

doi: 10.13241/j.cnki.pmb.2017.11.031

血清胃蛋白酶原联合 G-17 对萎缩性胃炎及胃癌早期诊断价值 *

薛 辉 辛凤池 穆素恩 杨 俭 赵树巧

(石家庄市第一医院消化内科 河北 石家庄 050011)

摘要 目的:探索检测血清胃蛋白酶原 I(PGI)、胃蛋白酶原 II(PGII)、胃泌素-17(G-17)在萎缩性胃炎及胃癌中的诊断价值。**方法:**收集医院 2015 年 2 月至 12 月门诊及住院的慢性非萎缩性胃炎 44 例(非萎缩性胃炎组),慢性萎缩性胃炎 47 例(萎缩性胃炎组),早期胃癌 42 例(胃癌组)。采用酶联免疫吸附试验(ELISA)测定各组血清 PGI、PGII、G-17 的水平,同时计算 PGI/PGII 的比值(PGR),比较各组指标间的差异,同时绘制各指标筛查萎缩性胃炎及胃癌的受试者工作曲线(ROC)曲线,分别评价其诊断价值。**结果:**胃癌组及萎缩性胃炎组的血清 PGI、PGR 水平较非萎缩性胃炎组明显下降,且胃癌组下降更明显,差异均具有统计学意义($P<0.05$),萎缩性胃炎组血清 PGII 显著低于非萎缩性胃炎组,差异均具有统计学意义($P<0.05$);胃癌组的血清 G-17 水平较非萎缩性胃炎组及萎缩性胃炎组均升高,差异有统计学意义($P<0.05$)。血清 PGI 筛查萎缩性胃炎的最佳界值为 $\text{PGI}<90\text{ ng/mL}$,其灵敏度和特异度分别为 71.5%和 51.0%,血清 PGR 筛查萎缩性胃炎的最佳界值为 $\text{PGR}<8$,其灵敏度和特异度分别为 71.9%和 54.0%,血清 G-17 筛查萎缩性胃炎的最佳界值为 $\text{G-17}<5\text{ pmol/L}$,其灵敏度和特异度分别为 66.1%和 64.0%。血清 PGI 筛查胃癌的最佳界值为 $\text{PGI}<73\text{ ng/mL}$,其灵敏度和特异度分别为 86.0%和 74.9%;血清 PGR 筛查胃癌的最佳界值为 $\text{PGR}<3$,其灵敏度和特异度分别为 90.2%和 62.5%;血清 G-17 筛查胃癌的最佳界值为 $\text{G-17}<4\text{ pmol/L}$,其灵敏度和特异度分别为 62.5%和 61.3%。**结论:**胃癌及萎缩性胃炎患者血清 PGI、PGR 水平下降明显,且胃癌患者的血清 G-17 异常升高,血清 PG 联合 GS-17 测定可用于萎缩性胃炎及胃癌的早期筛查。

关键词:胃蛋白酶原;胃泌素;萎缩性胃炎;胃癌;早期诊断

中图分类号:R573.32;R735.2 **文献标识码:**A **文章编号:**1673-6273(2017)11-2119-04

Early Diagnosis Value of Serum Pepsinogen Combined with G-17 for Atrophic Gastritis and Gastric Cancer*

XUE Hui, XIN Feng-chi, MU Su-en, YANG Jian, ZHAO Shu-qiao

(Third Department of Gastroenterology, The First Hospital of Shijiazhuang, Shijiazhuang, Hebei, 050011, China)

