doi:10.11659/jjssx.11E022012

·综 述·

感染性心内膜炎的诊断与治疗进展

朱云飞,励 峰 (上海交通大学医学院附属第六人民医院/上海市第六人民医院心血管外科,上海 200233)

[摘 要] 感染性心内膜炎(IE)是心内膜表面的一种感染性疾病,通常分为急性(症状持续在6周内)、亚急性(症状持续6周至3个月)和慢性(症状持续3个月以上)。IE是一种系统性疾病,其不仅累及心脏本身,还可影响全身多器官的功能。因此,IE的治疗需要多学科的共同参与,尤其是心胸外科、感染科和影像科。本研究对目前国内外关于IE的诊断与治疗的研究进展进行综述,以期为IE的诊治提供参考。

[关键词] 感染性心内膜炎;进展;多学科治疗
[中图分类号] R654.2 [文献标识码] A [收稿日期] 2022-11-03

Progress in the diagnosis and treatment of infective endocarditis

ZHU Yun-fei, LI Feng (Department of Cardiovascular Surgery, Sixth People's Hospital Affiliated to Shanghai Jiaotong University School of Medicine/Shanghai Sixth People's Hospital, Shanghai 200233, China)

Abstract: Infective endocarditis (IE) is an infectious disease on the endocardial surface, which is usually divided into acute (symptoms last for 6 weeks), sub-acute (symptoms last for 6 weeks to 3 months), and chronic (symptoms last for more than 3 months). IE is a systemic disease, which not only affects the heart itself, but also affects the function of multiple organs throughout the body. Therefore, the treatment of IE requires multidisciplinary involvement, especially the department of cardiothoracic surgery, infection department and imaging department. This study reviews the current research progress on the diagnosis and treatment of IE at home and abroad, in order to provide reference for the diagnosis and treatment of IE.

Keywords: infective endocarditis; progress; multidisciplinary therapy

感染性心内膜炎(infective endocarditis,IE)是心内膜表面的一种感染性疾病,最早在350年前被发现[1],通常涉及心脏瓣膜或腱索等结构,分为急性(症状持续在6周内)、亚急性(症状持续6周至3个月)和慢性(症状持续3个月以上)。有研究显示,1970年至2000年,IE的年发病率为5/100 000~7/100 000[2];自2000年以来发病率有所上升,在2011年接近15/100 000[3]。有研究显示,IE的发生与经济发展有关,在发展中国家,风湿性心脏病是引起IE的危险因素[4];而在发达国家,风湿性心脏病引起的IE发病率较低[5]。经历了长期的发展,IE主要的诊断与治疗方法都有了一定的进展。

1 诊断

随着科学技术的进步,临床对IE的认识逐渐加深,其诊断方法取得了巨大进展,诊断方式越来越先进,诊断的准确率也越来越高,现有的IE诊断方法如下。

[基金项目] 上海市科委科技创新行动计划(17411966600)
[通信作者] 励 峰,E-mail:cardiosh@aliyun.com

1.1 临床特征

IE的临床表现多样化,可累及各个器官系统。其心脏表现包括瓣膜增生、脓肿、环周扩张感染和心包炎等。除了心脏外,IE可累及动脉系统,其中霉菌性动脉瘤是IE的一种重要血管表现,未破裂和破裂的霉菌性动脉瘤的病死率分别为30%和80%[6-7],严重威胁患者的生命安全。IE常出现心脏赘生物,且可脱落,随血液循环转移到其他部位,导致栓塞。有研究报道IE引起的栓塞很常见,发生率高达50%,因此要注意抗菌药物的早期合理应用,以降低栓塞的发生风险[6-8]。

1.2 病原学

IE的致病微生物存在地域差异。金黄色葡萄球菌是世界上大部分地区IE的主要病因,约31%的IE患者存在金黄色葡萄球菌感染,其次是草绿色链球菌(17%)和肠球菌(10%)感染[9-10]。溶血性链球菌心内膜炎在欧洲比在北美洲更常见;由HACEK微生物(嗜血杆菌属、凝聚杆菌属、心杆菌属、艾肯菌属、金氏菌属)引起的心内膜炎,北美洲较南美洲更少见[9]。血培养阴性心内膜炎难以识别和诊断,其原因有:以前使用过抗菌药物的无菌血培养;有些有机体生长缓慢、需要复杂营养成分的有机体,如HACEK微生物、痤疮

角质杆菌(原丙酸杆菌)和念珠菌;以目前技术不能行常规血培养的病原体(如巴尔通体、衣原体和惠普滋养体)引起的心内膜炎[11]。在一项血培养阴性心内膜炎的前瞻性研究中,血清学检测可确定约50%的患者的致病微生物,其中贝氏柯克斯体和巴尔通体最为常见[12]。非感染性心内膜炎,包括非细菌性血栓性心内膜炎,偶尔可能由自身免疫或肿瘤引起。

目前,IE病原学诊断依赖于血培养及赘生物培养,然而术前使用抗菌药物可能会导致传统的病原学检测手段无法准确发挥效果,对血培养阴性的患者疾病的诊断与治疗都会产生影响,进而对患者的预后产生不利影响[13]。二代基因测序是一种快速、高敏的新兴技术,几乎不受术前使用抗菌药物的影响,可直接检测临床样本中所有类型的病原体,能早期确定病原菌,对治疗具有重要意义,在IE的诊断中发挥越来越重要的作用[14-15]。

