Original Article

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Associations of polygenic risk scores for preeclampsia and blood pressure with hypertensive disorders of pregnancy

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Background: Preexisting hypertension increases risk for preeclampsia. We examined whether a generic blood pressure polygenic risk score (BP-PRS), compared with a preeclampsia-specific polygenic risk score (PE-PRS), could better predict hypertensive disorders of pregnancy.

Methods: Our study sample included 141 298 genotyped FinnGen study participants with at least one childbirth and followed from 1969 to 2021. We calculated PRSs for SBP and preeclampsia using summary statistics for greater than 1.1 million single nucleotide polymorphisms.

Results: We observed 8488 cases of gestational hypertension (GHT) and 6643 cases of preeclampsia. BP-PRS was associated with GHT [multivariable-adjusted hazard ratio for 1SD increase in PRS (hazard ratio 1.38; 95% CI 1.35–1.41)] and preeclampsia (1.26, 1.23–1.29), respectively. The PE-PRS was also associated with GHT (1.16; 1.14–1.19) and preeclampsia (1.21, 1.18–1.24), but with statistically more modest magnitudes of effect ($P = 0.01$). The model c-statistic for preeclampsia improved when PE-PRS was added to clinical risk factors ($P = 4.6 \times 10^{-15}$). Additional increment in the c-statistic was observed when BP-PRS was added to a model already including both clinical risk factors and PE-PRS ($P = 1.1 \times 10^{-14}$).

Conclusion: BP-PRS is strongly associated with hypertensive disorders of pregnancy. Our current observations suggest that the BP-PRS could capture the genetic architecture of preeclampsia better than the current PE-PRSs. These findings also emphasize the common pathways in the development of all BP disorders. The clinical utility of a BP-PRS for preeclampsia prediction warrants further investigation.

Keywords: blood pressure, genetics, hypertension, polymorphism, preeclampsia, pregnancy-induced, risk factors, single nucleotide

Abbreviations: BP, blood pressure; BP-PRS, blood pressure polygenic risk score; CI, confidence interval; CS, continuous shrinkage; CVD, cardiovascular disease; DNA, deoxyribonucleic acid; FIMM, Institute for Molecular Medicine Finland; GHT, gestational hypertension; GWAS, genome-wide association study; ICD, International Classification of Diseases; IDI, Integrated Discrimination Index; IVF, in-vitro fertilization; NRI, Net Reclassification Index; PCA, principal component analysis; PE-PRS, Preeclampsia Polygenic Risk Score; PRS, Polygenic Risk Score; SD, standard deviation; SNP, single nucleotide polymorphism

INTRODUCTION

Preeclampsia is a leading cause of maternal and fetal morbidity and mortality worldwide, especially in low-income countries [1,2]. Preeclampsia is characterized by *de novo* hypertension during pregnancy after 20 weeks of gestation with proteinuria or other end-organ complications [3]. In women with chronic hypertension, which precedes pregnancy or develops prior to 20 weeks of gestation, superimposed preeclampsia can occur. Apart from these more serious conditions, new onset of hypertension in pregnancy without proteinuria is more common and is referred to as gestational hypertension (GHT). Chronic hypertension during pregnancy, GHT, preeclampsia, chronic

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hypertension with superimposed preeclampsia and eclampsia are collectively referred to as hypertensive disorders of pregnancy [3].

Considerable overlap and fluidity of diagnoses exist between various hypertensive disorders of pregnancy. For example, chronic hypertension diagnosed before pregnancy is an independent risk factor for preeclampsia [4]. On the other hand, preeclampsia is associated with an increased risk of chronic hypertension and cardiovascular disease later in life [5,6]. Prior data suggest that this overlap may be partly driven by genetic factors, as chronic hypertension has been associated with several autosomal single nucleotide polymorphisms (SNPs) [7]. A recent meta-analysis on genome-wide association studies (GWASs) for preeclampsia also identified five maternal genetic variants previously associated with chronic hypertension [8]. In addition, a polygenic risk score (PRS) for hypertension was associated with an increased risk of preeclampsia [8]. In a recent study by Kivioja *et al.* [9], a high BP-PRS score was associated with preeclampsia and especially its more severe forms. However, the associations between genetic propensity for chronic hypertension and other hypertensive disorders of pregnancy disorders remain unknown. In addition, the added predictive value of a blood pressure-specific PRS (BP-PRS) versus a preeclampsia-specific PRS (PE-PRS) is unclear.

