

心房颤动导管消融相关心房食管瘘的研究进展

于春鑫¹ 孙姣¹ 孙源君² 尹晓盟^{1,2}

(1. 大连医科大学研究生院,辽宁 大连 210200; 2. 大连医科大学附属第一医院心血管内科,辽宁 大连 210200)

【摘要】射频导管消融术和冷冻消融术是目前治疗心房颤动的重要手段。手术相关的心房食管瘘是最严重的并发症之一。该并发症发病隐匿,诊断困难,早期发现、诊断和治疗是改善预后的关键。现对消融手术相关的心房食管瘘的发病率、病理生理学、临床特点、诊断及鉴别诊断、损伤预防和损伤治疗进行综述。

【关键词】心房颤动;射频导管消融;冷冻消融;并发症;心房食管瘘

【DOI】10.16806/j.cnki.issn.1004-3934.2020.07.005

Atrioesophageal Fistula Associated with Catheter Ablation of Atrial Fibrillation

YU Chunxin¹, SUN Jiao¹, SUN Yuanjun², YIN Xiaomeng^{1,2}

(1. Graduate School of Dalian Medical University, Dalian 210200, Liaoning, China; 2. Department of Cardiology, The First Affiliated Hospital of Chongqing Medical University, Dalian 210200, Liaoning, China)

【Abstract】 Radiofrequency catheter ablation and cryoablation are important methods in the treatment of atrial fibrillation. Surgically related atrioesophageal fistula is one of the most serious complications. This complication is latent and difficult to diagnosis. Early detection, diagnosis and treatment are key to improve prognosis. This article reviews the prevalence, pathophysiology, clinical features, diagnosis and differential diagnosis, injury prevention and treatment of atrial esophageal fistula related to ablative surgery.

【Key words】Atrial fibrillation; Radiofrequency catheter ablation; Cryoablation; Complication; Atrioesophageal fistula

射频导管消融术是抗心律失常药物难治性心房颤动(房颤)的首选治疗方案,可改善症状,提高生活质量^[1]。术后相关并发症包括:卒中、心脏压塞、肺静脉狭窄和心房食管瘘等^[1-2],其中心房食管瘘的发生率较低,死亡率高^[3-4]。目前临幊上为了减少心房食管瘘的发生,术前和术后预防性应用胃黏膜保护剂及质子泵抑制剂,房颤手术过程中采用多种保护措施,术后及时观察患者的临幊表现,早期诊断,避免出现漏诊,及时治疗,改善预后。

1 心房食管瘘的发病率

房颤是心律失常最常见的疾病之一,房颤发病率随年龄增长而不断升高^[1]。针对抗心律失常药物难治性房颤,导管消融术为首选治疗方案^[1]。随着手术数量的逐渐增多,并发症的发生也越来越多。其中心房食管瘘虽发病罕见,但会引起血栓栓塞、卒中、胸膜炎、脓胸及脓毒血症等,由于疾病性质及诊断延迟,死亡率较高。有研究^[3]表明 5 721 例房颤患者射频导管消融术后,10 例患者出现心房食管瘘,发生率为

0.15%,其中 8 例患者死亡,死亡率为 80%。John 等^[4]研究表明 12 万余例患者应用冷冻消融术行肺静脉隔离,11 例患者出现心房食管瘘,发病率 1/10 000,其中 7 例患者死亡,死亡率为 64%。Guhl 等^[5]单中心研究了 450 例行冷冻消融术的患者,出现 1 例心房食管瘘,发病率为 0.22%。

2 心房食管瘘的病理生理学

心房食管瘘发病原因尚不完全明确。食管与心房的解剖位置关系可能是其中最主要的原因之一,并且二者之间的解剖位置关系可移动。导管消融可损伤左房后壁及食管,损伤程度取决于左房后壁(1~3 mm)、心脏外膜的脂肪组织及结缔组织(2~5 mm)和食管动脉外膜(2~5 mm)的厚度,由此可见,左房后壁至食管内膜最薄有 4~5 mm,而且在食管扩张及全麻情况下,食管可能会更薄,在导管消融术中更容易损伤^[6]。左房后壁与食管黏膜之间的组织屏障在接近肺静脉区域最薄弱,尤其是左下肺静脉。多个病例报告证实心房食管瘘多发生在左下肺静脉附近^[3,7-8]。

