Novel approaches for the treatment of ventricular tachycardia

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Abstract

Ventricular tachycardia (VT) is a crucial cause of sudden cardiac death (SCD) and a primary cause of mortality and morbidity in patients with structural cardiac disease. VT includes clinical disorders varying from benign to life-threatening. The targets of VT management are symptom alleviation, improved quality of life, reduced implantable cardioverter defibrillator shocks, prevention of reduction of left ventricular function, reduced risk of SCD, and improved overall survival. Antiarrhythmic drug therapy and endocardial catheter ablation remains the cornerstone of guideline-endorsed VT treatment strategies in patients with structural cardiac abnormalities. Novel strategies such as epicardial ablation, surgical cryoablation, transcoryonary alcohol ablation, pre-procedural imaging, and stereotactic ablative radiotherapy are an appealing area of res-
each. In this review, we gathered all recent advances in innovative therapies as well as experimental evidence focusing on different aspects of VT treatment that could be significant for future favorable clinical applications.

Key words: Ventricular tachycardia; Catheter ablation; Epicardial; Sudden cardiac death; Novel techniques; Substrate

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Core tip: Antiarrhythmic drug therapy and endocardial catheter ablation remains the cornerstone of ventricular tachycardia (VT) treatment management, but both treatments have limited efficacy and important adverse effects. Catheter ablation for cardiomyopathic (scar-related) VT is associated with recurrence rates as high as 50% at 6 mo. Implantable cardioverter defibrillator provides a safety net; however, there is an increased need for more effective and safer methods to decrease VT recurrence episodes. We sought to review current literature in order to summarize data on innovative techniques for VT treatment.

Spartalis M, Spartalis E, Tzatzaki E, Tsilimigras DI, Moris D, Kontogiannis C, Livas E, Liopoulos DC, Voudris V, Theodorakis GN. Novel approaches for the treatment of ventricular tachycardia. World J Cardiol 2018; 10(7): 52-59 Available from: URL: http://www.wjgnet.com/1949-8462/full/v10/i7/52.htm DOI: http://dx.doi.org/10.4330/wjc.v10.i7.52

INTRODUCTION

Sudden cardiac death (SCD) is a vital public health issue, accountable for almost 50% of all cardiovascular deaths[1]. In the last three decades, SCD was the leading cause for almost 230000 to 350000 deaths per annum in the United States[1]. Ventricular arrhythmias account for 25% to 36% of witnessed sudden cardiac arrests (SCA) at home and 38% to 79% of witnessed SCA in public[2].

Ischemic heart disease, structural disorders, various forms of cardiomyopathy associated with myocardial fibrosis, cardiac channeleopathies, myocarditis, congenital heart diseases, and other genetic rare disorders are associated with ventricular arrhythmias[3].

Even though treatment for heart failure lowers mortality and SCD, it was unsuccessful in lessening ventricular tachycardia (VT) recurrences[3]. Implantable cardioverter defibrillators (ICD) are very effective in eliminating VT episodes and in lowering the possibility of SCD, but they are not useful for arrhythmia prevention[4]. When the VT substrate manifests, anti-arrhythmic drug treatment or catheter ablation are the current choices to reduce VT episodes[5]. Catheter ablation and antiarrhythmic drug therapy though, are also limited by incomplete efficacy, unfavorable side effects, and procedural risk[5]. In this review, we outline the current advances in VT treatment options and describe the imaging modalities, progress, and novel strategies.

LITERATURE SEARCH

We have collected all experimental and clinical investigations focused on new aspects that could be essential for tailoring VT therapy according to underlying etiology, in order to achieve higher efficacy. The MEDLINE database was screened for studies with the medical term “ventricular tachycardia” and keywords “treatment”, or “ablation”, or “management”. We restricted our search to English literature.

