

经阴道彩色多普勒超声联合血清 miR-130a, miR-425-5p 水平检测对宫颈癌的诊断效能分析

赵白信, 于慧娟, 焦方杰, 邢丽丽, 黄 蕾, 姚辉梅

(郑州市第七人民医院功能科, 郑州 450000)

摘要:目的 分析经阴道彩色多普勒超声联合血清 miR-130a, miR-425-5p 水平检测对宫颈癌的诊断效能。方法 选取 2017 年 1 月~2019 年 1 月在郑州市第七人民医院诊治的宫颈癌患者 58 例和宫颈炎及宫颈上皮瘤变者 77 例分别为癌症组和疾病组, 60 例同期来院体检结果正常的健康女性为对照组。对三组实施经阴道彩色多普勒超声检查, 并使用实时荧光定量 PCR 法检测血清 miR-130a, miR-425-5p 水平。分析经阴道彩色多普勒超声联合血清 miR-130a, miR-425-5p 表达对宫颈癌的诊断效能。结果 癌症组、疾病组和对照组的收缩期血流速度 (peak systolic velocity, PSV) (12.01 ± 2.85 , 9.53 ± 1.98 和 8.52 ± 1.23 cm/s) 依次降低, 阻力指数 (resistive index, RI) (0.42 ± 0.10 , 0.58 ± 0.12 和 0.66 ± 0.14) 依次升高, 差异有统计学意义 ($F=43.178$, 60.098 , 均 $P < 0.001$); 癌症组、疾病组和对照组的血清 miR-130a (0.092 ± 0.030 , 0.045 ± 0.012 和 0.030 ± 0.008), miR-425-5p (0.733 ± 0.203 , 0.365 ± 0.098 和 0.205 ± 0.048) 表达水平依次升高, 差异有统计学意义 ($F=181.070$, 259.304 , $P < 0.001$)。受试者工作特征曲线 (receiver operating characteristic curve, ROC) 显示经阴道多普勒超声诊断宫颈癌的敏感度、特异度、准确度、曲线下面积 (area under curve, AUC) 分别为 77.59%, 87.01%, 82.96% 和 0.889; 血清 miR-130a 分别为 79.31%, 80.52%, 80.00% 和 0.820; 血清 miR-425-5p 分别为 74.14%, 77.92%, 76.30% 和 0.785; 联合诊断分别为 74.14%, 90.91%, 83.70% 和 0.932, 三者联合检测的 AUC 大于单独检测 ($P < 0.05$)。结论 阴道彩色多普勒超声联合血清 miR-130a 和 miR-425-5p 的表达对宫颈癌具有较高的诊断效能。

关键词: 宫颈癌; 阴道彩色多普勒超声; 微小核糖核酸 -130a; 微小核糖核酸 425-5p

中图分类号: R737.33; R730.43 文献标识码: A 文章编号: 1671-7414 (2021) 03-043-05

doi:10.3969/j.issn.1671-7414.2021.03.010

Analysis of Diagnostic Efficacy of Transvaginal Color Doppler Ultrasound Combined with Serum miR-130a and miR-425-5p Levels in Cervical Cancer

ZHAO Bai-xin, YU Hui-juan, JIAO Fang-jie, XING Li-li, HUANG Lei, YAO Hui-mei

(Department of Function, the Seventh People's Hospital of Zhengzhou City, Zhengzhou 450000, China)

