Advances in Clinical Medicine 临床医学进展, 2024, 14(12), 750-758
Published Online December 2024 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2024.14123143

不同起搏部位研究进展

钱雨婷[1]，杨　莹[2*]

[1]绍兴文理学院医学院，浙江　绍兴
[2]浙江大学医学院附属邵逸夫医院心内科，浙江　杭州

收稿日期：2024年11月18日；录用日期：2024年12月11日；发布日期：2024年12月18日

摘　要

心脏起搏60多年来在临床应用中不断发展，随着人们逐渐认识到传统起搏方式的不足后，更为符合生理的起搏方式应运而生。生理性起搏方式是否更符合预期，在临床结局上是否优于传统起搏方式，尚有待考究。本综述旨在全面概述不同起搏部位的优势和局限性，为临床应用提供参考，对不同起搏部位对比研究提出相关展望。

关键词

起搏部位，心室起搏，传导系统起搏，生理性起搏

Research Progress of Different Pacing Sites

Yuting Qian[1], Ying Yang[2*]

[1]School of Medicine, Shaoxing University, Shaoxing Zhejiang
[2]Department of Cardiology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou Zhejiang

Received: Nov. 18th, 2024; accepted: Dec. 11th, 2024; published: Dec. 18th, 2024

Abstract

Cardiac pacing for clinical application has been developing for more than 60 years. With the gradual recognition of the disadvantage of traditional pacing, physiological pacing has emerged. Whether physiologic pacing can meet more expectations and whether it is better than traditional pacing in clinical outcome remains to be studied. The purpose of this review is to give an overview of the advantages and limitations of different pacing sites, provide reference for clinical application, and propose prospects for studies for comparation of different pacing sites.

*通讯作者。

文章引用: 钱雨婷, 杨莹. 不同起搏部位研究进展[J]. 临床医学进展, 2024, 14(12): 750-758.
DOI: 10.12677/acm.2024.14123143

Keywords

Pacing Site, Ventricular Pacing, Conduction System Pacing, Physiological Pacing

1. 引言

对于有症状的心脏传导系统疾病，目前没有任何药物或其他非药物治疗可以逆转病因，起搏器植入是唯一有效的治疗方法[1]。由于人口老龄化，全球每年植入起搏器的总数持续增长，以帮助传导系统疾病患者提高生活质量并降低死亡率，来获得令人满意的结局[2]。自 1958 年第一例植入式起搏器以来，人们很快就发现，虽然这是一种挽救生命的疗法，但其起搏方式和自身传导不一致导致不符合心脏自身生理特性，带来的一系列问题还需要更多的临床进步空间。60 多年来，生理性心脏起搏一直是所追求的目标[3]。通过国内外的研究和临床的应用，起搏方式不断进展，从起搏部位上来看，常见的选择包括右心室心尖部起搏(right ventricular apex pacing, RVAP)、右心室间隔起搏(right ventricular septum pacing, RVSP)、双心室起搏(biventricular pacing, BVP)、希氏束起搏(his bundle pacing, HBP)、左束支起搏(left bundle branch pacing, LBBP)及左心室间隔起搏(left ventricular septal pacing, LVSP)等。本综述旨在讨论目前临床可用的不同起搏部位选择、局限性、并发症等，为临床应用提供参考，对不同起搏部位对比研究提出相关展望。

2. 不同起搏部位

2.1. 右心室起搏

2.1.1. 右心室心尖起搏

在初期应用时，右心室心尖部被认为是起搏器心室电极安置的最佳部位，因为易于定位，并且存在用于锚定被动导联的小梁，具有操作简单安全、导线易到位、长期稳定性好、使用经验丰富等优点[4]。几十年来，有大量双腔永久起搏器患者选择右心室心尖起搏。

但随着国内外的进一步研究，右心室心尖起搏的弊端也逐渐暴露。在许多患者中，右心室的心尖壁相对较薄，通常小于 1 mm，所以穿孔并不罕见[5] [6]。且在右心室心尖起搏期间，电传导通过心肌传播，其速度比希氏束－浦肯野纤维系统传导慢，可引起左心室延迟激活。长期右心室心尖起搏可引起高度房室传导阻滞患者的左右心室不同步，进而显著影响心脏形态和收缩功能[7]，可致左心室肥大，收缩功能进行性恶化。右心室心尖起搏和左心室收缩功能恶化之间的关联在起搏比例高的患者中尤其明显[8]，研究表明这可能与患者基线左心室射血分数，起搏比例以及永久性右心室心尖起搏产生非生理性的心室激活顺序，增加 QRS 波宽度相关[9] [10]。这种特殊的临床情况称为起搏诱导心肌病(pacing-induced cardiomyopathy, PICM)。超过 1/10 的长期右心室心尖起搏患者发展为起搏诱导心肌病[11]。其最佳的治疗方法尚不确定。

2.1.2. 右心室间隔起搏

右心室间隔起搏相较于右心室心尖起搏更符合生理，可能减少起搏诱导的不同步的不利影响。在起搏相关文献中，右心室间隔起搏的定义仍不明确，起搏部位包括右室流出道、右室中间隔，甚至与心尖相邻的间隔区域。尽管试图标准化非心尖起搏位点的命名，但这种混淆仍然存在，其中研究最多的是右

心室间隔流出道起搏。右心室间隔流出道起搏位于室上嵴，上部以肺动脉瓣为界，下部以三尖瓣为界，其被认为更接近希氏束－浦肯野纤维，提供了更多的生理性左心室激活，实际应用时该区域导线植入相对容易且稳定性好，具有良好的可行性及可重复性[12]。