NOVEL VT THERAPIES

Epicardial catheter ablation

Endocardial catheter ablation and antiarrhythmic drug treatment are currently the mainstays of VT treatment[1-3]. However, the procedural success rates of VT are quite variable due to the heterogeneous substrates that reflect the variety of pathophysiological processes[6,7]. The success rate of endocardial ablation in patients with outflow tract VT is 84%, in patients with papillary muscle VT is 60%, and in patients with idiopathic left ventricular VT is 70%[6]. Moreover, the VT recurrence rates of endocardial ablation in ischemic cardiomyopathy patients are between 23% and 49% and in dilated cardiomyopathy patients between 46% and 61%[7]. Non-ischemic cardiomyopathy patients have worse outcomes than ischemic cardiomyopathy patients due to scar patterns with epicardial and intramural sites[7].

Epicardial ablation has emerged as a potential alternative ablation strategy in order to increase the success rate in complex substrates and to eliminate VT in patients with different cardiomyopathies and more recently in patients with Brugada syndrome[8-11]. Percutaneous approach to the pericardial area facilitates epicardial ablation when the VT substrate is situated in the subepicardium[12] (Figure 1). Adjacency to coronary circulation and the phrenic nerve may hinder the procedure in certain situations[9]. In patients with previous heart surgery or previous epicardial ablation attempts, percutaneous access may not be possible and as such, video-assisted thoracoscopy may be a good and minimally invasive alternative to open surgery[12].

Epicardial ablation is a safe procedure with low complication rates[13]. Percutaneous effusion is the most common complication[13]. Damage to subdiaphragmatic organs and hemorrhage from diaphragmatic vessels have also been reported[13].

Della Bella et al[14] evaluated the possible benefit of endo-epicardial catheter ablation for the management of VT in 528 patients with any form of structural cardiac disorder (Figure 2). Endo-epicardial catheter ablation resulted in a VT recurrence rate of 34.1%, in comparison...
Cardiac sympathetic denervation

Accumulated evidence strongly suggests a role of sympathetic neuromodulation in controlling refractory VT\cite{14-24}. Cardiac sympathetic denervation surgery has been proven to be useful for the management of congenital long QT syndrome and catecholaminergic polymorphic VT\cite{21}. The procedure requires extraction of the lower fraction of the stellate ganglion and T2-T4 sympathetic thoracic ganglia\cite{21}. Complications regarding the procedure were infrequent, with 4% developing acute ptosis or Horner syndrome\cite{21}. Vaselli et al\cite{21} showed that cardiac sympathetic denervation has greater shock-free survival as well as a considerable decline in shock burden in patients with recurrent VT or VT storm, regardless of antiarrhythmic drug therapy and catheter ablation. In addition, bilateral cardiac sympathetic denervation appeared to be more efficacious than left-sided denervation\cite{21,22}.

Augmented sympathetic activity leads to early and delayed afterdepolarization, enhances diffuse repolarization, leading to ventricular electrical susceptibility and increases the possibility of malignant VT\cite{23}. Stellate ganglionectomy lengths the ventricular refractory period and raises the VF threshold, decreasing VT or VF inducibility in the context of myocardial infarction\cite{23,24}. Locally invasive sympathetic ganglion block could select individuals with greater possibilities of long-term clinical benefits prior to sympathetic denervation\cite{23,24}.

Renal sympathetic denervation

Enhanced sympathetic tone shortens the ventricular effective refractory period, enhances automaticity, and lowers the threshold for ventricular arrhythmias\cite{25-27}. Feyzi et al\cite{25} performed bilateral renal denervation in a patient with polymorphic VT with excellent results. Aksu et al\cite{27} also showed that catheter-based renal denervation was successful in a patient with an electrical storm due to catecholaminergic polymorphic VT. However, the microanatomy of human renal vessels has great variability. Accessory renal vessels that bifurcate early can also influence the result negatively, and there is still the absence of procedural endpoint during the technique\cite{26}.

As a result, renal sympathetic denervation is not currently recognized as an ideal or approved VT treatment method\cite{25-27}. However, certain ventricular arrhythmias do not terminate after catheter ablation, thus making renal sympathetic denervation a possible option for patients in whom other ablative approaches were ineffective\cite{25,27,28}.

