Magnetic resonance imaging of endocardial exits from epicardial ventricular tachycardia substrates in left ventricular nonischemic cardiomyopathy

Short title: MRI of epicardial VT substrates

Christopher Reithmann, M.D., Bernhard Herkommer, M.D., Theresia Kling, M.D., Cordula Brauns, Michael Fiek, M.D., Michael Ulbrich, M.D.

Medizinische Klinik 1, HELIOS Klinikum München-West, Akademisches Lehrkrankenhaus der Universität München, Germany

Disclosures: none

Correspondence to:

Prof. Dr. Christopher Reithmann

Medizinische Klinik 1

HELIOS Klinikum München-West

Akademisches Lehrkrankenhaus der Ludwig-Maximilians-Universität München

Steinerweg 5

D-81241 München

Germany

Tel. +49 89 8892 2307

Fax. +49 89 8892 2274

e-mail. Christopher.Reithmann@helios-gesundheit.de

ABSTRACT

Introduction: In patients with left ventricular (LV) nonischemic cardiomyopathy and monomorphic ventricular tachycardia (VT), midmyocardial and epicardial substrates are often involved but endocardial structures may also be affected. Delayed enhancement – magnetic resonance imaging (DE–MRI) was used to characterize the substrates of predominantly epicardial VT to improve identification of target sites for ablation.

Methods and Results: 12 patients with LV nonischemic cardiomyopathy and monomorphic VT (prior myocarditis in 9) had a predominantly epicardial (n = 8) or epicardial-only DE-MRI substrate (n = 4). Modest-sized endocardial involvement in predominantly epicardial substrates was identified by DE-MRI in 8 patients. Mapping of 22 VTs was performed in 12 patients using an endo-epicardial approach in 6 patients and an endocardial-only approach in 6 patients. Endocardial VT reentry circuit exit sites as defined by entrainment and pace mapping criteria corresponded to endocardial breakthroughs from predominantly epicardial DE-MRI substrates in 7 patients. The endocardial VT exits were located at the ventricular base near the mitral annulus in 6 patients. Successful endocardial ablation of at least one VT was accomplished in 5 patients. Epicardial ablation as a part of an endo-epicardial approach or as epicardial-only ablation was performed in 6 patients and was successful in 4 patients.

Conclusion: Endocardial breakthroughs from predominantly epicardial DE-MRI substrates are often located near the ventricular base in the perivalvular region and correlate with endocardial VT reentry circuit exit sites amenable to ablation.

Key words: Magnetic resonance imaging; ventricular tachycardia; mitral annulus; delayed enhancement; epicardial substrate

INTRODUCTION

Ventricular tachycardia (VT) in nonischemic cardiomyopathy often originate from midmyocardial or predominantly epicardial substrates in the left ventricle (LV). Previous electroanatomic mapping studies have shown a large area of LV epicardial low voltage and a narrow area of endocardial low voltage near the ventricular base in the perivalvular region in these patients (1-3). Endocardial VT ablation is associated with lower success rates when compared to VT ablation in patients with ischemic cardiomyopathy (1-3). Depending on wall thickness and transmural extension of the epicardial scar, successful endocardial ablation has been reported in some patients with predominantly epicardial substrates after prior myocarditis (4-6). Magnetic resonance imaging (MRI) of scar tissue and fibrosis is established as a method to characterize the substrate of monomorphic VT in nonischemic cardiomyopathy (7-9). The present study using delayed enhancement – magnetic resonance imaging (DE-MRI) was performed to visualize the VT substrate and to identify endocardial involvement of predominantly epicardial substrates in nonischemic cardiomyopathy as a possible target for endocardial VT ablation.

METHODS

Study population

50 consecutive patients with nonischemic cardiomyopathy underwent cardiac MRI prior to catheter ablation of monomorphic VT between September 2009 and September 2020 in our institution. Among them, 12 patients had an epicardial-only or predominantly epicardial DE-MRI substrate. The cardiac MRI studies were performed before ICD implantation in all patients included in this study. 12-lead ECG during the clinical VT allowed us to identify scar areas on DE-MRI that correlated to the clinical VT. The underlying structural heart disease was prior myocarditis in 9 patients (biopsy-proven viral myocarditis in 6 patients), nonischemic cardiomyopathy of unknown origin in two patients and polymyositis with axonal neuropathy in one patient. 5 patients had a prior unsuccessful endocardial ablation in another institution. Coronary angiography excluding coronary artery disease had been performed in all patients.

