Risk of coronary heart disease and risk of stroke in women with polycystic ovary syndrome: A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 1 May 2014
Accepted 29 June 2014
Available online 8 July 2014

Keywords:
Coronary disease
Stroke
Polycystic ovary syndrome
Obesity
PCOS

Women with polycystic ovary syndrome (PCOS), one of the commonest endocrine conditions in the human, are more likely than other women to have increased blood pressure, endothelial dysfunction, reduced arterial compliance, central obesity, dyslipidaemia, low grade chronic inflammation, and increased endothelin-1 and homocysteine [1]. A recent meta-analysis found an increased incidence of cardiovascular events in women with PCOS, but did not distinguish between coronary heart disease and stroke and did not consider fatal and non-fatal events separately [2]. The present meta-analysis aimed to quantify the risk of non-fatal stroke and coronary heart disease as separate disease events in women with PCOS compared to healthy women.

The Mantel–Haenszel method was used, with a random effects model in most cases, to generate an odds ratio (OR) for all included studies combined. Results were considered statistically significant where the probability value was below the 0.05 threshold. Review Manager statistical software, version 5.1, was used to analyse data. Heterogeneity was assessed using I^2 and chi square statistics.

Nine studies met the inclusion criteria (see list of included studies here [www.ijc.com/references). Women with PCOS were at increased risk of non-fatal stroke and non-fatal CHD but the odds ratios did not reach statistical significance (OR, 1.61; 95% CI, 0.82–3.15; P = 0.17 and OR, 1.63; 95% CI, 0.96–2.78; P = 0.07, respectively). In the five studies where the average age was more than 45 years old, the risk in PCOS was significantly increased for non-fatal stroke (OR, 1.94; 95% confidence interval, 1.19–3.17) and non-significantly increased in the six studies of CHD (OR, 1.70; 95% confidence interval, 0.92–3.11) (Fig. 1).

For the three studies where the BMI was similar and the mean age was over 45 in the groups the risk was non-significantly increased for women with PCOS for stroke (OR, 1.67; 95% confidence interval, 0.70–4.02) and for the three studies of CHD (OR, 2.04; 95% confidence interval, 0.60–6.97).

The Newcastle–Ottawa scale suggests that the methodological quality of the included studies was moderate. Funnel plots found that although publication bias cannot be ruled out, the asymmetry observed may be due to the relatively young age of the patients in one study.

Women with PCOS appear to be at increased risk of non-fatal stroke and possibly CHD. Although this study was not designed to investigate mechanism, the higher blood pressure and atherogenic lipid profile in women with PCOS may be contributory. In any case, clinicians and policymakers might focus on screening women with PCOS as soon as it is diagnosed, and focus on applying preventative measures, such as lifestyle interventions, appropriate to reducing the risk of stroke.

Whilst the results of the present meta-analysis did not provide evidence of increased risk of CVD in PCOS entirely independent of BMI, evidence of cardiovascular risk in lean women with PCOS [3] supports the hypothesis of the potential for an independent role of PCOS in CVD, perhaps due to the abdominal obesity in PCOS [5]. Future studies of PCOS should measure waist circumference in order to assess abdominal obesity. Furthermore, many women with PCOS receive treatments (the oral contraceptive pill, antiandrogens, insulin sensitizers or laparoscopic ovarian diathermy) which are likely to modify the risk of later cardiovascular events [4]. Future studies should therefore also assess the impact of these interventions on cardiovascular risk in women with PCOS.

These findings have important implications for disease prevention and screening in women. At present, weight management, changes in dietary composition and exercise should be the primary interventions, although pharmacologic treatment of hypertension, dyslipidaemia or insulin resistance may be required where lifestyle modification proves ineffective.

No funding supported the preparation of this paper.

The authors have nothing to disclose.

We would like to thank Dr Richard Morris of University College London for his advice on statistical matters.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2014.06.079.

References

[1] Fauser BCJM, Tarlatzis BC, Rebar RW, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril 2012;97 28-38.e25.
[2] De Groot PCM, Dekkers OM, Romijn JA, et al. PCOS, coronary heart disease, stroke and the influence of obesity: a systematic review and meta-analysis. Hum Reprod Update 2011;17:495–500.
[3] Conway GS, Agrawal R, Betteridge DJ, et al. Risk factors for coronary artery disease in lean and obese women with the polycystic ovary syndrome. Clin Endocrinol (Oxf) 1992;37:119–25.
[4] Lunde O, Tanbo T. Polycystic ovary syndrome: a follow-up study on diabetes mellitus, cardiovascular disease and malignancy 15–25 years after ovarian wedge resection. Gynecol Endocrinol 2007;23:704–9.
[5] Rexrode KM. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280:1843–8.