ABSTRACT Objective: To research the diagnostic value of measuring serum pepsinogen I(PGI), pepsinogen II(PGII) and gastrin-17 (G-17) for atrophic gastritis and gastric cancer. **Methods:** A total of 44 patients were diagnosed with non-atrophic gastritis(non-atrophic gastritis group), 47 patients were chronic atrophic gastritis(atrophic gastritis group), 42 were gastric cancer(gastric cancer group) were enrolled in the hospital February 2015 to December 2015. The serum PGI, PGII and G-17 levels were detected by enzyme-linked immunosorbent assay (ELISA), and PGI/II ratio (PGR) was calculated, compared above indexes in different groups, and drew the receiver operating curve (ROC) of above indexes, and analyzed their diagnostic value. **Results:** The levels of serum PGI and PGR in gastric cancer group and chronic atrophic gastritis group were significantly decreased than that of non-atrophic gastritis group, and gastric cancer group decreased more, the differences were statistically significant ($P<0.05$), the level of PGII in atrophic gastritis group was lower than non-atrophic gastritis group, the difference was statistically significant ($P<0.05$), the level of serum G-17 in gastric cancer were significantly increased than chronic atrophic gastritis and non-atrophic gastritis group, the differences were statistically significant ($P<0.05$). The optimal value of PGI screening for atrophic gastritis was $\text{PGI}<90\text{ ng/mL}$, its sensitivity and specificity were 71.5% and 51.0%, respectively. The optimal value of PGR screening for atrophic gastritis was $\text{PGR}<8$, its sensitivity and specificity were 71.9% and 54.0%, respectively. The optimal value of G-17 screening for atrophic gastritis was $\text{G-17}<5\text{ pmol/L}$, its sensitivity and specificity were 66.1% and 64.0%, respectively. The optimal value of PGI screening for gastric cancer was $\text{PGI}<73\text{ ng/mL}$, its sensitivity and specificity were 86.0% and 74.9%, respectively. The optimal value of PGR screening for gastric cancer was $\text{PGR}<3$, its sensitivity and specificity were 90.2% and 62.5%, respectively. The optimal value of G-17 screening for gastric cancer was $\text{G-17}<4\text{ pmol/L}$, its sensitivity and specificity were 62.5% and 61.3%, respectively. **Conclusion:** The levels of serum PGI and PGR in patients with gastric cancer and atrophic gastritis are significantly decreased, and the serum G-17 of the patients with gastric cancer are abnormally increased, detecting serum PG combined with G-17 can be used to screen early gastric cancer and chronic atrophic gastritis.

* 基金项目:2014 年度石家庄市科学技术研究与发展指导计划项目(141462833)

作者简介:薛辉(1973-),女,本科,副主任医师,从事肿瘤内科方面的研究,E-mail:xuehui12@163.com

(收稿日期:2016-10-28 接受日期:2016-11-21)

Key words: Pepsinogens; Gastrins; Atrophic gastritis; Gastric cancer; Early diagnosis

Chinese Library Classification(CLC): R573.32; R735.2 **Document code:** A

Article ID: 1673-6273(2017)11-2119-04

前言

胃癌是消化系统中较常见的恶性肿瘤,其死亡率占恶性肿瘤者五分之一左右,早期诊断率较低是其死亡率较高的一个重要原因^[1]。癌前疾病与癌前病变是导致胃癌的重要因素,慢性萎缩性胃炎是重要的癌前疾病之一,在我国发病率比较高,部分慢性萎缩性胃炎最终发展成为癌症,主要取决于萎缩部位,是否合并肠化及异型增生及萎缩的严重程度,且与患者基因型及遗传易感性有关^[1]。目前学术界普遍接受了从慢性非萎缩性胃炎-萎缩性胃炎-肠化生-异型增生-肠型胃癌的病变过程的多步骤假说。因此早期诊断萎缩性胃炎及胃癌对降低胃癌的死亡率显得尤为重要^[2]。监测患者血清中的胃蛋白酶原(Pepsinogen,PG)及胃泌素(gastrin,GS)水平是常用的非侵入性的监测方法,且在国内外已开展多年了。血清PG和GS是由胃粘膜不同部位的腺体及细胞合成并释放进入胃腔及外周血液循环的胃肠激素。PG根据其免疫活性不同可以分为PGI和PGII,二者的理化性质及来源不完全相同^[3]。GS是由G细胞分泌,其中胃泌素-17(Gastrin-17,G-17)含量约占80%-90%,它们由胃窦部的腺体分泌后可以直接进入血液循环,因此目前大部分学者认为G-17水平是G细胞功能的生物学标志,GS的主要功能在于调节胃酸的分泌和促进胃粘膜的生长,其与胃癌的发生也存在一定的关系。由于胃粘膜功能改变一般早于形态学改变,因此推测PG/GS水平可以早期反映胃粘膜不同部位腺体的形态和功能^[4,5]。本文正是在此基础上,进一步研究血PG及GS在萎缩性胃炎及胃癌患者中的变化及各指标筛查萎缩性胃炎及胃癌的界值。