1.3 影像学

超声心动图是IE诊断的影像学基础。目前超声心动图为可疑IE的常规检查,所有怀疑心内膜炎的患者都应进行经胸超声心动图(transthoracic echocardiogram,TTE)检查[16]。当TTE检查为阴性时,经食管超声心动图(transesophageal echocardiography,TEE)在IE的诊断、病变特征和确定局部并发症方面具有重要作用。TTE诊断假瓣膜患者的灵敏度约为50%[17],可能是由假瓣膜结构组件的阴影导致。TEE检查心内膜炎的灵敏度超过90%[18]。尽管TEE检查心内膜炎的灵敏度有所提高,但在评估心脏前结构(包括三尖瓣和右心室流出道)时的表现可能与TTE相似。对疑似右心内膜炎的静脉吸毒者进行研究发现,TTE检查赘生物的效果与TEE相当[19]。2011年发布的超声心动图的适当使用标准支持TTE用于疑似IE和血培养阳性或新杂音患者的初始评估[20]。此外,对于IE进展风险高或临床状态发生变化的患者,建议使用TTE重新评估;而对于非复杂性IE,如果没有预期的治疗改变,TTE的常规监测并不合适。2017年发布的多模态成像在瓣膜性心脏病中的适当使用标准也涉及IE[21]。与2011年发布的IE超声心动图指南相似,2017年的指南指出,即使治疗没有达到预期的效果,重复TTE检查也有益,可以用来评估抗菌药物治疗后的变化。TEE已广泛应用于心脏外科手术,对接受IE手术的患者有益。有研究发现,术中TEE可影响手术操作[22]。因为从初始诊断到手术开始往往存在一定的时间间隔,术中TEE检查结果可能与最初病变程度和范围不同,体外循环结束后TEE可检查是否有残余病变或心脏结构是否正常[23-24]。术中TEE可观察到IE的动态特性、赘生物大小的变化、瓣膜情况的迅速发展以及局部并发症的可能性,因此,在IE手术时应常规行术中TEE。

三维超声心动图的使用为IE的诊断提供了附加价值,并对传统的二维超声心动图进行了补充。三维超声心动图的主要优点是改善了心脏结构的空间分辨率,可以更好地显示赘生物、脓肿和瓣膜畸形。一项针对心脏手术中瓣膜赘生物患者的研究显示,三维超声心动图定位赘生物比二维超声心动图更准确,更能发现IE的并发症[25]。三维超声心动图也有助于手术的开展,如三维成像可从左心房观察二尖瓣,使二尖瓣可视化,并增加对先前未被识别的异常的了解,如二尖瓣裂和二尖瓣反流[26]。尽管三维超声心动图存在时间分辨率降低和伪影等局限性,但其依旧是二维超声心动图的重要辅助。

心内超声心动图(intracardiac echocardiography,ICE)已被用于IE的检查中。ICE是通过将装有换能器的导管插入股静脉,以显示心内结构。有研究发现,ICE在识别心内肿块方面优于TEE,尤其是在11%的可疑IE患者中,可以识别TEE未发现的肿块[27]。但其对IE的特异性可能会因为血栓和非感染性赘生物的假阳性而降低。如果ICE的优势在未来的前瞻性研究中得到证实,其可能成为IE的又一种重要的影像学检查方式。

替代成像方式在IE的诊断和治疗中发挥着越来越重要的作用,如心脏CT。尽管CT容易遗漏小赘生物(直径<4 mm),但在检查瓣膜赘生物的存在方面具有与TEE相似的诊断准确性[28],且其可检查瓣膜周围的感染和假性动脉瘤。有研究发现,多层螺旋CT在鉴别脓肿和假性动脉瘤方面优于TEE,能提供更准确的解剖信息[28-29]。与TEE相比,CT由于其优越的空间分辨率,能够提高对瓣膜周围脓肿和假性动脉瘤诊断的准确性;心脏CT在诊疗外科计划中可以提供冠状动脉疾病的无创评估。尽管心脏CT优势明显,但TEE能更好地评估瓣膜穿孔和心内瘘的存在[30]。TEE和CT结合使用能更好地诊断IE。

MRI可以指导IE的早期诊断,检查脑栓塞的情况。在法国的一项前瞻性队列研究中,约26%的患者经MRI检查从可疑IE确诊为IE[31]。脑MRI也可以影响手术计划,特别是手术时间。

正电子发射断层扫描(positron emission tomography,PET)已成为IE诊断的重要工具。PET诊断IE的原理是基于感染部位的白细胞和单核细胞对18F-氟脱氧葡萄糖(18F-fluorodeoxyglucose,FDG)的摄取。Saby等[32]的研究显示,当FDG PET/CT用于怀疑假体瓣膜心内膜炎患者的检查时,可明显减少可疑IE患者的比例。