Abstract: Objective To analyze the diagnostic efficacy of transvaginal color Doppler ultrasound combined with serum miR-130a and miR-425-5p levels in the diagnosis of cervical cancer. **Methods** A total of 58 patients with cervical cancer and 77 patients with cervicitis and cervical epithelial neoplasia who were diagnosed and treated in the Zhengzhou Seventh People's Hospital from January 2017 to January 2019 were selected as the cancer group and disease group, respectively, and 60 healthy women who came to the hospital with normal physical examination results. The three groups were examined by transvaginal color Doppler ultrasound, and the serum levels of miR-130a and miR-425-5p were detected by real-time fluorescent quantitative PCR. Analyzed the diagnostic efficacy of transvaginal color Doppler ultrasound combined with serum miR-130a and miR-425-5p expression in cervical cancer. **Results** There were significant differences in peak systolic velocity (PSV) (12.01 ± 2.85 , 9.53 ± 1.98 and 8.52 ± 1.23 cm/s) decreased sequentially, and resistive index (RI) (0.42 ± 0.10 , 0.58 ± 0.12 and 0.66 ± 0.14) increased sequentially between cancer group, disease group and control group, the differences were statistically significant ($F=43.178$, 60.098 , all $P < 0.001$). The expression levels of miR-130a (0.092 ± 0.030 , 0.045 ± 0.012 , 0.030 ± 0.008), miR-425-5p (0.733 ± 0.203 , 0.365 ± 0.098 , 0.205 ± 0.048) increased in the cancer group, disease group and control group were statistically different ($F=181.070$, 259.304 , all $P < 0.001$). Receiver operating characteristic curve (ROC) showed that the sensitivity, specificity, accuracy, and area under curve (AUC) of transvaginal Doppler ultrasound in the diagnosis of cervical cancer are 77.59%, 87.01%, 82.96% and 0.889, respectively. The serum miR-130a were 79.31%, 80.52%, 80.00% and 0.820, respectively.

作者简介: 赵白信 (1981-), 女, 本科, 主治医师, 研究方向: 成人腹部、浅表器官、小儿心脏及胎儿产前超声诊断。

通讯作者: 姚辉梅。

Serum miR-425-5p were 74.14%, 77.92%, 76.30% and 0.785, respectively. The combined diagnosis were 74.14%, 90.91%, 83.70% and 0.932 respectively, the AUC of the three combined detection was greater than that of the single detection ($P < 0.05$).

Conclusion Color Doppler ultrasound combined with the expression of mir-130a and mir-425-5p in serum has a high diagnostic efficacy for cervical cancer.

Keywords: cervical cancer; transvaginal color Doppler ultrasound; miR-130a; miR-425-5p; diagnosis efficiency

宫颈癌是威胁女性生命健康的生殖系统恶性肿瘤^[1]。流行病学显示^[2],我国宫颈癌的发病率居于女性恶性肿瘤的第2位,每年约有13万宫颈癌的新发病例,且发病年龄有年轻化趋势。做好宫颈癌的筛查诊断,及早采取有效地干预对于降低宫颈癌病死率有重要意义^[3]。目前影像学检查是恶性肿瘤诊断的常用辅助手段,彩色多普勒超声在传统二维超声结构图像的基础上,能提供浅表器官的血流动力学信息,是妇科疾病诊断中应用最广泛的影像学检查方式,但该方式受医生专业经验、体位等因素影响,常有漏诊或误诊的情况发生^[4-5]。近年来分子生物学标志物检测开始在疾病的诊断中应用,为恶性肿瘤的诊断提供了新途径。微小核糖核酸(micro ribonucleic acid, miRNA)是一类新发现的非编码小RNA,参与细胞的增殖、分化等生理过程,与多种恶性肿瘤的发生发展有关。研究表明^[6],miR-130a, miR-425-5p在宫颈癌患者中有异常表达,且与宫颈癌的病理参数密切相关,可作为宫颈癌的参考诊断标志物。目前关于彩色多普勒超声及血清分子生物学标志物在宫颈癌中的诊断研究较多,但关于二者联合应用的效能仍未明确。故此,本研究特探讨经阴道彩色多普勒超声联合血清 miR-130a, miR-425-5p 表达水平检测对宫颈癌的诊断效能,以为宫颈癌的早期诊断方式提供补充与参考。现报道如下。

1 材料与方法

1.1 研究对象 选取2017年1月~2019年1月郑州市第七人民医院收治的宫颈癌患者58例为癌症组,同期于门诊(体检)诊断为宫颈炎及宫颈上皮瘤变者77例为疾病组。癌症组及疾病组均经活检或手术病理检查确诊。癌症组年龄30~66岁,平均年龄 45.32 ± 6.35 岁;已婚48例,未婚10例;经产妇45例;症状表现:接触性阴道出血6例,高危型乳头瘤病毒(human papillomavirus, HPV)感染10例,绝经后阴道出血15例,宫颈刮片细胞学检查阳性或疑似阳性15例,碘试验或醋酸试验阳性12例。疾病组年龄28~65岁,平均年龄 45.02 ± 6.50 岁;已婚64例,未婚13例;经产妇63例;症状表现:接触性阴道出血24例,HPV感染28例,绝经后阴道出血13例,宫颈刮片细胞学检查阳性或疑似阳性7例,碘试验或醋酸试验阳性5例。另选取同期来院体检的健康女性60例为对照组,年

