

高危妊娠专题

基于人工智能模型量化视网膜血管特征参数预测子痫前期的可行性研究

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[摘要] **目的**· 基于人工智能 (artificial intelligence, AI) 模型, 探讨视网膜血管特征参数在子痫前期 (preeclampsia, PE) 中的预测能力。 **方法**· 回顾性纳入 2020 年 6 月—2021 年 1 月在妊娠 16 周前于同济大学附属妇产科医院建卡、规律产检、行眼底图像拍摄并于该院分娩的 789 例单胎活产孕妇。根据孕妇是否发生妊娠期高血压疾病 (hypertensive disorders of pregnancy, HDP), 将其分为正常妊娠组 ($n=685$) 和 HDP 组 ($n=104$); 根据是否发生 PE, 将 HDP 组分为妊娠期高血压 (gestational hypertension, GH) 组 ($n=36$) 和 PE 组 ($n=68$); 且根据发病孕周, 将 PE 组分为早发型 PE 组 (发病孕周 <34 周) 和晚发型 PE 组 (发病孕周 ≥ 34 周)。获取入组孕妇的眼底图像, 利用 AI 算法诊断眼底病变特征、量化视网膜血管特征参数并对眼底特征、视网膜血管特征参数进行比较分析。采用单因素 Logistic 回归模型分析 PE 发生的影响因素, 并采用多因素 Logistic 回归模型进一步评估视网膜血管特征参数等与 PE 发生的相关性。采用受试者操作特征曲线 (receiver operator characteristic curve, ROC curve, ROC 曲线) 的曲线下面积 (area under the curve, AUC) 分析视网膜血管特征参数等对 PE (早发型 PE 和晚发型 PE) 的预测能力。 **结果**· 眼底特征及视网膜血管特征参数的分析结果显示, 正常妊娠组和 PE 组孕妇的视网膜中央动脉直径等效值 (central retinal artery equivalent, CRAE)、视网膜中央静脉直径等效值 (central retinal vein equivalent, CRVE)、视网膜动静脉比值 (arteriole-to-venular ratio, AVR)、视网膜动脉弯曲度和视网膜动脉分形维数间差异具有统计学意义 (均 $P<0.05$)。单因素 Logistic 回归分析显示, 孕中期平均动脉压 (mean arterial pressure, MAP)、孕中期胎儿估计体质量 (estimated fetal weight, EFW)、CRAE、CRVE、AVR、视网膜动脉弯曲度和视网膜动脉分形维数是 PE 发生的影响因素 (均 $P<0.05$)。多因素 Logistic 回归分析显示, 孕中期 EFW、CRAE、CRVE、AVR、视网膜动脉弯曲度和视网膜动脉分形维数是 PE 发生的保护因素, 孕中期 MAP 是其危险因素 (均 $P<0.05$)。ROC 曲线的分析结果显示, 母体危险因素+孕中期产检资料 (包括 MAP 和 EFW)+视网膜血管特征参数模型对 PE 预测能力较好 [AUC (95% CI)=0.784 (0.725–0.843)], 且其对早发型 PE 的预测能力更优 [AUC (95% CI)=0.840 (0.756–0.924)]。 **结论**· 使用基于 AI 模型量化的视网膜血管特征参数联合母体危险因素、孕中期产检资料 (包括 MAP 和 EFW) 能够较好地预测 PE (特别是早发型 PE) 的发生。

[关键词] 子痫前期; 视网膜血管; 人工智能**[DOI]** 10.3969/j.issn.1674-8115.2024.05.002 **[中图分类号]** R714.7 **[文献标志码]** A

Feasibility study on quantifying retinal vascular features for predicting preeclampsia based on artificial intelligence models

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[Abstract] **Objective**· To explore the predictive capability of retinal vascular features in preeclampsia (PE) based on artificial intelligence (AI) models. **Methods**· This retrospective study enrolled 789 pregnant women who registered from June 2020 to January 2021 at Shanghai First Maternity and Infant Hospital of Tongji University in the first 16 weeks of gestation. These women underwent regular prenatal examinations, had retinal fundus images captured, and delivered singleton live births at the hospital. According to whether they developed hypertensive disorders of pregnancy (HDP), they were divided into unaffected group ($n=685$) and HDP group ($n=104$). Within the HDP group, pregnancies were further categorized into gestational hypertension (GH) group ($n=$