Sterotactic radioablative therapies

Despite catheter-oriented ablation, which applies radiofrequency or freezing to damage tissues, radiotherapy is based on photons from X-rays or gamma rays to injure the desired target, mainly cancer. Through novel distribution methods such as intensity-modulated radiotherapy, a dosage of radiotherapy can be precisely and accurately directed to the desired site, while diminishing...
ions, pneumonitis for chest therapies, myelopathy for spinal carcinomas, or bowel perforation for abdominal locations\textsuperscript{28,29}. In comparison to radiofrequency or cryo-energy, the damage from ablative radiotherapy progresses over days to months, needing time for the total tissue damage to be shown\textsuperscript{28,29}.

The first patient was treated on a robotic radiosurgery system (CyberKnife\textsuperscript{®}, Accuray, Sunnyvale, CA, United States) in 2012\textsuperscript{28}. The follow-up revealed no definite acute or late adverse effects, and a seven-month reduction burden in VT on standard antiarrhythmic drug therapy, suggesting a potential transient benefit of this method\textsuperscript{28}.

Cuculich \textit{et al}\textsuperscript{29} investigated five patients with increased-risk, refractory VT. The authors focused on arrhythmogenic scar sites by merging anatomical imaging with noninvasive electrocardiographic imaging during VT that was produced using an ICD\textsuperscript{29}. Patients were treated with a single dose of 25 Gy while awake, using a noninvasive distribution of accurate ablative radiation with stereotactic body radiation treatment\textsuperscript{29}. Cuculich \textit{et al}\textsuperscript{29} reported a reduction in events of VT in all five patients.

Cryoablation
Catheter radiofrequency ablation of VT originating from the left ventricle’s papillary muscles has been linked to conflicting outcomes\textsuperscript{30,31}. Rivera \textit{et al}\textsuperscript{31} investigated twenty-one patients with drug-refractory VT, who underwent catheter cryoablation or radiofrequency ablation. Cryoablation was correlated with greater success rates and smaller recurrence rates than radiofrequency procedures, superior catheter support, and smaller frequency of polymorphic arrhythmias\textsuperscript{31}. Marai \textit{et al}\textsuperscript{30} recently used cryoablation guided by intracardiac echocardiography, 3-dimensional mapping system, and image integration to treat a patient with refractory VT originating from papillary muscle with excellent results.

\textbf{Surgical therapy for VT}
Catheter ablation provides efficient outcomes for su-
stained monomorphic VT, but certain situations, such as the existence of mural thrombus and heavy calcification, can lead to adverse results[32,33]. Higuchi et al[33] successfully treated a 67-year-old patient with sustained monomorphic VT due to ventricular scar and resistant to endocardial radiofrequency ablation, by left ventricular reconstruction with cryoablation. Li et al[35] conducted a retrospective investigation of 38 consecutive surgical epicardial VT ablation procedures and compared the results with those of a propensity-matched percutaneous epicardial access control group. Surgical epicardial access after heart surgery for VT ablation showed no statistical difference in long-term results in comparison to the percutaneous epicardial group[36].

Recently, Berte et al[35] presented the first animal survey utilizing a more potent cryoablation system that can generate larger, transmural ventricular lesions from both the endocardium and the epicardium. Surgical cryoablation in sheep had no acute macroscopic vascular or extracardiac damage and resulted in 100% successful lesions at necropsy[36].

In some patients with non-ischemic cardiomyopathy and VT refractory to standard therapy or undergoing cardiac surgery, surgical ablation may be an alternative option for potentially reducing the burden of ICD shocks during long-term follow-up[36]. Liang et al[36] showed that detailed arrhythmic substrate in the electrophysiology lab before surgery, in conjunction with a direct scar and radiofrequency ablation lesion visualization in the operating room, is crucial for guiding surgical ablation.