FDG PET/CT成像有助于评估心脏装置感染情况，但手术、血管炎和其他炎症可能导致FDG PET/CT成像的假阳性。发生在人工瓣膜(prosthetic valves，PV)或心脏植入式电子设备(cardiac implantable electronic devices，CIED)的心内膜炎患者的预后比发生在天然瓣膜的心内膜炎患者更差，其诊断也更复杂。超声心动图，尤其是TEE及TTE，显示出较低的诊断效率；FDG PET/CT是一种新的成像工具，可更好地诊断发生在PV和CIED的IE，逐渐成为一种越来越重要的诊断方式[33-34]。

IE的诊断较复杂，目前公认的IE诊断依赖于Duke标准[35]，该标准最初于1994年提出，并于2000年进行了修改，在2015年再次进行了修改，修改后的Duke标准如下[35-36]。判定为阳性的主要标准：①IE血培养阳性，且有2种不同血培养的典型病原体；②任何生物体的血培养持续阳性(至少2个阳性培养样本，间隔12 h)；③Q热病原体单次血培养阳性或其IgG抗体滴度>1∶800；④IE超声心动图呈阳性，包括赘生物、脓肿、假体动脉瘤或新瓣膜反流。次要标准：①易感性，如易感性心脏疾病或静脉吸毒者；②体温在38 ℃及以上；③血管现象，包括动脉栓塞、脓毒性肺梗死、霉菌性动脉瘤、颅内出血、结膜出血、Janeway损害；④不符合主要标准的微生物证据；⑤血培养阳性，不符合主要标准；⑥免疫现象，包括Osler结节、Roth斑点、类风湿因子或肾小球肾炎。

满足2个主要标准或1个主要标准和3个次要标准，或5个次要标准，可诊断为IE。满足1个主要标准和1个次要标准或3个次要标准则为可疑IE。需要注意的是，IE的诊断在以下情况下可被否定：有明确的替代诊断；当症状或体征在应用抗菌药物治疗4 d后消失；手术时没有IE的病理证据(抗菌药物治疗4 d)；可能的IE标准不满足。尽管这些诊断标准被广泛用于IE的诊断，但仍有局限性[37]。

2 治疗

随着医疗技术的发展，对IE致病机制的认识逐渐加深，IE的治疗方法也取得了巨大进展，再加上近年来瓣膜置换手术的开展，以及多学科的治疗模式，较为复杂IE患者的预后也越来越好。

2.1 抗菌治疗

最初的抗菌治疗具有经验性，且基于患者病原学和流行病学因素。天然瓣膜心内膜炎最常见的病原体有金黄色葡萄球菌、草绿色链球菌、溶血性链球菌、肠球菌、HACEK微生物；人工瓣膜心内膜炎最常见的病原体有金黄色葡萄球菌、表皮葡萄球菌、肠球菌；血培养阴性心内膜炎最常见的病原体有贝氏柯克斯体、巴尔通体、布鲁氏菌[16]。草绿色链球菌或溶血性链球菌引起的链球菌IE的治疗有效率取决于青霉素最低抑菌浓度；在对青霉素高度敏感的链球菌菌株中发现，肠胃外青霉素或头孢曲松单药治疗非常有效[16-17]。对于不耐受青霉素治疗的患者，万古霉素是可接受的替代方案[38-39]。对于葡萄球菌引起的IE的治疗，不仅要判断其是凝固酶阳性(金黄色葡萄球菌)还是凝固酶阴性(表皮葡萄球菌)，还要观察是否存在人工瓣膜或人工材料。由对甲氧西林敏感的金黄色葡萄球菌引起的天然瓣膜心内膜炎通常用β-内酰胺类药物(萘夫西林)或头孢唑林(对β-内酰胺类过敏)治疗；而对于耐甲氧西林金黄色葡萄球菌，万古霉素是天然瓣膜心内膜炎的首选治疗药物。有研究发现，达托霉素对耐甲氧西林金黄色葡萄球菌同样有效，并且成为万古霉素的可接受替代品[40-41]。由于对青霉素和氨基糖苷类药物的耐药性增加，肠球菌引起的心内膜炎的治疗较为困难，可考虑采用氨苄西林与头孢曲松治疗[16]。

2.2 人工瓣膜置换术

IE的手术适应证有：心源性休克；抗菌治疗后仍存在持续菌血症、脓肿等并发症；活动性赘生物直径超过10 mm。在满足手术适应证的前提下，手术时机也是一个重要的考虑因素。IE引起瓣膜功能障碍导致急性心力衰竭，建议早期或急诊限期手术。有研究显示，手术可明显降低IE并发心衰患者的病死率[42]。金黄色葡萄球菌性IE预后差，易合并充血性心力衰竭、脓毒症等并发症，非手术治疗效果差，极大降低了患者的存活率[43]。适当使用抗菌药物后仍旧持续发热的患者，应尽早手术治疗[44-45]。对于活动性赘生物大于10 mm，且赘生物出现在二尖瓣前叶和有栓塞发作史的患者，也要尽早手术治疗[6,46]。除此之外，脑卒中患者的手术时机要严格把握，尤其是出血性脑卒中，因为脑卒中患者的术后病死率很高，尤其是在脑血管事件发生的最初4周内，美国心脏病学会指南建议，对于脑卒中患者，应延迟手术干预的时间至少4周[47]。