Cardiac MRI

Cardiac MRI was performed before ablation in our institution in 6 patients and in other institutions in 6 patients. The cardiac MRI studies were performed on a 3 T MRI scanner (Philips Achieva, Best, Netherlands) with a 5-element phased-array coil placed over the chest of patients in the supine position (10). Images were acquired with electrocardiographic gating during breath-holds. Dynamic short- and long-axis images of the heart were acquired using a segmented, k-space, steady-state, free-precession pulse sequence (30 phases, 1.4 x 1.4 mm in-plane resolution, 8-mm slice thickness). 10 minutes after administration of 0.15 mmol/kg of intravenous gadolinium DTPA (Gadovist^{R}, 1 mmol/ml), 3-dimensional delayed-enhancement imaging was performed using a 3-D inversion-recovery sequence (repetition time 6.7 ms, echo time 3.2 ms, in-plane spatial resolution 1.4 x 2.2 mm, slice thickness 8 mm) in the short- and long-axis of the LV. The inversion time (200 to 350 ms) was optimized to null the normal

myocardium by use of a look locker sequence. The DE–MRIs were reviewed for the presence and extension of delayed enhancement by two observers (B.H. and T.K.) blinded to the results of mapping and ablation. LV-EF was determined by cardiac MRI. For each patient, the maximum signal intensity (SI) in the LV myocardium was determined and scar / fibrosis was defined as myocardium with an SI ≥ 50 % of the maximum SI. The presence and extent of DE in the myocardial wall was determined in a four-chamber view and a short-axis view by manual tracing and not by a semiautomatic method. An epicardial-only DE-MRI substrate was defined as a subepicardial scar without transmurality (11). A predominantly epicardial DE-MRI substrate was characterized by a predominant affection of the subepicardium with varying progression to the midmyocardial wall and endocardium. Using DE-MRI, an endocardial breakthrough from an epicardial VT substrate was defined as a close contact of the epicardial DE substrate to the LV endocardium or the mitral valve annulus.

Electrophysiologic study

After giving informed consent, all patients underwent electrophysiological study. ICD therapies were de-activated during the procedures in all patients. Endocardial electrode catheters for programmed ventricular stimulation, mapping and ablation were introduced into the right and left ventricles through the right femoral vein and the right femoral artery. The stimulation protocol consisted of a programmed ventricular stimulation from the right ventricular apex and the right ventricular outflow tract at four cycle lengths with up to three extrastimuli (five captured beats at 600, 500, 400 and 330 ms cycle length). When the VT was not inducible by endocardial stimulation, stimulation was repeated under orciprenaline infusion (30ug/min). Endocardial mapping was performed with a three-dimensional mapping system (CARTO, Biosense Webster Inc., Baldwin Park, CA, USA) according to standard criteria (12). Epicardial mapping through a trans-pericardial access was performed using the technique of Sosa (13). In most cases, a 22 cm 8.5 F sheath was used to introduce the CARTO

mapping catheter in the pericardial space. Epicardial mapping and ablation was performed under general anesthesia in all patients. During mapping and ablation, 5000 IU heparine was given as a bolus, followed by 1000 IU/ h as an infusion. In the case of epicardial mapping, heparine was given after the pericardial puncture.

