New insights on post-myocardial infarction ventricular tachycardia ablation: defining patient-tailored endpoints to improve outcome

De Riva Silva, M.

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Fast non clinical ventricular tachycardia inducible after ablation in patients with structural heart disease: Definition and clinical implications

Marta de Riva, MD, Masaya Watanabe, MD, PhD, Sebastiaan R.D. Piers, MD, PhD, Olaf M. Dekkers, MD, PhD, Micaela Ebert, MD, PhD, Jeroen Venlet, MD, Serge A. Trines, MD, PhD, Martin J. Schalij, MD, PhD, Daniel A. Pijnappels, MD, PhD, Katja Zeppenfeld, MD, PhD

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ABSTRACT

Background

Noninducibility of ventricular tachycardia (VT) with an equal or longer cycle length (CL) than the clinical VT is considered the minimum ablation endpoint in patients with structural heart disease (SHD). Since their clinical relevance remains unclear, fast nonclinical VTs are often not targeted. However, an accepted definition for fast VT is lacking. The shortest possible CL of a monomorphic reentrant VT is determined by the ventricular refractory period (VRP).

Objectives

We propose a patient-specific definition for fast VT based on the individual VRP (fVT_{VRP}) and assess the prognostic significance of persistent inducibility after ablation of fVT_{VRP} for VT recurrence.

Methods

Out of 191 patients with prior myocardial infarction or with nonischemic cardiomyopathy undergoing VT ablation, 70 (63±13 years, 64% ischemic) remained inducible for a nonclinical VT and comprised the study population. A fVT_{VRP} was defined as any VT with CL ≤VRP_{400} +30ms. Patients were followed for VT recurrence.

Results

After ablation, 30 patients (43%) remained inducible exclusively for fVT_{VRP} and 40 (57%) for any slower VT. Patients with only fVT_{VRP} had a 3-year VT free-survival of 64% (CI95%:46-82%) compared to 27% (CI95%:14-48%) for patients with any slower remaining VT (P=0.013). Inducibility of only fVT_{VRP} was independently associated with lower VT recurrence (HR 0.38, CI95%:0.19-0.86; P=0.019). Within 36 patients inducible for any fVT_{VRP}, only one recurred with a fVT_{VRP}.

Conclusion

In patients with SHD, inducibility of exclusively fVT_{VRP} after ablation is associated with low VT recurrence.

INTRODUCTION

Noninducibility of the (presumed) clinical ventricular tachycardia (VT) is considered the minimum endpoint for radiofrequency catheter ablation (RFCA) in patients with structural heart disease (SHD)[1]. Since the clinical relevance of induced nonclinical fast VTs remains controversial[2-8], many laboratories only target VT with equal or longer cycle length (CL) than clinical VT but not fast remaining VTs (1). A major limitation for data comparison is the lack of an accepted definition for fast VT.

It is generally accepted that the majority of VTs in patients with SHD are caused by reentry facilitated by areas of slow conduction and fixed or functional conduction (pseudo-) block within the scar[9, 10]. Substrate-based ablation approaches target abnormal electrograms consistent with slow conduction during sinus rhythm assuming that all induced VTs depend on slow conducting regions[11-14]. However, fast nonclinical VTs may remain inducible even after complete ablation of the electroanatomical substrate[13, 14].

As the wavelength, the product of the myocardial conduction velocity and refractory period determines the shortest possible CL of a reentrant arrhythmia, Monomorphic VTs with a CL close to ventricular refractory period (VRP) may have a distinct underlying substrate, may require different induction protocols and may occur less often spontaneously.

The objectives of our study were 1) to propose a definition for fast VT based on the individual VRP (fVT_{VRP}) and 2) to assess the prognostic value of persistent inducibility of nonclinical fVT_{VRP} based on our proposed definition in patients with SHD.

