

doi: 10.13241/j.cnki.pmb.2022.22.024

慢阻肺伴左心衰竭临床特征与影响因素分析 *

李双双¹ 李超¹ 来静² 李娜³ 张怡^{1△}

(1 中国人民解放军空军第九八六医院呼吸内科 陕西 西安 710018;

2 安康市中心医院呼吸内科 陕西 安康 725099;3 西安交通大学第一附属医院检验科 陕西 西安 710061)

摘要 目的:探讨慢阻肺伴左心衰竭临床特征与影响因素。**方法:**回顾性选择 2019 年 1 月至 2020 年 12 月来我院诊治的慢性阻塞性肺疾病患者 150 例。根据是否合并心衰,将 150 例患者分为慢阻肺伴左心衰竭组(A 组)与慢阻肺未伴左心衰竭组(B 组)。分析 150 例患者中慢阻肺伴左心衰竭的占比,分析对比两组一般资料、习惯和疾病病史、肺功能、心脏彩超、心电图结果、血液指标水平与动脉血气指标,采用 Logistic 回归分析慢阻肺伴左心衰竭的影响因素。**结果:**(1)150 例患者中,慢阻肺伴左心衰竭者占比为 32.00 %,慢性阻塞性肺疾病未合并左心衰竭者占比为 68.00 %。(2)两组性别、年龄、患病时间、糖尿病史、吸烟史、高血压史、冠心病史、FEV₁/FVC、左房内径、左心室舒张末内径、左室重量分数、左后室壁厚度、肺动脉压、血小板计数、C 反应蛋白、降钙素原、凝血酶原时间、D-二聚体、白蛋白、肌酸激酶同工酶、N 末端脑钠肽前体、PaCO₂、PaO₂、SaO₂ 对比有差异($P < 0.05$)。(3)Logistic 回归分析结果表明、性别、年龄、糖尿病史、吸烟史、高血压史、冠心病史、左心室舒张末内径、肺动脉压是影响慢阻肺合并左心衰竭患者的影响因素($P < 0.05$)。**结论:**慢阻肺伴左心衰竭的占比较高,其与性别为男性、年龄偏大、有糖尿病史、吸烟史、高血压史、冠心病史、左心室舒张末内径升高、肺动脉压升高相关,需对以上因素给予积极干预及治疗。

关键词:慢性阻塞性肺疾病;左心衰竭;影响因素;临床特征

中图分类号:R563;R541.61 文献标识码:A 文章编号:1673-6273(2022)22-4326-05

Clinical Characteristics and Influencing Factors of Chronic Obstructive Pulmonary Disease with Left Heart Failure*

LI Shuang-shuang¹, LI Chao¹, LAI Jing², LI Na³, ZHANG Yi^{1△}

(1 Department of Respiratory medicine, The 986 hospital of Chinese People's Liberation Army Air Force, Xi'an, Shaanxi, 710018, China;

2 Department of Respiratory medicine, Ankang Central Hospital, Ankang, Shaanxi, 725099, China;

3 Department of Clinical Laboratory, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, China)

ABSTRACT Objective: To explore the clinical features and influencing factors of chronic obstructive pulmonary disease with left heart failure. **Methods:** A total of 150 patients with chronic obstructive pulmonary disease who came to our hospital for diagnosis and treatment from January 2019 to December 2020 were retrospectively selected. According to whether the patients were complicated with heart failure, 150 patients were divided into COPD with left heart failure group (group A) and COPD without left heart failure group (group B). The proportion of chronic obstructive pulmonary disease with left heart failure in 150 patients was analyzed, and the general data, habits and disease history, pulmonary function, echocardiography, electrocardiogram results, blood index levels and arterial blood gas indexes of the two groups were analyzed and compared. Risk factors for obstructive pulmonary disease with left heart failure. **Results:** (1) Among the 150 patients, COPD with left heart failure accounted for 32.00 %, and COPD without left heart failure accounted for 68.00 %. (2) The Gender, age, disease duration, diabetes history, smoking history, hypertension history, coronary heart disease history, FEV₁/FVC, left atrial diameter, left ventricular end-diastolic diameter, left ventricular weight fraction, left ventricular posterior wall thickness, pulmonary artery Blood pressure, platelet count, C-reactive protein, procalcitonin, prothrombin time, D-dimer, albumin, creatine kinase isoenzyme, N-terminal brain natriuretic peptide precursor, PaCO₂, PaO₂, SaO₂ in two groups were difference ($P < 0.05$). (3) Logistic regression analysis showed that gender, age, history of diabetes mellitus, smoking history, history of hypertension, history of coronary heart disease, left ventricular end-diastolic diameter and pulmonary artery pressure were the risk factors for patients with COPD complicated with left cardiac insufficiency ($P < 0.05$). **Conclusion:** The proportion of chronic obstructive pulmonary disease with left heart failure is high, which is related to male gender, older age, history of diabetes, smoking history, history of hypertension, history of coronary heart disease, increased left ventricular end-diastolic diameter, and increased pulmonary artery pressure, the above factors need