右心室流出道间隔起搏能获得较短的 QRS 持续时间，比右心室其他起搏部位都要短。这表明，右心室间隔起搏虽然不如自身传导系统起搏好，但可能是长期右心室起搏理想的部位，因为较短的 QRS 持续时间与左心室动力学的改善有关。但右心室间隔起搏的结局是否优于传统的右心室心尖起搏仍缺乏循证医学证据，有研究表明右心室间隔起搏并无法获得更优的左心室收缩功能[13]，在起搏诱导心肌病的发生率上两者亦未见明显差异[14]。但亦有研究在长期随访过程中发现，与右心室心尖起搏相比，右心室间隔起搏发生心力衰竭的风险降低 3.3 倍，而且没有显著增加手术复杂性或更高的并发症发生率[15]。因此，右心室间隔起搏是否优于右心室心尖起搏，仍需大量的临床对比研究的证实。

2.2. 双心室起搏

双心室起搏主要为心脏再同步化治疗，通过以下导线在两个部位同时或近乎同时刺激心室心肌来实现：植入冠状窦(coronary sinus, CS)分支中用于起搏心外膜的导线和右心室心内膜起搏导线。是旨在通过恢复更多生理激活来改善传导系统疾病患者心脏功能的起搏方法[16]。

双心室起搏适用于射血分数显著降低的左束支传导阻滞并且有临床症状的心力衰竭患者，或者有起搏需求且预期心室起搏比例高的心功能不全患者。随着研究深入，人们意识到它可以预防或逆转起搏诱导的左心室功能障碍，该类型占所有因不同步引起心力衰竭的 25%，大多数起搏诱导心肌病患者升级双心室起搏之后，左心室射血分数能得到改善，并减少心律失常事件[17]-[19]。双心室起搏可改善左束支传导阻滞患者的左心室的重塑和功能[20] [21]。然而，尽管有长期的临床证据，并且心脏电生理学家对植入技术很熟悉，但多达 1/3 的患者无法通过实现双心室起搏获益[22] [23]。这种无反应在很大程度上归因于绕过传导系统的非生理刺激[24]导致机械不同步、心肌瘢痕和左心室导线位置不理想[25]。因此，行双心室起搏应充分考虑以下 3 个方面：术前患者选择、电极植入和术后管理。首先，术前应排除未经治疗的心肌缺血、瓣膜性心脏病、机械性梗阻和未经治疗的心律失常诱发的心肌病患者，行心电图检查是筛选患者时最简便也最重要的。其次，植入电极时避免瘢痕至关重要，心脏磁共振是评估心肌结构和功能的金标准，因为它具有独特的心脏瘢痕成像能力。最后，术后的随访亦不可或缺，包括程控优化、心力衰竭及并发症治疗和日常康复[26]。

2.3. 希氏束起搏

近年来，永久性希氏束起搏已成为有右心室起搏和心脏再同步化治疗指征的患者的生理性起搏选择[27]。希氏束自房室结起，止于室间隔膜部，包含多个传导纤维。与传统起搏方式不同，希氏束起搏通过希氏－浦肯野纤维系统激动心室，通过相对正常的心室电激动传导顺序，产生较窄的 QRS 持续时间，保持了房室及心室间收缩同步性，可以防止有心动过缓起搏指征的患者发生右心室起搏诱导的心肌病。从理论上讲，希氏束起搏是最具生理意义的起搏方式，因为它可以保留或恢复心室的正常电激动顺序[28]。

与右心室起搏相比，希氏束起搏在长期随访中，死亡、因心衰住院和起搏器诱导心肌病的发生均明显低于右心室间隔或心尖起搏[29] [30]。且具有良好的电同步性和左室机械同步性[31] [32]。与双心室起搏相比，在需要心脏再同步化治疗的患者中，希氏束起搏对左心室收缩舒张功能及左心室射血分数的改善更大[33] [34]，且心衰和死亡的风险更低[35] [36]。此外，由于导联不穿过瓣膜，因此三尖瓣反流的发生率较低[37]。

然而，尽管近年来永久性希氏束起搏在电生理学家中获得了更多的认可，但技术困难仍然是一个主

要缺点，限制了该技术在临床实践中更广泛的应用。希氏束的直径只有 1~2 mm，位于中央纤维体，被心肌组织包围最少，起搏阈值高，且希氏束的解剖结构有 3 种常见变体：I 型，希氏束始终沿着室间隔膜部以下传导，覆盖着一层心肌纤维。II 型，希氏束远离室间隔膜部，通过较厚的心肌纤维包裹与周围组织绝缘。III 型，希氏束紧邻心内膜下方，裸露在外，与周围组织并未绝缘[38]。因而在实际应用中难以确定其确切位置，易损伤希氏束导致传导阻滞，手术难度大，后期阈值升高比例较高，增加患者经济负担等。可通过采用双导联法和稳定性评估技术等来增加希氏束起搏器植入的成功率[39] [40]。