龄26~65岁,平均年龄 43.50 ± 6.50 岁;已婚48例,未婚12例;经产妇43例。三组受检者的年龄、婚育史比较差异无统计学意义($P > 0.05$),具有可比性。本研究开展前已获得医院伦理委员会批准,纳入研究者均签署知情同意书。

1.2 试剂与仪器 Voluson E8(美国GE公司)多普勒超声诊断系统;miRNeasy Mini Kit试剂盒(德国Qiagen公司);Prime Script™反转录试剂盒(美国TaqMan);荧光定量PCR试剂盒检测(美国ABI公司)。

1.3 方法

1.3.1 宫颈癌诊断方法:参照《宫颈癌诊断与治疗指南(第四版)》^[7]:宫颈活检或实施宫颈高频电波刀(loop electrosurgical excision procedure, LEEP)宫颈锥切术病理检查确诊,以上诊断结果作为金标准。

1.3.2 阴道彩色多普勒超声检查:检查开始前叮嘱受检者排空膀胱,仰卧于检查床,取膀胱截石位,少量耦合剂涂抹于超声探头顶端后套上避孕套,将探头缓慢插入受检者阴道中段,进行横、纵、斜多切面检查,后观察宫颈内、外口,查看宫颈管回声及宫颈的整齐性。后使用彩色多普勒血流显像(color Doppler flow imaging, CDFI)查看宫颈血流分布,记录收缩期血流速度(peak systolic velocity, PSV)和阻力指数(resistive index, RI)。最后对宫体、卵巢及宫旁各组织情况进行仔细观察。超声检查均为具有5年以上临床经验的同一超声科医师进行操作。以Adler血流分级进行性质判断,其中0~I级为良性,II~III级为恶性。

1.3.3 血清 miR-130a, miR-425-5p 检测:抽取受检者空腹外周静脉血4 ml, 3 500 r/min离心10 min,离心半径12.5 cm,分离上层血清,保存于-80℃待检。提取总RNA,扩增反转录产物cDNA,取0.5 μl cDNA模板,以荧光定量PCR试剂盒检测血清中miR-130a, miR-425-5p水平,目的基因的相对表达量以 $2^{-\Delta\Delta C_t}$ 表示。实验步骤均严格按照试剂盒操作说明进行。

1.4 统计学分析 采用SPSS19.0统计学软件分析数据,正态分布资料以均数±标准差($\bar{x} \pm s$)表示,组间比较采用单因素方差分析,两两样本比较采用LSD-*t*检验;超声,miR-130a, miR-425-5p诊断效能评价采用灵敏度、特异度、准确度表示,

并以 Med Calc 绘制受试者工作特征曲线 (receiver operating characteristic curve, ROC) 分析单独检测和联合检测的诊断价值, 以 Hanley-McNeil 方法比较 ROC 曲线下面积 (area under curve, AUC)。以 $\alpha=0.05$ 为校验水准。

2 结果

2.1 经阴道彩色多普勒超声诊断参数比较 见表1。三组 PSV, RI 水平比较差异有统计学意义 ($P < 0.001$)；癌症组、疾病组、对照组的 PSV 依次降低, 两两比较差异均有统计学意义 (均 $P < 0.001$)；癌症组、疾病组和对照组的 RI 依次升高, 两两比较差异均有统计学意义 ($P < 0.001$)。

表2 三组的血清 miR-130a, miR-425-5p 表达情况比较 ($\bar{x} \pm s$)

项目	癌症组 (n=58)	疾病组 (n=77)	对照组 (n=60)	F	P
miR-130a	0.092 ± 0.030	0.045 ± 0.012	0.030 ± 0.008	181.070	< 0.001
miR-425-5p	0.733 ± 0.203	0.365 ± 0.098	0.205 ± 0.048	259.304	< 0.001

2.3 经阴道彩色多普勒超声与血清 miR-130a, miR-425-5p 单独及联合诊断宫颈癌的效能分析 见表3。以病理结果为标准, 分析经阴道彩色多普勒超声与血清 miR-130a, miR-425-5p 单独及联合诊断宫颈癌的灵敏度、准确度、特异度。阴道彩色多普勒超声与血清 miR-130a, miR-425-5p 联合检测的敏感度比单独检测低, 但特异度和准确度比单独检测高。

