DOI: 10.13241/j.cnki.pmb.2014.01.043

CRT_D 介导室性心动过速的研究进展

杨日升 梁兆光△ 徐义喜 王鑑萌 田凤祥

(哈尔滨医科大学附属第一医院心内科 黑龙江 哈尔滨 150001)

摘要:心室再同步心脏转复除颤器(CRT_D)可有效改善心力衰竭(CHF)患者的运动耐量和生活质量,预防猝死,提高生存率,但CRT_D植入后由于心室激动顺序的改变,使QT间期延长、跨室壁复极离散度(TDR)增加,潜在致室性心律失常风险;且CHF患者通常存在心肌解剖改变,传导的不均一性,也为折返性心动过速的发生提供了维持的机制;而多次电击也可导致肌钙蛋白升高,引起心肌损伤,局部心肌复极离散度增加(DRVR)和QT间期延长,以及电除颤后心肌纤维化和急性细胞损伤,反复室速、室颤也会引起进行性左心功能不全、心肌细胞凋亡、恶化心律失常基质和增加心律失常易感性。CRT_D潜在致室性心律失常作用逐渐引起人们的重视,本文就近年来CRT_D致室性心律失常的电生理机制与临床防治对策等做一综述。

关键词:心室再同步心脏转复除颤器;室性心动过速;跨室壁复极离散度

中图分类号:R541.71 **文献标识码**:A **文章编号**:1673-6273(2014)01-169-03

Advances in Ventricular Tachycardia Worsened by Cardiac Resynchronization Therapy Defibrillator

YANG Ri-sheng, LIANG Zhao-guang△, XU Yi-xi, WANG Jian-meng, TIAN Feng-xiang

(The first affiliated hospital of Harbin Medical University,cardiovascular department, Harbin, Heilongjiang, 150001, China)

ABSTRACT: Cardiac resynchronization therapy defibrillator (CRT_D) can improve heart failure patients exercise tolerance and the quality of life, to prevent sudden death and improve survival rate, but CRT_D implantation cause a reversal of the typical transmural activation sequence in ventricular, make QT interval prolongation, Transmural dispersion of repolarization (TDR) increases, the potential risk to ventricular arrhythmias; and CHF patients often exist myocardial anatomical change, conducting inhomogeneity, as well as the occurrence of reentrant tachycardia provides maintenance mechanism; and multiple shock can also lead to increased troponin, cause myocardial injury, the dispersion of regional ventricular repolarization (DRVR) increase and QT interval prolongation and electric defibrillation after acute myocardial fibrosis and cell damage, repeatedly ventricular tachycardia, ventricular fibrillation can also cause progressive left cardiac dysfunction, myocardial cell apoptosis, deteriorating cardiac arrhythmia matrix and increase arrhythmia susceptibility. The potential risk to ven-tricular arrhythmias gradually aroused people's attention,the article summarize the CRT_D electrophysiological mechanism of ventricular arrhythmia and clinical prevention and cure countermeasure, etc.

Key words: Cardiac resynchronization therapy defibrillator; Ventricular tachycardia; Transmural dispersion of repolarization

Chinese Library Classification(CLC): R541.71 Document code: A

Article ID: 1673-6273(2014)01-169-03

前言

心力衰竭进行性加重和致命性快速性室性心律失常(室性心动过速、心室颤动)是心力衰竭患者最常见的死亡原因,心力衰竭患者植入心室再同步心脏转复除颤器(CRT_D)能明显改善慢性心力衰竭患者的心功能,提高生活质量,降低心力衰竭导致的病死率;同时还可有效防治心脏性猝死[1-3]。然而,最近研究显示,CRT_D可能潜在致室性心律失常作用,并逐渐引起越来越多人的重视,本文就近年来CRT_D致室性心律失常的电生理机制与临床防治对策等做一综述。

1 CRT_D 潜在致室性心律失常风险

Medina-Rave ll[4]等对29例心衰病人分别进行右室心内膜、左室心外膜和双心室起搏,结果显示4例在双室起搏和左室心外膜起搏时出现频发的室性早搏或反复发作的多形性室性心动过速,而在右室心内膜起搏未能诱发,研究表明左室和双心室起搏存在致室性心律失常现象。