有报道表明在消融过程中,食管的位置也会发生移动,一般人在镇静状态下,食管的移动距离为 2 cm,少数人为 4 cm,在手术中利用食管的移动性可减少食管损伤^[9]。

心房食管瘘损伤另一种可能的重要机制:热损伤。热损伤使食管平滑肌中的结构蛋白受损,造成食管黏膜的损伤和溃疡的形成,可发展成心房食管瘘^[24,10-11]。研究发现热损伤导致食管溃疡是心房食管瘘的前提条件^[6,12]。Bastian 等^[13]研究证实在初次手术治疗房颤的患者,采用能量滴定的磁导单导管射频消融隔离肺静脉,使左房后壁射频能量降至 20~30 W,消融时间限制在 20 s,无需食管温度监测,对食管损伤无影响,安全可行。

即使温度控制在较低的范围内,仍有可能发生食管损伤,食管损伤引发食管瘘的影响因素还包括:食管狭窄、导管机械压力、导管大小、导管探头接触力、消融定位点以及冷冻球囊强冷冻作用等^[13-15]。

3 心房食管瘘的临床特点

导管消融可能会使左心房后壁及食管前壁变薄,当食管溃疡穿孔时,会形成单向瓣膜,导致液体只从食管流入心脏,而不会逆流^[7],胃内容物通过左心房后壁进入心脏,不会从左心房流入食管。心房食管瘘通常出现在房颤消融术后 1~6 周,常见临床表现:胸部不适、高热、疲劳、颈痛、吞咽困难、恶心、烧心、呕血或便血、心包或胸腔积液、癫痫和卒中等^[16-17]。如果不及时治疗,胃内容物进入纵膈,引起纵膈炎,发生严重炎症反应及脓毒血症,继续可发展为腹膜炎、低氧血症、败血症,甚至休克。临床反应性低和延误诊断,导致死亡率较高,即使诊断明确,复杂的手术治疗仍有很高的死亡风险^[11,18]。因此对于术后患者出现胸痛、寒战和发热等临床表现,应高度警惕该并发症的发生。

4 心房食管瘘的诊断及鉴别诊断

由于心房食管瘘发病率低,无完整的心房食管瘘的诊断流程,且发病时间延迟,对明确诊断产生一定的难度。对具有上述症状并且近期行房颤射频消融的患者,应高度警惕食管损伤及心房食管瘘的发生。怀疑心房食管瘘时,内镜检查会引起空气栓塞及永久性神经损伤,可加重病情,故应避免使用^[19]。食管穿孔主要的症状是严重的胸痛、发热及感染明显,心房食管瘘出现最早和最敏感的实验室指标是白细胞升高^[19]。应与感染相关性疾病相鉴别,比如感染性心内膜炎,可行血培养及心脏彩色超声进行鉴别。胸部 CT 检查可见心包积气和积脓,或可见空气气泡分布于心房后,以确诊心房食管瘘,也可结合血培养发现肠道菌群以明确诊断^[20-21]。有研究^[22]表明 88% 的患者术

后行胸部 CT 检查发现纵膈气胸(26%)、左房或左房内壁空气(24%);44% 的患者术后行头部 CT 检查,51% 的患者出现异常,其中 79% 可见弥漫性空气栓塞,食管造影剂外渗比率为 87%,血培养阳性率为 100%,其中以链球菌为主。

高度怀疑该并发症时,需结合临床症状、血常规、胸部 CT 及微生物检查以协助诊断,尽早治疗^[15-22]。

5 食管损伤的预防

5.1 术前预防措施

术前可行内镜检查和胸部 CT,明确食管与心房之间的解剖关系,为手术提供解剖位置,提示心房与食管的距离,注意食管已存在的黏膜病变^[23]。临术上术前或术后预防性应用胃黏膜保护剂和质子泵抑制剂以保护消化道黏膜,手术后需持续应用 1~6 周。