表3 经阴道彩色多普勒超声与血清 miR-130a, miR-425-5p 单独及联合诊断宫颈癌的效能 (%)

项目	敏感度	特异度	准确度
超声	77.59	87.01	82.96
miR-130a	79.31	80.52	80.00
miR-425-5p	74.14	77.92	76.30
联合诊断	74.14	90.91	83.70

2.4 经阴道彩色多普勒超声与血清 miR-130a, miR-425-5p 联合诊断宫颈癌的 ROC 曲线分析 见图1。经阴道彩色多普勒超声、血清 miR-130a, miR-425-5p 及联合诊断宫颈癌的 AUC 分别为 0.889, 0.820, 0.785, 0.932, 三者联合检测的 AUC 大于单独检测 ($P < 0.05$)。

3 讨论

宫颈癌在病变早期多无明显的症状体征, 容易被忽视、漏诊, 患者就诊时已进入中晚期, 病死率较高, 因此做好宫颈癌的早期筛查, 诊断是降低病死率的有效手段^[8]。目前宫颈癌的筛查方式较多, 如何需求一种安全、客观、有效、可重复性强的筛查方法是临床医师的关注重点。HPV 感染是导致宫颈癌病变的首要因素, 因此 HPV 是宫颈癌的主要筛查

表1 三组的 PSV, RI 水平比较 ($\bar{x} \pm s$)

项目	癌症组 (n=58)	疾病组 (n=77)	对照组 (n=60)	F	P
PSV (cm/s)	12.01 ± 2.85	9.53 ± 1.98	8.52 ± 1.23	43.178	< 0.001
RI	0.42 ± 0.10	0.58 ± 0.12	0.66 ± 0.14	60.098	< 0.001

2.2 血清 miR-130a, miR-425-5p 表达情况比较 见表2。三组的血清 miR-130a, miR-425-5p 表达水平比较差异有统计学意义 (均 $P < 0.001$)，癌症组的血清 miR-130a, miR-425-5p 表达水平均高于疾病组和对照组, 疾病组均高于对照组, 差异均有统计学意义 (均 $P < 0.001$)。

方式之一, 但该方式的敏感度和特异度不高, 临床应用具有一定的局限性^[9]。脱落细胞学、病理检查是指南推荐的宫颈癌诊断方式, 虽有较高的特异度, 但对检查技术的要求较高, 且费用昂贵^[10]。以彩色多普勒超声为主的影像学检查和分子生物学检测以安全、无创、可重复性好的特点成为临床首选。

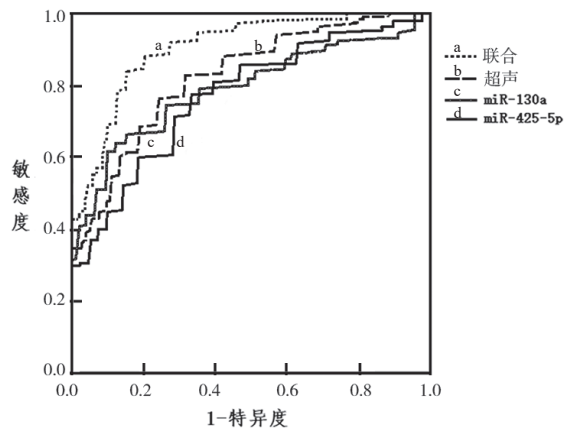


图1 系列联合检测 ROC 曲线图

本研究结果中, 癌症组的 PSV 大于疾病组和对照组, RI 小于疾病组和对照组, 血清 miR-130a, miR-425-5p 表达水平高于疾病组和对照组 ($P < 0.001$), 提示经阴道彩色多普勒超声对宫颈癌诊断有特异性, 且血清 miR-130a, miR-425-5p 表达水平与宫颈癌的发生有关。经阴道彩色多普勒超声是产科超声的新突破, 血流信息是彩色多普勒超声判断病灶性质的关键, 新生血管是恶性肿瘤生成和发展的基础。宫颈的恶性肿瘤因细胞生长活跃, 代谢和组织生长快速, 出现大量的异常新生血管结构, 并形成动静脉短路, 此类血管平滑肌相较于正常组织的血管弹性差, 经彩色多普勒超声检查可探