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36) and PE group ($n=68$) based on the occurrence of PE. Based on the gestational age at onset, the PE group was further divided into early-onset PE group (gestational age <34 weeks) and late-onset PE group (gestational age ≥ 34 weeks). Fundus images of the pregnant women were obtained, and an AI algorithm was utilized to diagnose retinal lesions and quantify retinal vascular features. Comparative analyses were conducted on fundus features and retinal vascular features. Univariate Logistic regression model was employed to analyze the influencing factors of PE occurrence, and multivariate Logistic regression model was further utilized to assess the correlation between retinal vascular features and the occurrence of PE. The predictive capability of retinal vascular features for PE (both early- and late-onset PE) was analyzed by using area under the curve (AUC) of receiver operator characteristic curve (ROC curve). **Results** The comparative analysis of fundus features and retinal vascular features demonstrated statistically significant differences between the unaffected group and PE group in terms of central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE), arteriole-to-venular ratio (AVR), retinal artery tortuosity and retinal artery fractal dimension (all $P < 0.05$). Univariate Logistic regression analysis indicated that second-trimester mean arterial pressure (MAP), second-trimester estimated fetal weight (EFW), CRAE, CRVE, AVR, retinal artery tortuosity and retinal artery fractal dimension were the influencing factors for PE occurrence (all $P < 0.05$). Multivariate Logistic regression analysis revealed that second-trimester EFW, CRAE, CRVE, AVR, retinal artery tortuosity and retinal artery fractal dimension were the protective factors for the occurrence of PE, while second-trimester MAP was the risk factor for PE (all $P < 0.05$). The analysis of ROC curves revealed that maternal risk factors along with second-trimester prenatal examination data (including MAP and EFW) and retinal vascular features model had good predictive ability for PE [AUC (95% CI)=0.784 (0.725—0.843)], and this model exhibited better predictive capability for early-onset PE, with an AUC (95% CI) of 0.840 (0.756—0.924). **Conclusion** The integration of quantified retinal vascular features based on AI models with maternal risk factors and second-trimester prenatal examination data (including MAP and EFW) enables a more effective prediction of PE occurrence, particularly early-onset PE.

[Key words] preeclampsia (PE); retinal vessel; artificial intelligence (AI)

子痫前期 (preeclampsia, PE) 是妊娠中晚期出现的以高血压、蛋白尿为主要临床特征的妊娠期特有疾病^[1]; 全球范围内其发病率为 3%~5%^[2], 且与孕产妇、胎儿的不良妊娠结局的发生率密切相关。临床上, 终止妊娠是治愈 PE 的唯一手段, 因此对 PE 进行早期、精准的预测具有重要意义。

目前在 PE 预测的相关研究中, 多数学者选择依据美国妇产科医师学会 (American College of Obstetricians and Gynecologists, ACOG) 发布的 *Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222* 指南^[3] 中母体危险因素进行预测。在该指南中, PE 的高危因素包括既往 PE 病史、多胎妊娠、肾脏疾病、自身免疫系统疾病、糖尿病及慢性高血压, 中危因素包括初次妊娠、年龄 ≥ 35 岁、肥胖、PE 家族史等; 同时, 将具有任一 PE 高危因素或 2 项及以上中危因素的孕妇定义为 PE 高风险孕妇。在使用母体危险因素进行预测时, 其优势为执行简单, 缺点则为预测 PE 的能力较差; 且有研究^[4-6] 显示, 仅使用母体危险因素预测 PE 的阳性率为 30.4% (95% CI 26.3%~34.6%)。而除了该危险因素外, 目前研究中常用的其他预测指标包括平均动脉压 (mean arterial pressure, MAP)、子宫动脉的多普勒血流参数及母体血清生物标志物; 其中, 母体血清生物标志物包括胎盘生长因子 (placental growth factor, PLGF)、可溶性 FMS 样酪氨酸激酶-1

(soluble FMS-like tyrosine kinase-1, sFlt-1)、妊娠相关血浆蛋白 A (pregnancy associated plasma protein A, PAPP-A) 等^[7]。研究^[8] 显示母体危险因素联合其他预测指标可提高 PE 的阳性预测率, 如母体危险因素联合 MAP 的阳性预测率为 49.3% (95% CI 40.8%~57.8%), 母体危险因素联合子宫动脉的多普勒血流参数的阳性预测率为 62.0% (95% CI 53.5%~70.0%), 母体危险因素联合 MAP、子宫动脉的多普勒血流参数、PAPP-A 及 PLGF 的阳性预测率为 81.0% (95% CI 73.6%~87.1%); 继而提示母体血清生物标志物能显著提高 PE 预测的阳性率, 但由于该检测方法具有一定的侵入性, 且高度依赖专业技术支持, 使得其在常规产检中较难被推广。因此, 积极探寻预测能力高、操作快捷且无创的预测指标十分必要。