**Extracorporeal life support for refractory VT**

Extracorporeal life support is a highly efficient bridging treatment in patients with refractory VT associated with cardiogenic shock[37]. Extracorporeal life support allows the usage of negative inotropic antiarrhythmic drug therapy, leading to the weaning of catecholamine delivery, thus resolving the dangerous period of the catecholamine driven electrical storm[37]. The utilization of extracorporeal life support maintains hemodynamic support during an ablation procedure, while mapping and induction of VT are commenced and provides sufficient vital organ perfusion in patients with refractory VT[37]. Current literature suggests the usage of extracorporeal life support, as it has proven to be a safe, practical and efficient therapeutic solution when traditional treatments have failed[37].

**Steroid pulse therapy**

Okabe et al[38] successfully treated a patient with cardiac sarcoidosis associated with VT using steroid pulse therapy.

**Gene therapy**

Catecholaminergic polymorphic VT (CPVT) is a rare cardiac ion channelopathy induced by anomalies in proteins that regulate Ca$^{2+}$ transport in heart cells that can lead to SCD[39,40]. CPVT is associated with mutations in the gene encoding the cardiac RyR2, a cardiac ryanodine receptor protein which is involved in calcium homeostasis and mutations in the gene that encodes calsequestrin (CASQ2), a protein that interacts with RyR2[39-41].

Denegri et al[42] showed that viral gene transfer of wild-type CASQ2 into the heart of mice prevented and reverted severe manifestations of CPVT. Furthermore, Lodola et al[43] infected induced pluripotent stem cells with an adeno-associated viral vector serotype 9 (AAV9) encoding the human CASQ2 gene and noticed a significant decline in the percentage of delayed afterdepolarizations. Li et al[44] used tetracaine, a local anesthetic drug with known RyR2 inhibiting action, in mice and showed that the drug efficiently halted the induction of VT in a mouse model of CPVT.

**INNOVATIVE MODALITIES FOR VT AND FUTURE CLINICAL APPLICATIONS**

Endo-epicardial ablation reduces VT recurrences, but not all patients have a VT substrate[45]. Contrast-enhanced magnetic resonance imaging (ceMRI) is utilized to identify VT substrate after myocardial infarction[46]. Arena et al[45] showed that ceMRI-based endo-epicardial signal intensity mapping in a porcine model allowed characterization of the epicardial VT substrate.

Klein et al[46] used 3D meta-iodobenzylguanidine (MIBG) imaging to guide VT ablation. MIBG innervation defects are greater than scars produced from bipolar voltage maps, and the investigation showed that 36% of successful ablative locations were situated in sections of irregular innervation and normal voltage, suggesting that innervation maps may identify additional VT ablation sites[46].

Zhang et al[47] investigated non-invasive high-resolution mapping and electrocardiographic imaging to provide epicardial substrate information. Electrocardiographic imaging identified scar electrophysiologic substrates in ischemic cardiomyopathy patients[47].

Cardiac ripple mapping for slow conducting channels is an innovative technique to integrate voltage and activation mapping[48,49]. Cardiac ripple mapping allows the concurrent vision of voltage and activation data and facilitates recognition of slow conduction channels within scar areas in the myocardium that could be probable VT ablation sites[48,49]. Table 1 summarizes the studies investigating novel approaches for the treatment of VT.

**CONCLUSION**

The management of patients with VT can be demanding. ICD implant led to a considerable difference in the survival of subjects with VT, but the estimate of subjects with recurrent ICD shocks is still a growing issue. Antiarrhythmic drug treatment has reduced effectiveness and is correlated with serious adverse effects. Catheter ablation remains the cornerstone in
the treatment of VT and efficiently lowers recurrent VT episodes but carries upfront procedural danger. Novel methods could enhance its future effectiveness. The final management strategy should be individualized utilizing clinical and imaging assessment, patient views and intentions, futility concerns, and operator’s catheter ablation experience.