Peichl P[5]等最先报道了1例55岁男性患者,CRT_D术后反复发作室速,经药物治疗无法有效控制其发作,当其开启左室起搏或双室起搏时出现频繁发作的室速,而调整为右室起搏或终止CRT_D工作后室速消失或能够有效被抑制,表明室速可能为CRT_D所致,因室速可以稳定诱发,且药物控制不佳,遂后行导管成功消融了室速,术后进行左室电极和双室电极起搏未诱发VT,CRT_D也可以正常工作。

居维竹[6]等报道一例CRT_D植入的患者,男性,45岁,扩张型心肌病病史十余年,因心功不全(LVEF35%),非持续性VT,植入CRT_D,术后频发室性心律失常,给予了足量的β-受体阻滞剂和胺碘酮,并且进行优化心功治疗,仍没有明显改善。心电图和Holter可见反复的单形态室速伴相同形态的室早,CRT_D时间日志提示近期有80多次抗VT治疗,并且有多次

作者简介:杨日升(1981-),男,硕士研究生,主要研究方向:心律失常,电话:15804622316,E-mail:yangrisheng206@163.com

△通讯作者:梁兆光,E-mail:supperzhaoguangliang@126.com

(收稿日期:2013-04-12 接受日期:2013-05-10)

放电,随后采用了导管射频消融的方法,由于心内膜消融无效,尝试采用经心外膜途径消融,并取得成功。

Takumi Yamada [7] 等也报道了一例心外膜导管消融治疗CRT_D 术后导致室速一例。64 岁男患因存在 VT 先行的 ICD 植入, 后因出现出现左束支传动阻滞,QRS 波群时限为 140 ms,心功能下降,升级为 CTR_D,患者出现频发的 VT,周期为 420 ms,较植入前明显增加,但未经历过任何晕厥发作,经药物治疗(胺碘酮,心得安、普鲁卡因胺、美西律)后不能有效控制 VT 的发作,随后进行了导管消融,术后观察三个月无室性事件发作,而且心功能也得到改善。

BharatK[8], Kantharia[8], DiCori[9], Mykytsey[10] 等多人都曾进行过 CRT_D 术后导致室性心律失常的相关报道。我们也注意到通常关闭左室电极,室性事件就能明显减少或消失,而左室打开时就易导致室性心律失常的发生,并且抗心律失常药物对由此引起的心律失常治疗效果很差, 而反复的 ATP 治疗和心内电除颤,不仅会严重困扰患者的生活,影响生活质量,也会缩短 CRT_D 使用年限。

2 CRT_D 介导室性心动过速相关实验研究

Medina-Rave ll[4]等的实验研究显示,左室心外膜起搏时的 QTc 比右室心内膜、双室起搏时明显延长 (587+35 ms vs 544+36 ms、535+38 ms,P<0.01)。左室心外膜起搏校正后跨室壁复极离散度(TDRc) 较右室内膜起搏时有明显延长(197+26 ms vs 163+25 ms,P<0.01)。他们从细胞机制方面进行研究,利用动脉灌注兔左室楔形模型,实验中同步记录从心内膜到心外膜的跨膜动作电位时程 (APD)、QT 间期与跨室壁复极离散度(TDR)。实验结果显示心外膜起搏较心内膜起搏时 QT 间期延长, TDR 增加。

Fish JM[11]等则采用了动脉灌注的犬左室楔形标本分别同步记录了心外膜与心内膜起搏时内、中、外三层心肌细胞的跨膜动作电位和跨壁心电图。当由心内膜起搏调整为心外膜起搏时,QT 间期和 TDR 均有显著增加,中层(M)细胞与心外膜细胞传导时间较心内膜起搏时显著延长。

Pang Y[12]等的研究显示,用不同能量腔内除颤,除颤的次数和能量的大小,会影响心室复极的离散度和 QT 延长,研究表明多次电击可导致肌钙蛋白升高,引起心肌轻度损伤,局部心肌复极离散度(DRVR)增加和 QT 延长。病理学研究近期电除颤后存在心肌纤维化和急性细胞损伤,反复室速,室颤,心肌细胞内钙的增加,也会引起进行性左心功能不全、心肌细胞凋亡、恶化心律失常基质和增加心律失常易感性。Brigadeau[13]等观察 128 例 ICD 或 CRT_D 植入患者共发了 294 次电交感风暴事件,其中 58%以上的患者经历了两次以上的电除颤,而且电风暴事件的间隔时间逐渐缩短。反复的放电引起的疼痛、精神紧张、焦虑或绝望等导致交感神经过度激活,释放大量儿茶酚胺,而加重室性心律失常发作的风险[14]。