1 资料与方法

1.1 临床资料

收集医院2015年2月至12月门诊及住院的慢性非萎缩性胃炎44例(非萎缩性胃炎组),慢性萎缩性胃炎47例(萎缩性胃炎组),早期胃癌42例(胃癌组),共133例。慢性萎缩性胃炎患者需从胃窦、胃体、胃底及小弯侧、大弯侧及非典型部位分别取材,胃癌患者的胃粘膜活检组织则经过内镜取材。所有患

者的胃镜检查均经有经验的内镜医师进行,病例取材的组织经病理实验室确证。纳入标准:内镜及病理诊断的慢性萎缩性胃炎、胃癌及慢性非萎缩性胃炎患者。排除标准:胃或十二指肠手术史;肝肾功能异常;正在服用或近4周服用PPI或H2R拮抗剂;近期抗生素使用史;既往HP根除史。

1.2 方法

1.2.1 材料与试剂 PGI检测试剂盒、PGII检测试剂盒、G-17检测试剂盒由芬兰必欧瀚集团提供:批号分别为17PA1304、21PB1303、17GC1302。吸水纸、蒸馏水、1000 mL量筒、稀释样本用混匀器、稀释样本用试管、采集血清样本的塑料管及一次性针头、冰水浴用容器、低温冰箱、全自动酶标仪、恒温箱、小型离心机。

1.2.2 实验方法 所有受检者空腹12 h后采血5 mL,即刻小型离心机以4000 r/min的速度离心5 min分离血清后-80℃冰箱冷冻保存待测,检测前将标本放入4℃冰箱12 h后再拿出至室温。应用酶联免疫吸附法(Enzyme-linked immunosorbent assay,ELISA)法通过全自动酶标仪来检测血清G-17、PGI、PGII的含量,计算PG比值(Pepsinogen ratio,PGR), $PGR=PGI/PGII$ 。检测过程严格按照说明书操作。

1.3 统计学方法

所得结果用SPSS20.0分析,结果以($\bar{x} \pm s$)表示,计量资料多组间均值比较,采用完全随机设计的单因素方差分析,组间多重比较采用LSD法,采用ROC曲线计算各指标筛查萎缩性胃炎及胃癌的最佳临界值。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 三组血清PGI、PGII、G-17的比较

胃癌组及萎缩性胃炎组中血清PGI、PGR水平均明显低于较非萎缩性胃炎组,且胃癌组明显低于萎缩性胃炎组,差异均具有统计学意义($P<0.05$),萎缩性胃炎组血清PGII显著低于非萎缩性胃炎组,差异均具有统计学意义($P<0.05$);胃癌组的血清G-17水平较非萎缩性胃炎组及萎缩性胃炎组均升高,差异有统计学意义($P<0.05$)。见表1。

表1 各组血清PGI、PGII、G-17及PGR水平比较

Table 1 Comparison of serum PGI, PGII, G-17 and PGR levels in different groups

Groups	n	PGI(ng/mL)	PGII (ng/mL)	PGR	G-17(pmol/L)
Non-atrophic gastritis group	44	138.2 $\pm$ 49.5	15.9 $\pm$ 12.8	13.2 $\pm$ 8.4	10.6 $\pm$ 10.2
Atrophic gastritis group	47	100.2 $\pm$ 42.2 ^a	13.3 $\pm$ 9.6 ^a	9.4 $\pm$ 5.2 ^a	7.7 $\pm$ 7.1
Gastric cancer group	42	52.8 $\pm$ 28.5 ^{a *}	13.9 $\pm$ 8.8	6.3 $\pm$ 5.9 ^{a *}	17.7 $\pm$ 12.6 ^{a *}
F		67.326	89.735	98.274	37.413
P		0.034	0.032	0.002	0.034

Note: Compared with non-atrophic gastritis group, ^a $P<0.05$; compared with atrophic gastritis group, ^{*} $P<0.05$.