5.2 手术过程中预防损伤的措施

5.2.1 食管温度监测

有学者研究表明食管温度监测会减少食管损伤^[24-26]。研究发现伴有食管损伤患者,食管管腔内的温度明显高于无食管损伤的患者,食管管腔内温度在 41℃ 以下时,食管损伤发生率较低^[25]。Kiuchi 等^[24]对 160 例阵发性房颤患者进行研究,其中 80 例患者在食管温度监测引导下行房颤消融,食管温度在 39.0℃ 时,可降低食管损伤的发生率(从 7.5% 降至 0%),并且对房颤的复发无影响。目前食管温度监测使用的探针有很多种^[23],单极传感器探头、多极传感器探头、热电阻传感器探头和可偏转探头等。研究发现无论哪一种类型的探头,对食管保护作用无明显差异^[26-28]。

5.2.2 导管消融中的食管移位

在消融过程中,食管与心房的解剖位置并非固定不变^[9-10]。研究^[29-30]发现消化道内窥镜可将食管移动至远离消融部位,但为了避免消融能量分散,消融时需将内窥镜取出,取出内窥镜后,无法确认消融时,食管与心房的位置关系是否不再出现改变,也无法确认对于食管损伤是否具有保护作用。超声心动图技术安全及无创,可协助心脏再同步化治疗,改善心力衰竭症状,降低心力衰竭死亡率^[31]。超声心动图在消融过程中,可以通过对食管移动,从而使食管远离心房,保护食管,降低心房食管瘘的发生率^[32]。Palaniswamy 等^[33]在食管内放入可锻金属探针,在消融过程中,可将食管偏离心房消融部位的距离最远至 20 mm,但只有少数患者可达到。Parikh 等^[34]使用最新的 EsoSure 装置(可膨胀式带薄膜测温的食管偏转装置),本身材质为记忆合金,根据食管温度而改变形状,不影响食管管腔内的温度,移动食管安全可靠。

5.2.3 食管冷却技术

有些研究在射频消融中利用食管冷却技术而保护食管。Sohara 等^[35]研究表明,在射频热能球囊系统中,当食管管腔内温度>39.0℃时,利用碘酰胺醇盐水灌注,可降低食管损伤发生率及严重程度。在一项猪动物实验中^[36],通过体外热交换装置,蒸馏水在4~42℃范围内,作为冷却剂,流速≥60 mL/h,润滑尖端置入食管管腔,最深可到达胸段食管,进入食管后与食管紧密接触,食管传热装置是一个闭环冷却装置,冷却温度越低,热损伤发生率越低,该研究有待临床进一步研究。

5.2.4 新的手术方式

Bourier 等^[37]改变了消融参数,分别采用 50 W, 13 s; 60 W, 10 s; 70 W, 7 s。与标准射频设置 30 W, 30 s 相比,通过离体猪大腿肌肉研究表明,与传统射频消融相比,短时间高功率所产生的病灶体积相似,但范围广、深度浅,安全可行。Vassallo 等^[38]回顾性分析了首次应用短时间高功率射频消融术的 76 例患者,与传统的射频消融相比,缩短了手术时间,降低了食管损伤的发生(传统射频消融组 74.6% 的食管腔温度升高,短时间高功率组 51.2% 的食管腔温度升高),是安全和有效的。Winkle 等^[39]研究也证实,针对 10 284 例患者行短时间高功率治疗术后,包括心房食管瘘在内,一共出现 4 例并发症,并发症发生率较低。目前短时间高功率射频消融术降低并发症发生率的作用明显。

6 食管损伤治疗

对于早期出现临床症状的患者,应警惕其心房食管瘘发生的可能,密切观察临床表现,结合血培养及胸部 CT 检查有助于明确患者的诊断,并尽快干预,阻止恶化,对于预后十分重要。具体治疗方案根据患者食管损伤程度、穿孔位置和个体身体情况而定。一般治疗包括护理气管、镇痛、肠道营养、液体复苏和广谱抗生素等。针对穿孔很小的患者,予积极抗生素、心包引流和食管支架植入微创手术等治疗^[20-21]。患者出现血流动力学不稳定,积极维持血流动力学稳定,并尽快采用外科手术治疗,包括体外循环下心脏胸腔联合手术、心房部分自体心包修复术、食管部分用胸膜或肌瓣修补术等。若患者病情危重,应在重症监护下,应用气管管理、抗生素和营养支持治疗^[21,25,32],必要时需胃肠科、心外科和胸外科联合手术治疗。