目前已有研究^[9] 证实, 视网膜微血管变化是高血压疾病的独立预测因素; 血压升高会导致血管发生生理性变化, 包括动脉壁增厚和透明样变性^[10]。而对 PE 的研究^[2] 发现, 全身血管内皮损伤是 PE 的发病机制之一; 且相关研究^[11-12] 表明, 25% 的重度 PE 患者和 50% 的 PE 患者均会出现视网膜血管异常, 包括小动脉狭窄、迂曲和节段性视网膜动脉血管痉挛等。眼底作为全身唯一可直接观察血管的区域, 对其图像的获取可通过眼底照相机这一无创的方式进行, 比母体血清生物标志物的获取更为便捷; 与此同时, 通过对眼底图像的分析可直接揭示视网膜微血管的变

化,从而反映心血管系统整体的状态。因此,我们认为视网膜血管特征参数有望成为快捷且无创的PE预测指标。近年来,随着人工智能(artificial intelligence, AI)技术在图像、数据处理领域的飞速发展,自动识别图像特征并进行定量评估的高精度算法不断涌现,这为输出图像的关键特征参数提供了强有力的支持^[13]。基于此,本研究通过AI模型对正常妊娠及PE孕妇的眼底图像进行分析,并对视网膜血管特征参数预测PE的能力展开分析,以评价该特征参数在PE中的预测价值。

1 对象与方法

1.1 研究对象

本研究对2020年6月—2021年1月在同济大学附属妇产科医院分娩的789例孕妇进行回顾性分析。纳入标准:①单胎妊娠。②妊娠16周前在该院建卡并行规律产检。③妊娠28周之前拍摄眼底图像。④于妊娠28~42周分娩。排除标准:①胎儿宫内死亡。②患有任​​何眼科疾病,如屈光性介质混浊或视网膜疾病。

1.2 研究方法

1.2.1 资料收集及分析 从电子病历系统中收集孕妇的临床资料和新生儿结局资料,并进行分析。孕妇的临床资料:①一般资料,包括年龄、妊娠前体质指数(body mass index, BMI)、既往PE史、本次妊娠的情况[是否为初次妊娠、是否通过辅助生殖技术(assisted reproductive technology, ART)受孕]、合并内科疾病[慢性高血压(chronic hypertension, CH)、肾脏疾病、自身免疫性疾病(autoimmune disease, AD)、孕前糖尿病(pregestational diabetes mellitus, PGDM)、妊娠期糖尿病(gestational diabetes mellitus, GDM)和多囊卵巢综合征(polycystic ovarian syndrome, PCOS)]。②产检资料,收集孕妇孕中期的收缩压和舒张压,计算得到孕中期平均动脉压(mean arterial blood pressure, MAP);收集孕中期胎儿超声检查结果,根据Hadlock公式^[14]获得估计胎儿体质量(estimated fetal weight, EFW)。③分娩资料,包括分娩方式(自然分娩、剖宫产)、分娩孕周、产后出血(postpartum hemorrhage, PPH)及分娩后住院天数。

④新生儿结局资料,包括出生体质量、1 min阿普加(Apgar)评分和5 min Apgar评分。

1.2.2 眼底图像获取、眼底特征评估及视网膜血管特征参数量化 眼底图像拍摄均在同一台非散瞳眼底照相机(佳能,日本)上,由经验丰富的眼科医师完成。在图像采集的过程中,眼科医师需以视神经和黄斑为中心,对每位孕妇的双眼进行拍照。

随后,对所有眼底图像进行匿名和去识别。使用北京鹰瞳科技发展股份有限公司开发的基于计算机视觉和深度学习的AI算法^[15-17]对眼底图像的眼底病变特征进行诊断,包括眼底动脉弹性减弱、豹纹样改变、动脉硬化、玻璃膜疣和视网膜零星出血;同时量化视网膜血管特征参数,包括视网膜中央动脉直径等效值(central retinal artery equivalent, CRAE)、视网膜中央静脉直径等效值(central retinal vein equivalent, CRVE)、视网膜动脉弯曲度、视网膜静脉弯曲度、视网膜动脉分形维数、视网膜静脉分形维数、垂直杯盘比(vertical C/D ratio, VCDR)和水平杯盘比(horizontal C/D ratio, HCDR),并根据CRAE和CRVE计算视网膜动静脉比值(arteriole to venular ratio, AVR)。

