Ten-Year, Thirty-Year, and Lifetime Cardiovascular Disease Risk Estimates Following a Pregnancy Complicated by Preeclampsia

Graeme N. Smith, MD, PhD,[1,2] Jessica Pudwell, MPH,[1,2] Mark Walker, MD, MSc,[3] Shi-Wu Wen, MB, PhD[3]; for the Pre-Eclampsia New Emerging Team

[1]Department of Obstetrics & Gynaecology, Kingston General Hospital, Queen's University, Kingston ON

[2]Department of Biomedical and Molecular Sciences, Kingston General Hospital, Queen's University, Kingston ON

[3]Department of Obstetrics and Gynecology, Ottawa Health Research Institute, University of Ottawa, Ottawa ON

Parts of this data were presented at the Society for Maternal–Fetal Medicine (2012) and Society for Gynecologic Investigation (2012).

Abstract

Objective: To calculate the cardiovascular disease (CVD) risk estimates for women following a pregnancy with or without preeclampsia.

Methods: We calculated 10-year, 30-year, and lifetime CVD risk estimates at one year postpartum for women recruited into the Pre-Eclampsia New Emerging Team's prospective cohort.

Results: Complete CVD risk screening data were obtained from 118 control women and 99 preeclamptic women. A total of 18.2% of preeclamptic women and 1.7% of control women had a high 10-year risk (OR 13.08; 95% CI 3.38 to 85.5), 31.3% of preeclamptic women and 5.1% of control women had a high 30-year risk (OR 8.43; 95% CI 3.48 to 23.23), and 41.4% of preeclamptic women and 17.8% of control women had a high lifetime risk for CVD (OR 3.25; 95% CI 1.76 to 6.11).

Conclusions: The association of preeclampsia with the future development of CVD makes pregnancy an early window of opportunity for the preservation of health and prevention of CVD.

Résumé

Objectif : Calculer les estimations du risque de maladie cardiovasculaire (MCV) chez les femmes à la suite d'une grossesse s'étant accompagnée ou non d'une prééclampsie.

Méthodes : Nous avons calculé des estimations du risque de MCV sur 10 ans, sur 30 ans et à vie à un an postpartum pour ce qui est des femmes ayant participé à la cohorte prospective *Pre-Eclampsia New Emerging Team*.

Résultats : Des données complètes sur le dépistage du risque de MCV ont été obtenues auprès de 118 témoins et de 99 femmes prééclamptiques. Au total, 18,2 % des femmes prééclamptiques et 1,7 % des témoins étaient exposées à un risque élevé de MCV sur 10 ans (RC, 13,08; IC à 95 %, 3,38 - 85,5), 31,3 % des femmes prééclamptiques et 5,1 % des témoins étaient exposées à un risque élevé de MCV sur 30 ans (RC, 8,43; IC à 95 %, 3,48 - 23,23), et 41,4 % des femmes prééclamptiques et 17,8 % des témoins étaient exposées à un risque élevé de MCV à vie (RC, 3,25; IC à 95 %, 1,76 - 6,11).

Conclusions : L'association entre la prééclampsie et l'apparition future d'une MCV fait en sorte que la grossesse constitue une période précocement très propice à la mise en œuvre de mesures visant le maintien de la santé et la prévention de la MCV.

Key Words: pregnancy, cardiovascular disease, preeclampsia, cardiovascular risk, risk estimates

Competing Interests: None declared.

Received on May 5, 2012

Accepted on June 7, 2012

J Obstet Gynaecol Can 2012;34(9):830–835

INTRODUCTION

It is well established that pregnancy is essentially a cardiovascular stress test.[1] The development of common pregnancy complications[2] (preeclampsia or gestational hypertension,[3,4] gestational diabetes or gestational impaired glucose intolerance,[5,6] clinically significant placental abruption,[7] preterm birth,[8] or delivery of a growth-restricted or low birth weight baby[4]) are some of the earliest clinically identifiable markers for increased risk of premature cardiovascular disease and cardiovascular death.