Our aim was to examine the common genetic background between chronic hypertension and hypertensive disorders of pregnancy. In this study, we investigated the association of a blood pressure-specific PRS (BP-PRS); preeclampsia-specific PRS (PE-PRS); and clinical risk factors with hypertensive disorders of pregnancy. We also compared the predictive ability of these risk factors in more than 140 000 previously pregnant FinnGen study participants.

METHODS

Study sample

Our cohort study sample consisted of 210 870 genotyped Finnish women from the FinnGen Data Freeze 9, which included participants from Finnish cohort studies and patients from national hospital biobanks [10]. Of these, 141 298 had given birth and were selected for further analysis. All participants provided written informed consent. This study protocol was approved by The Coordinating Ethical Committee of the Hospital District of Helsinki and Uusimaa, as described in the Supplemental Methods, http://links.lww.com/HJH/C113.

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be submitted through the Finnish Biobanks' Finngenious portal (https://site.fingenious.fi/en/) for longitudinal and genetic data.

Genotyping and polygenic risk scores

The collected DNA samples in FinnGen study were genotyped with Illumina (Illumina Inc., San Diego, California, USA) and Affymetrix (Thermo Fisher Scientific, Santa Clara, California, USA) arrays and genotype calls were made with zCall or GenCall algorithms (for Illumina) and AxiomGT1 algorithm (for Affymetrix) at the Institute for Molecular Medicine Finland (FIMM). Quality control exclusions were performed first sample-wise: ambiguous gender, high genotype missingness greater than 5%, excess heterozygosity greater than ±4SD, or non-European ancestry; and second, variant-wise: missingness greater than 2%, low Hardy–Weinberg equilibrium P less than 1×10^{-6}, minor allele count less than 3, were excluded. After quality control, the samples were prephased with Eagle 2.3.5 with default parameters and then genotypes were imputated with Beagle 4.1 (version 08Jun17.d8b) using a Finnish population-specific SISu v3 reference panel. Finally, to account for population structure in downstream analyses, genetic principal component analysis (PCA) was performed using a pruned set of SNPs of unrelated individuals. Detailed documentation of genotyping, imputation, and principal component analysis is available online [11].

BP-PRSs and PE-PRS were computed using the PRS-CS [12] pipeline with default parameters. PRS-CS computes SNP effect sizes by high-dimensional Bayesian regression with continuous shrinkage priors using the obtained GWAS summary statistics and a linkage disequilibrium reference panel. The summary statistics for SBP was obtained from UK Biobank [13,14] and it was based on 182 645 women. Preeclampsia summary statistics were obtained from previously published meta-analysis made by Genetics of Pre-Eclampsia Consortium [8]. However, to avoid potential overfitting because of Finnish participants in the GWAS, we obtained GWAS summary statistics from the authors of this report without the Finnish individuals included. Thus, the summary statistics for preeclampsia was based on 9115 cases of preeclampsia and 149 914 controls. The European linkage disequilibrium reference panel with 1.1 million variants was derived from samples of the 1000 Genomes Project [15]. The BP-PRS and PE-PRSs were based on 1 098 015 genetic variants common in the linkage disequilibrium reference panel and FinnGen.

Register-based outcomes

The calculated individual-level PRSs were linked to register-based predictors and outcomes using personal national identification codes. Every Finnish permanent resident is linked to National Hospital Discharge (from 1968) and Cause of Death (from 1969) Registers, which makes follow-up possible for all major clinical end points, including preeclampsia and GHT. Birth data was obtained from the Medical Birth and Population Information Registers, while disease events were retrieved from the Hospital Discharge and Causes-of-death Registers. The quality of the diagnoses in the Hospital Discharge and Causes-of-Death Registers is good and has been described in detail previously [16]. The clinical diagnoses in the registers are based on ICD codes made by the attending primary or secondary care physician and the definitions of the diagnoses used in this study are described in detail in the Supplementary Table S1, http://links.lww.com/HJH/C113. The following outcomes were used: GHT and preeclampsia. In analyses that assessed improvement in model fit, the variables included in the clinical model (age, obesity, hypertension, diabetes, gestational diabetes, multifetal pregnancy, in-vitro fertilization pregnancies, and renal insufficiency) were drawn from the same registers (Supplementary Table S1, http://links.lww.com/HJH/C113).