1.2.3 诊断标准及分组 中华医学会妇产科学分会妊娠期高血压疾病学组制定的《妊娠期高血压疾病诊治指南(2020)》^[18]指出,妊娠期高血压(gestational hypertension, GH)定义为妊娠20周后首次出现高血压[即收缩压 ≥ 140 mmHg和(或)舒张压 ≥ 90 mmHg(1 mmHg=0.133 kPa)],且尿蛋白检测呈阴性;PE定义为妊娠20周后孕妇出现收缩压 ≥ 140 mmHg和(或)舒张压 ≥ 90 mmHg,并伴有下列任一项:①尿蛋白定量 ≥ 0.3 g/24 h,或尿蛋白/肌酐比值 ≥ 0.3 ,或随机尿蛋白 $\geq (+)$ (无条件进行蛋白定量时的检查方法)。②无蛋白尿但伴有以下任一器官或系统受累(包括心、肺、肝、肾等重要器官),或血液系统、消化系统、神经系统的异常改变,胎盘-胎儿受到累及等。

根据上述指南的诊断标准,将本研究纳入的孕妇分为正常妊娠组($n=685$)和妊娠期高血压疾病(hypertensive disorders of pregnancy, HDP)组($n=104$),且HDP组可进一步分为GH组($n=36$)和PE组($n=68$);而根据发病孕周的不同,又将PE组分为早发型PE组(发病孕周 <34 周)和晚发型PE组(发病孕周 ≥ 34 周)。

1.3 统计学方法

采用R语言4.2.1版本进行统计分析。非正态分布的定量资料用 $M(Q_1, Q_3)$ 表示,组间比较用Wilcoxon秩和检验。定性资料用频数(百分率)表示,组间比较用 χ^2 检验或Fisher精确检验。对孕妇的产检资料进行数据标准化,即利用英国胎儿医学基金会(Fetal Medicine Foundation, FMF)的在线计算器(<https://fetalmedicine.org/research/mom>)获得孕中期MAP的中位数倍数(multiples of median, MoM),使用国际胎儿生长标准——EFW计算公式^[19]获得EFW的z-score值。采用单因素和多因素Logistic回归模型,分析产检资料、视网膜血管特征参数与GH、PE发生的关系,并计算比值比(OR)和相应的95%置信区间(95% CI)。采用受试者操作特征曲线(receiver operator characteristic curve, ROC curve, ROC曲线)

的曲线下面积(area under the curve, AUC)评估视网膜血管特征参数等对PE(早发型PE和晚发型PE)的预测能力。 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 孕妇的临床资料和新生儿结局资料分析

对入组孕妇的临床资料和新生儿结局资料进行分析,结果(表1)显示,孕中期MAP、分娩孕周、分娩后住院天数和5 min Apgar评分在正常妊娠组和GH组间的差异具有统计学意义(均 $P<0.05$);妊娠前BMI、ART、CH、PGDM、孕中期MAP、孕中期EFW、分娩方式、分娩孕周、分娩后住院天数、新生儿出生体质量和Apgar评分在正常妊娠组和PE组间、3组间的差异均具有统计学意义(均 $P<0.05$)。