METHODS

Study population

Consecutive patients referred for ablation of monomorphic VT after prior myocardial infarction (MI) or with nonischemic cardiomyopathy (NICM) to the Leiden University Medical Centre between January 2009 and December 2013 (post MI patients) and between January 2007 and December 2013 (NICM patients) and with partial success as acute procedural outcome were included. Partial success was defined as elimination of all clinical VTs but persistent inducibility of ≥1 nonclinical monomorphic VT.

All patients were treated according to our standard clinical protocol and provided informed consent. The Dutch Central Committee on Human-related Research (CCMO)

permits use of anonymous data without prior approval of an Institutional Review Board if the data are obtained for patient care and if the data do not contain identifiers that could be traced back to the individual patient.

Electrophysiological study

Before the procedure, antiarrhythmic drugs (AADs) except for amiodarone were discontinued. The programmed electrical stimulation (PES) protocol consisted of burst pacing and stimulation with 3 basic CLs (S1, 600, 500 and 400ms) and 1 to 3 extrastimuli (S2-S4) down to 200ms or refractoriness, from RV apex and RV outflow tract. A stimulus strength of twice the diastolic threshold was used for stimulation and a pause of 3 seconds between trains of ventricular pacing was applied. The first extrastimulus (S2) from the RV apex was used to determine the individual VRP for 2 drive CLs of 400 and 600ms: starting with a coupling interval (CI) of 350ms, S2 CI was decreased by 10ms until VRP was reached. Positive PES endpoint was the induction of a sustained monomorphic VT lasting >30 seconds or requiring termination because of hemodynamic instability. Induced VTs were classified as: clinical, in case of 12/12 lead electrocardiographic (ECG) match and a difference in VTCL ≤30ms with a previously documented VT, presumptive clinical, when VTCL was ±30ms of an ICD recorded VT, or nonclinical, when the previous criteria were not fulfilled.

Based on individual VRP at a drive CL of 400ms (VRP_{400}), VTs were defined as fast if VTCL was ≤VRP_{400} +30ms (fVT_{VRP}). This was based on the consideration that the possible shortest CL of a reentrant VT is determined by VRP in conjunction with the myocardial conduction velocity;[15] theoretically, no reentrant VT can have a shorter CL than the minimal VRP for a given situation. As the individual VRP may show variations (depending among others on the autonomic balance) we used VRP +30ms for the definition of fVT_{VRP}, which is in line with prior reports allowing a range of VTCL ±30ms for the definition of presumed clinical VT[5, 8, 16].

To evaluate the underlying VT mechanism, an attempt was made to entrain and terminate the VT by pacing unless VT was polymorphic.

Electroanatomical mapping and catheter ablation

Electroanatomical LV endocardial mapping was performed in all patients. Epicardial mapping was performed through a subxiphoid puncture if appropriate[5, 17]. Voltage maps were created with a 3.5mm irrigated-tip catheter (NaviStar ThermoCool; Biosense Webster, Inc., Diamond Bar, CA, USA) and the CARTO system. Electrograms were filtered at 30 to 400 Hz (bipolar) and 1 to 240 Hz (unipolar). The areas with bipolar voltage ≤0.5mV and 0.5-1.5mV were defined as dense scar and scar border zone respectively.

EGMs consistent with the presence of local slow conduction were tagged in the map (fragmented, late potentials [onset after QRS, separated by an isoelectric segment from the far-field signal >20ms). Reentry isthmus sites were identified with the combination of entrainment-, activation- and pace- mapping for stable VTs. For unstable VTs, re-entry isthmus sites were identified based on the combination of EGM characteristics and pace-mapping (morphologhy match with an induced VT ≥10/12 and stimulus-to-QRS delay >40ms). In addition, all late and prolonged, fragmented potentials were targeted, independently of their relation to an induced VT.[5, 8] RF energy was delivered at 35-50W (maximum temperature, 43°C; flow rate, 20-30ml/min) until pacing with 10mA and 2ms stimulus failed to capture.