2.4. 左束支区域起搏

2.4.1. 左束支起搏

2017 年首次报道了心力衰竭和左束支传导阻滞患者行左束支起搏的结果，起搏导线通过植入到右心室间隔深处，来夺获左束支区域[41]。左束支起源于希氏束的分支，位于室间隔膜部下方，形成左束支的所有纤维都位于同一平面上，呈扁带状结构，分布较广[42]。其解剖学特征决定了左束支起搏作为潜在生理起搏方式的可行性。成功夺获左束支的标准如下，需满足 3 条以上：第一，在左束支起搏后，单极起搏测试时心电图表现为右束支阻滞形态；第二，存在左束支电位，指行腔内心电图后检测到 QRS 波前 20~30 ms 的高频信号；第三，左心室达峰时间(pacing stimulus to left ventricular activation time, Stim-LVAT)随着高低电压输出有≥10 ms 的突变，或者短而稳定；第四，非选择性左束支起搏同时夺获左束支及局部心肌，而选择性左束支起搏仅夺获左束支，当非选择性向选择性转变时腔内心电图可观察到起搏钉与 QRS 波间的等位线；第五，通过标测导管和双导线记录到顺行左束支电位和逆行的希氏束电位[43]。左束支起搏可产生更窄 QRS，更快激活左心室，是实现左束支传导阻滞电再同步的可行有效方法。左束支起搏可在大多数患者中成功安全地进行，只有约 3%~20%可能因导线无法深入左室深部间隔以到达左束支、固定部位的隔膜疤痕/纤维化等原因植入失败[44]。

对成功植入左束支起搏的患者临床疗效进行研究，与右心室间隔或心尖起搏相比，左束支起搏可提供更好的心脏机电机械同步和比右心室起搏更有效的心肌工作，从而改善整体心脏功能，并且其操作安全且几乎没有严重的并发症[45]-[47]。存在右心室起搏诱导心肌病的患者亦可升级为左束支起搏来改善预后[48] [49]。与双心室起搏相比，左束支起搏显示出更好的机械、电再同步性和更高的临床和超声心动图反应[50] [51]。相较于希氏束起搏而言，左束支起搏植入手术相对容易，且具有低而稳定的起搏夺获阈值[52]-[54]。

左束支起搏在应用过程中存在相关的并发症，其中室间隔穿孔和血栓栓塞最常见，其余还包括冠状动脉损伤、导线脱落等。室间隔穿孔分为急性和慢性，其中急性占 3%，评估基础的室间隔厚度和导线植入的深度对于预防急性穿孔至关重要，一旦发生了急性穿孔，则应选择不同部位起搏[55]。

2.4.2. 左心室间隔起搏

2002 年，首次在动物研究中应用左心室间隔起搏，发现有改善左室泵功能的作用[56]。2016 年在具有双腔起搏器植入指征的心脏结构正常的病态窦房结综合征患者中也被证实是可行的。并且在所有患者中一致观察到左心室间隔起搏的急性血流动力学优于右心室间隔或心尖起搏。其不仅具有良好的血流动力学效应，而且左心室间隔起搏期间的 QRS 持续时间均短于右心室起搏[57]。左心室间隔起搏基于对缓慢的房间隔传导、短路径长度和快速心内膜传导的补偿，可提供更好的室间同步[58]。可获得与双心室起搏相当的同步性及血流动力学[59] [60]。亦有研究表明左心室间隔起搏可以克服希氏束的大部分局限性，并长期提供稳定的导联参数[61]。

左心室间隔起搏捕获心肌，左束支起搏捕获左束支，两者十分接近，因而存在一定的相似之处，都可显著改善心室的不同步性。尽管植入技术没有太大差异，但在左束支起搏中，需要更先进的电生理知

识和设备来验证左束支的夺获，因此左心室间隔起搏的植入相对直接。尽管左心室间隔起搏手术很简单，但有一些因素可能会使植入复杂化，若室间隔肥大、瘢痕增生、纤维化亦可引起导线固定困难，从而导致导线植入失败[41]。在左束支起搏的实践过程中，研究发现能成功夺获左束支的夺获率 60%至 90%不等，这意味着剩下 10%至 40%欲行左束支起搏的患者被动接受了左心室间隔起搏[62]-[64]。有研究通过使用超高频心电图来比较这两者之间心室除极的差异，发现左束支起搏保留了生理性的左心室去极化，但增加了心室间的不同步。而左心室间隔起搏期间左心室侧壁去极延长，但心室间同步得以保持[65]。上述大多数研究都集中在两者的急性或短期影响上，缺乏长期随访的数据，为后续的研究留下了空间。

Table 1. Comparison of different pacing sites
表 1. 不同起搏部位对比

起搏部位	适用人群[1]	优点	局限性	常见并发症	成本效益
右心室心尖起搏	多数具有起搏器植入指征患者或其他部位起搏不可行	简单安全、易植入、稳定性好、使用经验丰富	易穿孔、易致起搏诱导心肌病	穿孔；起搏诱导心肌病；心律失常；心力衰竭	操作成熟，手术价格低，再住院率高，后续经济负担大
右心室间隔起搏	多数具有起搏器植入指征、希望改善心室同步性的患者	易植入、稳定性好，具有良好的可行性及可重复性	长期安全性及预后尚未明确	穿孔；起搏诱导心肌病	较右室心尖起搏器植入价格相似，后续经济负担相对较小
双心室起搏	(1) 左束支传导阻滞伴宽 QRS 及收缩功能下降的患者；(2) 起搏诱导心肌病患者；(3) 接受房室交界区消融的射血分数降低的房颤患者	可预防或逆转起搏诱导的左心室功能障碍	约 1/3 患者无应答	导线脱位；膈神经刺激	手术时间长，失败率高，价格昂贵
希氏束起搏	(1) 永久房室传导阻滞伴窄 QRS 波，射血分数减少的患者；(2) 永久性房颤伴窄 QRS 波，射血分数减少需要使用房室结消融结合希氏束起搏的患者；(3) 房颤伴宽 QRS 波，需要心室起搏的患者；(4) 双心室起搏失败患者	生理性起搏，起搏相关并发症发生率小	植入困难、起搏阈值高、易损伤希氏束	导线移位；囊袋感染；传导阻滞；心室失夺获	操作困难，阈值高，耗电快，经济负担大
左束支起搏	(1) 预计心室起搏比例高，伴心脏重塑或射血分数下降者；(2) 慢性房颤需要心室起搏者；(3) 房室结病变或需要房室结消融的患者；(4) 双心室起搏失败患者	生理性起搏，起搏阈值低而稳定	缺乏统一术式及定位标准，可出现室间隔穿孔、血栓栓塞等并发症，长期安全性及有效性未知	室间隔穿孔；血栓栓塞；冠状动脉损伤；导线脱落	疗效明显，再住院率低，成本效益率相对较高[66]
左心室间隔起搏	较左束支起搏相似	生理性起搏，安全易植入	长期安全性及有效性未知	室间隔损伤；室间隔穿孔	疗效明显，再住院率低