表1 孕妇的临床资料和新生儿结局资料的比较

Tab 1 Comparison of clinical data of pregnant women and neonatal outcome data

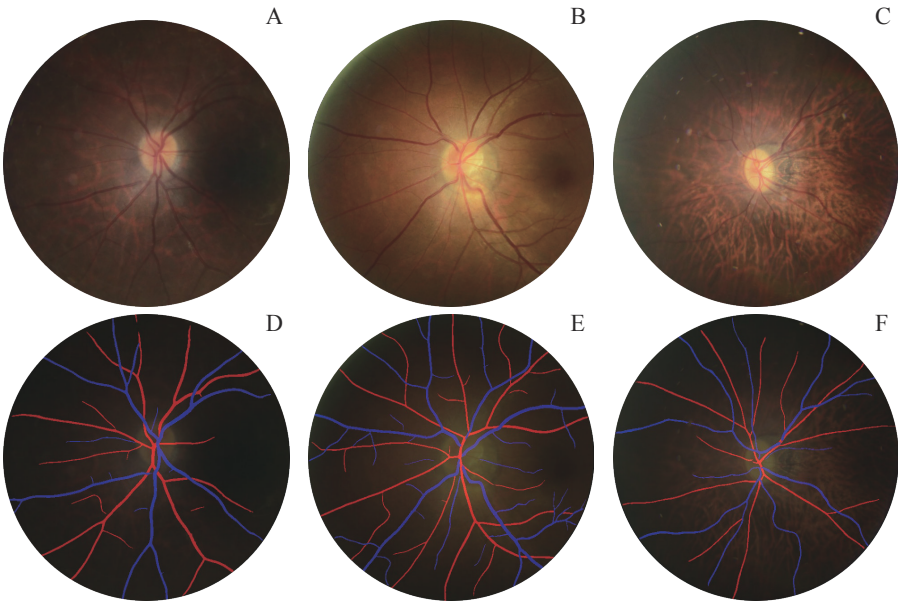
Characteristic	Unaffected group (n=685)	HDP group (n=104)				P^c value
		GH group (n=36)	P^a value	PE group (n=68)	P^b value	
Age/year	31.00 (29.00, 34.00)	32.00 (30.00, 34.00)	0.307	32.00 (29.00, 35.00)	0.153	0.234
Pre-pregnancy BMI/(kg·m ⁻²)	22.43 (20.32, 25.15)	22.72 (21.04, 27.29)	0.194	23.87 (20.77, 26.66)	0.013	0.025
Previous PE history/n(%)	5 (0.73)	1 (2.78)	0.265	0 (0)	1.000	0.317
Primiparity/n(%)	493 (71.97)	29 (80.56)	0.339	54 (79.41)	0.203	0.270
ART/n(%)	51 (7.45)	2 (5.56)	1.000	12 (17.65)	0.009	0.021
CH/n(%)	14 (2.04)	1 (2.78)	0.540	8 (11.76)	0.000	0.000
Renal disease/n(%)	3 (0.44)	0 (0)	1.000	2 (2.94)	0.067	0.080
AD/n(%)	29 (4.23)	2 (5.56)	0.664	5 (7.35)	0.222	0.318
PGDM/n(%)	4 (0.58)	1 (2.78)	0.227	3 (4.41)	0.019	0.016
GDM/n(%)	76 (11.09)	7 (19.44)	0.173	9 (13.24)	0.550	0.252
PCOS/n(%)	10 (1.46)	1 (2.78)	0.443	0 (0)	0.612	0.436
Second-trimester MAP/mmHg	82.67 (76.33, 88.33)	88.17 (85.67, 96.33)	0.000	91.33 (84.67, 95.33)	0.000	0.000
Second-trimester EFW/g	1 445.89 (1 320.37, 1 566.41)	1 443.56 (1 341.89, 1 583.57)	0.604	1 347.73 (1 218.09, 1 511.01)	0.003	0.009
Delivery method/n(%)			0.167		0.000	0.000
Spontaneous delivery	393 (57.37)	16 (44.44)		20 (29.41)		
Caesarean section	292 (42.63)	20 (55.56)		48 (70.59)		
Gestational weeks/week	39.43 (38.57, 40.14)	39.00 (38.29, 39.71)	0.028	37.64 (36.04, 39.00)	0.000	0.000
PPH/n(%)	19 (2.77)	1 (2.78)	1.000	4 (5.88)	0.146	0.283
Postpartum hospitalization days/n(%)	3.00 (3.00, 4.00)	4.00 (3.00, 5.00)	0.001	6.00 (5.00, 7.00)	0.000	0.000
Fetal birth weight/g	3 380.00 (3 115.00, 3 670.00)	3 407.50 (3 135.00, 3 655.00)	0.725	3 005.00 (2 446.25, 3 292.50)	0.000	0.000
1 min Apgar score/score	9.00 (9.00, 10.00)	9.00 (9.00, 10.00)	0.964	9.00 (9.00, 9.00)	0.000	0.000
5 min Apgar score/score	10.00 (10.00, 10.00)	10.0 (10.00, 10.00)	0.029	10.00 (9.00, 10.00)	0.000	0.000

Note: ^aComparison between the unaffected group and GH group; ^bComparison between the unaffected group and PE group; ^cComparison among the unaffected group, GH group and PE group.

2.2 眼底图像的获取、眼底特征及视网膜血管特征参数分析

图1显示了正常妊娠组、GH组、PE组孕妇的典型眼底图像及视网膜血管分割示意图。对该3组孕妇

的眼底特征及视网膜血管特征参数进行分析,结果(表2)显示,CRAE、CRVE、AVR、视网膜动脉弯曲度和视网膜动脉分形维数在正常妊娠组和PE组间、3组间的差异均具有统计学意义(均 $P<0.05$)。



Note: A–C. Typical fundus images of the unaffected group (A), GH group (B) and PE group (C). D–F. Schematic diagrams of segmentation of retinal blood vessels of the unaffected group (D), GH group (E) and PE group (F). The red lines represent the retinal arteries, while the blue lines represent the retinal veins.

