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Review Article

Cerebral Venous Sinus Thrombosis Following Oral Contraceptive Use: A Review of Published Cases

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Abstract

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon but potentially devastating stroke subtype affecting young women, and oral contraceptive (OCP) use is its most frequent reversible risk factor.

Objective: To review published case reports/series of OCP-associated CVST alongside the epidemiologic, pathophysiologic, diagnostic, and management literature.

Methods: Narrative review of case reports, case-control and cohort studies, meta-analyses, and guidelines.

Findings: CVST incidence is roughly 1.3 per 100,000 person-years, higher in reproductive-age women; OCP use confers a pooled odds ratio near 7-10, rising with inherited thrombophilia (prothrombin G20210A, Factor V Leiden). Published cases span isolated headache to fulminant, fatal disease, occasionally complicated by subdural hematoma or dural arteriovenous fistula. MRV/CTV is diagnostic; D-dimer has limited negative predictive value. Anticoagulation is first-line, with thrombectomy and decompressive craniectomy for refractory or malignant courses.

Conclusions: Prognosis is generally favorable with prompt anticoagulation and OCP discontinuation; guidelines support progestin-only or non-hormonal contraception thereafter.

Keywords: Cerebral venous sinus thrombosis; Oral contraceptives; Thrombophilia; Anticoagulation; Venous thromboembolism

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Introduction

Cerebral venous sinus thrombosis (CVST) accounts for roughly 0.5-1% of all strokes but disproportionately affects young adults, with a marked female predominance driven by hormonal risk factors [1,2]. Among these, combined oral contraceptive (OCP) use is the single most commonly identified provoking factor in women of reproductive age, first linked to cerebral venous thrombosis in observational studies of the 1990s and now supported by a substantial body of case reports, case-control studies, and meta-analyses [3,4]. Because CVST commonly presents

with nonspecific headache rather than a focal deficit, diagnosis is frequently delayed, and awareness of the OCP association is central to prompt recognition [5].

This is a narrative review, not a report of the authors' own patient, surveying published individual case reports and case series of OCP-associated CVST together with the epidemiologic, pathophysiologic, diagnostic, and management literature, to synthesize what the published record shows about presentation, workup, treatment — including options for refractory or malignant disease — and prognosis, including guidance on contraceptive choice after the event. Given the volume of the CVT literature broadly, this review deliberately concentrates on reports in which oral or other hormonal contraceptive use is explicitly identified as the provoking or contributing factor, supplemented by the larger cohort, case-control, and guideline literature needed to place those cases in context.

Epidemiology

The overall population incidence of CVST is approximately 1.32 per 100,000 person-years, rising to roughly 2 per 100,000 among women aged 31-50 [1]. In the largest published cohort, the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT), 75% of 624 patients were women, and a gender-specific risk factor — OCPs, pregnancy, puerperium, or hormone replacement — was identifiable in 65% of the female cohort [2].

Multiple case-control studies and meta-analyses quantify the OCP-specific risk. A systematic review and meta-analysis of 11 studies found the pooled odds of CVST in OCP users aged 15-50 were 7.59-fold higher than in non-users (95% CI 3.82-15.09) [6], corroborating an earlier meta-analysis of thrombophilic abnormalities and OCP use that reported a comparable, roughly sevenfold increase [7]. A recent case-control study of 206 CVST cases found combined hormonal contraceptive users had a

tenfold higher risk than non-users, with risk increasing in a dose-response manner with estrogen content and higher still with fourth-generation progestins [8]. Epidemiologic surveillance similarly shows current COC users carry an elevated venous thromboembolism risk that is highest in the first year of use [9]. Individual published cases mirror this pattern of risk concentrated in otherwise healthy young women, spanning duration of use from as little as 45 days [10] to two years or longer [5,11], and reinforcing that neither long-established use nor an apparently low-risk formulation reliably excludes the diagnosis. Notably, absolute risk remains low relative to the widespread prevalence of OCP use: most exposed women never develop CVST, and epidemiologic data are best interpreted as identifying a substantially elevated relative risk against a rare baseline event rather than a common individual outcome [1,9].