* 基金项目:陕西省重点研发计划项目(2021SF-312)

作者简介:李双双(1984-),女,本科,主治医师,研究方向:慢阻肺,发热伴肺部阴影,肺癌,

电话:15991781419,E-mail:xiaoyou01232022@163.com

△ 通讯作者:张怡(1985-),女,本科,主治医师,研究方向:呼吸内科、肺癌、慢阻肺、哮喘,

电话:15353529769,E-mail:xiaoyou01232022@163.com

(收稿日期:2022-05-10 接受日期:2022-05-30)

to be actively intervened and treated.

Key words: Chronic obstructive pulmonary disease; Left heart failure; Risk factors; Clinical features

Chinese Library Classification(CLC): R563; R541.61 Document code: A

Article ID: 1673-6273(2022)22-4326-05

前言

慢性阻塞性肺疾病的心血管合并症多包括缺血性心脏病、心力衰竭、心律失常、高血压等,其中心力衰竭因与慢性阻塞性肺疾病加重期症状相似,因此鉴别诊断较为困难^[1-3]。同时与单纯慢性阻塞性肺疾病相比,合并心力衰竭的慢性阻塞性肺疾病病情更加严重、复杂,若未及时诊断,则不能对合并心力衰竭的患者进行及时治疗,持续的左心衰竭会导致患者肺通气比例出现失调的情况,同时患者的心排量不足,会减少肋间肌、膈肌的血供,降低呼吸肌运动,进一步降低肺功能通气,从而加重患者的呼吸衰竭情况,引起疾病病情加重,甚至导致患者死亡^[4-6]。因此左心功能不全多出现在心力衰竭前,其起病较早,且临床症状较为隐匿,是导致慢性阻塞性肺疾病患者死亡的隐形杀手。因此临幊上对于慢阻肺伴左心衰竭需及早进行识别。临幊上无症状左心功能不全到有症状的心力衰竭存在潜伏期,因此若可以及早对慢阻肺伴左心衰竭的患者进行及早干预,可能会延缓或逆转慢性肺功能不全合并心力衰竭的疾病发生与发展^[7-9]。因此本文分析了慢阻肺伴左心衰竭患者的疾病患病情况,并对其临床特征进行分析,以为慢阻肺伴左心衰竭的疾病诊断、治疗提供支持与依据。

1 资料与方法

1.1 一般资料

回顾性选择2019年1月至2020年12月来我院诊治的慢性阻塞性肺疾病患者150例。

纳入标准:所有患者均符合慢性阻塞性肺疾病的疾病诊断标准(GOLD2017版),所有患者均存在慢性咳嗽、呼吸困难或者咳痰的临床症状,患者在吸入支气管舒张剂后行肺功能检查发现患者存在气流受限的情况,FEV₁/FVC低于70%;左心功能不全:符合评定左心衰竭的诊断标准:左室射血分数不超过50%同时E/e_r超过14或左室射血分数不低于50%且E/e_r在8~14间,同时符合(1)~(5)中的一项:(1)二尖瓣舒张早期血流速度/二尖瓣舒张晚期血流峰速<1;(2)脑钠肽或前体脑钠肽超过220 pg/mL;(3)左心房内径超过47 mm;(4)房颤;(5)男性左室质量指数超过149 g/m²,女性超过122 g/m²。