Procedural endpoint

All clinical VTs were targeted for ablation. Nonclinical VTs were also targeted with the exception of VTs with CL close to the VRP which were considered of unknown clinical relevance. The procedure was stopped when multiple electrical cardioversions for non-clinical VTs were required or no additional substrate for VTs could be identified.

Group definition

After ablation, the entire PES protocol was repeated. Patients were divided into 2 groups according to the CL of remaining nonclinical VTs: "FVT_{VRP} group" consisting of patients in whom only fVT_{VRP} were inducible after ablation and "Non-fVT_{VRP} group" in whom at least one slower VT remained inducible.

Post-procedural management and follow-up

Implantable cardioverter defibrillator (ICD) implantation was offered to all patients. All ICDs were programmed with the slowest VT detection zone at ≥10 bpm below the slowest clinical or induced VT (VT1). The programming of detection time/number of intervals for the VT1 zone was left at the discretion of the operator, tailored normally to the hemodynamic tolerance to prior documented VTs. In the VF zone (and if programmed, in the fast VT [VT2] zone) a detection time of 2.5 seconds or 18 of 24 intervals was programmed. Patients were followed at the outpatient clinic 3 months after RFCA and every 6 months thereafter or in case of ICD therapies or symptoms suggesting VT. For the analysis, the maximum follow-up period was set at 3 years to avoid the influence of disease progression on the occurrence of new arrhythmic events.

Endpoint definition

VT recurrence was considered as any VT treated by the ICD or registered in the monitor zone lasting>30 seconds. In patients without ICD, recurrence was defined as any VT >30 seconds documented on 12-lead ECG or 24-hour Holter. VT recurrence was further cat-

egorized in (1) any VT recurrence, regardless of VTCL and (2) fVT_{VRP} recurrence according to the definition.

Statistical analysis

Continuous variables are reported as mean±SD or medians with interquartile ranges (IQR) and compared using Student t-test or Mann–Whitney *U* test. Categorical variables are presented as numbers and percentages(%) and compared using Chi-squared test or Fisher exact test. Continuous paired variables were compared with Wilcoxon signed rank test. To estimate and compare freedom from VT recurrence between groups, Gray's test was performed to take competing risk of death into account. Predictors of VT recurrence were assessed by Fine-Gray subdistribution hazard model, considering all-cause death as competing risk. Independent predictors of VT recurrence were analysed with multivariable models using a backward stepwise selection. Variables with a p value ≤0.10 were initially included. At each step the least significant variable was removed from the model, until all variables reached a p value <0.20. All tests were 2-sided and a p value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS version 20.0 (SPSS Inc, Chicago, IL).

RESULTS

Patients

Baseline characteristics and procedural outcome of the entire 191 patients are shown in **Supplementary Table 1**. Of these patients, 70 (45 post-MI [64%] and 25 NICM [36%], 63±13 years, 89% male, LVEF 35±12%) with partial procedural success comprised the study population. Based on the CL of remaining VTs after ablation, 30 patients (43%) with only fVT_{VRP} constituted the "fVT_{VRP} group" and 40 patients (57%) with any slower VT the "non-fVT_{VRP} group". Six patients in non-fVT_{VRP} group remained also inducible for fVT_{VRP}.

Compared to the patients in fVT_{VRP} group, those in non-fVT_{VRP} group had lower LVEF (31±11% vs. 39±11%; P=0.007), had more frequently impaired renal function (58% vs. 10%; P<0.001), slower VTs at presentation (clinical VTCL 413±84ms vs. 344 ± 73ms; P <0.001) and were more often on amiodarone at admission (70% vs. 23%; P <0.001). Baseline characteristics of the patients are displayed in **Table 1.**

Electrophysiological study and catheter ablation

Electrophysiological parameters and procedural data are shown in **Supplementary Table 2**.