REFERENCES

1 Ak-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, Gillis AM, Hlatky MA, Granger CB, Hammill SC, Joglar JA, Kay GN, Matlock DD, Myerburg RJ, Page RL. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation 2017; pii: CIR.000000000000548 [PMID: 29084733 DOI: 10.1161/CIR.000000000000548]

2 Weisfeldt ML, Everson-Stewart S, Sitali C, Rea T, Aufderheide TP, Atkins DL, Bigham B, Brooks SC, Foester C, Gray R, Ornato JP, Powell J, Kudenchuk PJ, Morrison LJ; Resuscitation Outcomes Consortium Investigators. Ventricular tachyarrhythmias after cardiac arrest in public versus at home. N Engl J Med 2011; 364: 313-321 [PMID: 21268723 DOI: 10.1056/NEJMoa1010663]

3 Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggreve M, Cann J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolau N, Noreková TM, Spaulding C, Van Veldhuisen DJ; ESC Scientific Document Group. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015; 36: 2793-2867 [PMID: 26320108 DOI: 10.1093/eurheartj/ehv316]

4 Hohnloser SH, Israel CW. Current evidence base for use of the implantable cardioverter-defibrillator. Circulation 2013; 128: 172-183 [PMID: 23836830 DOI: 10.1161/CIRCULATIONAHA.112.000547]

5 Santangeli P, Muser D, Maeda S, Filtz A, Zado ES, Frankel DS, Dixit S, Epstein AE, Callans DJ, Marchlinski FE. Comparative effectiveness of antiarrhythmic drugs and catheter ablation for the prevention of recurrent ventricular tachycardia in patients with implantable cardioverter-defibrillators: A systematic review and meta-analysis of randomized controlled trials. Heart Rhythm 2016; 13: 1552-1559 [PMID: 26961297 DOI: 10.1016/j.hrthm.2016.03.004]

6 Dukkipati SR, Choudry S, Koruth JS, Miller MA, Whang W, Reddy VY. Catheter Ablation of Ventricular Tachycardia in Structurally Normal Hearts: Indications, Strategies, and Outcomes-Part I. J Am Coll Cardiol 2017; 70: 2909-2923 [PMID: 29216987 DOI: 10.1016/j.jacc.2017.10.031]

7 Dukkipati SR, Koruth JS, Choudry S, Miller MA, Whang W, Reddy VY. Catheter Ablation of Ventricular Tachycardia in Structural Heart Disease: Indications, Strategies, and Outcomes-Part II. J Am Coll Cardiol 2017; 70: 2924-2941 [PMID: 29216988 DOI: 10.1016/j.jacc.2017.10.030]

8 MacIntyre CJ, Sapp JL. Treatment of persistent ventricular tachycardia: Drugs or ablation? Trends Cardiovasc Med 2017; 27: 506-513 [PMID: 28625728 DOI: 10.1016/j.tcm.2017.05.004]
Baldinger SH, Stevenson WG, John RM. Ablation of ischemic ventricular tachycardia: evidence, techniques, results, and future directions. J Am Coll Cardiol 2016; 62: 31-39 [PMID: 26569083 DOI: 10.1016/j.jacc.2015.12.037]

Aryana A, d’Avila A. Epicardial Catheter Ablation of Ventricular Tachycardia. Card Electrophysiol Clin 2017; 9: 119-131 [PMID: 28167080 DOI: 10.1016/j.cecp.2016.10.009]

Nademaneke N, Hocini M, Haïssaguerre M. Epicardial substrate ablation for Brugada syndrome. Heart Rhythm 2017; 14: 457-461 [PMID: 27979714 DOI: 10.1016/j.hrthm.2016.12.001]

Aksu T, Erdem Goliev T, Yalın K. Successful ablation of an epicardial ventricular tachycardia by video-assisted thoracoscopy. Europace 2015; 17: 1116 [PMID: 25736561 DOI: 10.1093/europace/eu5012]

Graham AJ, Orini M, Lambiase P. Limitations and Challenges in Mapping Ventricular Tachycardia: New Technologies and Future Directions. Arrhythm Rythm Electrophysiol Rev 2017; 6: 118-124 [PMID: 29008159 DOI: 10.15420/aei.2017.20.1]

Della Bella P, Baratto F, Taischris D, Trevisi N, Vergara P, Bisciglja C, Petracca F, Baruccio C, Benussi S, Maisano F, Allieri O, Papapalardo F, Zangrillo A, Maccabello G. Management of ventricular tachycardia in the setting of a dedicated unit for the treatment of complex ventricular arrhythmias: long-term outcome after ablation. Circulation 2013; 127: 1359-1368 [PMID: 23439513 DOI: 10.1161/CIRCULATIONAHA.112.000872]