排除标准:既往已诊断为心力衰竭者、存在心脏瓣膜病、心肌疾病、感染性心内膜炎、心包疾病、主动脉夹层、成人先天性心脏病等心血管疾病者;存在支气管哮喘、肺炎、肺部肿瘤、间质性肺病、肺血栓栓塞、胸膜疾病等呼吸系统疾病;存在严重的肝肾功能异常者;存在严重的恶性肿瘤终末期疾病者;患者的临床资料不全者等。

根据是否合并心衰,将150例患者分为慢阻肺伴左心衰竭组(A组)与慢阻肺未伴左心衰竭组(B组)。

1.2 方法

收集150例慢阻肺伴左心衰竭患者的年龄、性别、体质量

指数、吸烟史等基础资料,是否存在高血压、冠状动脉粥样硬化、慢性肾脏病、糖尿病等基础疾病,以及既往的动脉pH值、脑钠肽或前体脑钠肽、肺功能指标(记录患者的一秒量FEV₁%、FEV₁/FVC)、心电图、血氧饱和度及心脏彩超(使用超声心动图检测患者的左房内镜、左心室舒张末内镜、左室后壁厚度、室间隔厚度、左室射血分数、二尖瓣舒张早期血流峰速度、二尖瓣舒张晚期血流峰速度)等资料。

1.3 观察指标

- (1)分析150例患者中慢阻肺伴左心衰竭的占比;
- (2)分析对比两组患者的一般资料、习惯和疾病病史、肺功能、心脏彩超和心电图结果;
- (3)分析对比两组患者的血液指标水平与动脉血气指标分析;
- (4)对自变量进行赋值,使用Logistic回归分析慢阻肺伴左心衰竭的危险因素。

1.4 统计学方法

使用Excel收集患者的资料,用SPSS22.0软件对比分析,计量资料用($\bar{x} \pm s$)表示,t检验分析,计数资料用频数表示,卡方检验分析,使用非条件Logistic回归分析法分析慢阻肺合并左心功能不全的危险因素,P<0.05为差异有统计学意义。

2 结果

2.1 分析150例患者中慢阻肺伴左心衰竭的占比

150例患者中,慢阻肺伴左心衰竭者例数为48例,占比为32.00%,慢阻肺未伴左心衰竭者102例,占比为68.00%。

2.2 对比一般资料、习惯和疾病病史、肺功能、心脏彩超和心电图结果

两组在性别、年龄、患病时间、糖尿病史、吸烟史、高血压史、冠心病史、FEV₁/FVC、左房内径、左心室舒张末内径、左室重量分数、左室后壁厚度、肺动脉压对比有差异(P<0.05)。

2.3 分析对比血液指标水平与动脉血气指标分析

两组的血小板计数、C反应蛋白、降钙素原、凝血酶原时间、D-二聚体、白蛋白、肌酸激酶同工酶、N末端脑钠肽前体、PaCO₂、PaO₂、SaO₂对比有差异(P<0.05)。

2.4 慢阻肺合并左心功能不全危险因素的Logistic回归分析

Logistic回归分析结果表明,性别、年龄、糖尿病史、吸烟史、高血压史、冠心病史、左心室舒张末内径、肺动脉压是影响慢阻肺伴左心衰竭患者的危险因素(P<0.05)。

3 讨论

慢性阻塞性肺疾病是一种异质性疾病,多是因气体或毒颗粒引起的肺泡或气道损害,从而导致患者出现持续的进行性不可逆气流受限或持续性呼吸症状,患者会出现以咳嗽、胸闷、呼吸困难、咳痰、气促的临床表现^[10-12]。心力衰竭是一种心脏功能异常、结构异常引起的综合征,患者会出现渐进性的室重构,

表 1 对比一般资料、习惯和疾病病史、肺功能、心脏彩超和心电图结果

Table 1 General information, habits and disease history, lung function, color doppler echocardiography and electrocardiogram results were compared