Statistical analyses

We used Cox proportional hazards model to assess the association between a 1SD increase in BP-PRS or PE-PRS and the outcomes. We also performed a sensitivity analysis by analyzing the individuals with and without a diagnosis of hypertension prior to the index pregnancy separately. The magnitudes of associations between different PRSs and outcomes were compared with Student's *t* test. The follow-up spanned from 1969 to 2021. An individual participant was censored only once at the first encountered episode of preeclampsia or GHT. Both cases and controls were censored at death or at the end of follow-up (age 55 or 11 October 2021). Age was considered as the timescale and we used collection year, genotyping batch, and the first 10 genetic principal components as covariates in all models. The proportional hazards assumption was validated by visual inspection of log-minus-log plots because of the large sample size.

Furthermore, we categorized the participants by their PRS-count percentiles (<2.5, 2.5–20, 20–80, 80–97.5, >97.5) and denoted the middle bin (20–80%) as the referent category. We then used Cox proportional hazards model for the four remaining categories to investigate the associations for preeclampsia and GHT using mother age as a timescale.

To include age at pregnancy as a covariate, we used logistic regression-based c-statistic to compare the predictive ability of three alternative models for predicting preeclampsia: clinical model, which included age at pregnancy, plus the following variables known to associate with preeclampsia: obesity, hypertension, diabetes, gestational diabetes, multifetal pregnancy, in-vitro fertilization, and renal insufficiency [17]; clinical model + PE-PRS; and clinical model + PE-PRS + BP-PRS. Previous preeclampsia was not included in the clinical model as we focused on the risk of first preeclampsia. Family history of preeclampsia was not included in the clinical model as this information was not available. All covariates included in the clinical model were observed before the outcome event of the index pregnancy. Also, pregnancy-related covariates were linked with the index pregnancy.

We also calculated the net reclassification index (NRI) and the integrated discrimination index (IDI) to further assess improvement in reclassification and risk discrimination. We used an 8% risk threshold for the categorical NRI, consistent with the lowest preeclampsia incidence observed in control groups in studies reviewed by a recent US Preventive Services Task Force Recommendation Statement [18]. Further, we assessed the variance explained by the models by calculating the pseudo-R-squared with the McKelvey–Zavoina method. We considered two-tailed *P* values of 0.05 as statistically significant and used R v.4.2.1 for all analyses.

RESULTS

Our study sample consisted of 141 298 women with childbirth with a mean age of 27.1 ± 5.2 years at time of first delivery. The characteristics of the study sample are shown in Table 1. We observed 8488 cases (6.1%) of GHT and 6643 cases (4.9%) of preeclampsia.

Both BP-PRS and PE-PRS were associated with GHT and preeclampsia (Table 2). For the BP-PRS, the hazard ratios for GHT and preeclampsia were 1.38 (95% CI 1.35–1.41; $P = 8.8 \times 10^{-194}$) and 1.26 (95% CI 1.23–1.29; $P = 3.5 \times 10^{-78}$), respectively. For PE-PRS, the corresponding hazard ratios were more modest – 1.16 (95% CI 1.14–1.19; $P = 1.5 \times 10^{-44}$), and 1.21 (95% CI 1.18–1.24; $P = 1.2 \times 10^{-55}$), respectively. The associations of BP-PRS with GHT and preeclampsia was stronger than those observed between PE-PRS and the clinical outcomes ($P < 0.01$ for all).

We also performed the analyses separately for individuals with and without a diagnosis of hypertension prior to the index pregnancy. We observed that the BP-PRS was associated with future eclampsia among the 135 687 individuals without a diagnosis of hypertension [6471 cases; hazard ratio 1.26 (95% CI 1.23–1.29)], but not among the 667 individuals who had hypertension [172 cases; hazard ratio 1.01 (95% CI 0.88–1.17)]. The results were similar for PE-PRS [hazard ratio 1.21 (95% CI 1.18–1.24) vs. hazard ratio 1.10 (95% CI 0.94–1.29)].