7 结语

术中对食管的保护及药物预防是防止食管损伤的关键。术前和术后口服抑酸保护胃黏膜药物,术中应用食管保护措施,可降低食管的损伤风险。术后高度重视患者相关临床不适症状,早期诊断,尽早干预,必要时行手术治疗可改善预后,减少不良后果的

发生。

参 考 文 献

- [1] Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation[J]. *Europace*, 2018, 20(1):1-160.
- [2] Kapur S, Barbhayia C, Deneke T, et al. Esophageal injury and atrioesophageal fistula caused by ablation for atrial fibrillation[J]. *Circulation*, 2017, 136(13):1247-1255.
- [3] Kim YG, Shim J, Choi JI, et al. Characteristics of atrial fibrillation patients suffering atrioesophageal fistula after radiofrequency catheter ablation[J]. *J Cardiovasc Electrophysiol*, 2018, 29(10):1343-1351.
- [4] John RM, Kapur S, Ellenbogen KA, et al. Atrioesophageal fistula formation with cryoballoon ablation is most commonly related to the left inferior pulmonary vein[J]. *Heart Rhythm*, 2017, 14(2):184-189.
- [5] Guhl EN, Siddoway D, Adelstein E, et al. Incidence and predictors of complications during cryoballoon pulmonary vein isolation for atrial fibrillation[J]. *J Am Heart Assoc*, 2016, 5(7):e003724.
- [6] Park J, Park CH, Lee HJ, et al. Left atrial wall thickness rather than epicardial fat thickness is related to complex fractionated atrial electrogram[J]. *Int J Cardiol*, 2014, 172(3):e411-e413.
- [7] Grubina R, Cha YM, Bell MR, et al. Pneumopericardium following radiofrequency ablation for atrial fibrillation: insights into the natural history of atrial esophageal fistula formation[J]. *J Cardiovasc Electrophysiol*, 2010, 21(9):1046-1049.
- [8] Patil KD, Spragg DD. How can we reduce the incidence of atrial-esophageal fistula[J]. *J Cardiovasc Electrophysiol*, 2018, 29(10):1352-1354.
- [9] Good E, Oral H, Lemola K, et al. Movement of the esophagus during left atrial catheter ablation for atrial fibrillation[J]. *J Am Coll Cardiol*, 2005, 46(11):2107-2110.
- [10] Knopp H, Halm U, Lamberts R, et al. Incidental and ablation-induced findings during upper gastrointestinal endoscopy in patients after ablation of atrial fibrillation: a retrospective study of 425 patients[J]. *Heart Rhythm*, 2014, 11(4):574-578.
- [11] Venkatesh K, Acevedo J, Kim R, et al. Pericardial-esophageal fistula after catheter ablation of atrial fibrillation[J]. *Pacing Clin Electrophysiol*, 2018, 41(3):331-333.
- [12] Halbfass P, Pavlov B, Muller P, et al. Progression from esophageal thermal asymptomatic lesion to perforation complicating atrial fibrillation ablation: a single-center registry[J]. *Circ Arrhythm Electrophysiol*, 2017, 10(8):e005233.
- [13] Bastian D, Schwab J, Steurer KT, et al. Oesophageal injury following magnetically guided single-catheter ablation for atrial fibrillation: insights from the MAGNA-AF registry[J]. *Europace*, 2018, 20(suppl 2):ii48-ii55.
- [14] Lin H, Chen YH, Hou JW, et al. Role of contact force-guided radiofrequency catheter ablation for treatment of atrial fibrillation: a systematic review and meta-analysis[J]. *J Cardiovasc Electrophysiol*, 2017, 28(9):994-1005.
- [15] Sandhu A, Zipse MM, Borne RT, et al. Esophageal position, measured luminal temperatures, and risk of atrioesophageal fistula with atrial fibrillation ablation[J]. *Pacing Clin Electrophysiol*, 2019, 42(4):458-463.
- [16] Schuring CA, Mountjoy LJ, Prioux AB, et al. Atrio-esophageal fistula: a case series and literature review[J]. *Am J Case Rep*, 2017, 18:847-854.
- [17] Khan MY, Siddiqui WJ, Iyer PS, et al. Left atrial to esophageal fistula: a case report and literature review[J]. *Am J Case Rep*, 2016, 17:814-818.
- [18] Khakpour H, Shemir RJ, Lee JM, et al. Atrioesophageal fistula after atrial fibrillation ablation: a single center series[J]. *J Atr Fibrillation*, 2017, 10(3):1654.
- [19] Dagres N, Kottkamp H, Piorkowski C, et al. Rapid detection and successful treatment of esophageal perforation after radiofrequency ablation of atrial fibrillation: lessons from five cases[J]. *J Cardiovasc Electrophysiol*, 2006, 17