Items	Classification	Group A (48 cases)	Group B (102 cases)
Gender	Male	30 [#]	80
	Femal	18	22
Age(Years)	-	70.33±5.78 [#]	65.89±4.15
BIM(kg/m ²)	-	21.45±2.12	20.89±1.89
Sick time(Years)	-	14.78±2.43 [#]	10.09±1.99
History of diabetes	Yes	10 [#]	5
	No	38	97
History of drinking	Yes	14	32
	No	34	70
History of smoking	Yes	33 [#]	45
	No	15	57
History of hypertension	Yes	38 [#]	35
	No	10	67
History of CHD	Yes	26 [#]	21
	No	22	81
FEV ₁ /FVC(%)	-	53.45±9.89 [#]	50.11±9.09
FEV ₁ (%)	-	52.56±10.34	54.99±11.24
Left atrial diameter(mm)		38.79±6.56 [#]	33.09±3.89
Interventricular septal thickness (mm)		10.38±1.34	10.43±1.45
Left ventricular end diastolic diameter(mm)		47.55±5.78 [#]	43.45±4.89
Left ventricular mass fraction(g/m ²)		101.78±18.89 [#]	86.89±16.45
Posterior wall thickness of left ventricle(mm)		9.76±1.02 [#]	9.28±0.89
Left ventricular ejection fraction(%)		62.13±9.89	63.67±10.34
Pulmonary artery pressure(mmHg)		37.34±10.89 [#]	30.25±8.34

Note: compared with the group B, [#]P<0.05, the same below.

从而导致患者出现射血脑功能受损及心室充盈,从而会降低患者的心室射血功能,从而出现血流动力学障碍,导致患者出现疲乏、呼吸困难、液体潴留等症状^[13-15]。临幊上慢性阻塞性肺疾病与心力衰竭两种疾病均有系统性炎症、烟草暴露、氧化应激等疾病的危险因素,同时有感染等疾病的诱发因素;两种疾病也会出现一定的发病年龄重叠^[16-18]。因感染引起的慢性阻塞性肺疾病患者随着进展,会对患者机体产生一定影响,随着感染低水平炎症因子会对患者心肌的进一步损伤,加剧心功能恶化,进而诱发心力衰竭。且发现慢性阻塞性肺疾病患者的主要死亡原因是冠状动脉性心脏病和心力衰竭,这些合并症的原因所导致的死亡比慢性阻塞性肺疾病急性加重引起的致死性呼吸衰竭更常见^[19-22]。因此慢性阻塞性肺疾病患者多存在心血管疾病,其是慢性阻塞性肺疾病的一种常见共患疾病^[23]。因此临幊上分析慢阻肺合并左心功能不全的疾病危险因素,以为降低慢阻肺伴左心衰竭发生率提供依据。

本文结果表明,150例患者中慢阻肺伴左心衰竭者占比为32.00%,占比较高,Cherneva Z H 等^[24]研究表明,104例慢性阻塞性肺疾病患者中,64%患者会出现应激性左室舒张功能不全,其比例较本研究较高,主要是由于其研究的是患者在运动高峰后容易出现左心功能不全者,而本研究研究的是患者在正常运动情况下的左心衰竭患病情况,也说明了慢性阻塞性肺疾病者出现左心功能不全的几率较高,与本研究类似;Jakub 等^[25]回顾性分析了450名慢性阻塞性肺疾病患者和122名年龄和性别匹配的健康人群,结果发现慢性阻塞性肺疾病患者与心肌纤维化独立相关,心肌纤维化与主要结局(心力衰竭住院和全因死亡率)独立相关,慢性阻塞性肺疾病患者、心肌炎症和心肌纤维化之间的联系,心肌纤维化的独立预后价值阐明了慢性阻塞性肺疾病患者和心衰之间潜在的病理生理联系,表明慢性阻塞性肺疾病患者与心力衰竭间存在一定的相关性,与本研究结果相似,心力衰竭是左心功能不全的疾病进展过程,因此也说

表 2 分析对比血液指标水平与动脉血气指标分析
Table 2 The blood index level and arterial blood gas index were analyzed and compared