3. 结论

心脏起搏器因其对心脏传导系统疾病的有效治疗作用而在世界范围内得到广泛应用，但起搏器植入部位的选择在实际临床应用中仍具有争议性。不同起搏部位特点对比可总结为上述表 1，传统右室心尖部起搏虽操作简单、稳定，但不符合正常的心脏传导顺序，为非生理性起搏，会产生起搏诱导心肌病、穿孔等一系列问题。右心室间隔起搏被认为更接近正常传导系统，曾一度被认为是长期右心室起搏理想

的部位，但现有研究仍无法证明其可获得比右心室心尖起搏更好的结局。以双心室起搏为代表的心脏再同步化治疗可一定程度上预防或逆转传统右心室起搏带来的起搏诱导心肌病，但在实际应用过程中对患者选择、电极植入和术后管理存在一定要求，可能出现无应答情况。作为心脏起搏领域研究热点和领先技术的希氏束起搏，是心肌起搏到传导系统起搏质的飞跃，其激动沿正常的心脏传导顺序下传，改善左心室收缩功能，但希氏束起搏定位困难、操作难度大、起搏阈值高、手术成功率低、潜在风险多等缺陷使其难以在临床广泛推广。新兴的左束支区域起搏具有低而稳定的起搏夺获阈值，能在一定程度上克服既往起搏部位的局限性，有助于维持令人满意的左心室同步性并产生良好的血流动力学效应，但应用时间较短，也因远期疗效及患者获益情况尚未得到大量实践验证而存在顾虑。

综上所述，寻找一种安全稳定、操作简单的、符合生理且成本效益高的电极植入部位一直是国内外电生理专家的研究热点，每个起搏部位在实际应用中均存在优缺点，目前多数研究存在研究对象局限，样本量少，随访时间短等问题，导致多种起搏部位长期有效性及安全性尚未明确，因而需充分了解各个起搏部位的特点以及其局限性，根据患者实际情况和相关临床经验选择不同的起搏部位，再通过大量的临床对比研究来佐证，后续在临床中可加强对患者长期随访，记录相关数据，追踪相关患者结局，进一步行不同部位起搏的对比研究，以期为患者提供个性化的最优起搏位点。

参考文献

[1] Chung, M.K., Patton, K.K., Lau, C., Dal Forno, A.R.J., Al-Khatib, S.M., Arora, V., *et al*. (2023) 2023 HRS/APHRS/LAHRS Guideline on Cardiac Physiologic Pacing for the Avoidance and Mitigation of Heart Failure. *Heart Rhythm*, **20**, e17-e91. https://doi.org/10.1016/j.hrthm.2023.03.1538

[2] Raatikainen, M.J.P., Arnar, D.O., Merkely, B., Nielsen, J.C., Hindricks, G., Heidbuchel, H., *et al*. (2017) A Decade of Information on the Use of Cardiac Implantable Electronic Devices and Interventional Electrophysiological Procedures in the European Society of Cardiology Countries: 2017 Report from the European Heart Rhythm Association. *EP Europace*, **19**, ii1-ii90. https://doi.org/10.1093/europace/eux258

[3] Biffi, M., Capobianco, C., Spadotto, A., Bartoli, L., Sorrentino, S., Minguzzi, A., *et al*. (2020) Pacing Devices to Treat Bradycardia: Current Status and Future Perspectives. *Expert Review of Medical Devices*, **18**, 161-177. https://doi.org/10.1080/17434440.2021.1866543

[4] Burri, H., Starck, C., Auricchio, A., Biffi, M., Burri, M., D'Avila, A., *et al*. (2021) EHRA Expert Consensus Statement and Practical Guide on Optimal Implantation Technique for Conventional Pacemakers and Implantable Cardioverter-Defibrillators: Endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), and the Latin-American Heart Rhythm Society (LAHRS). *EP Europace*, **23**, 983-1008. https://doi.org/10.1093/europace/euaa367

[5] Waddingham, P.H., Elliott, J., Bates, A., Bilham, J., Muthumala, A., Honarbakhsh, S., *et al*. (2022) Iatrogenic Cardiac Perforation Due to Pacemaker and Defibrillator Leads: A Contemporary Multicentre Experience. *EP Europace*, **24**, 1824-1833. https://doi.org/10.1093/europace/euac105