- (11):1213-1215.
- [20] Dive F, le Polain de Waroux JB, Pierard S, et al. Atrio-oesophageal fistula following atrial fibrillation ablation procedure; diagnosis with cardiac CT [J]. *Intensive Care Med*, 2018, 44(9):1565-1567.
- [21] Singh R, Landa EJ, Machado C. Atrial-esophageal fistula after catheter ablation: diagnosing and managing a rare complication of a common procedure [J]. *Am J Case Rep*, 2019, 20:557-561.
- [22] Ha FJ, Han HC, Sanders P, et al. Challenges and limitations in the diagnosis of atrioesophageal fistula [J]. *J Cardiovasc Electrophysiol*, 2018, 29(6):861-871.
- [23] Kadado AJ, Akar JG, Hummel JP. Luminal esophageal temperature monitoring to reduce esophageal thermal injury during catheter ablation for atrial fibrillation; a review [J]. *Trends Cardiovasc Med*, 2019, 29(5):264-271.
- [24] Kiuchi K, Okajima K, Shimane A, et al. Impact of esophageal temperature monitoring guided atrial fibrillation ablation on preventing asymptomatic excessive transmural injury [J]. *J Arrhythm*, 2016, 32(1):36-41.
- [25] Halm U, Gaspar T, Zachaus M, et al. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias [J]. *Am J Gastroenterol*, 2010, 105(3):551-556.
- [26] Kuwahara T, Takahashi A, Takahashi Y, et al. Incidences of esophageal injury during esophageal temperature monitoring; a comparative study of a multi-thermocouple temperature probe and a deflectable temperature probe in atrial fibrillation ablation [J]. *J Interv Card Electrophysiol*, 2014, 39(3):251-257.
- [27] Miyazaki S, Nakamura H, Taniguchi H, et al. Esophagus-related complications during second-generation cryoballoon ablation-insight from simultaneous esophageal temperature monitoring from 2 esophageal probes [J]. *J Cardiovasc Electrophysiol*, 2016, 27(9):1038-1044.
- [28] Tscharbrom CM, Silverstein J, Berzin T, et al. Comparison between single- and multi-sensor oesophageal temperature probes during atrial fibrillation ablation: thermodynamic characteristics [J]. *Europace*, 2015, 17(6):891-897.
- [29] Chugh A, Rubenstein J, Good E, et al. Mechanical displacement of the esophagus in patients undergoing left atrial ablation of atrial fibrillation [J]. *Heart Rhythm*, 2009, 6(3):319-322.
- [30] Koruth JS, Reddy VY, Miller MA, et al. Mechanical esophageal displacement during catheter ablation for atrial fibrillation [J]. *J Cardiovasc Electrophysiol*, 2012, 23(2):147-154.
- [31] 黄晓凤,熊峰.超声心动图技术在优化心脏再同步化治疗效果中的应用 [J]. 心血管病学进展,2019,40(7):1043-1046.
- [32] Mateos JC, Mateos EI, Peña TG, et al. Simplified method for esophagus protection during radiofrequency catheter ablation of atrial fibrillation—Prospective study of 704 cases [J]. *Rev Bras Cir Cardiovasc*, 2015, 30(2):139-147.
- [33] Palaniswamy C, Koruth JS, Mittnacht AJ, et al. The extent of mechanical esophageal deviation to avoid esophageal heating during catheter ablation of atrial fibrillation [J]. *JACC Clin Electrophysiol*, 2017, 3(10):1146-1154.
- [34] Parikh V, Lavu M, Jazayeri MA, et al. Use of an esophageal retractor to prevent thermal injuries during atrial fibrillation ablation: a multi-center experience [J]. *J Am Coll Cardiol*, 2017, 69(11):406.
- [35] Sohara H, Satake S, Takeda H, et al. Prevalence of esophageal ulceration after atrial fibrillation ablation with the hot balloon ablation catheter: what is the value of esophageal cooling? [J]. *J Cardiovasc Electrophysiol*, 2014, 25(7):686-692.
- [36] Montoya MM, Mickelsen S, Clark B, et al. Protecting the esophagus from thermal injury during radiofrequency ablation with an esophageal cooling device [J]. *J Atr Fibrillation*, 2019, 11(5):2110.
- [37] Bourier F, Duchateau J, Vlachos K, et al. High power short duration vs. standard RF ablation: insights on lesion metrics [J]. *J Cardiovasc Electrophysiol*, 2018, 29(11):1570-1575.
- [38] Vassallo F, Cunha C, Serpa E, et al. Comparison of high-power short-duration (HPSD) ablation of atrial fibrillation using a contact force-sensing catheter and conventional technique: initial results [J]. *J Cardiovasc Electrophysiol*, 2019, 30(10):1877-1883.
- [39] Winkle RA, Mohanty S, Patrawala RA, et al. Low complication rates using high power (45-50 W) for short duration for atrial fibrillation ablations [J]. *Heart Rhythm*, 2019, 16(2):165-169.