Items	Group A (48 cases)	Group B (102 cases)
Red cell count($\times 10^{12}/L$)	4.45±0.89	4.50±0.91
Hemoglobin content(g/L)	128.45±26.78	129.10±27.34
White blood cell count($\times 10^9/L$)	8.06±1.78	7.67±1.99
Neutrophil count($\times 10^9/L$)	6.10±1.78	5.89±1.67
Lymphocyte count($\times 10^9/L$)	1.19±0.23	1.24±0.29
Erythrocyte sedimentation rate(mm/h)	27.34±3.14	26.99±2.89
Activated partial post-coagulation enzyme time(s)	39.10±5.78	38.99±6.23
fibrinogen(g/L)	3.78±0.78	3.91±0.89
Creatine kinase(U/L)	95.34±17.89	93.17±14.56
Platelet count(PLT)	168.45±23.45 [#]	198.67±31.34
C-reactive protein(mg/L)	66.34±10.78 [#]	21.09±3.45
Calcitonin original(ng/mL)	1.77±0.25 [#]	0.23±0.04
Prothrombin time(s)	14.56±2.89 [#]	12.02±2.04
Thrombin time(s)	17.45±3.45	16.34±2.78
D - dimer($\mu g/mL$)	3.01±0.34 [#]	0.72±0.18
Albumin(g/L)	36.29±3.89 [#]	40.99±4.12
Creatine kinase isoenzyme(U/L)	18.89±2.34 [#]	14.88±1.89
N-terminal brain natriuretic peptide precursor($\mu g/mL$)	4.67±0.89 [#]	0.32±0.07
pH	7.42±0.09	7.39±0.11
PaCO ₂ (%)	49.87±10.89 [#]	41.23±9.89
PaO ₂ (%)	61.78±11.23 [#]	73.34±12.45
SaO ₂ (%)	88.78±10.34 [#]	94.89±12.34

表 3 慢阻肺伴左心衰竭危险因素的 Logistic 回归分析
Tab 3 Logistic regression analysis of risk factors for COPD with left heart failure

Variable	B	S.E	Wald χ^2	P	OR	95%CI
Gender	-1.038	0.408	6.341	0.010	0.344	0.145~0.789
Age	0.041	0.017	6.889	0.008	1.041	1.008~1.088
History of diabetes	1.841	0.579	10.048	0.003	6.321	2.021~18.998
History of Smoking	0.934	0.375	6.298	0.014	2.634	1.887~3.989
History of hypertension	0.781	0.300	6.432	0.011	2.212	1.198~4.897
History of CHD	0.671	0.327	3.879	0.045	1.879	1.011~3.823
Left ventricular end diastolic diameter	0.308	0.567	4.781	0.039	0.378	0.132~0.775
Pulmonary artery pressure	0.065	0.017	16.789	<0.001	1.087	1.031~1.134

明慢性阻塞性肺疾病患者容易出现左心功能不全。慢阻肺合并急性左心衰竭时,因心脏收缩力严重减弱,心排血量迅速减少,肺静脉回流不畅,毛细血管通透性增高,使血管内液渗入肺间质和肺泡内形成肺水肿,导致通气血流比例失调,氧弥散障碍,同时左心室的跨壁压以及后负荷增大,心输出量减少,氧向呼吸机的输送量继而减少,导致心力衰竭和呼吸衰竭加重,严重的缺氧亦可抑制心脏收缩力,甚至可导致心脏停搏。

两组在性别、年龄、患病时间、糖尿病史、吸烟史、高血压史、冠心病史、FEV₁/FVC、左房内径、左心室舒张末内径、左室重量分数、左室后壁厚度、肺动脉压、血小板计数、C 反应蛋白、降钙素原、凝血酶原时间、D-二聚体、白蛋白、肌酸激酶同工酶、N 末端脑钠肽前体、PaCO₂、PaO₂、SaO₂ 对比无统计学意义, Logistic 回归分析结果表明、性别、年龄、糖尿病史、吸烟史、高血压史、冠心病史、左心室舒张末内径、肺动脉压是影响慢阻肺