Mapping

Bipolar endocardial and epicardial mapping filtered at 30 and 5000 kHz during sinus rhythm and VT were recorded on the Electrophysiological LAB system (PRUCKA Engineering, Houston, TX, USA). An endocardial voltage map of the LV during sinus rhythm was constructed in all patients. The endocardial exit site of the VT was defined as the endocardial site with earliest local electrograms during the VT preceding QRS by a maximum of 30 % of the VT cycle length with concealed entrainment or pace mapping being performed with the QRS configuration identical or very similar to that of the spontaneous VT (14). Epicardial voltage maps during sinus rhythm were constructed in five patients. Low voltage was defined as an endocardial or epicardial region with a voltage < 1.5 mV. Very low voltage was defined if the voltage was < 0.5 mV. Sites at the mitral annulus or adjacent to the mitral annulus were defined by 1) a characteristic mitral annular location and motion when viewed in right and left anterior oblique fluoroscopic views and 2) the ratio of atrial to ventricular electrograms at this site being < 1, if the atrial electrograms were clearly discernible and the ventricular electrograms were > 0,5mV (15). In epicardial voltage maps, we attempted to exclude the regions of the large coronary vessels and the AV groove from the assessment of epicardial low voltage and very low voltage areas according to prior coronary angiography (16). Detailed epicardial voltage mapping in the region of the arrhythmia substrate was performed during sinus rhythm, and all sites demonstrating late potentials or isolated diastolic potentials were identified. Epicardial pace mapping at high output power (12 V, 2 ms duration) was used in and around the abnormal substrate to define the approximate epicardial exit site of the

VT circuit and to identify sites with a long stimulus to QRS interval and a good QRS match suggesting an epicardial critical isthmus or exit site of the VT reentry circuit.

Catheter ablation

A 500 kHz radiofrequency (RF) ablation unit (Stockert-Cordis) was used for ablation. The ablation catheter was a 3.5 or 4 mm tipped irrigated ablation catheter (CARTO, Biosense Webster). The current was initially applied at a power of 20 W and was increased every 5 to 10 s to a maximum output of 50 W for endocardial ablation and 40 W from the pericardial space. RF energy application from the pericardial space was performed at sites where the distance to the adjacent coronary artery was > 5 mm detected by simultaneous coronary angiography (16). Endocardial ablation was performed in most patients during the clinical VT according to standard entrainment and pace mapping criteria (12). The endpoint of endocardial ablation was termination and non-inducibility of the clinical VT and of VTs with a similar or larger cycle length. Due to the poor inducibility of the clinical VT under general anesthesia in 4 patients, epicardial RF energy delivery was mainly performed as a substrate-based ablation during sinus rhythm in these patients. The combination of late or isolated diastolic potentials during sinus rhythm, a good pace map QRS match and a long stimulus – QRS interval during pace mapping suggested the likelihood of proximity to epicardial VT origin / circuit and was used to define the target of substrate – based epicardial ablation. In addition to non-inducibility of the clinical VT, the endpoint of epicardial ablation was complete elimination of all potentials with late or isolated diastolic electrograms in a region of very low voltage (< 0.5 mV) that was identified as an appropriate target for ablation by pace mapping. All patients underwent an electrophysiologic re-evaluation consisting of repetition of the initial stimulation protocol in the absence and presence of orciprenaline and 12-lead ECG recording for 30 min after the ablation.

Follow-up

One patient without ICD had a control electrophysiologic study including programmed ventricular stimulation within 3 months after the successful epicardial-only ablation. Follow-up information was obtained from patient visits and ICD interrogation every 3 months in our outpatient clinic.

RESULTS

Delayed enhancement - magnetic resonance imaging of epicardial VT substrates

12 patients with LV nonischemic cardiomyopathy undergoing DE – MRI and catheter ablation for drug-refractory sustained VT (11 male, 62 ± 17 years) had a predominantly epicardial (n = 8) (fig. 1A, 2A, 3A) or epicardial-only DE-MRI substrate (n = 4) (fig. 4A). Mean left ventricular ejection fraction (LV-EF) in the 12 patients was 54 ± 7 % (Table 1). An implantable cardioverter defibrillator (ICD) was implanted before (n = 5) or after ablation (n = 2) in 7 patients. Mean cycle length of the predominant clinical VT was 333 ± 45 ms. The main location of the epicardial LV DE–MRI substrate was lateral or posterolateral in 8 patients, anterior or anterolateral in 3 patients and circular in 1 patient. Endocardial involvement in predominantly epicardial substrates as a defined breakthrough from the epicardial DE-MRI substrate to the LV endocardium was found in 8 patients (fig. 1B - C, 2B, 3B). The location of the endocardial breakthroughs was at the base of the LV adjacent or in proximity to the mitral annulus in 6 patients (fig. 1B - C, 2B). In 4 patients, the DE – MRI substrates were epicardial-only without transmural extensions to the endocardium (fig. 4B).

