections of leuprorelin and choriogonadotropin alfa on the 12th day to trigger ovulation. Her estrogen levels were monitored throughout this process and peaked at 1057 pg/mL just before triggering ovu-

Stroke. 2021;52:e554–e557.

TVC durant la grossesse et le post-partum

- Incidence
  - 10/ 100 000 accouchements dans les pays développés (5-20% de toutes les TVC)
  - 10 fois plus en Inde ou au Mexique (60% de toutes les TVC)
- 10 à 15% des TVC survenant chez les femmes en âge de procréer
- La majorité des TVC associées à la grossesse surviennent durant le troisième trimestre
- Préférer l'IRM avec angio-IRM veineuse (sans injection de gadolinium) et séquence T2* pour le diagnostic de TVC durant la grossesse
- Traitement par HBPM durant la grossesse (pas de passage transplacentaire)
- Le risque de TVC est nettement plus important durant le post-partum (x 13)

Coutinho *et al*., *Stroke* 2009; Bousser et Crassard, *Thrombosis Research* 2012

TVC du post-partum

- **Le risque est maximal durant les 6 semaines qui suivent l'accouchement (état pro-thrombotique)**
- Facteurs de risque de TVC
  - Age maternel
  - Multiparité
  - Accouchement à domicile
  - Césarienne
  - Hypertension artérielle
  - Infection
  - Déshydratation
  - Vomissements
  - Anémie
  - Hypotension intracrânienne après anesthésie péridurale

Coutinho *et al*., *Stroke* 2009; Bousser et Crassard, *Thrombosis Research* 2012