2.3 CIED术后IE

CIED较为常用，包括永久性起搏器、植入式心律转复除颤器和心脏再同步治疗设备等。然而与CIED相关的感染率增加并不与CIED的植入成正比。CIED感染可能发生在设备口袋、引线和/或心内膜表面。发生CIED感染的危险因素包括设备翻修、设备口袋血肿以及患者存在合并症，如糖尿病、癌症、心力衰竭等[48]。60%~80%的CIED感染由葡萄球菌属导致，可通过患者的临床表现、血培养结果、超声心动图、FDG PET/CT等进行诊断[49-50]。一旦确诊CIED感染，需尽早完整移除设备及引线，同时依据血培养结果给予适

当的抗菌治疗[51]。

2.4 左心室辅助装置(left ventricular assist device, LVAD)植入术后IE

LVAD是终末期心衰的终极疗法或心脏移植桥接的重要方法之一,然而LVAD植入术后特异性感染(35%)和脓毒症(36%)的发生率较高[52]。LVAD相关感染可发生在动力传动系统部位、装置口袋部位或靠近心内膜的泵内表面,其中动力传动系统部位感染是LVAD相关感染的最常见类型[53]。LVAD相关IE病死率比天然瓣膜IE更高;与单纯内科治疗相比,外科手术干预(如更换心内辅助装置或心脏移植手术)能提高患者生存率[54]。

2.5 心脏介入手术后IE

心脏瓣膜介入手术是治疗瓣膜性心脏病的常见方法,包括经导管主动脉瓣置换术(transcatheter aortic valve replacement,TAVR)、经皮瓣膜修复术等。有研究显示,在中风险和高风险手术患者中,TAVR和外科主动脉瓣置换术治疗人工瓣膜心内膜炎的风险相近[55]。自20世纪70年代以来,卵圆孔未闭和房间隔缺损闭合装置已被用于IE的治疗,研究认为在装置植入后的数周至数月内,发生IE的风险最高,并且认为缺乏装置内皮化是导致患者发生晚期细菌性心内膜炎的原因[56]。目前,评估左心耳封堵器植入后IE发生率的研究较少,值得临床深入研究。

2.6 妊娠合并IE

有研究显示,妊娠合并IE较为少见,其发病率约为6/100 000;然而,合并IE的孕妇及其胎儿的病死率很高,约为22%和15%[57-58]。对于合并IE的孕妇,早期诊断非常重要,应密切监测孕妇的体温、脉搏等生命体征,及时关注患者心脏杂音情况。妊娠合并IE患者的手术指征包括瓣膜功能不全、心力衰竭、感染持续加重且有心内扩散、难治性微生物感染(如假单胞菌和真菌感染)、持续性菌血症、大的活动性赘生物等。尽管对于妊娠合并IE患者的手术时机选择困难[59],手术甚至可能增加胎儿死亡风险,但对于伴瓣膜严重功能障碍且具有IE早期手术指征的孕妇,建议在妊娠期间行心脏手术[17,60]。IE的及时诊断和合理治疗对降低孕妇和胎儿的病死率非常重要。

2.7 IE合并脑卒中

美国一项全国性调查研究表明,约13%的IE患者合并脑卒中或中枢神经系统感染,尤其是老年住院IE患者,脑卒中发病常见,而脑卒中会显著增加IE患者病死率[61]。对于IE伴有脑卒中以及神经功能障碍的患者,应对手术必要性与术中卒中加重风险进行权衡,决定手术时机[61]。若存在预计生存期较短(尤其是80岁以上的高龄患者)、多器官功能衰竭、出血性卒中合并症、脑脓肿形成或感染性脑动脉瘤等,宜从脑血管事件发生后,延迟手术至少4周以上[62-63]。对于伴有严重神经功能损害或意识障碍的缺血性卒中IE患者,术后神经系统并发症加重和死亡风险较高,应视情况严格把握手术时机。对于出血性卒中IE患者,若血流动力学稳定,建议延迟手术至少4周以上。有研究显示,对于无症状轻微栓塞、短暂性脑缺血发作、脑脓肿、无出血征象和严重神经功能损害的缺血性卒中患者,若具备早期手术指征,建议尽早手术[64-65]。对于伴出血性卒中的IE患者,4周内手术病死率明显高于较晚手术者(75% *vs.* 40%)[47]。有研究显示,出血性卒中IE患者延迟手术可显著降低术后病死率及神经系统并发症发生率[66]。对于存在神经系统症状的IE患者,应考虑颅内感染性动脉瘤的可能,建议行CT或MRI血管造影辅助诊断;如果颅内感染性动脉瘤巨大,有扩张或破裂风险,建议与神经外科会诊,行神经外科手术或血管内治疗,待血流动力学稳定后,进一步治疗IE。

2.8 右心系统IE

右心系统IE占IE患者的5%~10%,最常见于静脉吸毒者、先天性心脏病患者及安装起搏器、植入型心律转复除颤器、中心静脉导管的患者,尤其是免疫功能不全的患者;金黄色葡萄球菌是其主要感染病原体,常累及三尖瓣[67]。右心系统IE通常表现为菌血症、持续发热以及肺栓塞,对患者危害大,其诊断依赖于TTE。随着抗菌药物应用的增多,耐甲氧西林菌株越来越常见,万古霉素的应用逐渐增加。对于内科治疗无效者,应进行手术治疗。右心系统IE的手术指征包括持续性菌血症、赘生物直径超过20 mm或严重的右心衰竭。有研究表明,早期手术瓣膜修复成形的治疗成功率更高,有助于改善预后,但不建议行三尖瓣置换术[68]。