Kim SM, Virgadamo S, Gurlay J, Elayi CS. Use of Cardioplegia to Guide Alcohol Ablation for Incipient Ventricular Tachycardia. Pacing Clin Electrophysiol 2017; 40: 213-226 [PMID: 27565512 DOI: 10.1111/pacme.12945]

Markowitz SM, Minutillo RM, Kim JK, Ip JE, Thomas G, Lerman BB. Treatment of intramural ventricular tachycardia in cardiac sarcoidosis with transcoronary ethanol ablation. European 2017; 19: 1921 [PMID: 29126258 DOI: 10.1093/europeexu/cex277]

Sapp JL, Berte B, Sanadi AM, Yalın K. Renal sympathetic denervation assisted treatment of electrical storm due to polymorphic ventricular tachycardia. Eur J Intern Med 2017; 45: e694 [PMID: 27570715 DOI: 10.7759/cureus.694]

Cuculich PS, Schill MR, Kashani R, Mutic S, Lang A, Cooper D, Faddis M, Gleva N, Noheria A, Smith TW, Hallahan D, Ruddy R, Robinson CG. Noninvasive Cardiac Radiation for Ablation of Ventricular Tachycardia. N Engl J Med 2017; 377: 2325-2336 [PMID: 29236642 DOI: 10.1056/NEJMoai1617373]

Marai I, Andria N, Gurevitz O. Cryoablaction for Ventricular Tachycardia Originating from Anterior Papillary Muscle of Left Ventricle Guided by Intracardiac Echocardiography. Card Electrophysiol Rep 2017; 11: 9734795 [PMID: 28512586 DOI: 10.1155/2017/9734795]

Rivera S, Ricapito Mde L, Tomas L, Parodi J, Bardera Molina G, Banega R, Bueti P, Oroso A, Reinoso M, Caro M, Belardi D, Albina G, Giniger A, Scaszfuso F. Results of Cryoenergy and Radiofrequency-Based Catheter Ablation for Treating Ventricular Arrhythmias Arising From the Papillary Muscles of the Left Ventricle, Guided by Intracardiac Echocardiography and Image Integration. Circ Arrhythm Electrophysiol 2016; 9: e003874 [PMID: 27069089 DOI: 10.1161/CIRCEP.115.003874]

Shenasa M, Miller JM, Callans DJ, Almendral JM, Marchlinski FE, Buxton AE. Conquest of Ventricular Tachycardia: Insights Into Mechanisms, Innovations in Management: Contribution of Mark E. Josephson, MD, to Clinical Electrophysiology. Cir Arrhythm Electrophysiol 2017; 10: pii: e005150 [PMID: 28487348 DOI: 10.1161/CIRCEP.117.005150]

Higuchi T, Tsutsui Y, Monta O, Asada S, Matsumoto R, Yamada S, Ohashi H. Surgical treatment for endocardial radiofrequency ablation-resistant sustained monomorphic ventricular tachycardia with mural thrombus including dense calcification in the left ventricle. Gen Thorac Cardiovasc Surg 2017; Epub ahead of print [PMID: 29188428 DOI: 10.1007/s11748-017-0855-2]

Li A, Hayase J, Do D, Buch E, Vaseghi M, Ajioka OA, Macias C, Kroshkava V, Khakpour H, Boyle NK, Shenharash P, Binwale R, Shvikumar K, Bradfield JS. Hybrid surgical vs percutaneous access epicardial ventricular tachycardia ablation. Heart Rhythm 2018; 15: 512-519 [PMID: 29132931 DOI: 10.1016/j.hrthm.2017.11.009]

Berte B, Sacher F, Wielandts JY, Mahdia S, Polios X, Weerasooriya R, Bemus O, Jais P. A new cryoenergy for ventricular tachycardia ablation: a proof-of-concept study. Europace 2018; 19: 1401-1407 [PMID: 29709704 DOI: 10.1177/1040139318750393]