3 CRT_D 介导室性心动过速电生理机制

心肌分为内、中、外三层,通常心外膜心肌是最早开始复极的,其复极时间也最短,最先完成复极;而中层心肌最后完成复极,复极时间最长。三层心肌复极时间的差异性(最长与最短之差)即为跨室壁复极离散(TDR),TDR 在正常心脏中存在,在病理状态下增大,而在心外膜起搏时 TDR 增加更明显,而 TDR 增加是恶性心律失常发生的基础[15-17]。

在生理情况下,心室肌的跨室壁除极是从心内膜往心外膜方向进行的, 而复极过程则是从心外膜往心内膜方向进行。CRT_D 植入的患者,在心外膜起搏时,室壁心肌除极顺序发生了变化,而心肌跨室壁传导的速度与激动的传播方向与处极顺序是相关联的,心肌的跨室壁激动顺序发生逆转后,延长心肌的复极时间并增大跨室壁复极离散度,从而为促进恶性心律失常的发生提供了诱因[4]。同时电除颤也会导致局部心肌复极离散度(DRVR)增加,反复的腔内电除颤,引起心肌损伤,心肌纤维化和性细胞损伤,都潜在加重室性心律失常风险[11]。

并不是所有心外膜起搏都容易诱发室性心律失常,CRT_D 患者多数存在心肌病变,病变造成心肌的纤维化和脂肪组织的代替,在传导上表现为不均一性,这些区域会形成一条或多条缓慢传导通道,为产生和维持心律失常提供了病理基础[6]。

因此,CRT_D 患者,其心肌通常存在病变,如:瘢痕组织、狭长通道等, 这些病理基础的改变为 VT 发作提供了解剖基质, 而这些解剖基质的异常病变为 VT 发作提供了维持机制,当心外膜起搏时心室激动顺序的改变和室壁离散度的增加,则成为 VT 发作的触发机制,因此当心外膜起搏时,在非生理情况下除极顺序的改变和 TDR 增加, 以及心肌本身病变造成心肌传导的不均一性, 都是 CRT_D 潜在致室性心律失常的风险因素。而当室性心动过速发作时,多次除颤也会引起左心功能下降、心肌凋亡、恶化心律失常基质,同时增加局部心肌复极离散度(DRVR)和延长 QT 间期,进一步增加致室性心动过速的风险。

4 CRT_D 致室性心律失常的对策

4.1 药物治疗

常用的药物主要包括 β- 受体阻滞剂和胺碘酮,β- 受体阻滞剂能有效逆转交感神经的激活和抑制交感神经过度兴奋,而且可以通过抑制儿茶酚胺分泌,减少其心肌细胞的毒性,降低心率,使室颤阈值升高 [18];同时在电交感风暴时 β- 受体阻滞剂能逆转心室的多种离子通道的异常,降低心肌的耗氧量,改善心肌的缺血,提高心肌的电稳定性。胺碘酮对室速 / 室颤复发能有效抑制,ACC /AHA /ESC 室性心律失常的诊疗和心源性猝死预防指南中指出, 交感风暴时可以行胺碘酮和 β- 受体阻滞剂联合治疗。它是多通道阻滞剂,包括:钠、钾通道的阻滞作用及弱的钙通道阻滞作用,还可阻滞 α,β- 受体,胺碘酮也能削弱交感肾上腺素能系统的活性,防治室速 / 室颤,降低猝死率,但药物治疗对 CRT_D 介导的室性心动过速效果不佳, 即使被抑制,也通常会复发,未能从本质上解决室性心律失常的诱因。

4.2 射频消融

针对药物控制无效或不佳的患者, 可以选择行射频消融治疗,改良局部基质,利用电压标测潜在的电解剖基质(瘢痕,通道及边缘区), 特殊的标测系统以及应用常规电生理方法 (起搏,拖带,激动)标测关键点,帮助我们发现持续性 VT 缓慢传导通道,对瘢痕区周围的浦氏电位及峡部通道进行消融,能有效终止或减少 VT 的发作[19-22]。Carbucicchio C[23]等对 95 例药物