The American Heart Association's 2011 update to their evidence-based guidelines for the prevention of CVD in women now identifies these complications of pregnancy as relevant in the determination of CVD risk in women.[9]

Given that the majority of pregnant women access the health care system on a regular basis, it is hypothesized that pregnancy is an ideal starting point to determine which women should enter into CVD risk screening programs. The goal of this study was to determine whether women with and without preeclampsia had 10-year, 30-year, and lifetime CVD risk estimates at one year postpartum that were high enough to identify them as warranting further counselling and follow-up regarding lifestyle modification and/or pharmacotherapy.

METHODS

The Pre-Eclampsia New Emerging Team (PE-NET) prospective longitudinal cohort was initiated to study preeclampsia and its association with metabolic and cardiovascular risk factors. The cohort is made up of two groups: women who had a pregnancy complicated by preeclampsia (PE group) and women who had never had a pregnancy complicated by preeclampsia (control group). The diagnosis and recruitment process has previously been described.[3] Women are followed up after one year, three years, and five years in this ongoing cohort study; the present study was a secondary analysis in which all women who had a complete CVD risk screen performed at one year postpartum were included in the CVD risk calculations.

Data collected both at time of recruitment into the study and at follow-up after one year were used to calculate each individual's 10-year,[10] 30-year,[11] and lifetime[12] risk estimates for CVD. For each risk estimate method a two-group Mann-Whitney *U* test was used to determine whether there was a significant difference in the distribution of CVD risk estimates between the PE group and the control group. Additionally, for each risk estimate method a mid-*P* exact chi-square test was used to compare the number of individuals in the PE and control groups who had high risk estimates. For the 10-year risk estimate method two definitions of a high risk score ($\geq 5\%$[13] and $\geq 10\%$[10]) were considered. For the 30-year risk estimate method, a high risk score was defined as $\geq 10\%$.[11] Finally, for the lifetime risk estimation method a high risk score was defined as $\geq 39\%$.[12] The statistical analysis was performed using R version 2.10.1 (R Foundation for Statistical Computing, Vienna, Austria) and OpenEpi version 2.3.1.

ABBREVIATIONS

CVD	cardiovascular disease
PE	preeclampsia

RESULTS

Baseline demographic characteristics for women in the control group (n = 118) and PE group (n = 99) who had complete CVD risk screening performed at one year postpartum is presented in Table 1. For all variables, except maternal education level, the groups did not differ significantly at baseline. Forty women with PE and 35 control subjects were recruited but were lost to follow-up after one year. Baseline characteristics for those lost to follow-up and those actually seen were not different (Table 1).

The variables used in each of the 10-year,[10] 30-year,[11] and lifetime[12] CVD risk estimate methods are listed in Table 2. The 10-year, 30-year, and lifetime risk analyses for the control and PE groups are presented in Table 3. For all three scoring methods the two-group Mann-Whitney *U* test demonstrated a significant difference between the PE and control groups ($P < 0.001$). This test indicates that the distribution of risk score estimates differed significantly, with the PE group scoring higher than the control group. For the 10-year risk estimate method no woman scored higher than 9%; therefore, it was found that the suggested cut-off value of $\geq 10\%$ for further follow-up or intervention may be inappropriate in this population. However, the JUPITER study[13] indicates individuals with a risk $\geq 5\%$ may benefit from intervention; therefore, this was considered as an alternative cut-off value. The mid-*P* exact chi-square test for each of the risk estimate methods demonstrates that significantly more women in the PE group met or exceeded the risk scores proposed as cut-off values for further follow-up or intervention ($P < 0.005$). We identified 18.2% of women in the PE group and 1.7% of women in the control group as having a high 10-year risk (i.e., > 5%) (OR 13.08; 95% CI 3.38 to 85.5), 31.3% of women in the PE group and 5.1% of women in the control group as having a high 30-year risk (i.e., > 10%) (OR 8.43; 95% CI 3.48 to 23.23), and 41.4% of women in the PE group and 17.8% of women in the control group as having a high lifetime risk (i.e., > 39%) (OR 3.25; 95% CI 1.76 to 6.11). With respect to lifetime risk, the majority of control women who were classified as being at high risk were classified as such because of a history of smoking, unlike the PE group. Control and PE 10- and 30-year risk scores and the proportion of women in each group with a high lifetime risk of CVD at one year postpartum are shown in the Figure. Baseline and one-year