2.9 辅助治疗

有研究显示,接受抗凝治疗的人工瓣膜心内膜炎患者的病死率明显高于天然瓣膜心内膜炎患者,并且约73%的人工瓣膜IE患者死于中枢神经系统并发症[69]。对于有中枢神经系统栓塞的IE和机械瓣膜患者,应停止抗凝治疗至少2周,以改善患者预后。有研究发现,使用他汀类药物的住院患者,治疗后3个月和12个月病死率明显低于非他汀类药物使用者[70]。但目前关于他汀类药物治疗IE的报道较少,尚需进一步研究报道。

2.10 预防性使用抗菌药物

预防性使用抗菌药物预防IE的概念已经出现超过60年,可以追溯到1955年的AHA指南[71],该指南建议在牙科手术前对风湿性心脏病和冠心病患者使用

肌内青霉素[72]。牙科手术前使用抗菌药物预防IE的适应证有:人工心脏瓣膜;IE史;先天性心脏病,尤其是未修复的紫绀性心脏病或使用假体材料修复6个月后的先天性心脏病,如果存在残留缺陷,则终身用药。尽管对于预防性应用抗菌药物存在争议,但目前在牙科手术前预防性应用抗菌药物,一定程度上权衡了治疗的风险和益处,对可能因IE产生重大不良后果的高危人群起到了一定的保护作用[73]。

随着医疗技术的发展,目前关于IE的诊断与治疗方式取得了巨大的进展,IE患者的预后也越来越好。但IE仍旧是危及患者生命安全的疾病,每年依旧有许多患者死于IE。IE作为一种复杂的系统性疾病,不仅影响心脏本身,还会对全身其他器官系统的功能造成影响。对于IE应继续深入研究,整合多学科的力量,以期找到更安全、更有效、更经济的治疗方法。

[参考文献]

[1] Geller SA. Infective endocarditis: a history of the development of its understanding[J]. Autops Case Rep, 2013, 3(4): 5-12. doi: 10.4322/acr.2013.033.

[2] Tleyjeh IM, Steckelberg JM, Murad HS, et al. Temporal trends in infective endocarditis: a population-based study in Olmsted county, Minnesota[J]. JAMA, 2005, 293(24): 3022-3028. doi: 10.1001/jama.293.24.3022.

[3] Wurcel AG, Anderson JE, Chui KK, et al. Increasing infectious endocarditis admissions among young people who inject drugs[J]. Open Forum Infect Dis, 2016, 3(3): ofw157. doi: 10.1093/ofid/ofw157.

[4] Yew HS, Murdoch DR. Global trends in infective endocarditis epidemiology[J]. Curr Infect Dis Rep, 2012, 14(4): 367-372. doi: 10.1007/s11908-012-0265-5.

[5] Rwebembera J, Nascimento BR, Minja NW, et al. Recent advances in the rheumatic fever and rheumatic heart disease continuum[J]. Pathogens, 2022, 11(2): 179. doi: 10.3390/pathogens11020179.

[6] Vilacosta I, Graupner C, San Román JA, et al. Risk of embolization after institution of antibiotic therapy for infective endocarditis[J]. J Am Coll Cardiol, 2002, 39(9): 1489-1495. doi: 10.1016/s0735-1097(02)01790-4.

[7] Steckelberg JM, Murphy JG, Ballard D, et al. Emboli in infective endocarditis: the prognostic value of echocardiography[J]. Ann Intern Med, 1991, 114(8): 635-640. doi: 10.7326/0003-4819-114-8-635.

[8] Pawar NH, Nickalls OJ, Tan KL, et al. Invasive streptococcus pneumoniae infection causing cardioembolic stroke: a clinical proximity to austrian syndrome[J]. Cureus, 2017, 9(12): e1960. doi: 10.7759/cureus.1960.

[9] Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study[J]. Arch Intern Med, 2009, 169(5): 463-473. doi: 10.1001/archinternmed.2008.603.

[10] Fowler VG Jr, Miro JM, Hoen B, et al. Staphylococcus aureus endocarditis: a consequence of medical progress[J]. JAMA, 2005, 293(24): 3012-3021. doi: 10.1001/jama.293.24.3012.

[11] Tattevin P, Watt G, Revest M, et al. Update on blood culture-negative endocarditis[J]. Med Mal Infect, 2015, 45(1/2): 1-8. doi: 10.1016/j.medmal.2014.11.003.

[12] Fournier PE, Thuny F, Richet H, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases[J]. Clin Infect Dis, 2010, 51(2): 131-140. doi: 10.1086/653675.

[13] Bağ Soytaş R, Ünal D, Arman P, et al. Factors affecting mortality in geriatric patients hospitalized with COVID-19[J]. Turk J Med Sci, 2021, 51(2): 454-463. doi: 10.3906/sag-2008-91.

[14] Lecuit M, Eloit M. The diagnosis of infectious diseases by whole genome next generation sequencing: a new era is opening[J]. Front Cell Infect Microbiol, 2014, 4: 25. doi: 10.3389/fcimb.2014.00025.