图1 典型眼底图像和视网膜血管分割示意图

Fig 1 Typical fundus images and schematic diagrams of segmentation of retinal blood vessels of the three groups

表2 3组孕妇的眼底特征及视网膜血管特征参数比较

Tab 2 Comparison of fundus characteristics and retinal vascular characteristic parameters among the three groups of pregnant women

Characteristic	Unaffected group (n=685)	HDP group (n=104)			P^b value	P^c value
		GH group (n=36)	P^a value	PE group (n=68)		
Decreased elasticity of retinal arteries/n(%)	196 (28.61)	12 (33.33)	0.572	23 (33.82)	0.401	0.532
Leopard pattern change/n(%)	456 (66.57)	23 (63.89)	0.721	48 (70.59)	0.589	0.746
Arteriosclerosis/n(%)	4 (0.58)	1 (2.78)	0.227	1 (1.47)	0.378	0.181
Vitreous warts/n(%)	42 (6.13)	2 (5.56)	1.000	4 (5.88)	1.000	1.000
Retinal sporadic bleeding/n(%)	7 (1.02)	1 (2.78)	0.338	1 (1.47)	0.533	0.337
CRAE	94.00 (87.00, 99.00)	89.00 (86.00, 95.00)	0.150	87.00 (80.00, 94.00)	0.000	0.000
CRVE	122.00 (116.00, 129.00)	120.00 (116.00, 122.50)	0.101	120.00 (111.00, 126.50)	0.017	0.019
AVR	0.75 (0.71, 0.81)	0.74 (0.70, 0.79)	0.432	0.72 (0.67, 0.77)	0.002	0.006
Retinal artery tortuosity	0.05 (0.04, 0.07)	0.04 (0.04, 0.07)	0.567	0.04 (0.03, 0.06)	0.004	0.015
Retinal vein tortuosity	0.09 (0.07, 0.11)	0.07 (0.06, 0.11)	0.186	0.08 (0.06, 0.10)	0.120	0.141
Retinal artery fractal dimension	1.48 (1.41, 1.54)	1.47 (1.41, 1.51)	0.245	1.45 (1.38, 1.51)	0.003	0.007
Retinal vein fractal dimension	1.49 (1.42, 1.56)	1.51 (1.45, 1.55)	0.569	1.48 (1.44, 1.55)	0.990	0.848
VCDR	0.28 (0.22, 0.34)	0.29 (0.20, 0.33)	0.688	0.27 (0.22, 0.34)	0.522	0.764
HCDR	0.39 (0.31, 0.46)	0.40 (0.31, 0.45)	0.967	0.39 (0.31, 0.45)	0.740	0.941

Note: ^aComparison between the unaffected group and GH group; ^bComparison between the unaffected group and PE group; ^cComparison among the unaffected group, GH group and PE group.

2.3 PE发生的影响因素的单因素和多因素 Logistic 回归分析

为分析PE发生的相关影响因素,我们对上述与

之相关的有统计学意义的产检资料和视网膜血管特征量化参数开展单因素 Logistic 回归分析,结果(表3)显示孕中期 MAP、孕中期 EFW、CRAE、CRVE、

AVR、视网膜动脉弯曲度和视网膜动脉分形维数是影响PE发生的主要因素(均 $P<0.05$)。将ACOG指南定义的母体危险因素作为混杂因素调整后,进一步行多因素Logistic回归分析,结果(表3)显示孕中期