Liang JJ, Betensky BP, Muser D, Zado ES, Anter E, Desai ND, Callans DJ, Deo R, Frankel DS, Hutchinson MD, Lin D, Riley MP, Schaller RD, Supple GE, Santangeli P, Acker MA, Bavaria JE, Schiller MR, Kashani R, Mutic S, Lang A, Cooper D, Faddis M, Gleva N, Noheria A, Smith TW, Hallahan D, Ruddy R, Robinson CG. Noninvasive Cardiac Radiation for Ablation of Ventricular Tachycardia in Patients with Non-ischemic Cardiomyopathy. Europace 2018; 20: e30-e41 [PMID: 28402404 DOI: 10.1093/europace/eux029]

Bhandary SP, Joseph N, Hofmann JP, Saranteas T, Padimos TJ. Extracorporeal i.v. support for refractory ventricular tachycardia. Ann Trans Med 2017; 5: 73 [PMID: 28275618 DOI: 10.21037/atm.2017.01.39]

Okabe T, Yukashii T, Hiroe M, Oyama Y, Iwaga W, Ono M, Kido T, Ebara S, Yamashita K, Yamamoto MH, Saito S, Hoshimoto K, Aksu T, Guler TE, Ozcan KS, Bozyel S, Yalın K. Renal sympathetic denervation assisted treatment of electrical storm due to polymorphic ventricular tachycardia in a patient with catecholaminergic polymorphic ventricular tachycardia. Turk Kardiol Dern Ars 2017; 45: 441-449 [PMID: 28694398 DOI: 10.5453/tkda.2017.72773]

Aksu T, Güler E. Percutaneous renal sympathetic denervation in catecholaminergic polymorphic ventricular tachycardia. J Arrhythm 2017; 33: 245 [PMID: 28607624 DOI: 10.1016/j.joa.2016.12.004]

Wang L, Fahimian B, Softs SG, Zi F, Lo A, Gardner EA, Maguire PJ, Loo DW Jr. Stereotactic Arrhythmia Radioablation (STAR) of Ventricular Tachycardia: A Treatment Planning Study. Curr Heart Rhythm 2016; 9: e694 [PMID: 27570715 DOI: 10.7759/cureus.694]

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Neth Heart J 2017; 25: 596-597 [PMID: 28608267 DOI: 10.1007/s12471-017-1012-1]
Spartalis M et al. Novel treatments of ventricular tachycardia

39 Roston TM, Cunningham TC, Sanatani S. Advances in the diagnosis and treatment of catecholaminergic polymorphic ventricular tachycardia. Cardiol Young 2017; 27: 549-556 [PMID: 28084961 DOI: 10.1017/S1047951116002237]

40 Arakawa J, Hamabe A, Aiba T, Nagai T, Yoshida M, Touya T, Ishigami N, Hisadome H, Katsushika S, Tabata H, Miyamoto Y, Shimizu W. A novel cardiac ryanodine receptor gene (RyR2) mutation in an athlete with aborted sudden cardiac death: a case of adult-onset catecholaminergic polymorphic ventricular tachycardia. Heart Vessels 2015; 30: 835-840 [PMID: 25092222 DOI: 10.1007/s00380-014-0555-y]

41 Kawata H, Ohno S, Aiba T, Sakaguchi H, Miyazaki A, Sumitomo N, Kamakura T, Nakajima I, Inoue YY, Miyamoto K, Okamura H, Noda T, Kusano K, Kamakura S, Miyamoto Y, Shiraiishi I, Horie M, Shimizu W. Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Associated With Ryanodine Receptor (RyR2) Gene Mutations- Long-Term Prognosis After Initiation of Medical Treatment. Circ J 2016; 80: 1907-1915 [PMID: 27452199 DOI: 10.1255/circj.CJ-16-0250]