2.2 血清PGI、PGR及G-17对萎缩性胃炎的诊断价值

萎缩性胃炎血清PGI、PGR及G-17的ROC曲线显示,血

清PGI的线下面积为0.689,最佳临界值为PGI<90 ng/mL,其灵敏度和特异度分别为71.5%和51.0%;血清PGR线下面积为

0.649,最佳临界值为 $PGR < 8$,其灵敏度和特异度分别为 71.9% 和 54.0%;血清 G-17 线下面积为 0.622,最佳临界值为 $G-17 < 5$ pmol/L,其灵敏度和特异度分别为 66.1%和 64.0%。见图 1。

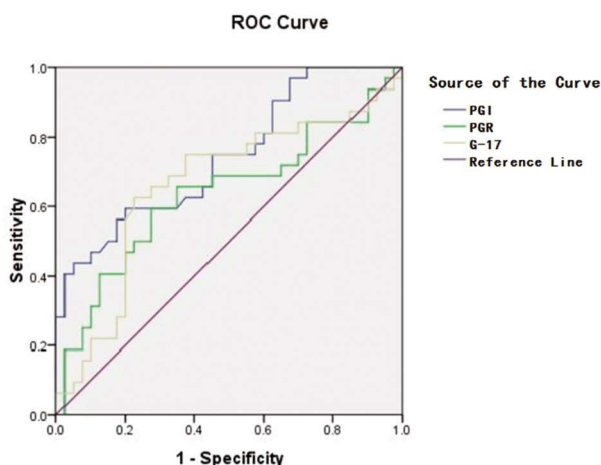


图 1 血清 PGI、PGR 及 G-17 诊断萎缩性胃炎的 ROC 曲线

Fig.1 The ROC curve of serum PGI, PGR and G-17 for the diagnosis of atrophic gastritis

2.3 PGI、PGR 及 G-17 对胃癌的诊断价值

胃癌血清 PGI、PGR 及 G-17 ROC 曲线显示,血清 PGI 线下面积为 0.901,最佳临界值为 $PGI < 73$ ng/mL,其灵敏度和特异度为 86.0%、74.9%;血清 PGR 线下面积为 0.757,最佳临界值为 $PGR < 3$,其灵敏度和特异度为 90.2%、62.5%;血清 G-17 筛查胃癌的 ROC 曲线下面积为 0.682,最佳界值为 $G-17 < 4$ pmol/L,其灵敏度和特异度分别为 62.5%和 61.3%。见图 2。

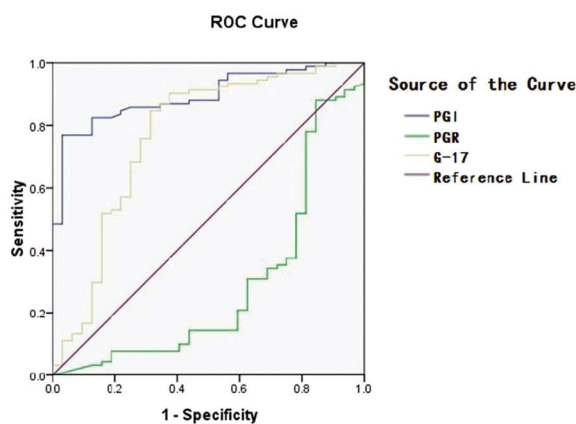


图 2 PGI、PGR 及 G-17 诊断胃癌的 ROC 曲线

Fig.2 The ROC curve of serum PGI, PGR and G-17 for the diagnosis of gastritis cancer