Endocardial mapping and ablation

Among the 12 patients with epicardial DE – MRI substrates, endocardial voltage mapping revealed discrete very low voltage areas (voltage < 0.5 mV) in 6 patients that correlated to the endocardial breakthroughs in DE-MRI (fig. 1E). No or only minimal endocardial low voltage was found in 6 patients (fig. 3 C, 4C). Endocardial activation and entrainment mapping demonstrated endocardial VT reentry circuit exit sites adjacent or in proximity to the mitral annulus in 6 patients (fig. 1F, 2D) and at another LV endocardial sites in 2 patients (fig. 3D). The endocardial exits of VT reentry circuits correlated with endocardial breakthroughs from predominantly epicardial DE-MRI substrates in 7 patients. In 4 patients with epicardial-only DE-MRI substrates, no endocardial reentry circuit exit sites were identified by entrainment

and pace mapping. Endocardial ablation was attempted in 9 patients and was successful in 5 patients in the elimination of at least one VT (fig. 1F, 2D, 3E). VT with both endocardial and epicardial reentry circuit exits were found in 3 patients (fig. 1).

Epicardial mapping and ablation

6 patients agreed to undergo transpericardial epicardial mapping and ablation as a combined endo-epicardial ablation approach (n = 3) or as an epicardial-only ablation approach (n = 3). In one patient (pt. 5), ablation was unsuccessful and an ICD was implanted. Epicardial ablation was mainly performed during sinus rhythm as a substrate-based ablation guided by abnormal epicardial electrograms in a low voltage or very low voltage area (ablation area 14.2 ± 9.4 cm^2) in combination with a good pace map QRS match (fig. 1 G - K, 4 E - F). Elimination of all abnormal epicardial electrograms in the target region and non-inducibility of the clinical VT at the end of the epicardial ablation procedure was achieved in 5 patients. 3 of the 5 patients undergoing epicardial ablation had signs of a temporary sterile pericarditis after the procedure that reversed after administration of steroids within few days.

Follow-up

During the follow-up of 30 ± 27 months after ablation, one of the 12 patients (pt. 1) had an episode of polymorphic VT one day after epicardial ablation but was free of further ICD interventions during the follow-up of 6 months. None of the patients died. The two patients with unsuccessful endocardial ablation without epicardial ablation received an ICD, and one was treated with amiodarone. The patient with unsuccessful epicardial ablation (pt. 5) received an ICD and was treated with amiodarone after two adequate ICD shocks. None of the 5 patients who were left without an ICD after successful endocardial (n = 4) or epicardial (n = 1) ablation, had a recurrent symptomatic VT during the follow up (amiodarone in one patient).

DISCUSSION

Endocardial involvement in epicardial VT substrates

VT in patients after prior myocarditis often originate from the epicardium (1-3). A nonischemic pattern with typical delayed enhancement of the epicardial LV myocardium has also been described in patients with cardiac sarcoidosis, Anderson-Fabry, Chagas Disease and polymyositis (16-18). In these patients, the lateral, posterolateral and inferolateral wall are frequently involved and the subepicardium is usually affected with varying progression towards the midmyocardial and subendocardial wall (19).

In our series of patients referred for VT ablation who underwent DE – MRI, 12 patients had a predominantly epicardial or epicardial-only DE – MRI substrate in the free wall of the LV with various degree of extension of myocardial fibrosis or scar to the midmyocardium and endocardium. Our results are in agreement with previous studies demonstrating larger areas of low voltage and electrogram abnormalities in the LV epicardium and a narrow region of endocardial low voltage in the perivalvular region (1-3). In half of our patients, modest-sized breakthroughs from the epicardial scar to the endocardium near the ventricular base adjacent or in proximity to the mitral annulus were detected by DE – MRI. This extension of epicardial scar to the endocardium after prior myocarditis and in other forms of nonischemic cardiomyopathy may have relevance for the ablation approach in these patients.