Table 1. Baseline clinical characteristics

	All (n=70)	FVT_{VRP} (n=30)	Non-fVT_{VRP} (n=40)	P
Age, years	63±13	60±15	65±12	0.159
Male sex	62 (89%)	28 (93%)	34 (85%)	0.278
Underlying disease				
Prior MI	45(64%)	21(70%)	24(60%)	0.386
NICM	25(36%)	9(30%)	16(40%)	0.386
LVEF, %	35±12	39±11	31±11	0.007
Prior admission for heart failure	29(41%)	10(33%)	19(48%)	0.234
Hypertension	22(31%)	7(23%)	15(38%)	0.206
Diabetes Mellitus	5(7%)	4(13%)	1(3%)	0.082
History of atrial flutter/fibrillation	23(33%)	9(30%)	14(35%)	0.659
Renal failure	26(37%)	3(10%)	23(58%)	<0.001
ICD before ablation	54(77%)	21(70%)	33(83%)	0.218
Prior VT ablation	15(21%)	6(20%)	9(23%)	0.801
Clinical VT CL, ms	384±86	344±73	413±84	<0.001
VT clinical presentation				
Electrical storm*	11(16%)	2(7%)	9(23%)	0.072
Incessant VT	11(16%)	3(10%)	8(20%)	0.255
ICD shocks	36(51%)	15(50%)	21(53%)	0.836
Below ICD detection	10(14%)	4(13%)	6(15%)	0.844
First episode	17(24%)	10(33%)	7(18%)	0.126
Failed AADs before ablation				
Amiodarone	35(50%)	7(23%)	28(70%)	<0.001
Sotalol	25(36%)	13(40%)	12(30%)	0.249
Class 1 AAD	7 10%)	3(10%)	4(10%)	1.000

VT indicates ventricular tachycardia; MI, myocardial infarction; NICM, nonischemic cardiomyopathy; LVEF, left ventricular ejection fraction; ICD, implantable cardioverter defibrillator; CL, cycle length and AAD, anti-arrhythmic drug. *Electrical storm: ≥3 ICD shocks within 24 hours.

VRP at a drive CLs of 600 and 400ms were comparable between fVT_{VRP} and non-fVT_{VRP} groups (260±31ms and 226±23ms vs. 267±23ms and 234±26ms; P=0.387 and P=0.236 respectively).

Patients in non-fVT_{VRP} group were inducible for a larger number of distinct VTs (median 4 [IQR 3-6] vs. 3 [IQR 2-5]; P=0.005) which were slower (mean VTCL 370±61ms vs. 286±53ms; P <0.001) and had more often a left bundle branch block morphology (80% vs. 53%; P=0.017).

Characteristics of remaining VTs

After ablation, a total of 87 nonclinical VTs (median 1 VT per patient [IQR 1-1]) remained inducible. Remaining VTCL was 230±24ms in fVT_{VRP} and 310±41ms in non-fVT_{VRP} groups. With regard to the induction protocol for post-RFCA remaining VTs, more often triple extrastimuli (94% VTs in fVT_{VRP} vs. 72% in non-fVT_{VRP} group, P=0.01) and the shorter CIs of the extrastimuli (224±30ms in fVT_{VRP} vs. 257±28ms in non-fVT_{VRP} group; P <0.001) were required in the fVT_{VRP} group. An attempt of rapid pacing for entrainment and VT termination was performed in 80 (92%) of 87 remaining VTs, resulting in successful VT termination in 36 VTs (45%; 12 (39%) in fVT_{VRP} vs. 24 VTs (49%) in non-fVT_{VRP} group; P=0.368). Details of the induction mode and response to overdrive pacing of remaining VTs are shown in **Supplementary Table 3**.