[6] Israel, C.W., Tribunyan, S., Yen Ho, S. and Cabrera, J.A. (2022) Anatomy for Right Ventricular Lead Implantation. *Herzschrittmachertherapie + Elektrophysiologie*, **33**, 319-326. https://doi.org/10.1007/s00399-022-00872-w

[7] Xin, M., Gao, p. and Zhang, S. (2021) Effects of Long-Term Right Ventricular Apex Pacing on Left Ventricular Dyssynchrony, Morphology and Systolic Function. *International Journal of Cardiology*, **331**, 91-99. https://doi.org/10.1016/j.ijcard.2021.01.042

[8] Osiecki, A., Kochman, W., Witte, K.K., Mańczak, M., Olszewski, R. and Michałkiewicz, D. (2022) Cardiomyopathy Associated with Right Ventricular Apical Pacing-Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, **11**, Article No. 6889. https://doi.org/10.3390/jcm11236889

[9] Chango-Azanza, D.X., Munín, M.A., Sánchez, G.A., Arévalo-Pérez, L.M., Chango-Azanza, J.J., Pelayo, M.E., *et al*. (2020) La asincronía ventricular izquierda como resultado de la estimulación apical permanente por dispositivos en el ventrículo derecho. *Archivos de Cardiología de México*, **90**, 328-335. https://doi.org/10.24875/acm.20000003

[10] Chávez-González, E., Nodarse-Concepción, A., Donoiu, I., Rodríguez-González, F., Puerta, R.C., Elizundia, J.M.C., *et al*. (2021) Increased QRS Duration and Dispersion Are Associated with Mechanical Dyssynchrony in Patients with Permanent Right Ventricular Apical Pacing. *Discoveries*, **9**, e128. https://doi.org/10.15190/d.2021.7

[11] Somma, V., Ha, F.J., Palmer, S., Mohamed, U. and Agarwal, S. (2023) Pacing-Induced Cardiomyopathy: A Systematic Review and Meta-Analysis of Definition, Prevalence, Risk Factors, and Management. *Heart Rhythm*, **20**, 282-290.

https://doi.org/10.1016/j.hrthm.2022.09.019

[12] Da Costa, A., Gabriel, L., Romeyer-Bouchard, C., Géraldine, B., Gate-Martinet, A., Laurence, B., *et al*. (2013) Focus on Right Ventricular Outflow Tract Septal Pacing. *Archives of Cardiovascular Diseases*, **106**, 394-403. https://doi.org/10.1016/j.acvd.2012.08.005

[13] Galand, V., Martins, R.P., Donal, E., Behar, N., Crocq, C., Soulié, G.G., *et al*. (2022) Septal versus Apical Pacing Sites in Permanent Right Ventricular Pacing: The Multicentre Prospective SEPTAL-PM Study. *Archives of Cardiovascular Diseases*, **115**, 288-294. https://doi.org/10.1016/j.acvd.2021.12.007

[14] Yoshiyama, T., Shimeno, K., Hayashi, Y., Ito, A., Iwata, S., Matsumura, Y., *et al*. (2022) Risk Factors of Pacing-Induced Cardiomyopathy—Insights from Lead Position. *Journal of Arrhythmia*, **38**, 408-415. https://doi.org/10.1002/joa3.12712

[15] Dias-Frias, A., Costa, R., Campinas, A., Alexandre, A., Sá-Couto, D., Sousa, M.J., *et al*. (2022) Right Ventricular Septal versus Apical Pacing: Long-Term Incidence of Heart Failure and Survival. *Journal of Cardiovascular Development and Disease*, **9**, Article No. 444. https://doi.org/10.3390/jcdd9120444

[16] Simader, F., Arnold, A. and Whinnett, Z. (2023) Comparison of Methods for Delivering Cardiac Resynchronization Therapy: Electrical Treatment Targets and Mechanisms of Action. *Expert Review of Medical Devices*, **20**, 337-348. https://doi.org/10.1080/17434440.2023.2199925

[17] Khurshid, S. and Frankel, D.S. (2023) Pacing-Induced Cardiomyopathy. *Cardiology Clinics*, **41**, 449-461. https://doi.org/10.1016/j.ccl.2023.03.010

[18] Merkely, B., Hatala, R., Wranicz, J.K., Duray, G., Földesi, C., Som, Z., *et al*. (2023) Upgrade of Right Ventricular Pacing to Cardiac Resynchronization Therapy in Heart Failure: A Randomized Trial. *European Heart Journal*, **44**, 4259-4269. https://doi.org/10.1093/eurheartj/ehad591

[19] Khurshid, S., Obeng-Gyimah, E., Supple, G.E., Schaller, R., Lin, D., Owens, A.T., *et al*. (2018) Reversal of Pacing-Induced Cardiomyopathy Following Cardiac Resynchronization Therapy. *JACC*: *Clinical Electrophysiology*, **4**, 168-177. https://doi.org/10.1016/j.jacep.2017.10.002

[20] Lu, D., Zhang, H. and Zhang, H. (2018) Cardiac Resynchronization Therapy Improves Left Ventricular Remodeling and Function Compared with Right Ventricular Pacing in Patients with Atrioventricular Block. *Heart Failure Reviews*, **23**, 919-926. https://doi.org/10.1007/s10741-018-9722-z