Endocardial exit sites from epicardial VT circuits as targets for endocardial ablation

Several studies have previously reported that a subgroup of patients with epicardial VT can be successfully treated by endocardial ablation. Dello Russo et al were able to successfully ablate drug-refractory VT in 70 % of patients after myocarditis using endocardial ablation alone while in the remaining 30 % ablation of the clinical VT required epicardial ablation (5). On the other hand, Komatsu et al. showed that ablation of epicardial local abnormal ventricular activities (LAVA) from the endocardium was ineffective at sites where neither endocardial

LAVA nor wall thinning were present, and an epicardial approach was required in these patients (6). The present study suggests that endocardial ablation of predominantly epicardial VTs can be successfully performed if transmural progression of the epicardial scar or a defined breakthrough to the endocardium allows targeting of critical components of the VT reentry circuit from the endocardium. In our study, endocardial breakthroughs on DE – MRI correlated with endocardial exit sites of the reentry circuit as defined by entrainment and pace mapping. Both, endocardial breakthroughs on DE – MRI and successful endocardial ablation sites were located near the ventricular base in the perivalvular region in most patients. Other authors have also reported successful endocardial ablation of epicardial VTs near the mitral annulus in patients with nonischemic cardiomyopathy (1-3, 20).

Ablation approach for epicardial VT in nonischemic cardiomyopathy

Depending on the transmural extension of epicardial scar or fibrosis, a combined endo- and epicardial ablation or epicardial-only ablation was reported to be associated with a favourable long-term outcome of VT ablation in nonischemic cardiomyopathy (1, 3). Maccabelli et al. reported that pre-procedural scar imaging by DE-MRI and electroanatomical mapping support the necessity of epicardial ablation approach in patients with prior myocarditis (4). The results of Berte et al. also showed a good qualitative correlation between epicardial abnormal ventricular activities (LAVA) and the distribution of scar on DE-MRI in patients with epicardial-only substrates after prior myocarditis (11). In agreement with these results, our data demonstrate that patients with epicardial-only DE-MRI substrates without endocardial involvement had no or only minimal endocardial low voltage and epicardial ablation was needed in all patients. However, epicardial ablation in the basal lateral LV may be complicated by the proximity to the circumflex artery and epicardial fat tissue in the atrioventricular groove. Endocardial exit sites from midmyocardial or epicardial VT reentry circuits can be an appropriate target for endocardial ablation of nonischemic VT in some

patients. Preprocedural DE –MRI may help to detect endocardial targets for ablation of monomorphic VT in patients with LV nonischemic cardiomyopathy.

Limitations

The study was a retrospective case series of 12 patients with predominantly epicardial scars on DE-MRI in nonischemic cardiomyopathy and not a prospectively designed study. Cardiac 3 T –MRI studies were performed before ICD implantation in all patients of this study. Unfortunately, in our institution many patients with recurrent VT in nonischemic cardiomypathy cannot undergo MRI because of a non-MRI compatible device. It is possible that the freedom from VT recurrence after prior myocarditis may be due to a favourable spontaneous progress of the disease rather than to the effect of ablation in some patients. The number of patients is too small to propose recommendations for ablation of monomorphic epicardial VT in nonischemic cardiomyopathy but the results of this study strongly confirm the clinical relevance of preprocedural DE – MRI in patients with monomorphic VT in nonischemic cardiomyopathy.

CONCLUSION

Endocardial breakthroughs from predominantly epicardial DE –MRI substrates in LV nonischemic cardiomyopathy are often located near the ventricular base in the perivalvular region and correlate with endocardial exit sites from predominantly epicardial VT reentry circuits. DE – MRI may help to identify endocardial ablation targets in patients with VT after prior myocarditis and other forms of nonischemic cardiomyopathy.

Author contribution

CR gave the concept, designed the study, analyzed and interpreted the data, statistics and approved the article. BH, TK, CB, MF and MU analyzed, interpreted, and collected the data and approved the article.