The analyses examining the association of PRS quantiles and GHT and preeclampsia are reported in Fig. 1 and Table 3. For GHT, the spread of hazard ratios between the low-risk and high-risk categories was wider when BP-PRS category was used as the exposure variable, as compared with the PE-PRS category (Fig. 1).

We then assessed the improvements in risk discrimination and reclassification when the PE-PRS and/or the BP-PRS were included in a model with known clinical preeclampsia risk factors (Table 4). The addition of PE-PRS in the clinical model significantly increased the c-statistic (c-statistic increment

TABLE 1. The characteristics of the study sample by outcome status

Characteristic	Gestational hypertension		Preeclampsia	
	Yes	No	Yes	No
n	8488	129 829	6643	129 711
Age (mean ± SD)	30.1 ± 5.7	27.1 ± 5.1	29.1 ± 5.7	27.1 ± 5.1
Multifetal pregnancy [*n* (%)]	216 (2.5)	1581 (1.2)	288 (4.3)	1553 (1.2)
IVF [*n* (%)]	16 (0.2)	163 (0.1)	11 (0.2)	163 (0.1)
Hypertension [*n* (%)]	273 (3.2)	470 (0.4)	172 (2.6)	495 (0.4)
Obesity [*n* (%)]	310 (3.7)	891 (0.7)	166 (2.5)	897 (0.7)
Diabetes [*n* (%)]	1186 (14.0)	5633 (4.4)	904 (13.6)	5616 (4.3)
Renal failure [*n* (%)]	8 (0.1)	38 (0.03)	8 (0.1)	38 (0.03)

Characteristics for the controls are reported at the time of first pregnancy. Gestational diabetes is included to the diabetes. IVF, in-vitro fertilization.

TABLE 2. Association of polygenic risk scores for blood pressure with hypertensive disorders of pregnancy

			Blood pressure PRS		Preeclampsia PRS		
Endpoint	Cases	Controls	HR (95% CI)	*P* value	HR (95% CI)	*P* value	*P* value for HR difference
Gestational hypertension	8488	129 829	1.38 (1.35–1.41)	8.8×10^{-194}	1.16 (1.14–1.19)	1.5×10^{-44}	1.7×10^{-31}
Preeclampsia	6643	129 711	1.26 (1.23–1.29)	3.5×10^{-78}	1.21 (1.18–1.24)	1.2×10^{-55}	0.01

We adjusted the models for collection year, genotyping batch, and the first 10 genetic principal components. Hazard ratios are reported per 1SD increment in polygenic risk score. CI, confidence interval; HR, hazard ratio; PRS, polygenic risk score.

0.015; 95% CI 0.011–0.018; $P = 4.6 \times 10^{-15}$). However, including the BP-PRS among the predictor variables resulted in an additional improvement in the c-statistic (0.013; 95% CI 0.001–0.017, $P = 1.1 \times 10^{-14}$). Also, the strength of the associations of both PRSs with preeclampsia remained similar when clinical covariates were included in the same model (Table S2, http://links.lww.com/HJH/C113). The NRI and IDI increased significantly ($P = 4.5 \times 10^{-5}$ and 6.2×10^{-32}, respectively) when the PE-PRS was included in the clinical model. However, additional increase was observed in NRI and IDI when BP-PRS (NRI = 0.023, $P = 7.8 \times 10^{-13}$, IDI = 0.0029, $P = 4.1 \times 10^{-41}$) was added in the model that included the clinical variables and the PE-PRS. Variances of the Cox models assessed with the pseudo-R^2 were 5.5% for the clinical model, 6.6% for the clinical + PE-PRS -model and 8% for the clinical + PE-PRS + BP-PRS model (Table 4).

DISCUSSION

In a study sample of 141 298 women with childbirth, we demonstrate that BP-PRS is strongly associated with preeclampsia and that this association is even stronger for GHT (Table 2). Our current observations suggest a strong common genetic background for chronic hypertension, preeclampsia, and hypertensive disorders of pregnancy.

Epidemiological studies have demonstrated that maternal, paternal, and fetal components of the genetic susceptibility for preeclampsia exist [19,20]. Our results elucidate that this susceptibility may be partially driven by BP, a strongly polygenic trait [21–28]. The relation between high BP and hypertensive disorders of pregnancy has also been observed in epidemiological studies in which chronic hypertension diagnosed before pregnancy was related to fivefold increase in the risk of preeclampsia [4,17].