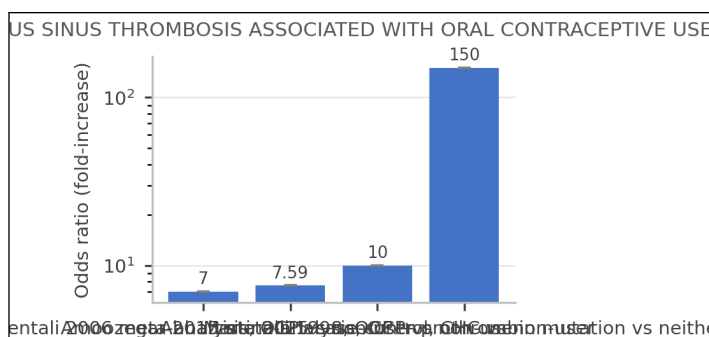


Figure 1: Odds/relative risk of cerebral venous sinus thrombosis in oral or combined hormonal contraceptive users: ~7-fold [7], 7.59-fold [6], 10-fold [8], and ~150-fold when combined with a prothrombin gene mutation [3].

Pathophysiology

Estrogen-containing contraceptives promote a prothrombotic state through several converging mechanisms: increased hepatic synthesis of coagulation factors (fibrinogen, factors VII, VIII, and X), reduced levels of the natural anticoagulants protein S and antithrombin, and acquired resistance to activated protein C, together with impaired fibrinolysis [5,7]. This effect is markedly amplified by inherited thrombophilia. Carriers of the prothrombin G20210A gene mutation who also use OCPs

have a roughly 150-fold increased risk of cerebral vein thrombosis compared with women with neither risk factor, far exceeding the additive risk of either alone [3]. A parallel case-control study of hereditary prothrombotic conditions (Factor V Leiden, protein C/S and antithrombin deficiency) found similarly synergistic risk in OCP users who were carriers [4], echoing the foundational description of markedly increased venous thrombosis risk in Factor V Leiden carriers using OCPs for systemic venous thromboembolism [12]. This gene-environment interaction underlies ongoing debate about pre-prescription thrombophilia screening, addressed explicitly in current OCP case reports discussing an affected patient's subsequent contraceptive counseling [5,13]. Routine universal screening before OCP initiation is not generally recommended, given the rarity of CVST relative to the cost and anxiety of population-wide testing, but targeted testing after a first thrombotic event — as performed in several of the cases reviewed here — is standard, both to inform anticoagulation duration and to guide future contraceptive choice [5,14].

Clinical Presentation

Published cases illustrate a spectrum from indolent headache to fulminant, fatal disease. A 32-year-old woman on combined OCPs for two years presented with four days of worsening headache, nausea, vomiting, and right-sided weakness, with superior sagittal and right transverse sinus thrombosis and venous infarction; she survived with anticoagulation and permanent OCP discontinuation [5]. A 31-year-old woman taking cyproterone-acetate/ethinyl estradiol for only 45 days developed an 11-day headache before three-site sinus/vein thrombosis was diagnosed, and later relapsed symptomatically when antiplatelet therapy was withdrawn [10]. In a 42-year-old woman, OCP use taken briefly to delay menses was initially withheld from clinicians and only surfaced on directed questioning after

an otherwise cryptogenic presentation with sudden focal neurological deficit — underscoring how easily the history can be missed [11].

Table 1: Published cases of oral/hormonal contraceptive-associated cerebral venous sinus thrombosis reviewed here [5,15,10,11,18,17,13,16]; N = 8 reports.					
Report	Age	Contraceptive / duration	Sinus(es) involved	Treatment	Outcome
Amri 2025	32	Combined OCP, 2 years	Superior sagittal, right transverse	LMWH to warfarin	Survived, partial recanalization
Huang 2019	22	OCP, >2 months	Left transverse-sigmoid, IJV	Thrombolysis, anticoagulation, fistula clipping	Survived, dAVF at 3 months
Moeindarbari 2022	31	Diane-35, 45 days	Right transverse, posterior SSS	Enoxaparin/warfarin, then clopidogrel	Survived, symptomatic recurrence
Sheerani 2006	42	OCP, short-term	Not stated	Not stated	Not stated
Galarza 2009, n=15	23-45	OCP, not stated	Not stated	Neurosurgical management	Not stated
Uemura 2016	20	Low-dose CHC, recent start	Not stated	None (fatal before treatment)	Fatal
Kilavuz Suman 2013	Not stated	OCP, not stated	Not stated	Not stated	Not stated
Arrighi 2024	Not stated	OCP, not stated	Not stated (subdural hematoma)	Anticoagulation	Not stated