[15] Yu X, Newland SA, Zhao TX, et al. Innate lymphoid cells promote recovery of ventricular function after myocardial infarction[J]. J Am Coll Cardiol, 2021, 78(11): 1127-1142. doi: 10.1016/j.jacc.2021.07.018.

[16] Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American heart association[J]. Circulation, 2015, 132(15): 1435-1486. doi: 10.1161/CIR.0000000000000296.

[17] Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)[J]. Eur Heart J, 2015, 36(44): 3075-3128. doi: 10.1093/eurheartj/ehv319.

[18] Mügge A, Daniel WG, Frank G, et al. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by the transthoracic and the transesophageal approach[J]. J Am Coll Cardiol, 1989, 14(3): 631-638. doi: 10.1016/0735-1097(89)90104-6.

[19] San Román JA, Vilacosta I. Role of transesophageal echocardiography in right-sided endocarditis[J]. Echocardiography, 1995, 12(6): 669-672. doi: 10.1111/j.1540-8175.1995.tb00860.x.

[20] American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians[J]. J Am Soc Echocardiogr, 2011, 24(3): 229-267. doi: 10.1016/j.echo.2010.12.008.

[21] Doherty JU, Kort S, Mehran R, et al. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2019 appropriate use criteria for multimodality imaging in the assessment of cardiac structure and function in nonvalvular heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiog-

raphy and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons[J]. J Am Coll Cardiol, 2019, 73(4): 488-516. doi:10.1016/j.jacc.2018.10.038.

[22] Gadhinglajkar S, Sreedhar R, Karunakaran J, et al. Tricuspid valve excision using off-pump inflow occlusion technique: role of intra-operative trans-esophageal echocardiography [J]. Ann Card Anaesth, 2010, 13(2): 148-153. doi:10.4103/0971-9784.62929.

[23] Eltzschig HK, Rosenberger P, Loffler M, et al. Impact of intraoperative transesophageal echocardiography on surgical decisions in 12,566 patients undergoing cardiac surgery[J]. Ann Thorac Surg, 2008, 85(3): 845-852. doi:10.1016/j.athoracsur.2007.11.015.

[24] Emily J, MacKay DO, Bo Zhang, et al. Association of intraoperative transesophageal echocardiography and clinical outcomes after open cardiac valve or proximal aortic surgery[J]. JAMA Netw Open, 2022, 5(2): e2147820. doi:10.1001/jamanetworkopen.2021.47820.

[25] Hansalia S, Biswas M, Dutta R, et al. The value of live/real time three-dimensional transesophageal echocardiography in the assessment of valvular vegetations [J]. Echocardiography, 2009, 26(10): 1264-1273. doi:10.1111/j.1540-8175.2009.01042.x.

[26] Saxena P, Malouf JF, Click R, et al. 3D echocardiography in cardiac surgery [J]. J Card Surg, 2014, 29(1): 51-54. doi: 10.1111/jocs.12256.

[27] Narducci ML, Pelargonio G, Russo E, et al. Usefulness of intracardiac echocardiography for the diagnosis of cardiovascular implantable electronic device-related endocarditis[J]. J Am Coll Cardiol, 2013, 61(13): 1398-1405. doi:10.1016/j.jacc.2012.12.041.

[28] Feuchtner GM, Stolzmann P, Dichtl W, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings [J]. J Am Coll Cardiol, 2009, 53(5): 436-444. doi: 10.1016/j.jacc.2008.01.077.

[29] Hryniewiecki T, Zatorska K, Abramczuk E, et al. The usefulness of cardiac CT in the diagnosis of perivalvular complications in patients with infective endocarditis[J]. Eur Radiol, 2019, 29(8): 4368-4376. doi:10.1007/s00330-018-5965-2.

[30] Kim IC, Chang S, Hong GR, et al. Comparison of cardiac computed tomography with transesophageal echocardiography for identifying vegetation and intracardiac complications in patients with infective endocarditis in the era of 3-dimensional images[J]. Circ Cardiovasc Imaging, 2018, 11(3): e006986. doi: 10.1161/CIRCIMAGING.117.006986.

[31] Duval X, Iung B, Klein I, et al. Effect of early cerebral magnetic resonance imaging on clinical decisions in infective endocarditis: a prospective study[J]. Ann Intern Med, 2010, 152(8): 497-504. doi: 10.7326/0003-4819-152-8-201004200-00006.

[32] Saby L, Laas O, Habib G, et al. Positron emission tomography/computed tomography for diagnosis of prosthetic valve endocarditis: increased valvular 18F-fluorodeoxyglucose uptake as a novel major criterion [J]. J Am Coll Cardiol, 2013, 61(23): 2374-2382. doi: 10.1016/j.jacc.2013.01.092.

[33] Kestler M, Muñoz P, Rodríguez-Créixems M, et al. Group for the Management of Infectious Endocarditis (GAME). Role of (18)F-FDG PET in patients with infectious endocarditis[J]. J Nucl Med, 2014, 55(7): 1093-1098. doi:10.2967/jnumed.113.134981.