伴左心衰竭患者的危险因素。本研究因素结果表明,患者的肺动脉压出现异常,可能会影响机体的心血管细胞,引起左心室功能不全。Yogita S 等研究^[26]回顾性分析了 35 岁以上的慢性阻塞性肺疾病患者,其机体中的 C 反应蛋白水平明显升高,且与患者的 FEV₁、6 分钟步行距离呈明显负相关,本研究结果发现,慢性阻塞性肺疾病患者的 C 反应蛋白水平明显升高,而其不是危险因素,可能与本研究样本量不足有一定关系。Anker S D 等^[27]研究表明,7,020 例慢性阻塞性肺疾病合并 2 型糖尿病患者中 707 例出现了心力衰竭,慢性阻塞性肺疾病合并 2 型糖尿病增加了心力衰竭的发生率,本研究发现,糖尿病病史是慢阻肺伴左心衰竭的危险因素,与本研究结果类似。Yangui F 等^[28]研究表明,慢性阻塞性肺病吸烟患者合并缺血性心脏病的发病率较高,且大多数有症状但未能确诊,本研究发现,吸烟会增加慢阻肺伴左心衰竭的发生率,与 Yangui F 等研究相似。Gsb A 等^[29]研究表明,在慢性阻塞性肺疾病合并心力衰竭患者中,运动时会增加患者的心率、血压和自主反应,本研究发现,既往有高血压史的慢性阻塞性肺病吸烟患者合并左心功能不全患者的发病率较高,本研究与 Gsb A 等研究均表明高血压与慢性阻塞性肺疾病合并心脏疾病有一定的相关性。Evdokimov V 等^[30]研究表明,385 例 NYHA 分级为 II~III 的心力衰竭患者均存在中重度慢性阻塞性肺疾病,LVEF 低于 45%,本研究发现,冠心病史会增加慢阻肺伴左心衰竭的发病几率,与 Evdokimov V 等研究类似,主要是由于患者既往存在冠心病,与慢性阻塞性肺疾病间会相互影响,加重疾病病情。

总之,慢阻肺伴左心衰竭的占比较高,其与性别为男性、年龄偏大、有糖尿病史、吸烟史、高血压史、冠心病史、左心室舒张末内径升高、肺动脉压升高相关,需对以上因素给予积极干预及治疗。

参考文献(References)

- [1] Zhang C, Zhang M, Wang Y, et al. Efficacy and cardiovascular safety of LAMA in patients with COPD: a systematic review and meta-analysis[J]. *J Invest Med*, 2021, 69(8): 1141-1148
- [2] Llc A, Hmla B, Fan M W, et al. Association of Cardiovascular Health with Mortality Among COPD Patients: National Health and Nutrition Examination Survey III[J]. *Resp Med Res*, 2021, 80(11): 11860
- [3] Fiorentino G, Esquinas AM, Annunziata A. Exercise and Chronic Obstructive Pulmonary Disease (COPD)[J]. *Adv Exp Med Biol*, 2020, 12(7): 355-368
- [4] Horodinschi RN, Bratu OG, Dediu GN, et al. Heart failure and chronic obstructive pulmonary disease: a review[J]. *Acta Cardiol*, 2020, 75(2): 97-104
- [5] André S, Conde B, Fragoso E, et al. COPD and Cardiovascular Disease [J]. *Pulmonology*, 2019, 25(3): 168-176
- [6] Kotlyarov S, Kotlyarova A. Atherosclerosis as a risk factor in the prognosis of the survival of patients with COPD [J]. *Eur Heart J Acute Card Care*, 2021, 10(4): 223
- [7] Groff P, Petrelli G, Giorgini P, et al. Clinical heterogeneity of a population of patients admitted to the Emergency Department with a diagnosis of COPD-exacerbation: Relevance of cardiovascular comorbidities[J]. *Emerg Care J*, 2021, 17(1): 1123-1130
- [8] Km Y, Gm P. Left Ventricular Systolic and Diastolic Dysfunction in Chronic Obstructive Pulmonary Disease[J]. *J Assoc Physicians India*, 2020, 68(1): 52
- [9] Hilde JM, Hisdal J, Skjörten I, et al. Left ventricular dysfunction in COPD without pulmonary hypertension [J]. *PLoS One*, 2020, 15(7): e0235075
- [10] S HK, Vishwanath BM. Study of Left Ventricular Dysfunction in Chronic Obstructive Pulmonary Disease Patients [J]. *J Assoc Physicians India*, 2020, 68(1): 80
- [11] Ye J, Yao P, Shi X, et al. A systematic literature review and meta-analysis on the impact of COPD on atrial fibrillation patient outcome [J]. *Heart Lung*, 2022, 51(2): 67-74
- [12] A Fernández-García, M Pérez-Ríos, A Fernández-Villar, et al. Four Decades of COPD Mortality Trends: Analysis of Trends and Multiple Causes of Death[J]. *J Clin Med*, 2021, 10(5): 1171
- [13] Francis G S, Cleveland F, Ohio, et al. Heart Failure Heart Failure from the Point of View of Quantitative Anatomy [J]. *Eur Heart J Open*, 2021, 33(2): 291-294
- [14] Horodinschi RN, Bratu OG, Dediu GN, et al. Heart failure and chronic obstructive pulmonary disease: a review [J]. *Acta Cardiol*, 2020, 75(2): 97-104
- [15] Güder G, Störk S. COPD and heart failure: differential diagnosis and comorbidity[J]. *Herz*, 2019, 44(6): 502-508
- [16] Axson E L, Bottle A, Cowie M R, et al. Relationship between heart failure and the risk of acute exacerbation of COPD [J]. *Thorax*, 2021, 16(8): 216390
- [17] Hamada S Y, Hoshy M, Hoshy M, et al. Study of Pulmonary Hypertension and Its Predictors in Patients with Chronic Obstructive Pulmonary Disease[J]. *Eur Heart J Suppl*, 2021, 23(sD): suab069.015
- [18] Hesse K, Bourke S, Steer J. Heart failure in patients with COPD exacerbations: Looking below the tip of the iceberg [J]. *Resp Med*, 2022, 196(5): 106800
- [19] Jain S, Obeid M J, Yenigalla S, et al. Impact of Chronic Obstructive Pulmonary Disease in Heart Failure with Preserved Ejection Fraction [J]. *Amer J Cardiol*, 2021, 149(2): 47-56
- [20] Pellicori P, Cleland JGF, Clark AL. Chronic Obstructive Pulmonary Disease and Heart Failure: A Breathless Conspiracy [J]. *Heart Fail Clin*, 2020, 16(1): 33-44
- [21] Lagan J, Schelbert EB, Naish JH, et al. Mechanisms Underlying the Association of Chronic Obstructive Pulmonary Disease With Heart Failure[J]. *JACC Cardiovasc Imaging*, 2021, 14(10): 1963-1973
- [22] Berge J, Vark L, Postmus D, et al. Determinants of quality of life in acute heart failure patients with and without comorbidities: a prospective, observational study [J]. *Eur J Cardiovasc Nurs*, 2021, 21(3): 1132-1140
- [23] Terraneo S, Rinaldo R F, Papa G, et al. Distinct Mechanical Properties of the Respiratory System Evaluated by Forced Oscillation Technique in Acute Exacerbation of COPD and Acute Decompensated Heart Failure[J]. *Diagnostics*, 2021, 11(3): 554
- [24] Cherneva Z H, Cherneva R. Left ventricular diastolic dysfunction in non-severe chronic obstructive pulmonary disease as a step forward in cardiovascular comorbid dome[J]. *Eur Heart J*, 2021, 42(S1): ehab724.055