Complications reported in the literature include dural arteriovenous fistula formation, illustrated by a 22-year-old woman whose transverse-sigmoid sinus and jugular vein thrombosis was followed three months later by a fistula requiring surgical clipping [15], and spontaneous subdural hematoma, described in an index case and systematic review identifying four total published instances of this complication in OCP users [16]. At the most severe end of the spectrum, a 20-year-old woman died shortly after starting a low-dose estrogen contraceptive, with the diagnosis established only postmortem by 3T-MRI and autopsy [17]. A 15-patient

neurosurgical case series spanning 1990-2007 similarly found severe headache the most common presenting symptom, followed by focal motor deficits and coma in patients requiring surgical intervention [18] — together with the fatal case above, demonstrating that OCP-associated CVST is not uniformly benign.

Diagnostic Approach

Because presentation is dominated by nonspecific headache, guidelines emphasize a low threshold for neuroimaging in young women, particularly those using estrogen-containing contraception [19]. Magnetic resonance imaging with venography (MRV) is the preferred initial modality per both American Heart Association and European Stroke Organization guidance, with CT venography (CTV) an acceptable alternative when MRI is unavailable or contraindicated; non-contrast CT alone has poor sensitivity and can miss thrombus entirely [19,20]. D-dimer testing carries important caveats: a systematic review and meta-analysis found it sensitive but with a meaningful false-negative rate, particularly in patients presenting with isolated headache or with thrombosis of more than a week's duration, so a normal D-dimer does not reliably exclude CVST [21]. In several published cases, elevated D-dimer prompted the imaging that confirmed diagnosis [5,15], while thrombophilia panels (protein C/S, antithrombin, lupus anticoagulant, anticardiolipin antibodies, Factor V Leiden) were sent in parallel but returned negative, reinforcing exogenous estrogen as the presumed primary driver in several reports [5,10].

Management

First-line therapy is anticoagulation, initiated even in the presence of hemorrhagic venous infarction, per AHA and ESO guidance [19,20]. Low-molecular-weight heparin transitioning to a vitamin K antagonist has been standard, reflected in several published cases [5,10], though direct oral anticoagulants are increasingly used: the exploratory RE-SPECT CVT trial randomized 120 clinically stable

patients to dabigatran or dose-adjusted warfarin and found comparably low rates of recurrent venous thromboembolism and bleeding in both arms, supporting dabigatran as a reasonable alternative [22]. Immediate, permanent discontinuation of estrogen-containing contraception is uniformly recommended once OCP-associated CVST is diagnosed [5,14].

Table 2: Guideline recommendations for diagnosis, initial management, and contraceptive counseling in oral-contraceptive-associated cerebral venous sinus thrombosis [19,20,14].				
Source (year)	Preferred imaging	D-dimer role	First-line treatment	Contraception after CVST
AHA/ASA (2024)	MRI/MRV; CTV if MRI unavailable	Adjunct only; not exclusionary	Anticoagulation regardless of hemorrhage	Discontinue estrogen-containing methods
ESO/EAN (2017)	MRV or CTV	Limited negative predictive value	Parenteral anticoagulation; decompressive surgery if herniating	Avoid estrogen-containing contraception
ASRM (2016)	Not applicable (contraception guideline)	Not applicable	Not applicable	Progestin-only or non-hormonal methods

