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Title: Do progestin-only oral contraceptives increase cardiovascular risk?

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Evidence-Based Answer:

Probably not. There does not appear to be an increased risk of progestogen/ progestin-only contraceptive (POC) use and cardiovascular disease (CVD), venous thromboembolism (VTE), thromboembolic stroke, or acute MI. There may be a risk of VTE among injectable POC users, although more studies are needed (SOR: B, meta-analysis of observational trials, case control trials).

Evidence Summary:

The World Health Organization (WHO) Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception (SHC) examined the association between cardiovascular disease and use of oral, injectable progestogen-only, and combined injectable contraceptives. This was a hospital-based, international, multicenter, case-control trial, from 21 centers in 17 countries. Women aged 15-49 who had CVD (N= 3,697) and were using contraception were studied compared to controls (N= 9,997). When compared to the control group, there was no difference in risk of CVD with oral POC (OR)1.1; 95% CI, 0.79–1.6), injectable POC (OR 1.0; 95% CI, 0.68–1.5), or combined injectable contraceptives (OR 0.95; 95% CI, 0.49–1.9).¹

A multicenter, case-control study of European women aged 16-44, from 16 centers in 5 countries, examined oral POC and risk of CVD in patients with a diagnosed cardiovascular event (N= 394) and compared them to a control group (N= 2,366). There was no increase in CVD risk with oral POC use (OR 0.84; 95% CI, 0.45-1.6) compared to the non-user group. There was no increased risk for myocardial infarction (OR 0.94; 95% CI, 0.31-2.9), thromboembolic CVA (OR 1.6; 95% CI, 0.24-10.72), or VTE (OR 0.68; 95% CI, 0.28-1.66).²

A meta-analysis of 8 observational studies evaluated for increased risk of VTE among women <50 years old with/ without a documented VTE (N=147 and 346 respectively) who were using oral, injectable, or intrauterine POCs. There was no increased risk for VTE in women using progestin-only pills or intrauterine devices (8 trials; N= 493; RR 1.0 (95% CI, 0.76-1.4; RR 0.61; 95% CI, 0.24-1.5) respectively. However, in a subgroup analysis, there was a significant increased risk of VTE among injectable progestin users (2 trials, N=38; RR 2.7, 95%CI, 1.3-5.5). This suggests that injectable POC use in patients at higher risk of developing VTE (i.e. thrombophilic patients) should be limited; but further studies are indicated to make this conclusion.³

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1. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. *Contraception*. 1998 May;57(5):315-2. [LOE: 3b]
 2. Heinemann LA, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the Health of Young Women. *Eur J Contracept Reprod Health Care*. 1999 Jun;4(2):67-73. [LOE: 3b]
 3. Mantha S, Karp R, Raghavan V, Terrin N, Bauer KA, Zwicker JI. Assessing the risk of venous thromboembolic events in women taking progestin-only contraception: a meta-analysis. *BMJ*. 2012 Aug 7;345:e4944. doi: 10.1136/bmj.e4944. [LOE: 2a]

Continuing Education Question:

Although further study needs to be done, which of these cardiovascular diseases may have an associated risk with injectable progestogen/ progestin-only contraceptives use?

1. Stroke
2. Myocardial infarction
3. VTE
4. PVD

The correct answer is 3.