控制不佳的 CRT、ICD 及 CRT_D 的患者进行了射频消融治疗,平均随访 22 月,成功率达 89%,该研究表明射频消融治疗是有效的,但有时候心内膜消融并不能成功,必要时需采用心外膜消融[24]。

4.3 重视 CRT_D 的无痛治疗,减少放电

尽量使用抗心动过速起搏(ATP)终止 VT 的发作,实现无痛治疗,ATP 终止 VT 安全有效,减少放电次数,减轻心肌损伤,避免过度激活交感神经的兴奋[25],加重恶性心律失常反复发作的趋势。

4.4 更换左室电极位置

如进行上述治疗仍无法有效终止 VT 发作,也可以考虑更换左室电极位置,BharatK[7]等曾报告一例 CRT_D 术后顽固的室性心动过速,最终更换左室电极位置后 VT 有效被终止。现在有相关报道提出进行左室电极心内膜的植入,能够提供更多、更有效起搏点,更接近生理起搏,减少心肌复极的离算度,减少室性心动过速的发作,但其存在血栓栓塞并发症以及造成二尖瓣关闭的冲突,加重二尖瓣关闭不全和增加感染率[26],因此该技术的效果还需要等待大规模的临床实验进一步验证该技术的远期疗效及安全性。

5 小结与展望

CHF 患者存在心肌解剖和电学重构异常,左心室心外膜起搏和双心室起搏延长心肌复极时间并增大跨室壁心肌复极离散度,以及传导的不均一性,从而为促进恶性心律失常的发生提供了基质。CRT_D 引起的电生理异常无疑会加重这一类人群发生恶性心律失常的危险性。目前 CRT_D 在临床上的应用方兴未艾,其改善症状和心功能,预防猝死的作用毋庸置疑,但临床医生也必须对由 CRT_D 引起的室性事件有充分的认识,对由此产生的不良后果可能会在某种程度上抵消 CRT_D 给患者带来的益处。同时随着射频消融的三维标测(Carto 和 Ensite)技术和非接触性标测的发展,对各种 VT(如心室辅助装置后的 VT)消融成功率升高,减少了心内除颤给患者带来的痛苦[27]。因此临床医生为患者植入 CRT_D 必须对此有充分的认识,要结合指南及适应症,权衡利弊,提高警惕,如出现相关并发症及时处理,避免因为反复除颤造成心肌的损伤、炎症、心室重构及心肌应激性增加,加重室性心律失常的发作趋势,从而提高患者生活质量及生存率,让植入 CRT_D 的患者最终受益。

参考文献(References)

[1] George J, Barsheshet A, Moss AJ, et al. Effectiveness of cardiac resynchronization therapy in diabetic patients with ischemic and nonischemic cardiomyopathy[J]. Ann Noninvasive Electroca- rdiol, 2012, 17: 14-21

[2] Jons C, Thomsen P E. Treating cardiac arrhythmias detected with an implantable cardiac monitor in patients after an acute myocardial infarction[J]. Curr Treat Options Cardiovasc Med, 2012, 14: 39-49

[3] Epstein AJ, Polsky D, Yang F, et al. Groeneveld PW. Geographic variati-on in implantable cardi-overter defibrillator use and heart failure survival[J]. Med Care, 2012, 50: 7-10

[4] Medina-Ravell VA, Lankipalli RS, Yan GX, et al. Effect of epicardial or biventricular pacing to prolong QT interval and increase transmural dispersion of repolarization: does resynchronization therapy pose a risk for patients predisposed to long QT or torsade de pointes[J]. Circulation, 2003, 107(5): 740-746

[5] Peichl P, Mlcochova H, Kautzner J, et al. Successful catheter ablation of two types of vent- ricular tachycardias triggered by cardiac resynchron-ization therapy: a case report[J]. J Cardovasc Electrophysiol, 2007, 18(2): 218-221

[6] 居维竹,陈明龙,杨兵,等. 经心外膜消融治疗非缺血性扩张性心肌病心脏再同步治疗后室性心动过速"风暴"一例[J].中国心律失常杂志, 2011, 6: 462-463
Ju Wei-long, Chen Ming-long, Yang Bing, at el. The epicardial ablation treatment of nonischemic dilated cardiomyopathy ventricular tachycardia "storm" worsened by cardiac resynchronization therapy[J]. Chin J Cardiac Arrhyth, 2011, 6: 462-463