[34] Jiménez-Ballvé A, Pérez-Castejón MJ, Delgado-Bolton RC, et al. Assessment of the diagnostic accuracy of 18F-FDG PET/CT in prosthetic infective endocarditis and cardiac implantable electronic device infection: comparison of different interpretation criteria [J]. Eur J Nucl Med Mol Imaging, 2016, 43(13): 2401-2412. doi: 10.1007/s00259-016-3463-9.

[35] Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service[J]. Am J Med, 1994, 96(3): 200-209. doi:10.1016/0002-9343(94)90143-0.

[36] Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis[J]. Clin Infect Dis, 2000, 30(4): 633-638. doi:10.1086/313753.

[37] Habib G, Derumeaux G, Avierinos JF, et al. Value and limitations of the Duke criteria for the diagnosis of infective endocarditis[J]. J Am Coll Cardiol, 1999, 33(7): 2023-2029. doi: 10.1016/s0735-1097(99)00116-3.

[38] Francioli P, Etienne J, Hoigné R, et al. Treatment of streptococcal endocarditis with a single daily dose of ceftriaxone sodium for 4 weeks: efficacy and outpatient treatment feasibility[J]. JAMA, 1992, 267(2): 264-267. doi:10.1001/jama.1992.03480020074034.

[39] Verhagen DW, Vedder AC, Speelman P, et al. Antimicrobial treatment of infective endocarditis caused by viridans streptococci highly susceptible to penicillin: historic overview and future considerations[J]. J Antimicrob Chemother, 2006, 57(5): 819-884. doi:10.1093/jac/dkl087.

[40] Fowler VG Jr, Boucher HW, Corey GR, et al. Daptomycin versus standard therapy for bacteremia and endocarditis caused by Staphylococcus aureus[J]. N Engl J Med, 2006, 355(7): 653-665. doi:10.1056/NEJMoa053783.

[41] Carugati M, Bayer AS, Miró JM, et al. International collaboration on endocarditis. High-dose daptomycin therapy for left-sided infective endocarditis: a prospective study from the international collaboration on endocarditis[J]. Antimicrob Agents Chemother, 2013, 57(12): 6213-6222. doi:10.1128/AAC.01563-13.

[42] Kiefer T, Park L, Tribouilloy C, et al. Association between valvular surgery and mortality among patients with infective endocarditis complicated by heart failure[J]. JAMA, 2011, 306(20): 2239-2247. doi:10.1001/jama.2011.1701.

[43] Remadi JP, Habib G, Nadji G, et al. Predictors of death and impact of surgery in Staphylococcus aureus infective endocarditis [J]. Ann Thorac Surg, 2007, 83(4): 1295-1302. doi:10.1016/j.athoracsur.2006.09.093.

[44] Hill EE, Herijgers P, Claus P, et al. Abscess in infective endocarditis: the value of transesophageal echocardiography and outcome: a 5-year study[J]. Am Heart J, 2007, 154(5): 923-928. doi: 10.1016/j.ahj.2007.06.028.

[45] Sohail MR, Martin KR, Wilson WR, et al. Medical versus surgical management of Staphylococcus aureus prosthetic valve endocarditis [J]. Am J Med, 2006, 119(2): 147-154. doi: 10.1016/j.amjmed.2005.09.037.

[46] Fosbøl EL, Park LP, Chu VH, et al. The association between vegetation size and surgical treatment on 6-month mortality in left-sided infective endocarditis [J]. Eur Heart J, 2019, 40(27): 2243-2251. doi:10.1093/eurheartj/ehz204.

[47] García-Cabrera E, Fernández-Hidalgo N, Almirante B, et al. Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study [J]. Circulation, 2013, 127(23): 2272-2284. doi: 10.1161/

CIRCULATIO NAHA. 112. 000813.

[48] Voigt A, Shalaby A, Saba S. Continued rise in rates of cardiovascular implantable electronic device infections in the United States: temporal trends and causative insights[J]. Pacing Clin Electrophysiol, 2010, 33(4): 414-419. doi: 10. 1111/j. 1540-8159. 2009. 02569. x.

[49] Blomström-Lundqvist C, Traykov V, Erba PA, et al. European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections-endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)[J]. Europace, 2020, 22(4): 515-549. doi: 10. 1093/europace/euz246.

[50] Victor F, De Place C, Camus C, et al. Pacemaker lead infection: echocardiographic features, management, and outcome[J]. Heart, 1999, 81(1): 82-87. doi: 10. 1136/hrt. 81. 1. 82.

[51] Chrapko BE, Chrapko M, Nocuń A, et al. Role of 18F-FDG PET/CT in the diagnosis of inflammatory and infectious vascular disease[J]. Nucl Med Rev Cent East Eur, 2016, 19(1): 28-36. doi: 10. 5603/NMR. 2016. 0006.

[52] Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device[J]. N Engl J Med, 2009, 361(23): 2241-2251. doi: 10. 1056/NEJMoa0909938.

[53] Nienaber J, Wilhelm MP, Sohail MR. Current concepts in the diagnosis and management of left ventricular assist device infections[J]. Expert Rev Anti Infect Ther, 2013, 11(2): 201-210. doi: 10. 1586/eri. 12. 163.