Prior maternal GWASs on preeclampsia have discovered associations with several genetic variants that are also associated with BP [8,29]. Moreover, an association between a PRS for hypertension and preeclampsia has also been formerly identified by a meta-analysis of 9515 preeclamptic women and 157 719 controls from five cohorts [8]. In a recent smaller study of 1514 preeclamptic individuals and 983 controls, a BP-PRS above the 95th percentile was associated with 1.7-fold greater odds of preeclampsia and especially its more severe forms. However, this association was not statistically significant after adjustment for the first antenatal blood pressure measurement [9]. This risk increase is similar to that observed for a BP-PRS in the top 2.5 percentile in our study. However, over 95% of individuals in our study were normotensive before the index pregnancy. Our results expand these prior results by providing a comprehensive analysis on the associations between a BP-PRS and hypertensive disorders of pregnancy in a relatively unselected cohort over a follow-up period spanning 50 years.

The exact mechanism of the observed common genetic background for preeclampsia, chronic hypertension, and future cardiovascular disease (CVD) risk remains still unclear. Preeclampsia is an independent risk factor for several cardiovascular diseases later in life including chronic hypertension, stroke, coronary artery disease, and heart failure [5,30–32]. However, it is debated, whether the defective placentation followed by maternal manifestations leads to permanent alterations in the vasculature and increased CVD risk, or whether there are an underlying maternal susceptibility for preeclampsia, hypertension, and CVD that is unveiled by the pregnancy [33–35]. It is clear that several pathogenetic mechanisms of preeclampsia exist apart from genetic hypertension risk, such as

TABLE 3. Risk of hypertensive disorders of pregnancy by blood pressure and preeclampsia polygenic risk score bins

	Blood pressure PRS				Preeclampsia PRS			
PRS (%)	Cases	Controls	HR (95% CI)	*P* value	Cases	Controls	HR (95% CI)	*P* value
Gestational hypertension								
<2.5%	103	3369	0.51 (0.42–0.62)	1.7×10^{-11}	151	3319	0.75 (0.64–0.88)	4.2×10^{-4}
2.5–20%	974	23 418	0.69 (0.64–0.74)	1.2×10^{-26}	1288	23 026	0.90 (0.85–0.96)	6.4×10^{-4}
20–80%	4815	77 990	–	–	4913	78 031	–	–
80–97.5%	2169	22 034	1.55 (1.47–1.63)	3.4×10^{-64}	1814	22 323	1.26 (1.20 -1.33)	1.3×10^{-17}
>97.5%	427	3018	2.17 (1.96–2.39)	7.8×10^{-53}	322	3130	1.58 (1.41–1.77)	1.4×10^{-15}
Preeclampsia								
<2.5%	77	3368	0.46 (0.37–0.57)	1.3×10^{-11}	98	3335	0.60 (0.49–0.74)	7.7×10^{-7}
2.5–20%	878	23 344	0.75 (0.70–0.81)	2.2×10^{-14}	954	23 049	0.84 (0.78–0.90)	9.2×10^{-7}
20–80%	3928	77 819	–	–	3867	77 900	–	–
80–97.5%	1518	22 110	1.34 (1.27–1.43)	1.7×10^{-22}	1456	22 311	1.30 (1.22–1.38)	2.1×10^{-17}
>97.5%	242	3070	1.53 (1.35–1.74)	1.3×10^{-10}	268	3116	1.68 (1.49–1.90)	2.0×10^{-16}

CI, confidence interval; HR, hazard ratio; PRS, polygenic risk score. We adjusted the models for collection year, genotyping batch, and the first 10 genetic principal components.