3 讨论

全球每年死于胃癌的人数 70 万左右,严重威胁着人类的健康^[6]。我国属于胃癌的高发地区。胃癌是长期多因素互相作用的结果。其癌前情况包括胃萎缩、肠化及异型增生。报道显示,每年大概有 0-1.8%的萎缩性胃炎、0-10%的肠化、0-73%的异型增生演变为胃癌^[7]。研究表明,早期诊断的胃癌患者五年生存率可以达到 90%以上,而中晚期诊断的患者五年生存率低于 50%^[8]。目前主要依靠胃镜加病理活检诊断胃癌,但胃镜检查存在对内镜医师的技术要求高,有些患者由于耐受性差,存在禁忌等

不能行内镜检测,病理活检则存在取材不满意、技术要求高的问题,因此尚不能作为普查手段^[9]。而肿瘤标志物检测则存在灵敏度及特异性低及费用较高的缺点,亦不能在基层医院普及。X 线透视检查可以作为胃癌的筛查,但其存在着射线辐射,而且仅能发现晚期病变,对发现早期病变存在一定的困难,且其对特殊人群如孕妇等并不可行。因此亟待寻找一种新型的,可方便快捷、无创地进行早期萎缩性胃炎及胃癌的筛查诊断方法^[10,11]。

PG 本身不具有活性,是胃蛋白酶的前体,主要存在于人体的胃液中,血清及 24 h 尿液中也可检测到 PG 的存在。因此通过测定血清 PG 的含量可以间接反应胃粘膜腺体及细胞的数量。根据血清 PG 免疫活性的差异分成 PGI 和 PGII。胃底腺颈粘液细胞主要分泌 PGI,胃体部位的萎缩导致分泌 PGI 的主细胞数量减少,PGI 分泌量减少,因此血清 PGI 可以作为胃体的血清学标志物^[12]。因分泌 PGII 的腺体及细胞分布广泛,因此其水平与胃窦或胃体萎缩水平并不一致,但考虑 PGII 可能与肠化及异型增生相关。本实验结果显示胃癌组及萎缩性胃炎组中血清 PGI、PGR 水平均明显低于较非萎缩性胃炎组,且胃癌组明显低于萎缩性胃炎组($P < 0.05$)。说明在 PG 在萎缩性胃炎-胃癌的病变进展过程不断下降,可能是当慢性萎缩性胃炎进展至肠化阶段,假幽门腺代替了部分主细胞,从而导致 PGII 水平增加,PGR 水平降低。此外本研究发现 PGI 筛查胃癌的最佳临界值为 $PGI < 73$ ng/mL,PGR 筛查胃癌的最佳临界值为 $PGR < 3$ 。不同地方报道的萎缩性胃炎及胃癌的诊断界值不同,可能是由萎缩程度、肿瘤位置及临床分期差异、生活饮食习惯不同引起的^[13,14]。且有关研究显示^[14]PG 及 GS 水平与年龄、性别、身高、体重、饮酒等均有关,因此建议行大规模的分级、分期研究,制定各地的界值,从而提供更好的参考价值。

G-17 主要是由胃窦部的 G 细胞分泌的一种胃肠激素,其含量主要受 G 细胞数量及功能的影响,也受胃内酸度的负反馈调节,其生理作用主要是调节胃酸的分泌及胃粘膜的生长及分泌功能^[15]。一般情况下胃窦部萎缩性病变进展时 G 细胞数量的减少可以导致外周血清中 G-17 水平减低。本研究发现,胃癌组的 G-17 水平较非萎缩性胃炎组及萎缩性胃炎组均升高,差异有统计学意义($P < 0.05$),究其原因,可能与胃部萎缩过程中,胃酸分泌水平降低,引起 G 细胞数量增加,导致 G-17 水平上升有关^[16,17]。本研究通过分别绘制萎缩性胃炎及胃癌患者的 PGI、PGR 及 G-17 的 ROC 曲线,发现这些指标对萎缩性胃炎及胃癌的灵敏度和特异度均较高,说明通过测定 PG 及 GS 水平可以筛查出该疾病的高危人群,对早期诊断率、及时采取干预措施具有重要作用,且血清学检测具有无创、廉价、方便简便等特点,可大规模推广^[18-20]。