收稿日期:2019-11-07

(上接第 686 页)

- [15] Gao S, Liu Q, Ding X, et al. Predictive value of the acute-to-chronic glycemic ratio for in-hospital outcomes in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention [J]. *Angiology*, 2020, 71(1):38-47.
- [16] Kosiborod M, Deedwania P. An overview of glycemic control in the coronary care unit with recommendations for clinical management [J]. *J Diabetes Sci Technol*, 2009, 3(6):1342-1351.
- [17] Lazaros G, Tsiahris D, Vlachopoulos C, et al. Distinct association of admission hyperglycemia with one-year adverse outcome in diabetic and non-diabetic patients with acute ST-elevation myocardial infarction [J]. *Hellenic J Cardiol*, 2013, 54(2):119-125.
- [18] Mladenovic V, Zdravkovi V, Jovi M, et al. Influence of admission plasma glucose level on short and long-term prognosis in patients with ST-segment elevation myocardial infarction [J]. *Vojnosanit Pregl*, 2010, 67(4):291-295.
- [19] Kim EJ, Jeong MH, Kim JH, et al. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients [J]. *Int J Cardiol*, 2017, 236:9-15.
- [20] Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention; the HORIZONS-AMI trial [J]. *Int J Cardiol*, 2013, 167(6):2572-2579.
- [21] Marik PE, Raghavan M. Stress-hyperglycemia, insulin and immunomodulation in sepsis [J]. *Intensive Care Med*, 2004, 30(5):748-756.
- [22] Goglia F, Skulachev VP. A function for novel uncoupling proteins: antioxidant defense of mitochondrial matrix by translocating fatty acid peroxides from the inner to the outer membrane leaflet [J]. *FASEB J*, 2003, 17(12):1585-1591.
- [23] Silveira A. Postprandial triglycerides and blood coagulation [J]. *Exp Clin Endocrinol Diabetes*, 2001, 109(4):S527-S532.
- [24] Das UN. Insulin in sepsis and septic shock [J]. *J Assoc Physicians India*, 2003, 51:695-700.
- [25] Kitano D, Takayama T, Nagashima K, et al. A comparative study of time-specific oxidative stress after acute myocardial infarction in patients with and without diabetes mellitus [J]. *BMC Cardiovasc Disord*, 2016, 16:102.
- [26] Esposito K, Nappo F, Marfella R, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress [J]. *Circulation*, 2002, 106(16):2067-2072.
- [27] Jeschke MG, Klein D, Herndon DN. Insulin treatment improves the systemic inflammatory reaction to severe trauma [J]. *Ann Surg*, 2004, 239(4):553-560.
- [28] 王芳,何胜虎.应激性高血糖与急性心肌梗死相关研究进展 [J]. 心血管病学进展,2018,39(5):831-834.
- [29] Marik PE, Preiser JC. Toward understanding tight glycemic control in the ICU: a systematic review and metaanalysis [J]. *Chest*, 2010, 137(3):544-551.

收稿日期:2019-12-05