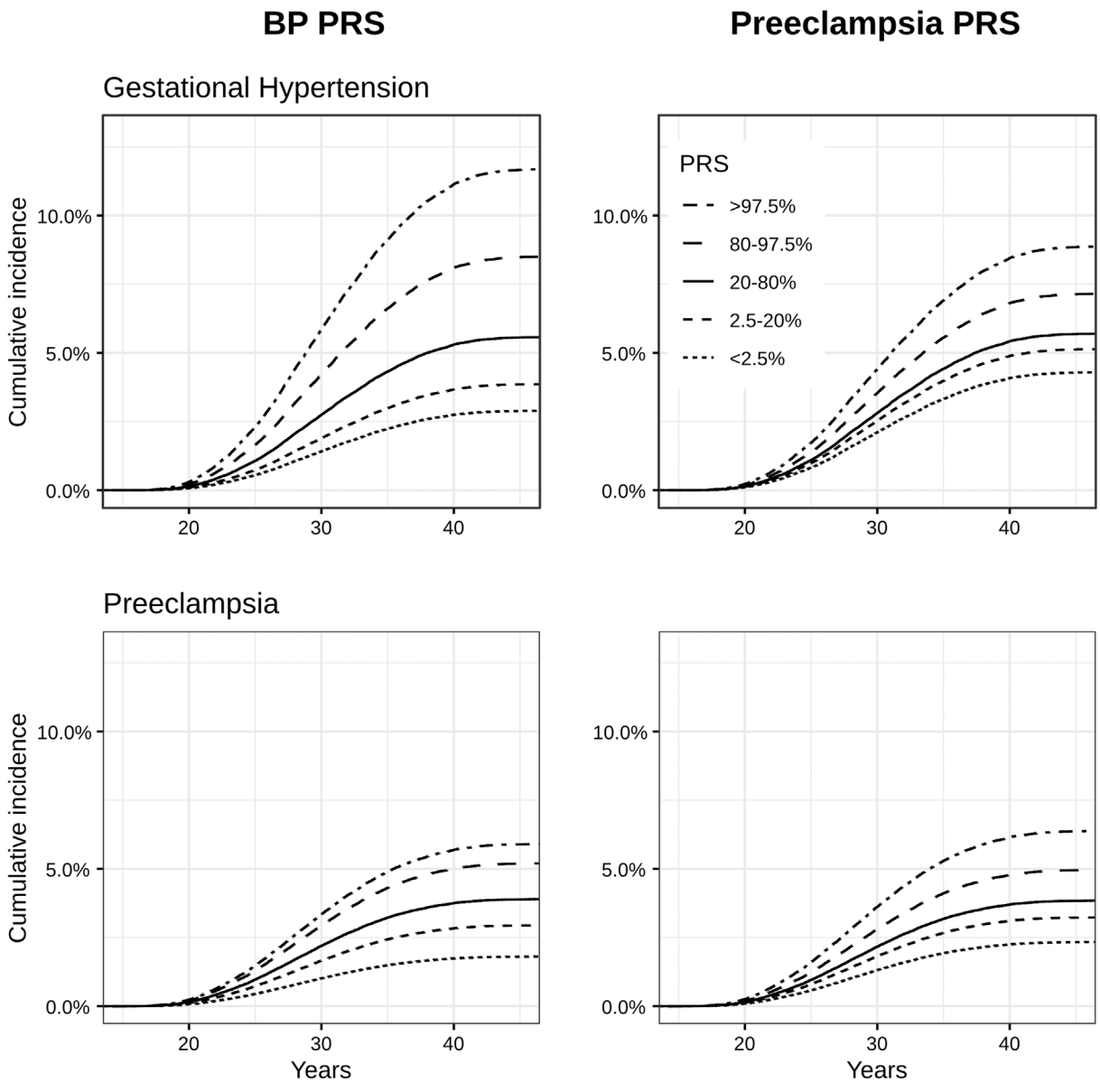

FIGURE 1 Cumulative incidence of hypertensive disorders of pregnancy by blood pressure and preeclampsia polygenic risk score bins. The survival curves are from Cox proportional hazards models. We adjusted the models for collection year, genotyping batch and the first 10 genetic principal components. BP, blood pressure; PRS, polygenic risk score.

defective spiral artery modelling, systemic inflammation, and immunologic response [36]. These mechanisms may also differ between early and late preeclampsia [36]. However, as the clinical [17], epidemiological [19], and genetic links [8,29,36] between preeclampsia and hypertension have been demonstrated, hypertension is clearly one of the major contributors to risk of preeclampsia. Our study with BP-PRS enforces the approach that there is a preexisting maternal genetic influence behind both preeclampsia and chronic hypertension with the latter being known, strong risk factor for CVD.