42 Denegri M, Lodola F, Boncompagni S, De Giusti VC, Avelino-Cruz JE, Liu N, Persampieri S, Cucurto A, Esposito F, Pietrangelo L, Marty I, Villani L, Moiyo A, Baiardi P, Auricchio A, Protasi F, Napolitano C, Priori SG. Single delivery of an adeno-associated viral vector to transfer the CASQ2 gene to knock-in mice affected by catecholaminergic polymorphic ventricular tachycardia is able to cure the disease from birth to advanced age. Circulation 2014; 129: 2673-2681 [PMID: 24888331 DOI: 10.1161/CIRCULATIONAHA.113.069601]

43 Lodola F, Morone D, Denegri M, Bongianino R, Nakahama H, Rutigliano G, Losetti R, Rizzo G, Vollero A, Buonocore M, Napolitano C, Cordorelli G, Priori SG, Di Pasquale E. Adeno-associated virus-mediated CASQ2 delivery rescues phenotypic alterations in a patient-specific model of recessive catecholaminergic polymorphic ventricular tachycardia. Cell Death Dis 2016; 7: e2393 [PMID: 27711080 DOI: 10.1038/cddis.2016.304]

44 Li N, Wang Q, Sibrian-Vazquez M, Klipp RC, Reynolds JO, Word TA, Scott L Jr, Salama G, Strongin RM, Abramson JJ, Wehrens XHT. Treatment of catecholaminergic polymorphic ventricular tachycardia in mice using novel RyR2-modifying drugs. Int J Cardiol 2017; 227: 668-673 [PMID: 27838126 DOI: 10.1016/j.ijcard.2016.10.078]

45 Arenal A, Pérez-David E, Avila P, Fernández-Portales J, Crisóstomo V, Báez C, Jiménez-Candil J, Rubio-Guiveraun JL, Ledesma-Carbayo MJ, Loughlin G, Bermejo J, Sánchez-Margallo FM, Fernández-Avilés F. Noninvasive identification of epicardial ventricular tachycardia substrate by magnetic resonance-based signal intensity mapping. Heart Rhythm 2014; 11: 1456-1464 [PMID: 24747421 DOI: 10.1016/j.hrthm.2014.04.022]

46 Klein T, Abdulghani M, Smith M, Huang R, Asoglu R, Remo BF, Turgeman A, Mesubi O, Sidhu S, Symowski S, Saltaris A, See V, Shorofsky S, Chen W, Diluzio V, Dickfeld T. Three-dimensional 123I-meta-iodobenzylguanidine cardiac innervation maps to assess substrate and successful ablation sites for ventricular tachycardia: feasibility study for a novel paradigm of innervation imaging. Circ Arrhythm Electrophysiol 2015; 8: 583-591 [PMID: 25713216 DOI: 10.1161/CIRCEP.114.002105]

47 Zhang J, Cooper DH, Desouza KA, Cuculich PS, Woodard PK, Smith TW, Rudy Y. Electrophysiologic Scar Substrate in Relation to VT: Noninvasive High-Resolution Mapping and Risk Assessment with ECGI. Pacing Clin Electrophysiol 2016; 39: 781-791 [PMID: 27197804 DOI: 10.1111/pace.12882]

48 Luther V, Linton NW, Jamil-Coley S, Koai-Wing M, Lim PB, Qureshi N, Ng GS, Hayat S, Whinnett Z, Davies DW, Peters NS, Kanagaratnam P. A Prospective Study of Ripple Mapping the Post-Infarct Ventricular Scar to Guide Substrate Ablation for Ventricular Tachycardia. Circ Arrhythm Electrophysiol 2016; 9: pii: e004072 [PMID: 27307519 DOI: 10.1161/CIRCEP.114.004072]

49 Jamil-Coley S, Vergara P, Carbucicchio C, Linton N, Koai-Wing M, Luther V, Francis DP, Peters NS, Davies DW, Tondo C, Della Bella P, Kanagaratnam P. Application of ripple mapping to visualize slow conduction channels within the infarct-related left ventricular scar. Circ Arrhythm Electrophysiol 2015; 8: 76-86 [PMID: 25527678 DOI: 10.1161/CIRCEP.114.001827]