REFERENCES

1. Cano O, Hutchinson M, Lin D, et al. Electroanatomic substrate and ablation outcome for suspected epicardial ventricular tachycardia in left ventricular non-ischemic cardiomyopathy. J Am Coll Cardiol 2009; 54: 799-808.
2. Hsia HH, Callans DJ, Marchlinski FE. Characterization of endocardial electrophysiological substrate in patients with nonischemic cardiomyopathy and monomorphic ventricular tachycardia. Circulation 2003; 108: 704-710.
3. Soejima K, Stevenson WG, Sapp JL, et al. Endocardial and epicardial radiofrequency ablation of ventricular tachycardia associated with dilated cardiomyopathy: the importance of low-voltage scar. J Am Coll Cardiol 2004; 43: 1834-1842.
4. Maccabeli G, Tsiachris, D, Silberbauer J, et al. Imaging and epicardial substrate ablation of ventricular tachycardia in patients late after myocarditis. Europace 2014; 16: 1363-1372.
5. Dello Russo A, Casella M, Pieroni M, et al. Drug-refractory ventricular tachycardia following myocarditis : endocardial and epicardial radiofrequency catheter ablation. Circ Arrhythm Electrophysiol 2012; 5: 492-498.
6. Komatsu Y, Daly M, Sacher F, et al. Endocardial ablation to eliminate epicardial arrhythmia substrate in scar-related ventricular tachycardia. J Am Coll Cardiol 2014; 63: 1416-1426.
7. Nazarian S, Bluemke DA, Lardo AC, et al. Magnetic resonance assessment of the substrate for inducible ventricular tachycardia in nonischemic cardiomyopathy. Circulation 2005; 112: 2821-2825.
8. Bogun FM, Desjardins B, Good E, et al. Delayed – enhancement magnetic resonance imaging in non-ischemic cardiomyopathy : utility for identifying the ventricular arrhythmia substrate. J Am Coll Cardiol 2009; 53: 1138-1145.

9. Mukherjee RK, Whitaker J, Willians SE, et al. Magnetic resonance imaging guidance for the optimazation of ventricular tachycardia ablation. Europace 2018; 20: 1721-1732.
10. Herkommer B, Fiek M, Reithmann C. Findings on magnetic resonance imaging of fascicular ventricular tachycardia. J Interv Cardiac Electrophysiol 2014; 7: 456-462.
11. Berte B, Sacher F, Cochet H, et al. Postmyocarditis ventricular tachycardia in patients with epicardial-only scar: a specific entity requiring a specific approach. J Cardiovasc Electrophysiol 2015; 26: 42-50.
12. Aliot EM, Stevenson WG, Almentdral-Garrote JM, et al. EHRA/HRS Expert consensus on catheter ablation of ventricular arrhythmias: developed in a partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the Heart Rhythm Society (HRS); in collaboration with the American College of Cardiology (ACC) and the American Heart Assocation (AHA). Heart Rhythm 2009; 6: 866-933.
13. Sosa E, Scanavacca M, D´Avila A, et al. A new technique to perform epicardial mapping in the electrophysiology laboratory. J Cardiovasc Electrophysiol 1996; 7: 531-536.
14. Stevenson WG, Friedman PL, Sager PT, et al. Exploring postinfarction reentrant ventricular tachycardia with entrainment mapping. J Am Coll Cardiol 1997; 29: 1180-1189.
15. Tada H, Ito S, Naito S, et al. Idiopathic ventricular arrhythmia arising from the mitral annulus. A distinct subgroup of idiopathic ventricular arrhythmias. J Am Coll Cardiol 2005; 45: 877-886.
16. Reithmann C, Herkommer B, Fiek M. Epicardial ventricular tachycardia substrate visualized by magnetic resonance imaging: need for a transpericardial ablation approach? Clin Res Cardiol 2016; 105: 827-837.

17. Mahrholdt H, Goedecke C, Wagner A, et al. Cardiovascular magnetic resonance assessment of human myocarditis: a comparison to histology and molecular pathology. Circulation 2004; 109: 1250-1258.
18. Arenal A, Perez-David E, Avila P, et al. Noninvasive identification of epicardial ventricular tachycardia substrate by magnetic resonance-based signal intensity mapping. Heart Rhythm 2014; 11: 1456-1464.
19. Karamitsos TD, Francis JM, Myerson S, et al. The role of cardiovascular magnetic resonance imaging in heart failure. J Am Coll Cardiol 2018; 54: 1407-1424.
20. Itoh T, Doppalapudi H, Yamada T et al. Epicardial ventricular tachycardia successfully ablated from the left atrium in a case with a prior mitral valve repair. Europace 2017; 8:1356.