Compared with PE-PRS, the association between BP-PRS and hypertensive disorders of pregnancy was stronger. Several prior GWASs have identified genetic variants related to preeclampsia [29,37–40], but genetic risk scores based on preeclampsia-related SNPs have produced only modest results [41,42]. In this article, we demonstrate that using a BP-PRS to predict hypertensive disorders of pregnancy is equal or even better than conventional approach of using a PE-PRS as the predictor. However, these findings applied only to women who were nonhypertensive before the index pregnancy. Possible explanations on the lack of associations in the hypertensive individuals include the low number of individuals with hypertension preceding pregnancy and the confounding effects of antihypertensive therapy among the hypertensive individuals [43,44].

Further, our results in c-statistic, NRI, IDI, and R^2 demonstrate that the improvement in risk prediction and discrimination of preeclampsia is only marginal when a PE-PRS is used (Table 4). In addition, an additional improvement in all these indices was observed when BP-PRS was included, even when a diagnoses of prior hypertension and other clinical risk

TABLE 4. Model fit, calibration, and discrimination statistics for different preeclampsia risk prediction models

	c-statistic			NRI				IDI		
Model	c-statistic	Increment (95% CI)	*P* value	NRI (95% CI)	*P* value	Correctly reclassified cases (%)	Correctly reclassified controls (%)	IDI (95% CI)	*P* value	Pseudo R^2 (%)
Clinical model[a]	0.634									5.5
Clinical model + preeclampsia PRS	0.649	0.015 (0.011–0.018)	4.6×10^{-15}	0.011 (0.006–0.017)	4.5×10^{-5}	4.3	11.6	0.0022 (0.0018–0.0025)	6.2×10^{-32}	6.6
Clinical model + preeclampsia PRS + blood pressure PRS	0.661	0.013 (0.001–0.017)	1.1×10^{-14}	0.023 (0.017–0.029)	7.8×10^{-13}	6.5	15.2	0.0029 (0.0024–0.0033)	4.1×10^{-41}	8.0

CI, confidence interval; IDI, integrated discrimination index; NRI, net reclassification index; PRS, polygenic risk score.
[a]Model includes age, hypertension, obesity, diabetes, gestational diabetes, multifetal pregnancies, in-vitro fertilization and renal failure. NRI cut off was set at 8%.

factors were already included in the model. Thus, BP-PRS could, therefore, be potentially used in clinical practice for assessing risk of preeclampsia.

Despite the strengths of our study, such as a large sample size, a standardized and reliable method for assessing a wide range of clinical outcomes, and application of a PRS derived from over 1.1 million SNPs, the results of our study must be interpreted within the context of potential limitations. First, we used outcome data from Finnish nationwide healthcare registers, which are generally complete and accurate, but may nevertheless lack the granularity of detailed clinical data [16]. However, this potential limitation is similar for both BP-PRS and PE-PRS and is, therefore, unlikely to have a major effect on our findings. Second, as in most GWAS, we analyzed only autosomal SNP variants, which may omit important genetic information from the sex chromosomes. Third, given that our sample constituted mainly of individuals of Northern European ancestry, further studies are needed to determine generalizability of findings to other groups. Fourth, some relevant preeclampsia risk factors, such as family history of preeclampsia, inflammation indices, and glomerular filtration rate were not available in the FinnGen data. Similarly, the prevalence of cardiovascular disease was too low for it to be included in the statistical models. Finally, as the diagnoses of hypertension and preeclampsia in our study are register-based and span five decades, we do not have information on the exact blood pressure measurement methods for each individual.

Perspectives

In conclusion, we demonstrate in a sample of more than 140 000 previously pregnant women that genetic autosomal polymorphism related to BP is strongly associated with increased risk of preeclampsia and gestational hypertension. In addition, this association appears to be stronger than what is observed for PE-PRS and preeclampsia. The exact mechanisms of this dual effect on the development of essential hypertension and preeclampsia and increased risk of cardiovascular disease later in life are unknown, but may point to a common pathway of development, which warrants further investigation. Furthermore, prospective trials are needed to evaluate the value of BP-PRSs as a clinical screening tool and to define clinically significant cutoff values for BP-PRS.

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Conflicts of interest

There are no conflicts of interest.

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