- Gestational Diabetes Mellitus in China [J]. Int J Environ Res Public Health, 2020, 17(24): 9517
- [12] 李彦荣, 侯爱琴, 樊阳阳, 等. 妊娠期糖尿病患者血清 PGRN、FGF21、Vaspin 水平与糖脂代谢及胰岛素抵抗的相关性分析[J]. 现代生物医学进展, 2021, 21(8): 1580-1583, 1554
- [13] Castling ZA, Farrell T. An analysis of demographic and pregnancy outcome data to explain non-attendance for postpartum glucose testing in women with gestational diabetes mellitus: Why are patients missing follow-up? [J]. Obstet Med, 2019, 12(2): 85-89
- [14] Powe CE. Early Pregnancy Biochemical Predictors of Gestational Diabetes Mellitus[J]. Curr Diab Rep, 2017, 17(2): 12
- [15] Hermann A, Sirdikova G. Homocysteine: Biochemistry, Molecular Biology and Role in Disease[J]. Biomolecules, 2021, 11(5): 737
- [16] Zhang N, Shi F, Liang H, et al. The feasibility of using Hey, CRP, and Cys-C to analyze AMI patients' disease conditions and prognoses[J]. Am J Transl Res, 2021, 13(4): 2724-2730
- [17] Muzurović E, Kraljević I, Solak M, et al. Homocysteine and diabetes: Role in macrovascular and microvascular complications [J]. J Diabetes Complications, 2021, 35(3): 107834
- [18] Tomić M, Vrabec R, Ljubić S, et al. Plasma homocysteine is associated with nonproliferative retinopathy in patients with type 2 diabetes without renal disease[J]. Diabetes Metab Syndr, 2022, 16(1): 102355
- [19] 王静, 王立媛, 王妍. 血清 HCY、APN、chemerin 在妊娠期糖尿病中的表达及与围生儿结局的关系 [J]. 实用预防医学, 2021, 28(2): 225-228
- [20] Zheng J, Xu J, Zhang Y, et al. Effects of insulin combined with metformin on serum cystatin C, homocysteine and maternal and neonatal outcomes in pregnant women with gestational diabetes mellitus[J]. Exp Ther Med, 2020, 19(1): 467-472
- [21] Zhang F, Zhu X, Wang P, et al. The cytokine FAM3B/PANDER is an FGFR ligand that promotes posterior development in Xenopus [J]. Proc Natl Acad Sci U S A, 2021, 118(20): e2100342118
- [22] Shehata MM, Kamal MM, El-Hefnawy MH, et al. Association of serum pancreatic derived factor (PANDER) with beta-cell dysfunction in type 2 diabetes mellitus[J]. J Diabetes Complications, 2017, 31(4): 748-752
- [23] Robert-Cooperman CE, Dougan GC, Moak SL, et al. PANDER transgenic mice display fasting hyperglycemia and hepatic insulin resistance[J]. J Endocrinol, 2014, 220(3): 219-231
- [24] Chi Y, Meng Y, Wang J, et al. FAM3B (PANDER) functions as a co-activator of FOXO1 to promote gluconeogenesis in hepatocytes[J]. J Cell Mol Med, 2019, 23(3): 1746-1758
- [25] Li JB, Asakawa A, Cheng K, et al. Biological effects of obestatin[J]. Endocrine, 2011, 39(3): 205-211
- [26] Cowan E, Burch KJ, Green BD, et al. Obestatin as a key regulator of metabolism and cardiovascular function with emerging therapeutic potential for diabetes[J]. Br J Pharmacol, 2016, 173(14): 2165-2181
- [27] Kołodziejski PA, Pruszyńska-Oszmałek E, Strowski MZ, et al. Long-term obestatin treatment of mice type 2 diabetes increases insulin sensitivity and improves liver function[J]. Endocrine, 2017, 56(3): 538-550
- [28] Wang JL, Xu XH, Zhang XJ, et al. The role of obestatin in roux-en-Y gastric bypass-induced remission of type 2 diabetes mellitus [J]. Diabetes Metab Res Rev, 2016, 32(6): 470-477
- [29] Granata R, Gallo D, Luque RM, et al. Obestatin regulates adipocyte function and protects against diet-induced insulin resistance and inflammation[J]. FASEB J, 2012, 26(8): 3393-3411
- [30] Khaleel EF, Abdel-Aleem GA. Obestatin protects and reverses nonalcoholic fatty liver disease and its associated insulin resistance in rats via inhibition of food intake, enhancing hepatic adiponectin signaling, and blocking ghrelin acylation [J]. Arch Physiol Biochem, 2019, 125(1): 64-78