EFW、CRAE、CRVE、AVR、视网膜动脉弯曲度和视网膜动脉分形维数是PE发生的保护因素,孕中期MAP是其危险因素(均 $P<0.05$)。

表3 PE发生的影响因素的单因素和多因素Logistic回归分析

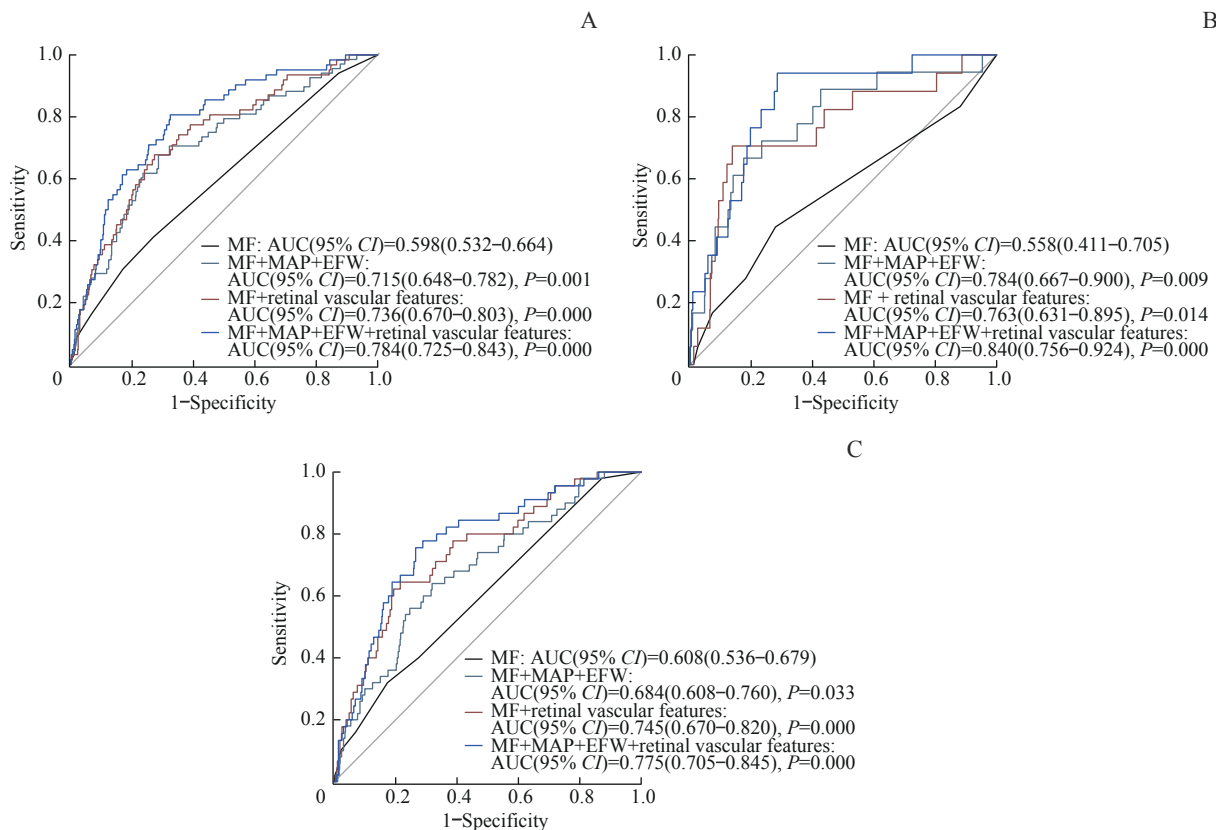
Tab 3 Univariate and multivariate Logistic regression analysis of the influencing factors of PE occurrence

Characteristic	Univariate Logistic analysis			Multivariate Logistic analysis		
	OR	95% CI	P value	aOR	95% CI	P value
Second-trimester MAP	1.110	1.076–1.148	0.000	1.106	1.068–1.147	0.000
Second-trimester EFW	0.702	0.571–0.869	0.001	0.700	0.560–0.870	0.000
CRAE	0.936	0.904–0.965	0.000	0.940	0.910–0.970	0.000
CRVE	0.972	0.952–0.993	0.009	0.970	0.950–0.990	0.010
AVR	0.010	0.000–0.288	0.008	0.020	0.000–0.500	0.020
Retinal artery tortuosity	0.000	0.000–0.012	0.012	0.000	0.000–0.050	0.020
Retinal artery fractal dimension	0.046	0.006–0.393	0.004	0.070	0.010–0.720	0.020

2.4 视网膜血管特征参数预测PE的ROC分析

在多因素Logistic回归分析的基础上,我们对PE发生的相关影响因素进行了ROC曲线分析,并考虑4种模型[①单独使用母体危险因素、②母体危险因素+孕中期产检资料(包括MAP和EFW)、③母体

危险因素+视网膜血管特征参数、④母体危险因素+孕中期产检资料(包括MAP和EFW)+视网膜血管特征参数]的预测能力。结果显示(图2),模型②($P=0.001$)、模型③($P=0.000$)、模型④($P=0.000$)的预测能力均优于模型①,且模型④的预测能力更佳



Note: Predictive performance for PE (A), early-onset PE (B) and late-onset PE (C). MF—maternal risk factors.