及丰富的血流信号,频谱多普勒内为低阻动脉血流,PSV数值明显增加,RI较小^[11-12]。慢性宫颈炎或宫颈上皮瘤变者患者多存在宫颈囊肿和肥大,可发现少量宫颈血流信号,而正常宫颈组织无明显的血流信号,因此其PSV值小,而RI值大^[13]。何玉春等^[14]研究结果中显示癌症组的PSV,RI与其他疾病患者有显著差异,与本研究结果相似,证实经阴道彩色多普勒超声对宫颈癌的诊断鉴别有一定的价值。

miRNA作为非编码的RNA分子,主要参与真核生物转录后基因的表达与调控,与细胞的增殖、分化与凋亡等生理过程密切相关,在多种癌组织的病理中均有异常表达^[15]。马向薇等研究显示^[16],miR-130a可促进恶性肿瘤细胞的增殖与转移,其机制与激活NF- κ B等信号通路有关。朱军等^[17]研究显示,miR-425-5p能抑制程序性细胞死亡因子10(programmed cell death 10, PDCD10)的表达,促进肿瘤的增殖、迁移和侵袭。以上分析与结果说明血清miR-130a,miR-425-5p参与卵巢癌的发生发展,可作为潜在分子生物学标志物。

经阴道彩色多普勒超声在宫颈癌的诊断鉴别中虽可清晰的显示病灶声像特征及血流信息,但早期的宫颈癌及癌前应变者宫颈阴道外观多正常,且未出现浸润和远处转移,超声声像图表现不典型,无明显的血流信号,有误诊及漏诊的可能^[18]。miRNA在外周血中含量较为丰富且稳定,在胃癌、结直肠癌、卵巢癌等恶性肿瘤中均有异常表达,作为潜在的肿瘤分子生物学标志物,对于诊断宫颈癌的特异度不高^[19-20]。本研究中ROC曲线分析显示,经阴道彩色多普勒超声联合血清miR-130a,miR-425-5p诊断宫颈癌的敏感度、特异度、准确度、AUC分别为74.14%,90.91%,83.70%和0.932,阴道多普勒超声分别为77.59%,87.01%,82.96%和0.889,血清miR-130a分别为79.31%,80.52%,80.00%和0.820,miR-425-5p分别为74.07%,65.19%,76.30%和0.785,提示经阴道彩色多普勒超声联合血清miR-130a,miR-425-5p诊断宫颈癌有更高的特异度、准确度和AUC,具有良好的诊断效能。

综上所述,在宫颈癌的诊断中,应用经阴道彩色多普勒超声、血清miR-130a,miR-425-5p联合诊断较单独应用具有更高的效能,且具有安全、无创、可重复强的优势,可作为宫颈癌筛查、诊断的首选方式。宫颈癌的发生涉及因素较多且机制复杂,是否有其更加特异性生化指标有待进一步探讨,且是下一步研究方向。

参考文献:

[1] GAO Chundi, ZHOU Chao, ZHUANG Jing, et al. MicroRNA expression in cervical cancer: Novel diagnosis

tic and prognostic biomarkers[J].J CellBiochem, 2018, 119(8):7080-7090.