Post-procedural management

All but one patient were discharged with an ICD. In the majority, AAD regimen remained unchanged after ablation. Thirty-four patients (49%) were discharged on amiodarone, 18 on sotalol (26%) and 6 (9%) on a class I AAD. Patients in non-fVT_{VRP} group were more often discharged on amiodarone (27 patients [68%] vs. 7 [23%] in fVT_{VRP} group; P <0.001)

Impact of remaining VT cycle length on the incidence and characteristics of recurrent VTs

During a median follow-up of 31 months (IQR 16-36), 36 patients (51%) had VT recurrence (median time to recurrence 61 days (IQR 30-407)). Only one patient was lost to follow-up.

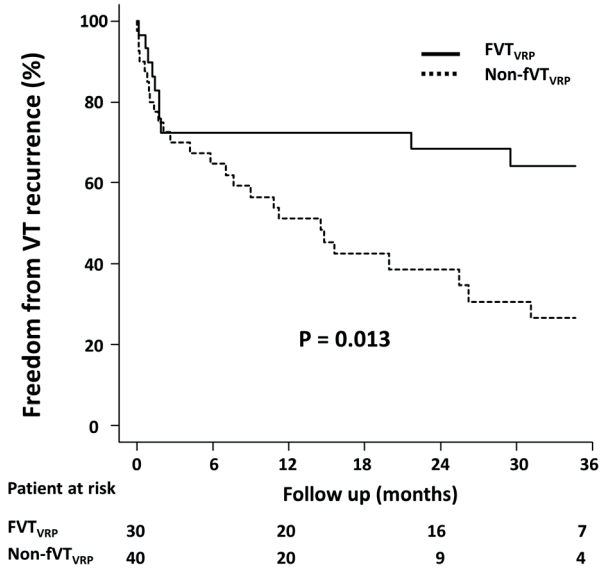
Compared to non-fVT_{VRP} group, patients in fVT_{VRP} group had a significantly lower incidence of VT recurrence (10 [33%] vs. 26 patients [65%], HR 0.40: CI95% 0.18-0.80; P=0.01). Patients in fVT_{VRP} group had a 3-year VT recurrence-free survival of 64% (CI95% 46-82%) compared to 27% (CI 95% 14-48%) for those in non- fVT_{VRP} group (P=0.013) **(Figure 1)**.

The predictive value of inducibility of only fast VT_{VRP} for absence of VT recurrence was 90% in our population. If a fixed arbitrary value for the definition of fast VT was used (VT CL ≤ 250ms), the predictive value for absence of VT recurrence decreased to 84%. This difference did not reach, however, statistical significance, probably because of the limited number of patients included in the study (P=0.257).

Since patients in the non-fVT_{VRP} group were more often on amiodarone at the time of the procedure, which may have had an effect both in the induced VTCL but also in the outcome after ablation, we performed a subanalysis including only patients off amiodarone. This analysis showed a similar trend of lower VT recurrence in the fVT_{VRP} group (3-year

VT free survival 63% [95% CI 38-79%] in fVT_{VRP} group vs 20% (95% CI 1-54%) in non-fVTgroup; P=0.12). Recurrent VTs were significantly slower than remaining VTs in both groups (remaining VTCL and VTCL of first recurrent VT were 235±28ms vs. 311±61ms in fVT_{VRP} and 303±41ms vs. 381±74ms in non-fVT_{VRP} group; both P <0.001). However, there was no significant difference between the clinical VTCL before RFCA and the recurred VTCL (349±80ms vs. 311±61ms in fVT_{VRP} and 399±84ms vs. 381±74 ms in non-fVT_{VRP} group; P=0.54 and 0.755, respectively). In **Figure 2**, the CLs of clinical, remaining and first recurrent VT for each individual patient who had VT recurrence in fVT_{VRP} **(A)** and non-fVT_{VRP} group **(B)** are depicted.

Figure 1.
VT-free survival according to groups



fVT_{VRP} indicates fast ventricular tachycadia based on the individual ventricular refractory period; VT ventricular tachycardia.