Table 1. Baseline demographic characteristics of preeclamptic and control women who were seen at one year postpartum and of those lost to follow-up

	Subjects followed at one year		Subjects lost to follow-up at one year	
	Preeclampsia (n = 99)	Control subjects (n = 118)	Preeclampsia (n = 40)	Control subjects (n = 35)
Maternal age (y), mean (SD)	30.3 (5.7)	30.3 (4.1)	27.4 (5.6)	29.3 (4.4)
Maternal race, n (%)				
White	95 (96.0)	118 (100.0)	32 (80.0)	33 (94.0)
Other	4 (4.0)	0 (0.0)	8 (20.0)	2 (6.0)
Maternal education level, n (%)				
High school or less	16 (16.1)	5 (4.2)	11 (27.5)	6 (17.1)
Postsecondary not complete	9 (9.1)	17 (14.4)	4 (10.0)	5 (14.3)
Postsecondary complete	74 (74.8)	96 (81.4)	25 (62.5)	24 (68.6)
Household income ($), n (%)				
≤ 29 999	8 (8.3)	8 (7.0)	10 (25.0)	4 (11.4)
30 000 to 59 999	21 (21.9)	17 (14.9)	14 (35.0)	6 (17.1)
60 000 to 89 999	29 (30.2)	30 (26.3)	8 (20.0)	7 (20.0)
≥ 90 000	38 (39.6)	59 (51.8)	6 (15.0)	15 (42.9)
Did not respond	3 (3.0)	4 (3.9)	2 (5.0)	3 (8.6)
Maternal smoking, n (%)				
Yes	9 (9.1)	5 (4.2)	8 (20.0)	7 (20.0)
No	90 (90.9)	113 (95.8)	32 (80.0)	28 (80.0)
Parity, n (%)				
Nulliparous	64 (64.6)	73 (61.9)	23 (57.5)	17 (48.6)
Multiparous	35 (35.4)	45 (38.1)	17 (42.5)	18 (51.4)
Previous pregnancy with PE, n (%)				
Yes	8 (8.1)	0 (0.0)	7 (17.5)	0 (0.0)
No	91 (91.9)	118 (100.0)	33 (82.5)	35 (100.0)
Maternal weight (kg), mean (SD)	71.3 (15.7)	70.1 (14.8)	73.9 (18.5)	66.1 (10.6)
Maternal BMI (kg/m^2), mean (SD)	26.7 (5.7)	25.5 (5.1)	28.2 (7.5)	23.9 (3.6)

characteristics of the control and PE women who were classified either as having a high lifetime risk or having a low lifetime risk of CVD were compared (data not shown). In women with PE at the time of delivery, their smoking status, average pre-pregnancy BMI, and proportion with a pre-pregnancy BMI ≥ 30 differed between those with a high lifetime and those with a low lifetime risk; preterm birth (< 34 or < 37 weeks' gestation), IUGR, and other markers of severity of PE did not differ. At the time of the one-year follow-up, differences were noted between these two groups in their systolic and diastolic blood pressure, use of antihypertensive medication, total serum cholesterol, serum LDL cholesterol, serum triglycerides, average BMI, and proportion with BMI ≥ 30. In control subjects, only smoking status differed between those with a high lifetime and those with a low lifetime risk. At the one-year follow-up, differences were also noted in total serum cholesterol and serum LDL cholesterol.