[7] Takumi Yamada, Paul B.Tabereaux, H, et al. Successful catheter ablation of epicardial ventricular tachycardia worsened by cardiac resynchronization therapy[J]. Europace, 2010, 12(3): 437-440

[8] Bharat K. Kantharia, Jigar A. Patel, et al. Electrical storm of monomorphic ventricular tachyc- ardia after a cardiac-resynchronizationtherapy-defibrillator upgrade[J]. Europace, 2006, 8: 625-628

[9] DiCoriA, Bongiorni MG, A rena G, et al. New-onset ventricular tachycardia after cardiac resyn-chronization therapy[J]. J Interv Card Electrophysiol, 2005, 12(3): 231

[10] Mykytsey A, Maheshwari P, DharG, et al. Ventricular tachycardia induced by biventricular pacing in patient with severe ischemic cardiomyopathy[J]. J Cardiovasc Electrophysiol, 2005, 16(6): 655

[11] Fish JM, Di Diego JM, Nesterenko V, et al. Epicardial activation of left ventricular wall pro- longs QT interval and transmural dispersion of repolarization: implications for biventricular pacing[J]. Circulation, 2004, 109(17): 2136-2142

[12] Pang Y, Jin Q, Zhang N, et al. High-energy defibrillation increases the dispersion of regional ventricular repolarization [J]. J Interv Card Electrophysiol, 2011, 32(2): 81-86

[13] Brigadeau F, Kouakam C, Klug D, et al. Clinical predictors and prognostic significance of el- ectrical storm in patients with implantable cardioverter defibrillators[J]. Eur Heart J, 2006, 27(6): 700-707

[14] Andrsova I, Valaskova I, Kubus P, et al. Clinical characteristics and mutational analysis of the RyR2 gene in seven Czech families with catecholaminergic polymorphic ventricular tachycardia[J]. Pacing Clin Electrophysiol, 2012, 35(7): 798-803

[15] Gardner MJ, Montague TJ, Armstrong CS, et al. Vulnerability to Ventricular arrhythmia: assessment by mapping of body surface potential [J]. Circulation, 1986, 73: 684

[16] Liu DW, Gintant GA, Antzelevitch C. Ionic basis for electrophysiological distinctions among epicardial, midmyocardial, and endocardial myocytes from the free wall of the canine left ventricle [J]. CircRes, 1993, 72: 671

[17] Scicouri S, Antzelevitch C. Electrophysiologic characteristics of M cells in the canine left ventricular free wall [J]. J Cardiovasc Electrophysiol, 1995, 6: 591

[18] Davis JE, Curtis LA, Rashid H. Idiopathic cardiac electricalstorm[J]. J Emerg Med, 2007, 37(3): 264-268

(下转第 179 页)

基因释放、能规模化生产和储存稳定。目前尚不能达到这些目标，需要进一步研究开发。随着各项研究的不断深入，相信非病毒基因治疗所遇到各种问题将会得到解决，使基因治疗成为临床治疗的新手段。

参考文献(References)

[1] Rosenberg SA, Aebersold P, Cornetta K, et al. Gene transfer into humans-immunotherapy of patients with advanced melanoma, using tumor-infiltrating lymphocytes modified by retroviral gene transduction[J]. New England Journal of Medicine, 1990, 323: 570-578

[2] Edelstein ML, Abedi MR, Wixon J. Gene therapy clinical trials worldwide to 2007-an update[J]. The journal of gene medicine, 2007, 9: 833-842

[3] Erbacher P, Roche AC, Monsigny M, et al. Glycosylated polylysine/DNA complexes: gene transfer efficiency in relation with the size and the sugar substitution level of glycosylated polylysines and with the plasmid size[J]. Bioconjugate chemistry, 1995, 6: 401-410

[4] Luby-Phelps K, Castle PE, Taylor DL, et al. Hindered diffusion of inert tracer particles in the cytoplasm of mouse 3T3 cells [J]. Proceedings of the National Academy of Sciences, 1987, 84: 4910-4913

[5] Erbacher P, Roche AC, Monsigny M, et al. Putative role of chloroquine in gene transfer into a human hepatoma cell line by DNA/ lactosylated polylysine complexes[J]. Experimental cell research, 1996, 225: 186-194