[21] Rickard, J., Patel, D., Park, C., Marine, J.E., Sinha, S., Tang, W.H.W., *et al*. (2021) Long-Term Outcomes in Patients with a Left Ejection Fraction ≤ 15 % Undergoing Cardiac Resynchronization Therapy. *JACC*: *Clinical Electrophysiology*, **7**, 36-46. https://doi.org/10.1016/j.jacep.2020.07.025

[22] Green, P.G., Herring, N. and Betts, T.R. (2022) What Have We Learned in the Last 20 Years about CRT Non-Responders? *Cardiac Electrophysiology Clinics*, **14**, 283-296. https://doi.org/10.1016/j.ccep.2021.12.019

[23] Naqvi, S.Y., Jawaid, A., Goldenberg, I. and Kutyifa, V. (2018) Non-response to Cardiac Resynchronization Therapy. *Current Heart Failure Reports*, **15**, 315-321. https://doi.org/10.1007/s11897-018-0407-7

[24] Daubert, C., Behar, N., Martins, R.P., Mabo, P. and Leclercq, C. (2016) Avoiding Non-Responders to Cardiac Resynchronization Therapy: A Practical Guide. *European Heart Journal*, **38**, 1463-1472. https://doi.org/10.1093/eurheartj/ehw270

[25] Pezel, T., Mika, D., Logeart, D., Cohen-Solal, A., Beauvais, F., Henry, P., *et al*. (2020) Characterization of Non-Response to Cardiac Resynchronization Therapy by Post-Procedural Computed Tomography. *Pacing and Clinical Electrophysiology*, **44**, 135-144. https://doi.org/10.1111/pace.14134

[26] Zhu, H., Zou, T., Zhong, Y., Yang, C., Ren, Y. and Wang, F. (2019) Prevention of Non-Response to Cardiac Resynchronization Therapy: Points to Remember. *Heart Failure Reviews*, **25**, 269-275. https://doi.org/10.1007/s10741-019-09834-w

[27] Glikson, M., Nielsen, J.C., Kronborg, M.B., Michowitz, Y., Auricchio, A., Barbash, I.M., *et al*. (2021) 2021 ESC Guidelines on Cardiac Pacing and Cardiac Resynchronization Therapy. *EP Europace*, **24**, 71-164. https://doi.org/10.1093/europace/euab232

[28] Sharma, P.S., Vijayaraman, P. and Ellenbogen, K.A. (2019) Permanent His Bundle Pacing: Shaping the Future of Physiological Ventricular Pacing. *Nature Reviews Cardiology*, **17**, 22-36. https://doi.org/10.1038/s41569-019-0224-z

[29] Vijayaraman, P., Naperkowski, A., Subzposh, F.A., Abdelrahman, M., Sharma, P.S., Oren, J.W., *et al*. (2018) Permanent His-Bundle Pacing: Long-Term Lead Performance and Clinical Outcomes. *Heart Rhythm*, **15**, 696-702. https://doi.org/10.1016/j.hrthm.2017.12.022

[30] Huang, W., Su, L., Wu, S., Xu, L., Xiao, F., Zhou, X., *et al*. (2018) Long-Term Outcomes of His Bundle Pacing in Patients with Heart Failure with Left Bundle Branch Block. *Heart*, **105**, 137-143. https://doi.org/10.1136/heartjnl-2018-313415

[31] Zhang, J., Guo, J., Hou, X., Wang, Y., Qian, Z., Li, K., *et al*. (2017) Comparison of the Effects of Selective and Non-Selective His Bundle Pacing on Cardiac Electrical and Mechanical Synchrony. *EP Europace*, **20**, 1010-1017. https://doi.org/10.1093/europace/eux120

[32] Li, Y., Tian, H., Zhang, J., *et al.* (2021). Effects of His Bundle Pacing and Right Ventricular Apex Pacing on Cardiac electrical and Mechanical Synchrony and Cardiac Function in Patients with Heart Failure and Atrial Fibrillation. *American Journal of Translational Research*, **13**, 3294-3301.

[33] Vijayaraman, P., Pokharel, P., Subzposh, F.A., Oren, J.W., Storm, R.H., Batul, S.A., *et al.* (2023) His-Purkinje Conduction System Pacing Optimized Trial of Cardiac Resynchronization Therapy vs Biventricular Pacing: HOT-CRT Clinical Trial. *JACC*: *Clinical Electrophysiology*, **9**, 2628-2638. https://doi.org/10.1016/j.jacep.2023.08.003

[34] Kato, H., Yanagisawa, S., Sakurai, T., Mizuno, C., Ota, R., Watanabe, R., *et al*. (2022) Efficacy of His Bundle Pacing on LV Relaxation and Clinical Improvement in HF and LBBB. *JACC*: *Clinical Electrophysiology*, **8**, 59-69. https://doi.org/10.1016/j.jacep.2021.06.011

[35] Vijayaraman, P., Zalavadia, D., Haseeb, A., Dye, C., Madan, N., Skeete, J.R., *et al.* (2022) Clinical Outcomes of Conduction System Pacing Compared to Biventricular Pacing in Patients Requiring Cardiac Resynchronization Therapy. *Heart Rhythm*, **19**, 1263-1271. https://doi.org/10.1016/j.hrthm.2022.04.023

[36] Wang, Y., Liu, F., Liu, M., Wang, Z., Lu, X., Huang, J., *et al*. (2023) His-Purkinje System Pacing versus Biventricular Pacing in Clinical Efficacy: A Systematic Review and Meta-Analysis. *BMC Cardiovascular Disorders*, **23**, Article No. 285. https://doi.org/10.1186/s12872-023-03307-7