FIGURES LEGENDS

Fig. 1. VTs with endocardial and epicardial exits associated with a predominantly epicardial VT substrate in a 69 year-old patient with prior myocarditis (pt. 1). **A** DE-MRI in a short-axis view demonstrating the epicardial DE-MRI substrate. DE-MRI in long axis view (**B**) and modified 2-chamber view (**C**) showing the breakthrough from the epicardial substrate to the endocardium adjacent to the mitral annulus. MV, mitral valve. **D** 12-lead ECG of the clinical VT1 with endocardial exit. **E** Endocardial electroanatomical map (CARTO) in a left lateral projection. Red represents areas of very low voltage (< 0.5mV). The red dots indicate endocardial sites where VT1 could be successfully ablated. The white dot indicates the site where concealed entrainment of VT1 was performed. **F** Left. Concealed entrainment of VT1 by pacing from an endocardial site at the border of the low voltage area. VT cycle length was 320ms. Stimulus – QRS (S – QRS) interval was 70ms. Post pacing interval was 330ms. Right. Intracardiac electrograms during sinus rhythm at the successful ablation site showing a small atrial and large ventricular potential consistent with a site near the mitral annulus. **G** Left.12-lead ECG of the clinical VT2 with epicardial exit. Right. Epicardial pace map with a S – QRS interval of 60 ms and a good QRS match at a site at the superior aspect of the epicardial very low voltage region (white dot). **H** Left. 12-lead ECG of the clinical VT3 with epicardial exit. Right. Epicardial pace map with a S – QRS interval of 50 ms and a QRS match in 11/12 ECG leads at the inferior aspect of the epicardial very low voltage region (white dot). **I** Abnormal epicardial electrograms (isolated diastolic potentials) during sinus rhythm within the epicardial low voltage zone. **K** Epicardial electroanatomical map (CARTO) in a posterior projection. Red represents areas of very low voltage (< 0.5mV). The red dots indicate epicardial sites where VT2 and VT3 could be successfully ablated in a very low voltage zone between the exits of VT2 and VT3.

Fig. 2. Successful endocardial-only VT ablation in a 72 year-old patient with predominantly epicardial VT substrate. (pt. 2) **A** DE-MRI in a short axis view demonstrating the epicardial VT substrate. **B** DE-MRI in 2-chamber view showing the endocardial breakthrough from the epicardial substrate near the mitral annulus. LAA, left atrial auricle. **C** 12-lead ECG of the VT. **D** Left. Intracardiac electrograms from the distal electrode pair of the ablation catheter (ABLd) at the successful endocardial ablation site in the anterolateral LV. Right. Intracardiac electrograms during sinus rhythm at the successful ablation site showing a very small atrial and large ventricular electrogram consistent with a site in proximity to the mitral annulus.

Fig.3. Predominantly epicardial VT substrate with transmural progression in a 46 year-old patient with VT post-myocarditis (pt. 7). **A** DE-MRI in short axis view demonstrating the epicardial VT substrate. **B** DE-MRI in long axis showing the endocardial breakthrough from the epicardial substrate. **C** Electroanatomical map of the endocardial LV in modified left anterior oblique projection. Purple represents areas of highest voltage (normal endocardium). The red dots indicate sites where the VT could be successfully ablated at the endocardial exit site of the VT reentry circuit. **D** Left. 12-lead ECG of the VT. Right. Pace map with a good QRS match at the endocardial site in LV where the VT could be successfully ablated. **E** Intracardiac electrograms from the distal and proximal electrode pair of the ablation catheter (ABLd and ABLp) at the successful endocardial ablation site in the posterolateral LV.

Fig.4. Epicardial-only VT substrate in a 67 year-old patient after prior myocarditis (pt. 10). DE-MRI in short axis view (**A**) and long axis view (**B**) demonstrating the epicardial-only VT substrate. **C** Endocardial electroanatomical map (CARTO) of the LV in a LAO projection. No endocardial very low voltage was detected and no endocardial ablation was performed. **D** 12-lead ECG of the clinical VT. **E** Epicardial recordings (ABLd and ABLp) showing abnormal epicardial electrograms (isolated diastolic potentials) at sites with a good pace map QRS match and a prolonged stimulus – QRS interval. **F** Epicardial electroanatomical map (CARTO) in a left lateral projection. Potential-guided ablation (red dots) was successfully performed in a region of low voltage (< 1,5mV) with a good pace map QRS match and a prolonged S – QRS interval.