- [2] Kanyina E W, Kamau L, Muturi M. Cervical precancerous changes and selectedcervical microbial infections, Kiambu County, Kenya, 2014: a cross sectionalstudy[J].BMC Infect Dis, 2017, 17(1):647.
- [3] 陈慎,杜明君,宋雅琴. 宫颈组织HPV DNA与血清Chemerin,Leptin水平联合检测对宫颈癌早期诊断的价值分析[J]. 现代检验医学杂志, 2019, 34(3):42-46. CHEN Shen, DU Mingjun, SONG Yaqin. Value of combined detection of HPV DNA and serum levels of chemerin and leptin in early diagnosis of cervical cancer[J]. J Mod Lab Med, 2019, 34(3):42-46.
- [4] THÉODORE C, LEVAILLANT J M, CAPMAS P, et al. MRI and ultrasound fusion imaging for cervical cancer[J].Anticancer Res, 2017, 37(9):5079-5085.
- [5] ZHANG Lu, ZHOU Wei, ZHAN Weiwei. Role of ultrasound in the assessment of percutaneous laser ablation of cervical metastatic lymph nodes from thyroid carcinoma[J].Acta Radiol,2018, 59(4):434-440.
- [6] 庄小捷,曹成莉,李云,等. 血清miR-130a, miR-425-5p表达水平与宫颈癌患者临床病理参数的关系及其诊断价值分析[J]. 中国妇幼保健, 2019, 34(9): 1966-1969. ZHUANG Xiaojie, CAO Chengli, LI Yun, et al. Analysis on the relationships between serum miR-130a and miR-425-5p expression levels and clinicopathological parameters of cervical cancer patients and the diagnostic value[J]. Maternal & Child Health care of China, 2019, 34(9):1966-1969.
- [7] 中国抗癌协会妇科肿瘤专业委员会. 宫颈癌诊断与治疗指南(第四版)[J]. 中国实用妇科与产科杂志, 2018, 34(6):613-622. Chinese Society of Gynecological Oncology. Guidelines for the diagnosis and treatment of cervical cancer (4th Edition)[J]. Chin J Pract Gynecol Obstet, 2018, 34(6):613-622.
- [8] GRADÍSSIMO A, BURK R D. Molecular tests potentially improving HPV screening and genotyping for cervical cancer prevention[J].Expert Rev Mol Diagn, 2017, 17(4):379-391.
- [9] MUSA J, ACHENBACH C J, O'DWYER L C, et al. Effect of cervical cancer education and provider recommendation forscreening on screening rates: A systematic review and meta-analysis[J].PLoS One, 2017, 12(9):e0183924.
- [10] LI Hai, WANG Xubo, GENG Jianxiang, et al. Clinical study of styping detection of human papillomavirus (HPV) infection with microarray from paraffinembedded specimens of cervical cancer and precursor lesions[J].J Nanosci Nanotechnol, 2015, 15(9):6423-6428.
- [11] WANG Pingping, SUN Wenqing, WANG Longxia, et al. Correlations of p53 expressionwith transvaginal color Doppler ultrasound findings of cervical cancer after radiotherapy[J].J BUON, 2018, 23(3):769-775.
- [12] LIU Yingxia, LIU Yan, XU Jinmei, et al. Color Doppler

- ultrasound and contrast-enhanced ultrasound in the diagnosis of lacrimal apparatus tumors[J]. *Oncol Lett*, 2018, 16(2):2215-2220.
- [13] ZHU Yi, ZHANG Guonan, ZHANG Ruibo, et al. Sonographic image of cervixepithelioid trophoblastic tumor coexisting with mucinous a denocarcinoma in apostmenopausal woman: A case report[J]. *Medicine (Baltimore)*, 2017, 96(38):e7731.
- [14] 何玉春, 李慧敏, 李邱静, 等. 经阴道彩色多普勒超声病灶内微血管与早期宫颈癌预后发展的关系 [J]. *实用癌症杂志*, 2017, 32(2):335-338.
- HE Yuchun, LI Huimin, LI Qiujing, et al. Relationship between the transvaginal color doppler flow imaging(TV-CDFI) of intralesional capillaries and prognosis of early cervical cancer[J]. *Practic J Cancer*, 2017, 32(2):335-338.
- [15] MASOOD N, BASHARAT Z, KHAN T, et al. Entangling relation of micro RNA-let7, miRNA-200 and miRNA-125 with various cancers[J]. *Pathol Oncol Res*, 2017, 23(4):707-715.
- [16] 马向薇, 曹东华, 仲美琦. miR-130a 靶向调节 SMAD4 基因对卵巢癌 SKOV3 细胞增殖和侵袭的影响 [J]. *解剖科学进展*, 2018, 24(2):118-121.
- MA Xiangwei, CAO Donghua, ZHONG Meiqi. Effects of miR-130a targeting SMAD4 gene on the proliferation and invasion of ovarian cancer SKOV3 cells[J]. *Prog Anat Sci*, 2018, 24(2):118-121.
- [17] 朱军, 赵琴. miR-425-5p 在宫颈癌中的表达及临床意义 [J]. *中国生育健康杂志*, 2017, 28(4):361-363.
- ZHU Jun, ZHAO Qin. Expression and clinical significance of mir-425-5p in cervical cancer[J]. *Chin J Reprod Health*, 2017, 28(4):361-363.
- [18] WANG H R, LIN Y, ZHANG X Y, et al. Transvaginal color doppler sonography combined with colposcopy for diagnosis of early stage cervical cancer and precancerous lesions[J]. *J Biol Regul Homeost Agents*, 2018, 32(1):123-126.
- [19] PARK S, EOM K, KIM J, et al. MiR-9, miR-21, and miR-155 as potential biomarkers for HPV positive and negative cervical cancer[J]. *BMC Cancer*, 2017, 17(1):658.
- [20] 冯磊, 常春红, 管晓卿, 等. 宫颈癌患者血浆 miRNA-10b 的表达及其临床意义 [J]. *现代检验医学杂志*, 2018, 33(1):52-55, 58.
- FENG Lei, CHANG Chunhong, GUAN Xiaoping, et al. Expression of plasma miRNA-10b in patients with cervical cancer and its clinical significance[J]. *J Mod Lab Med*, 2018, 33(1):52-55, 58.