综上所述,胃癌及萎缩性胃炎患者血清 PGI、PGR 水平下降明显,且胃癌患者的血清 G-17 异常升高,血清 PG 联合 GS 测定可用于萎缩性胃炎及胃癌的早期筛查。

参考文献 (References)

- [1] Nejadi-Kelarijani F, Roshandel G, Semnani S, et al. Diagnostic values of serum levels of pepsinogens and gastrin-17 for screening gastritis and gastric cancer in a high risk area in northern Iran [J]. Asian Pac J Cancer Prev, 2014, 15(17): 7433-7436
- [2] McNicholl AG, Forné M, Barrio J, et al. Accuracy of GastroPanel for

- the diagnosis of atrophic gastritis [J]. *Eur J Gastroenterol Hepatol*, 2014, 26(9): 941-948
- [3] Tu H, Sun L, Dong X, et al. Temporal changes in serum biomarkers and risk for progression of gastric precancerous lesions: a longitudinal study[J]. *Int J Cancer*, 2015, 136(2): 425-434
- [4] Švagelj D, Terzić V, Dovhanj J, et al. Superoxide dismutases in chronic gastritis[J]. *APMIS*, 2016, 124(4): 252-256
- [5] Pohjanen VM, Koivurova OP, Huhta H, et al. Toll-Like Receptor 4 Wild Type Homozygosity of Polymorphisms +896 and +1196 Is Associated with High Gastrin Serum Levels and Peptic Ulcer Risk[J]. *PLoS One*, 2015, 10(7): e0131553
- [6] Ohashi T, Komatsu S, Ichikawa D, et al. Tumor Index as a Combined Indicator of Tumor Depth and Size in Gastric Cancer [J]. *Anticancer Res*, 2016, 36(4): 1895-1900
- [7] Tanaka T, Mulyadi IK, Moestikaningsih, et al. Rare *Helicobacter pylori* Infection May Explain Low Stomach Cancer Incidence: Ecological Observations in Bali, Indonesia[J]. *Asian Pac J Cancer Prev*, 2016, 17(3): 979-984
- [8] Xie XQ, Zheng KC, Wu BS, et al. Differences in the levels of gastric cancer risk factors between Nanjing and Minqing counties, China[J]. *J Prev Med Public Health*, 2014, 47(5): 281-287
- [9] Masci E, Pellicano R, Mangiavillano B, et al. GastroPanel® test for non-invasive diagnosis of atrophic gastritis in patients with dyspepsia [J]. *Minerva Gastroenterol Dietol*, 2014, 60(1): 79-83
- [10] Makki AM, Aldaqa SM, Alorabi SH, et al. Chronic Gastritis in Morbidly Obese Patients with Sleeve Gastrectomy[J]. *Electron Physician*, 2016, 8(1): 1786-1790
- [11] Adamczyk M, Peczek Ł, Rudnicki C, et al. The clinical significance of GastroPanel in diagnostics of *Helicobacter pylori* eradication efficiency in patients with dyspepsia with correlation of family history of gastric cancer[J]. *Pol Merkuriusz Lekarski*, 2013, 35(207): 141-147
- [12] De Re V, Orzes E, Canzonieri V, et al. Pepsinogens to Distinguish Patients With Gastric Intestinal Metaplasia and *Helicobacter pylori* Infection Among Populations at Risk for Gastric Cancer [J]. *Clin Transl Gastroenterol*, 2016, 7(7): e183
- [13] Benberin V, Bektayeva R, Karabayeva R, et al. Prevalence of *H. pylori* infection and atrophic gastritis among symptomatic and dyspeptic adults in Kazakhstan. A hospital-based screening study using a panel of serum biomarkers[J]. *Anticancer Res*, 2013, 33(10): 4595-4602
- [14] Eybpoosh S, Talebkhan Y, Saberi S, et al. Age-Specific Gastric Cancer Risk Indicated by the Combination of *Helicobacter pylori* Sero-Status and Serum Pepsinogen Levels[J]. *Version 2. Iran Biomed J*, 2015, 19(3): 133-142