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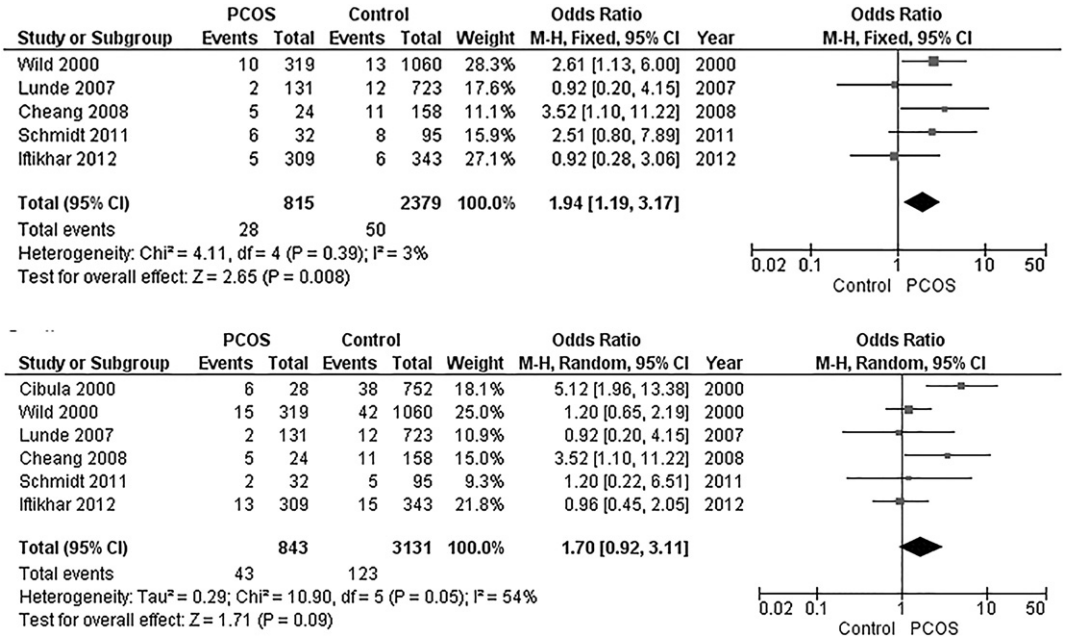

Fig. 1. Forest plot comparing risk of non-fatal stroke in women with PCOS compared to controls in the older age group (mean > 45 years) (above) and forest plot comparing risk of non-fatal CHD in women with PCOS compared to controls in the older age group (mean > 45 years) (below).

http://dx.doi.org/10.1016/j.ijcard.2014.06.079

Direct medical costs of hypertension and associated co-morbidities in South Korea

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ARTICLE INFO

Article history:
Received 30 April 2014
Accepted 29 June 2014
Available online 8 July 2014

Keywords:
Hypertension
Medical expenditure
Heart failure
Nephropathy

Hypertension (HTN) is a primary risk factor for cardiovascular disease. The costs following cardiovascular events in hypertensive patients are reportedly substantial [1,2]. The estimated direct and indirect costs of HTN among Americans in 2007 totaled $66.4 billion, making HTN the second most costly cardiovascular-related disorder [1]. Lloyd et al. estimated that UK patients with failure to achieve blood pressure targets experience 58,000 unnecessary major cardiovascular events annually, at a cost of £97.2 million [2]. These studies have emphasized the disease burden of uncontrolled HTN, causing considerable increases in medical expenditure and in comorbid disease.

In South Korea, the total prevalence rate of HTN in people aged 30 years and over was 26.9% in 2010 [3]. During the 4-year period from 2005 through 2009, HTN therapy costs increased by 64.3% from $1.4 billion to $2.3 billion [4]. Moreover, medical expenditure to treat (primary) HTN and other hypertensive diseases is an estimated 2.5 trillion KRW [4]. Given that the proportion of HTN-associated comorbidities is estimated to be 50% [5] and given that the South Korean population is aging rapidly, the future cost burden of HTN and its comorbid conditions will be profound.

In this study, we calculated the direct medical costs of treating HTN and associated comorbidities in South Korea.

This study analyzed data from the 2009 South Korean Health Insurance Review and Assessment Service-National Patients Sample (HIRA-NPS) data. The HIRA database contains reimbursement records from all medical facilities, including both hospitalized cases and outpatient clinic cases, in South Korea. The 2009 HIRA-NPS contains approximately 700,000 in patients (13% of total in patients) and approximately 400,000 outpatients (1% of total outpatients) extracted

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