For patients who deteriorate despite adequate anticoagulation, endovascular therapy is a recognized rescue strategy; a systematic review of 185 published cases of mechanical thrombectomy in CVST reported its use predominantly in severe or progressive disease [23]. For malignant courses with impending herniation from venous infarction and cerebral edema, decompressive craniectomy is a life-saving option: a review of its role in CVST management found favorable functional recovery achievable even in comatose patients with bilateral fixed pupils [24], and an individual case report describes bilateral decompressive craniectomy in a puerperal woman with progressive deterioration despite anticoagulation [25]. The earliest published neurosurgical case series in this specific OCP-associated population likewise supports surgical intervention, including decompressive procedures, in patients with severe or

progressive disease [18]. Across these reports, the treatment sequence follows a consistent escalation logic: anticoagulation first regardless of hemorrhagic transformation, endovascular thrombectomy for clinical deterioration despite adequate anticoagulation, and decompressive craniectomy reserved for impending or established herniation, mirroring the pathway now codified in AHA and ESO guidance [19,20].

Outcomes and Prognosis

Overall prognosis in CVST is more favorable than historically assumed: in the 624-patient ISCVT cohort, most patients achieved good functional outcome, though a clinically identifiable 13% subgroup remained at increased risk of death or dependency [26]. Women fared significantly better than men (complete recovery 81% versus 71%), attributed partly to their younger age and more often reversible, hormonally-related provoking factor [2]. Published OCP-associated cases mostly describe favorable outcomes with prompt anticoagulation and OCP cessation — survival with partial or complete recanalization [5,10,15] — but the literature also documents fatal outcomes, particularly with delayed recognition [17] or severe presentation requiring surgery [18].

Contraceptive counseling after CVST is a recurring theme: estrogen-containing methods are contraindicated (WHO category 4) after a personal history of CVST, and cohort data specifically evaluating progestin-only contraception after a first venous thromboembolic event found it did not meaningfully increase recurrence risk, supporting current guideline recommendations for progestin-only pills, levonorgestrel-releasing intrauterine devices, or non-hormonal methods thereafter [27,14]. Multiple individual case reports explicitly document this counseling in practice, with patients advised to permanently discontinue OCPs and offered alternative, non-estrogen contraception at discharge [5,10]. Long-term anticoagulation duration is individualized:

provoked cases such as most reviewed here are typically treated for 3-12 months, whereas recurrent thrombosis, persistent severe thrombophilia, or continued hormonal exposure prompts consideration of extended or indefinite therapy [20,19].

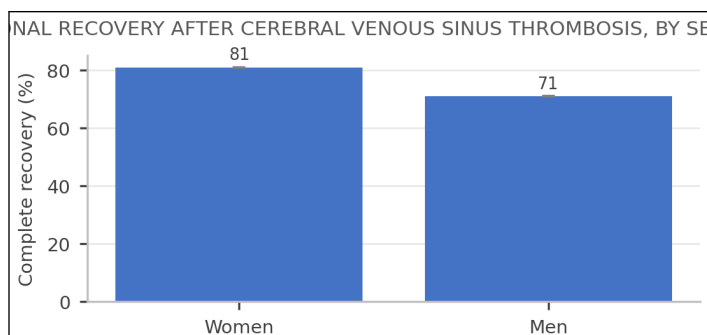


Figure 2: Complete functional recovery after cerebral venous sinus thrombosis by sex in the 624-patient ISCVT cohort: 81% in women versus 71% in men (P=0.01) [2].

Conclusion

The published case literature on OCP-associated CVST — from isolated headache diagnosed early to fatal, fulminant disease diagnosed only at autopsy — together with epidemiologic, pathophysiologic, and guideline evidence, describes a rare but important and largely preventable-in-hindsight complication of a widely used medication class. Risk is substantially amplified by inherited thrombophilia, diagnosis rests on a low threshold for MRV/CTV given D-dimer's limitations, and management follows a clear escalation pathway from anticoagulation through endovascular thrombectomy to decompressive craniectomy in malignant disease. Prognosis is favorable overall, particularly in women, and durable secondary prevention depends on permanent discontinuation of estrogen-containing contraception with transition to progestin-only or non-hormonal alternatives.

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