[6] Curiel DT, Agarwal S, Wagner E, et al. Adenovirus enhancement of transferrin-polylysine-mediated gene delivery [J]. Proceedings of the National Academy of Sciences, 1991, 88: 8850-8854

[7] Plank C, Oberhauser B, Mechtler K, et al. The influence of endosome-disruptive peptides on gene transfer using synthetic virus- like gene transfer systems[J]. Journal of Biological Chemistry, 1994, 269: 12918-12924

[8] Behr JP. The proton sponge: a trick to enter cells the viruses did not exploit[J]. CHIMIA International Journal for Chemistry, 1997, 51: 1-2

[9] Haensler J, Szoka Jr FC. Polyamidoamine cascade polymers mediate efficient transfection of cells in culture [J]. Bioconjugate chemistry, 1993, 4: 372-379

[10] Niidome T, Huang L. Gene therapy progress and prospects: nonviral vectors[J]. Gene therapy, 2002, 9: 1647-1652

[11] Felgner PL, Gadek TR, Holm M, et al. Lipofection: a highly efficient, lipid-mediated DNA-transfection procedure [J]. Proceedings of the National Academy of Sciences, 1987, 84: 7413-7417

[12] Koltover I, Salditt T, R dler JO, et al. An inverted hexagonal phase of cationic liposome-DNA complexes related to DNA release and delivery[J]. Science, 1998, 281:78-81

[13] Zabner J. Cationic lipids used in gene transfer [J]. Advanced drug delivery reviews, 1997, 27: 17-28

[14] Nguyen J, Szoka FC. Nucleic Acid Delivery: The Missing Pieces of the Puzzle[J]. Accounts of Chemical Research, 2012, 45: 1153-1162

[15] 徐松琳,金拓. 新型聚乙烯亚胺衍生物体内转染活性的研究 [J]. 现代生物医学进展, 2008, 8(12): 2242-2243
Xu Song-lin, Jin Tuo. Transfection activity of a novel polyethyleneimine derivative in vivo[J]. Progress in Modern Biomedicine, 2008, 8 (12): 2242-2243

(上接第 171 页)

[19] Cano O, Hutchinson M, Lin D, et al. Electroanato mic substrate and ablation outcome for suspected epicardial ventricular tachycardia in left ventricular nonischemic cardiomyopathy [J]. J Am Coll Cardiol, 2009, 54(9): 799-808

[20] MBCHB DB, deKemp RA, Ruddy TD, et al. Effect of lateral wall scar on reverse remodeling with cardiac resynchronization therapy[J]. Heart Rhythm, 2009, 6: 1721-1726

[21] Tung R, Mathuria N, Michowitz Y, at el. Functional pace-mapping responses for identification of targets for catheter ablation of scar-mediated ventricular tachycardia[J]. Circ Arrhythm Electrophysiol, 2012, 5(2): 264-272

[22] Ciaccio EJ. Characteristics of critical isthmus sites during reentrant ventricular tachycardia[J]. Heart Rhythm, 2011, 8(12): 1950-1951

[23] Carbucicchio C, Santamaria M, Trevisi N, et al. Catheter ablation for the treatment of elect-rical storm in patients with implantable cardioverter-defibrillators: short-and long-term outcomes in a prospective single-center study[J]. Circulation, 2008, 117(4): 462-469

[24] Tschabrunn CM, Haqqani HM, Zado ES, et al. Repeat Percutaneous Epicardial Mapping and Ablationof Ventricular Tachycardia: Safety and Outcome[J]. J Cardiovasc Electrophysiol, 2012, 23(7): 744-749

[25] Credner SC, Klingenheben T, Mauss O, et al. Electrical storm in patients with transvenous implantable cardioverter-defibrillators. Incidence, management and prognostic implications [J]. J Am Coll Cardiol, 1998, 32: 1909

[26] Van deursen C, Van geldorp IE, Rademakers LM, et al. Left ventricular endocardial pacing im- proves resynchronization therapy in canine left bundle-branch hearts [J]. Circ Arrhythm Electrophysiol, 2009, 2 (5): 580-587

[27] Cesario DA, Saxon LA, Cao MK, et al. Ventricular tachycardia in the era of ventricular assist devices[J]. J Cardiovasc Electrophysiol, 2011, 22(3): 359-363