DISCUSSION

Cardiovascular disease risk scoring is routinely used in older men and women to predict the risk of atherosclerosis and/or major cardiovascular events within a given period of time.[14] However, the short-term (10-year) risk estimate scores (e.g., the Framingham Heart Study[10] and Reynolds Risk Score[15]) and longer-term (30-year) risk estimate score[11] place significant weight on age in predicting absolute risk; therefore, typically only older patients exceed thresholds for treatment in guidelines. This emphasis on age obscures the important contributions that modifiable risk factors make in young adults[14]; modestly elevated cardiovascular risk factors in young adults may have little effect on short-term risk but can substantially elevate lifetime risk for cardiovascular disease. It could be argued that it is appropriate not to intervene until an individual either manifests any cardiovascular risks or reaches the age at

Table 2. Variables utilized in each method of cardiovascular disease risk estimation

	10-year risk[10]	30-year risk[11]	Lifetime risk[14]
Sex	X	X	X
Age	X	X	
Smoking	X	X	X
BMI	X		
Serum total cholesterol		X	X
Serum LDL cholesterol	X		
Serum HDL cholesterol	X		
Fasting plasma glucose	X	X	X
Systolic blood pressure	X	X	X
Diastolic blood pressure			X
Antihypertensive usage	X	X	X

Table 3. Ten-year, thirty-year, and lifetime risk of cardiovascular disease at one-year postpartum for women who did or did not have a pregnancy complicated by preeclampsia

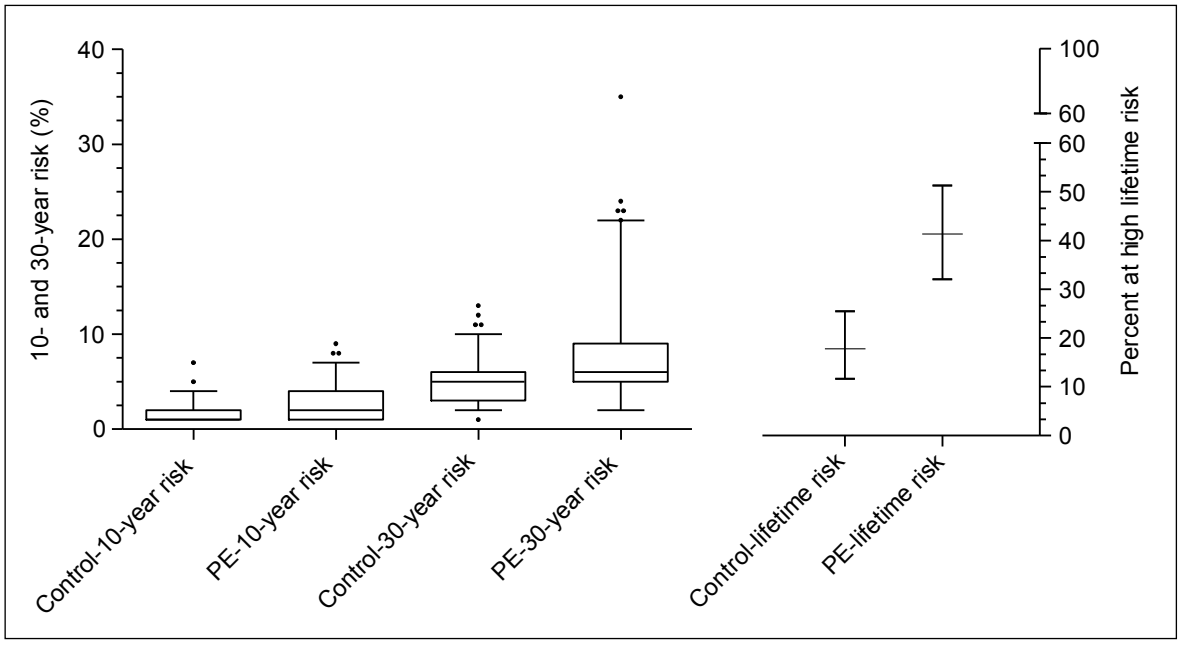
Statistical test	Sample size	Number of women with elevated risk scores	*P*	OR (95% CI)
10-year risk				
2-group Mann-Whitney *U* test	PE = 97 Control subjects = 118		< 0.001	
Chi-square CVD risk score < 5% vs. ≥ 5%	PE = 97 Control subjects = 118	n = 18 n = 2	< 0.005	13.08 (3.38 to 85.5)
Chi-square CVD risk score < 10% vs. ≥ 10%	PE = 97 Control subjects = 118	n = 0 n = 0	NA	NA
30-year risk				
2-group Mann-Whitney *U* test	PE = 99 Control subjects = 118		< 0.001	
Chi-square CVD risk score < 10% vs. ≥ 10%	PE = 99 Control subjects = 118	n = 31 n = 6	< 0.005	8.43 (3.48 to 23.23)
Lifetime risk				
2-group Mann-Whitney *U* test	PE = 99 Control subjects = 118		< 0.001	
Chi-square lifetime CVD risk score ≤ 27% vs. ≥ 39%	PE = 99 Control subjects = 118	n = 41 n = 21	< 0.001	3.25 (CI 1.76 to 6.11)