[54] Patel S, Rizvi SSA, Choi JH, et al. Management and outcomes of left ventricular assist device-associated endocarditis: a systematic review[J]. Ann Cardiothorac Surg, 2019, 8(6): 600-609. doi: 10. 21037/acs. 2019. 04. 04.

[55] Summers MR, Leon MB, Smith CR, et al. Prosthetic valve endocarditis after TAVR and SAVR: insights from the PARTNER trials[J]. Circulation, 2019, 140(24): 1984-1994. doi: 10. 1161/CIRCULATIO NAHA. 119. 041399.

[56] Slesnick TC, Nugent AW, Fraser CD Jr, et al. Images in cardiovascular medicine. Incomplete endothelialization and late development of acute bacterial endocarditis after implantation of an Amplatzer septal occluder device[J]. Circulation, 2008, 17(18): e326-e327. doi: 10. 1161/CIRCULATIONAHA. 107. 754069.

[57] Montoya ME, Karnath BM, Ahmad M. Endocarditis during pregnancy[J]. South Med J, 2003, 96(11): 1156-1157. doi: 10. 1097/01. SMJ. 0000054503. 18393. 1E.

[58] Campuzano K, Roqué H, Bolnick A, et al. Bacterial endocarditis complicating pregnancy: case report and systematic review of the literature[J]. Arch Gynecol Obstet, 2003, 268(4): 251-255. doi: 10. 1007/s00404-003-0485-x

[59] Kaoutzanis C, Evangelakis E, Kokkinos C, et al. Urgent aortic valve replacement for infective endocarditis during the 23rd week of pregnancy[J]. Gen Thorac Cardiovasc Surg, 2013, 61(5): 296-300. doi: 10. 1007/s11748-012-0140-1.

[60] Ramlakhan KP, Johnson MR, Roos-Hesselink JW. Pregnancy and cardiovascular disease[J]. Nat Rev Cardiol, 2020, 17(11): 718-731. doi: 10. 1038/s41569-020-0390-z.

[61] Bor DH, Woolhandler S, Nardin R, et al. Infective endocarditis in the U. S., 1998-2009: a nationwide study[J]. PLoS One, 2013, 8(3): e60033. doi: 10. 1371/journal. pone. 0060033.

[62] Sorabella RA, Han SM, Grbic M, et al. Early operation for endocarditis complicated by preoperative cerebral emboli is not associated with worsened outcomes[J]. Ann Thorac Surg, 2015, 100(2): 501-508. doi: 10. 1016/j. athoracsur. 2015. 03. 078.

[63] Kitai T, Masumoto A, Okada T, et al. Optimal timing of surgery for patients with active infective endocarditis[J]. Cardiol Clin, 2021, 39(2): 197-209. doi: 10. 1016/j. ccl. 2021. 01. 002.

[64] Thuny F, Avierinos JF, Tribouilloy C, et al. Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study[J]. Eur Heart J, 2007, 28(9): 1155-1161. doi: 10. 1093/eurheartj/ehm005.

[65] Yanagawa B, Pettersson GB, Habib G, et al. Surgical management of infective endocarditis complicated by embolic stroke: practical recommendations for clinicians[J]. Circulation, 2016, 134(17): 1280-1292. doi: 10. 1161/CIRCULATIONAHA. 116. 024156.

[66] Tam DY, Yanagawa B, Verma S, et al. Early *vs.* late surgery for patients with endocarditis and neurological injury: a systematic review and meta-analysis[J]. Can J Cardiol, 2018, 34(9): 1185-1199. doi: 10. 1016/j. cjca. 2018. 05. 010.

[67] Gaca JG, Sheng S, Daneshmand M, et al. Current outcomes for tricuspid valve infective endocarditis surgery in North America[J]. Ann Thorac Surg, 2013, 96(4): 1374-1381. doi: 10. 1016/j. athoracsur. 2013. 05. 046.

[68] Akinosoglou K, Apostolakis E, Koutsogiannis N, et al. Right-sided infective endocarditis: surgical management[J]. Eur J Cardiothorac Surg, 2012, 42(3): 470-479. doi: 10. 1093/ejcts/ezs084.

[69] Tornos P, Almirante B, Mirabet S, et al. Infective endocarditis due to Staphylococcus aureus: deleterious effect of anticoagulant therapy[J]. Arch Intern Med, 1999, 159(5): 473-475. doi: 10. 1001/archinte. 159. 5. 473.

[70] Papazian L, Roch A, Charles PE, et al. Effect of statin therapy on mortality in patients with ventilator-associated pneumonia: a randomized clinical trial[J]. JAMA, 2013, 310(16): 1692-1700. doi: 10. 1001/jama. 2013. 280031.

[71] The Subcommittee of Principal Investigators of the American Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association. TREATMENT of acute rheumatic fever in children a co-operative clinical trial of A. C. T. H., cortisone, and aspirin[J]. Br Med J, 1955, 1(4913): 555-574.

[72] Kerdemelidis M, Lennon DR, Arroll B, et al. The primary prevention of rheumatic fever[J]. J Paediatr Child Health, 2010, 46(9): 534-548. doi: 10. 1111/j. 1440-1754. 2010. 01854. x.

[73] Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group[J]. J Am Dent Assoc, 2007, 138(6): 739-745. doi: 10. 14219/jada. archive. 2007. 0262.

(编辑:贺绍梅)