- [15] Mansour-Ghanaei F, Joukar F, Rajpout Y, et al. Screening of precancerous gastric lesions by serum pepsinogen, gastrin-17, anti-*Helicobacter pylori* and anti- CagA antibodies in dyspeptic patients over 50 years old in Guilan Province, north of Iran [J]. *Asian Pac J Cancer Prev*, 2014, 15(18): 7635-7638
- [16] Leja M, Lapina S, Polaka I, et al. Pepsinogen testing for evaluation of the success of *Helicobacter pylori* eradication at 4 weeks after completion of therapy[J]. *Medicina(Kaunas)*, 2014, 50(1): 8-13
- [17] Lundell L, Vieth M, Gibson F, et al. Systematic review: the effects of long-term proton pump inhibitor use on serum gastrin levels and gastric histology[J]. *Aliment Pharmacol Ther*, 2015, 42(6): 649-663
- [18] Gong Y, Wei W, Jingwei L, et al. *Helicobacter pylori* Infection Status Correlates with Serum Parameter Levels Responding to Multi-organ Functions[J]. *Dig Dis Sci*, 2015, 60(6): 1748-1754
- [19] Ishimura N, Owada Y, Aimi M, et al. No increase in gastric acid secretion in healthy Japanese over the past two decades [J]. *J Gastroenterol*, 2015, 50(8): 844-852
- [20] Sillakivi T, Suumann J, Kirsimägi U, et al. Plasma levels of gastric biomarkers in patients after bariatric surgery: biomarkers after bariatric surgery [J]. *Hepatogastroenterology*, 2013, 60(128): 2129-2132
- (上接第 2136 页)
- [13] Sandoval-Talamantes AK, Brito-Luna MJ, Fafutis-Morris M, et al. The 3'UTR 1188A/C polymorphism of IL-12p40 is not associated with susceptibility for developing plaque psoriasis in Mestizo population from western Mexico[J]. *Immunol Lett*, 2015, 163(2): 221-226
- [14] Wu Y, Lu Z, Chen Y, et al. Association of IL-12B gene rs6887695 polymorphism with hereditary susceptibility and clinical characterization of psoriasis vulgaris in the Chinese Han population[J]. *Arch Dermatol Res*, 2013, 305(6): 477-482
- [15] Hébert HL, Bowes J, Smith RL, et al. Identification of loci associated with late-onset psoriasis using dense genotyping of immune-related regions[J]. *Br J Dermatol*, 2015, 172(4): 933-939
- [16] Karabacak E, Aydin E, Ozcan O, et al. Methylenetetrahydrofolate reductase (MTHFR) 677C>T gene polymorphism as a possible factor for reducing clinical severity of psoriasis [J]. *Int J Clin Exp Med*, 2014, 7(3): 697-702
- [17] Prieto-Pérez R, Solano-López G, Cabaleiro T, et al. The polymorphism rs763780 in the IL-17F gene is associated with response to biological drugs in patients with psoriasis [J]. *Pharmacogenomics*, 2015, 16(15): 1723-1731
- [18] Li B, Tsoi LC, Swindell WR, et al. Transcriptome analysis of psoriasis in a large case-control sample: RNA-seq provides insights into disease mechanisms[J]. *J Invest Dermatol*, 2014, 134(7): 1828-1838
- [19] Jókai H, Szakonyi J, Kontár O, et al. Impact of effective tumor necrosis factor- α inhibitor treatment on arterial intima-media thickness in psoriasis: results of a pilot study [J]. *J Am Acad Dermatol*, 2013, 69(4): 523-529
- [20] Oostveen AM, Bergboer JG, Van de Kerkhof PC, et al. Genotype-phenotype correlations in a prospective cohort study of paediatric plaque psoriasis: lack of correlation between HLA-C*06 and family history of psoriasis[J]. *Acta Derm Venereol*, 2014, 94(6): 667-671