NA: not applicable

which the 10-year CVD risk exceeds 5% or 10%. However, this approach results in clinicians treating adults who are older, who have had risk factors for a longer time, and who may have a greater burden of established atherosclerosis; such an approach does not reduce risk to the same extent as maintaining favourable risk factor levels throughout adulthood.[14]

We previously reported using 10-year risk scores to demonstrate that women who had a pregnancy complicated by PE were at greater risk for a significant cardiovascular event than women who had not had PE, although none met either a 5% or 10% cardiovascular risk score, which is the recommended level for further follow-up.[3] Ten-year risk scores for women who had a pregnancy complicated by a hypertensive disorder are also being proposed as part of the HyRAS Study,[16] and recently 10-year CVD risk scores were calculated 18 years after pregnancy in the Avon Longitudinal Study of Parents and Children.[17] In that study also, it was determined that women who had a pregnancy complicated by PE had increased calculated risks compared with control subjects, although the authors did not state

Different cardiovascular risk scores for control and preeclamptic women at one year postpartum. Ten- and 30-year risks of developing CVD (left-side y axis) are presented as box and whisker plots (± 95% CI) and proportion at high lifetime risk of CVD (right-side axis) is presented as a line with whiskers (± 95% CI) for control subjects (n = 118) and women with PE (n = 99) one year postpartum.



whether any of the women would have reached the threshold for intervention (a > 10% risk). In the present study, we demonstrated that there were significantly elevated 10-year, 30-year, and lifetime cardiovascular risk scores in the PE group compared with control subjects. There was also a greater chance of exceeding the 5% cut-off for the 10-year risk[13] (OR 13.08; 95% CI 3.38 to 85.5), the 10% cut-off for the 30-year risk [11] (OR 8.43; 95% CI 3.48 to 23.23), and the 39% cut-off for the lifetime risk[12] (OR 3.25; 95% CI 1.76 to 6.11) for women with PE compared to control subjects. The sample size was not sufficient to compare risk estimates for subgroups of women with PE (e.g., first time vs. recurrent cases, severe vs. mild, or early onset vs. late onset).

Large retrospective database studies[7,8] have suggested that there are different subgroups within the population of women with PE in terms of future CVD risk. Women with PE who deliver prematurely, have a growth-restricted baby, or have a pregnancy complicated by placental abruption are examples of subgroups with an apparent increased CVD risk. We did not observe a difference in these subgroups between women who were found to be at high lifetime risk of CVD and women at low lifetime risk. Similarly, the Avon Longitudinal Study[17] did not identify a difference in 10-year risk scores between the different subsets of women with hypertensive disorders of pregnancy. Both the Avon Longitudinal Study and our study are limited by sample size and length of postpartum follow-up; only a very large long-term longitudinal study of such women would have the statistical power to demonstrate subgroup differences if they exist. Such a study would need to include ethnicity as a variable, because some ethnic groups have a greater risk of both PE and cardiovascular disease.[4]

This study has a number of limitations. Firstly, this is a secondary analysis of data from an ongoing cohort study, and the statistical power of the study may be limited with the current sample size. Secondly, CVD risk scoring systems were originally developed using older populations of men and women, and they may not be directly applicable to younger populations of women. Furthermore, the lifetime risk scoring system was based on a study population at 50 years of age, which may actually underestimate the lifetime risk when used in significantly younger individuals; the average age of the women in our cohort was 30 years. It would require a very long-term follow-up of a large cohort of postpartum women to determine alternate cut-offs for 10-year, 30-year, or lifetime risk estimates for major cardiovascular events.