[37] Zaidi, S.M.J., Sohail, H., Satti, D.I., Sami, A., Anwar, M., Malik, J., *et al*. (2022) Tricuspid Regurgitation in His Bundle Pacing: A Systematic Review. *Annals of Noninvasive Electrocardiology*, **27**, e12986. https://doi.org/10.1111/anec.12986

[38] Vijayaraman, P., Chung, M.K., Dandamudi, G., Upadhyay, G.A., Krishnan, K., Crossley, G., *et al.* (2018) His Bundle Pacing. *Journal of the American College of Cardiology*, **72**, 927-947. https://doi.org/10.1016/j.jacc.2018.06.017

[39] Su, L., Wu, S., Wang, S., Wang, Z., Xiao, F., Shan, P., *et al*. (2018) Pacing Parameters and Success Rates of Permanent His-Bundle Pacing in Patients with Narrow QRS: A Single-Centre Experience. *EP Europace*, **21**, 763-770. https://doi.org/10.1093/europace/euy281

[40] Keene, D., Arnold, A.D., Jastrzębski, M., Burri, H., Zweibel, S., Crespo, E., *et al.* (2019) His Bundle Pacing, Learning Curve, Procedure Characteristics, Safety, and Feasibility: Insights from a Large International Observational Study. *Journal of Cardiovascular Electrophysiology*, **30**, 1984-1993. https://doi.org/10.1111/jce.14064

[41] Ali, N., Arnold, A.D., Miyazawa, A.A., Keene, D., Peters, N.S., Kanagaratnam, P., *et al*. (2023) Septal Scar as a Barrier to Left Bundle Branch Area Pacing. *Pacing and Clinical Electrophysiology*, **46**, 1077-1084. https://doi.org/10.1111/pace.14804

[42] Elizari, M. (2017) The Normal Variants in the Left Bundle Branch System. *Journal of Electrocardiology*, **50**, 389-399. https://doi.org/10.1016/j.jelectrocard.2017.03.004

[43] Huang, W., Chen, X., Su, L., Wu, S., Xia, X. and Vijayaraman, P. (2019) A Beginner's Guide to Permanent Left Bundle Branch Pacing. *Heart Rhythm*, **16**, 1791-1796. https://doi.org/10.1016/j.hrthm.2019.06.016

[44] Li, Y., Chen, K., Dai, Y., Li, C., Sun, Q., Chen, R., *et al.* (2019) Left Bundle Branch Pacing for Symptomatic Bradycardia: Implant Success Rate, Safety, and Pacing Characteristics. *Heart Rhythm*, **16**, 1758-1765. https://doi.org/10.1016/j.hrthm.2019.05.014

[45] Wang, P., Yang, L., Zheng, S., Mai, J., Wei, Y., Liu, Y., *et al*. (2022) Left Bundle Branch Pacing on Mechanical Synchrony and Myocardial Work in Bradycardia Patients. *The International Journal of Cardiovascular Imaging*, **39**, 369-378. https://doi.org/10.1007/s10554-022-02742-5

[46] Mao, Y., Duchenne, J., Yang, Y., Garweg, C., Yang, Y., Sheng, X., *et al*. (2023) Left Bundle Branch Pacing Better Preserves Ventricular Mechanical Synchrony than Right Ventricular Pacing: A Two-Centre Study. *European Heart Journal—Cardiovascular Imaging*, **25**, 328-336. https://doi.org/10.1093/ehjci/jead296

[47] Liu, X., Li, W., Wang, L., Tian, S., Zhou, X. and Wu, M. (2021) Safety and Efficacy of Left Bundle Branch Pacing in Comparison with Conventional Right Ventricular Pacing: A Systematic Review and Meta-Analysis. *Medicine*, **100**, e26560. https://doi.org/10.1097/md.0000000000026560

[48] Rademakers, L.M., Bouwmeester, S., Mast, T.P., Dekker, L., Houthuizen, P. and Bracke, F.A. (2022) Feasibility, Safety and Outcomes of Upgrading to Left Bundle Branch Pacing in Patients with Right Ventricular Pacing Induced Cardiomyopathy. *Pacing and Clinical Electrophysiology*, **45**, 726-732. https://doi.org/10.1111/pace.14515

[49] Qian, Z., Wang, Y., Hou, X., Qiu, Y., Wu, H., Zhou, W., *et al*. (2021) Efficacy of Upgrading to Left Bundle Branch Pacing in Patients with Heart Failure after Right Ventricular Pacing. *Pacing and Clinical Electrophysiology*, **44**, 472-480. https://doi.org/10.1111/pace.14147

[50] Wang, Y., Zhu, H., Hou, X., Wang, Z., Zou, F., Qian, Z., *et al*. (2022) Randomized Trial of Left Bundle Branch vs Biventricular Pacing for Cardiac Resynchronization Therapy. *Journal of the American College of Cardiology*, **80**, 1205-1216. https://doi.org/10.1016/j.jacc.2022.07.019

[51] Chen, X., Ye, Y., Wang, Z., Jin, Q., Qiu, Z., Wang, J., *et al*. (2021) Cardiac Resynchronization Therapy via Left Bundle Branch Pacing vs. Optimized Biventricular Pacing with Adaptive Algorithm in Heart Failure with Left Bundle Branch

Block: A Prospective, Multi-Centre, Observational Study. *EP Europace*, **24**, 807-816. https://doi.org/10.1093/europace/euab249