收稿日期: 2020-07-01

修回日期: 2020-09-05

(上接第22页)

- WANG Tingting, SHAN Chao, ZHAO Jin. Research progress in the association between interleukin-17 gene polymorphism and periodontitis and rheumatoid arthritis[J]. *Journal of Xinxiang Medical University*, 2020, 37(5):498-501.
- [13] 陈建芸, 廖海平, 孙朝晖, 等. 类风湿性关节炎患者血清 RA-CP、抗 CCP 抗体及 RF 检测对 RA 的实验诊断意义 [J]. *现代检验医学杂志*, 2020, 35(5):38-40, 50.
- CHEN Jianyun, LIAO Haiping, SUN Zhaohui, et al. Significance of the detection of RA-CP, Anti-CCP antibody and RF in the laboratory diagnosis of rheumatoid arthritis [J]. *Journal of Modern Laboratory Medicine*, 2020, 35(5):38-40, 50.
- [14] 赵玉霞, 梅红, 彭罕鸣, 等. 白细胞介素 38 通过核因子- κ B 与信号转导及转录激活因子 3 信号通路抑制儿童炎症性肠病的分子机制 [J]. *中华消化杂志*, 2019, 39(4):237-243.
- ZHAO Yuxia, MEI Hong, PENG Hanming, et al. Molecular mechanisms of interleukin-38 inhibiting inflammatory bowel disease in children by regulating nuclear factor- κ B and signal transduction and activator of transcription 3 pathway [J]. *Chinese Journal of Digestion*, 2019, 39(4):237-243.
- [15] 刘珍星, 张山锋, 杨钟华. IL-38 通过调控 PI3K/Akt/GSK3 β /NFATc1 信号通路抑制骨质疏松的机制研究 [J]. *中国免疫学杂志*, 2018, 34(2):251-255.
- LIU Zhenxing, ZHANG Shanfeng, YANG Zhonghua. IL-38 inhibits osteoporosis via regulating PI3K/Akt/GSK3 β /NFATc1 signaling pathway [J]. *Chinese Journal of Immunology*, 2018, 34(2):251-255.
- [16] 廖林波, 王小超, 梁俊卿, 等. 类风湿关节炎易感基因多态性研究进展 [J]. *现代免疫学*, 2017, 37(5):433-436, 432.
- LIAO Linbo, WANG Xiaochao, LIANG Junqing, et al. Susceptibility gene polymorphism and rheumatoid arthritis[J]. *Current Immunology*, 2017, 37(5):433-436, 432.
- [17] 陈萍, 李亮亮, 梁申菊, 等. IL-17F 基因多态性与类风湿关节炎发病风险关系的 Meta 分析 [J]. *中国免疫学杂志*, 2017, 33(8):1218-1222.
- CHEN Ping, LI Liangliang, LIANG Shenju, et al. Association of IL-17F rs763780 and rs2397084 polymorphisms with rheumatoid arthritis: a meta-analysis [J]. *Chinese Journal of Immunology*, 2017, 33(8):1218-1222.
- [18] LEE Y H, BAE S C. Associations between circulating IL-17 levels and rheumatoid arthritis and between IL-17 gene polymorphisms and disease susceptibility: a meta-analysis[J]. *Postgraduate Medical Journal*, 2017, 93(112): 465-471.
- [19] DHAOUADI T, CHAHBI M, HAOUAMI Y, et al. IL-17A, IL-17RC polymorphisms and IL17 plasma levels in Tunisian patients with rheumatoid arthritis[J]. *PLoS One*, 2018, 13(3): e0194883.

收稿日期: 2021-03-09

修回日期: 2021-03-21