Approximately 80% of cardiovascular disease is largely preventable through lifestyle modification and/or pharmacotherapy[18]; early identification of individuals at risk and subsequent screening would go a long way

towards achieving this goal. For the majority of women of reproductive age, pregnancy and the postpartum period provides an opportunity to identify risk factors early and to improve their long-term health. Because the lifetime cardiovascular disease risk score identified a larger proportion of women with PE who are at increased risk of future cardiovascular disease than did either the 10-year or 30-year risk scores, we feel that this is the scoring method that should be considered for women postpartum.

Given that pregnant women access the health-care system regularly and are perhaps seen by a health-care provider for the first time, pregnancy is an ideal time to identify young women at future risk for CVD to initiate health preservation and disease prevention strategies.

ACKNOWLEDGEMENTS

Funding for the PE-NET cohort was provided by the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Canada.

The authors wish to thank Heather Ramshaw, Michelle Roddy, and Ruth White for their dedicated assistance in recruitment, follow-up, and data collection.

REFERENCES

1. Williams D. Pregnancy: a stress test for life. Curr Opin Obstet Gynecol 2003;15:465–71.
2. Smith GN. The development of pre-eclampsia provides a window of opportunity for early cardiovascular risk screening and intervention. Expert Rev Obstet Gynecol 2009;4:355–7.
3. Smith GN, Walker M, Liu A, Wen SW, Swansburg M, Ramshaw H, et al. A history of preeclampsia identifies women who have underlying cardiovascular risk factors. Am J Obstet Gynecol 2009;200:58.e1–e58.e8.
4. Smith GCS, Pell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129,290 births. Lancet 2001;357:2002–6.
5. Retnakaran R. Glucose tolerance status in pregnancy: a window to the future risk of diabetes and cardiovascular disease in young women. Curr Diabetes Rev 2009;5:239–44.
6. Retnakaran R, Shah BR. Mild glucose intolerance in pregnancy and risk of cardiovascular disease: a population-based cohort study. CMAJ 2009;181:371–6.
7. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. Lancet 2005;366:1797–803.
8. Irgens HU, Reisaeter L, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. BMJ 2001;323:1213–7.
9. Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, Lloyd-Jones D, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update. J Am Coll Cardiol 2011;57:1404–23.
10. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain MR, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The Framingham Heart Study. Circulation 2008;117:743–53.
11. Pencina MJ, D'Agostino RB, Larson MG, Massaro JM, Vasan RS. Predicting the 30-year risk of cardiovascular disease: the Framingham Heart Study. Circulation 2009;119:3078–84.
12. Lloyd-Jones D, Leip EP, Larson MG, D'Agostino RB, Beiser AS, Wilson PW, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. Circulation 2006;113:791–8.
13. Ridker PM, Macfadyen JG, Nordestgaard BG, Koenig W, Kastelein JJ, Genest J, et al. Rosuvastatin for primary prevention among individuals with elevated high-sensitivity c-reactive protein and 5% to 10% and 10% to 20% 10-year risk. Implications of the Justification for Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial for "intermediate risk". Circ Cardiovasc Qual Outcomes 2010;3:447–52.
14. Lloyd-Jones D. Short-term versus long-term risk for coronary artery disease: implications for lipid guidelines. Curr Opin Lipidol 2006;17:619–25.
15. Ridker PM, Buring JE, Rifai N. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: The Reynolds Risk Score. JAMA 2007;297:611–9.
16. Hermes W, Franx A, van Pampus MG, Bloemenkamp KW, van der Post JA, Porath M, et al. 10-year cardiovascular event risks for women who experienced hypertensive disorders in late pregnancy: the HyRAS study. BMC Pregnancy Childbirth 2010;10:28.
17. Fraser A, Nelson SM, Macdonald-Wallis C, Cherry L, Butler E, Sattar N, et al. Association of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: The Avon Longitudinal Study of Parents and Children. Circulation 2012;125:1367–80.
18. Smith ER. Canadian heart health strategy and action plan (CHHS-AP). 2010. Available at: http://www.chhs.ca. Accessed July 5, 2011.