图2 不同模型分别预测PE、早发型PE和晚发型PE的ROC曲线分析

Fig 2 Analysis of ROC curves for predicting PE, early-onset PE and late-onset PE using different models

(AUC>0.750)。

为进一步探究上述模型对不同亚型PE（早发型PE、晚发型PE）的预测能力，我们采用ROC曲线对该2亚型PE进行分析，结果（图2）显示，在预测早发型PE中，模型②（ $P=0.009$ ）、模型③（ $P=0.014$ ）、模型④（ $P=0.000$ ）的预测能力均优于模型①，且这3种模型的预测能力均较好（AUC>0.750）；在预测晚发型PE中，该3种模型的预测能力亦均优于模型①（均 $P<0.05$ ），且模型④的预测能力更佳（AUC>0.750）。

3 讨论

在本研究中，我们评估了基于AI模型量化的视网膜血管特征参数在预测PE中的应用潜力。结果显示，孕中期EFW、CRAE、CRVE、AVR、视网膜动脉弯曲度、视网膜动脉分形维数是PE发生的保护因素，孕中期MAP是其危险因素；母体危险因素+孕中期产检资料（包括MAP和EFW）+视网膜血管特征参数模型具有较好的PE预测能力，在早发型PE的预测方面表现更佳；这些结果表明，视网膜血管特征参数在预测PE（特别是早发型PE）的发生具有潜在的临床价值。

PE是一种妊娠期特有的疾病，其基本病理变化之一为血管内皮细胞损伤，可导致全身各脏器血流灌注不足，从而对孕妇和胎儿的健康造成重大风险。既往已有研究证实，视网膜微血管的变化在PE的早期阶段就已经显现^[20]，且使用视网膜血管特征参数可有效评估高血压和冠状动脉疾病的严重程度^[21]。基于此，本研究对孕妇的视网膜血管特征进行了详细的量化分析，并证实了视网膜血管特征参数在PE（尤其是早发型PE）中的预测能力，为PE及其早预测提供了潜在的生物标志物；同时，本研究亦对GH组开展了同样的分析，却未得到有统计学意义的结果（未在文中展示），这表明GH组孕妇的视网膜血管特征参数并未表现出显著的差异或变化，提示使用视网膜血管特征参数尚无法准确预测GH。

此外，本研究采用的技术具有一定的优势：①目前普及的PE预测方法^[22-24]依赖于血清生物标志物检测及超声检查，这些方法存在一定的侵入性以及对该技术人员的依赖性；本研究通过非散瞳眼底照相监测孕妇眼底微血管变化，是一种无创、简便的替代方案。②AI技术的应用可显著提高图像处理及特

征提取的效率和准确性，深度学习算法也已被应用于自动测量视网膜血管直径方面，且与专业人工分级的测量结果高度一致^[25]；本研究基于AI模型^[15-17]能自动提取视网膜眼底图像中动静脉结构、检测视盘和黄斑区域并量化视网膜血管特征参数，大幅提高了处理和分析视网膜眼底图像的效率。

然而，本研究尚存在一些局限性：①样本量较小，在一定程度上可能导致模型的泛化能力受限并影响模型的可推广性。②本研究尚未在其他医疗保健机构中进行外部验证，可能难以评估模型的稳健性。未来我们计划扩大样本量并进行多中心数据收集，通过大量的数据训练来提高模型的准确性和可靠性。

总体而言，本研究发现视网膜血管特征参数可作为PE的预测因素，且与母体危险因素及孕中期产检资料（包括MAP和EFW）联合预测PE（特别是早发型PE）具有较好的预测能力，初步证实了利用AI模型量化视网膜血管特征参数预测PE的可行性，或将为无创、快捷的PE预测方法的探索提供一定的方向。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

All authors disclose no relevant conflict of interests.

伦理批准和知情同意/Ethics Approval and Patient Consent

本研究经同济大学附属妇产科医院伦理委员会批准（审批号：KS20268），并获得所有参与者的知情同意。所有试验过程均遵照《赫尔辛基宣言》的条例进行。

This study was approved by Ethics Committee of Shanghai First Maternity and Infant Hospital of Tongji University (Approval Letter No. KS20268), and obtained informed consent from all participants. All experimental protocols were carried out by following the guidelines of Declaration of Helsinki.

作者贡献/Authors' Contributions

花晓琳构思并设计了这项研究，周天凡、邵飞雪、万盛进行了数据分析及论文撰写，周晨晨负责论文修改，周思锦负责深度学习算法和人工智能模型的设计及应用。所有作者均阅读并同意最终稿件的提交。

HUA Xiaolin conceived and designed this research. ZHOU Tianfan, SHAO Feixue and WAN Sheng performed data analysis and drafted the manuscript. ZHOU Chenchen revised the manuscript. ZHOU Sijin was responsible for the design and application of deep-learning algorithms and AI models. All the authors have read the last version of paper and consented for submission.

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