(上接第 4330 页)

- [25] Jakub, Lagan, Erik B, et al. Mechanisms Underlying the Association of Chronic Obstructive Pulmonary Disease With Heart Failure. [J]. JACC. Cardiovasc Imag, 2021, 14(10): 1963-1973
- [26] Yogita S, Santosh M, Pratap S D. To Study the Correlation of CRP Levels with Functional Ability in Chronic Obstructive Pulmonary Disease Patients in Tertiary Health Care in Western Up [J]. Rad Res Acad, 2021, 32(10): 1101-1112
- [27] Anker S D, Sander L E, Fitchett D H, et al. Empagliflozin in patients with type 2 diabetes mellitus and chronic obstructive pulmonary disease[J]. Diabet Res Clin Pract, 2022, 186(4): 109837
- [28] Yangui F, Touil A, Antit S, et al. COPD prevalence in smokers with stable ischemic heart disease: A cross-sectional study in Tunisia[J]. Resp Med, 2021, 179(4): 106335
- [29] Gsb A, Cdlg A, Frc A, et al. Noninvasive ventilation can modulate heart rate variability during high-intensity exercise in COPD-CHF patients[J]. Heart Lung, 2021, 50(5): 609-614
- [30] Evdokimov V, Yushchuk E, Evdokimova A, et al. Efficacy and safety of beta-blockers and prolonged bronchodilators in patients with heart failure with coronary artery disease and moderate to severe COPD[J]. Eur Heart J, 2020, 41(S2): 1143-1150