[52] Bozorgi, A. (2023) Left Bundle Branch Pacing. *The Journal of Tehran University Heart Center*, **17**, 165-167. https://doi.org/10.18502/jthc.v17i4.11602

[53] Huang, W., Wu, S., Vijayaraman, P., Su, L., Chen, X., Cai, B., *et al*. (2020) Cardiac Resynchronization Therapy in Patients with Nonischemic Cardiomyopathy Using Left Bundle Branch Pacing. *JACC*: *Clinical Electrophysiology*, **6**, 849-858. https://doi.org/10.1016/j.jacep.2020.04.011

[54] Hou, X., Qian, Z., Wang, Y., Qiu, Y., Chen, X., Jiang, H., *et al*. (2019) Feasibility and Cardiac Synchrony of Permanent Left Bundle Branch Pacing through the Interventricular Septum. *EP Europace*, **21**, 1694-1702. https://doi.org/10.1093/europace/euz188

[55] Vijayaraman, P., Subzposh, F.A., Naperkowski, A., Panikkath, R., John, K., Mascarenhas, V., *et al*. (2019) Prospective Evaluation of Feasibility and Electrophysiologic and Echocardiographic Characteristics of Left Bundle Branch Area Pacing. *Heart Rhythm*, **16**, 1774-1782. https://doi.org/10.1016/j.hrthm.2019.05.011

[56] Prinzen, F.W. and Peschar, M. (2002) Relation between the Pacing Induced Sequence of Activation and Left Ventricular Pump Function in Animals. *Pacing and Clinical Electrophysiology*, **25**, 484-498. https://doi.org/10.1046/j.1460-9592.2002.00484.x

[57] Mafi-Rad, M., Luermans, J.G.L.M., Blaauw, Y., Janssen, M., Crijns, H.J., Prinzen, F.W., *et al*. (2016) Feasibility and Acute Hemodynamic Effect of Left Ventricular Septal Pacing by Transvenous Approach through the Interventricular Septum. *Circulation*: *Arrhythmia and Electrophysiology*, **9**, e003344. https://doi.org/10.1161/circep.115.003344

[58] Heckman, L., Luermans, J., Salden, F., Stipdonk, A.M.W.v., Mafi-Rad, M., Prinzen, F., *et al*. (2021) Physiology and Practicality of Left Ventricular Septal Pacing. *Arrhythmia & Electrophysiology Review*, **10**, 165-171. https://doi.org/10.15420/aer.2021.21

[59] Rademakers, L.M., van Hunnik, A., Kuiper, M., Vernooy, K., van Gelder, B., Bracke, F.A., *et al*. (2016) A Possible Role for Pacing the Left Ventricular Septum in Cardiac Resynchronization Therapy. *JACC*: *Clinical Electrophysiology*, **2**, 413-422. https://doi.org/10.1016/j.jacep.2016.01.010

[60] Salden, F.C.W.M., Luermans, J.G.L.M., Westra, S.W., Weijs, B., Engels, E.B., Heckman, L.I.B., *et al*. (2020) Short-term Hemodynamic and Electrophysiological Effects of Cardiac Resynchronization by Left Ventricular Septal Pacing. *Journal of the American College of Cardiology*, **75**, 347-359. https://doi.org/10.1016/j.jacc.2019.11.040

[61] Huang, W., Su, L., Wu, S., Xu, L., Xiao, F., Zhou, X., *et al*. (2017) A Novel Pacing Strategy with Low and Stable Output: Pacing the Left Bundle Branch Immediately Beyond the Conduction Block. *Canadian Journal of Cardiology*, **33**, 1736.e1-1736.e3. https://doi.org/10.1016/j.cjca.2017.09.013

[62] Heckman, L.I.B., Luermans, J.G.L.M., Curila, K., Van Stipdonk, A.M.W., Westra, S., Smisek, R., *et al*. (2021) Comparing Ventricular Synchrony in Left Bundle Branch and Left Ventricular Septal Pacing in Pacemaker Patients. *Journal of Clinical Medicine*, **10**, Article No. 822. https://doi.org/10.3390/jcm10040822

[63] Jastrzębski, M., Kiełbasa, G., Curila, K., Moskal, P., Bednarek, A., Rajzer, M., *et al*. (2021) Physiology-Based Electrocardiographic Criteria for Left Bundle Branch Capture. *Heart Rhythm*, **18**, 935-943. https://doi.org/10.1016/j.hrthm.2021.02.021

[64] Heckman, L., Vijayaraman, P., Luermans, J., Stipdonk, A.M.W., Salden, F., Maass, A.H., *et al*. (2020) Novel Bradycardia Pacing Strategies. *Heart*, **106**, 1883-1889. https://doi.org/10.1136/heartjnl-2020-316849

[65] Curila, K., Jurak, P., Jastrzebski, M., Prinzen, F., Waldauf, P., Halamek, J., *et al*. (2021) Left Bundle Branch Pacing Compared to Left Ventricular Septal Myocardial Pacing Increases Interventricular Dyssynchrony but Accelerates Left Ventricular Lateral Wall Depolarization. *Heart Rhythm*, **18**, 1281-1289. https://doi.org/10.1016/j.hrthm.2021.04.025

[66] Wang, S., Xue, S., Jiang, Z., Hou, X., Zou, F., Yang, W., *et al*. (2024) Cost-Effectiveness Ratio Analysis of LBBaP versus BVP in Heart Failure Patients with LBBB. *Pacing and Clinical Electrophysiology*, **47**, 1539-1547. https://doi.org/10.1111/pace.15077