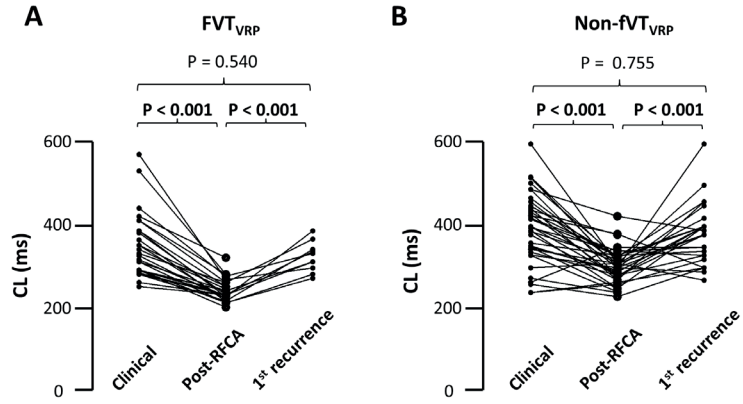
Predictors of VT recurrence

On multivariate analysis, inducibility of only fVT_{VRP} after ablation was independently associated with lower VT recurrence (HR 0.38: CI95% 0.19–0.86; P=0.019) **(Figure 3)**.

Recurrence and new occurrence of fVT_{VRP}s after ablation

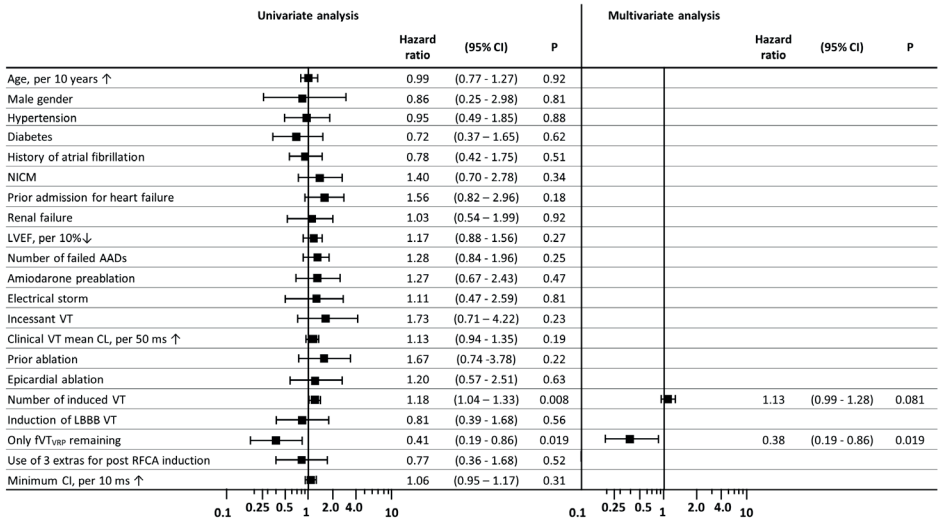
Among 36 patients in whom ≥1 fVT_{VRP} was inducible after RFCA (including 6 patients in non-fVT_{VRP} group), only one patient recurred with a fVT_{VRP} 2 months after the procedure. Three additional patients in non-fVT_{VRP} group experienced a fVT_{VRP} which was not induced during the procedure 4 days, 4 and 28 months after ablation. **Figure 4** shows the survival curve free from fVT_{VRP} for both groups. See **Supplementary Figure 1** for details.

Figure 2.



Cycle length of clinical, remaining VT (Post-RFCA) and recurrent VT at first recurrent event (1st Recurrence) in fVT_{VRP} (left panel) and non-fVT_{VRP} groups (right panel).
CL indicates cycle length; fVT_{VRP}, fast ventricular tachycadia based on the individual ventricular refractory period; RFCA, radiofrequency catheter ablation.

Figure 3.
Predictors of VT recurrence

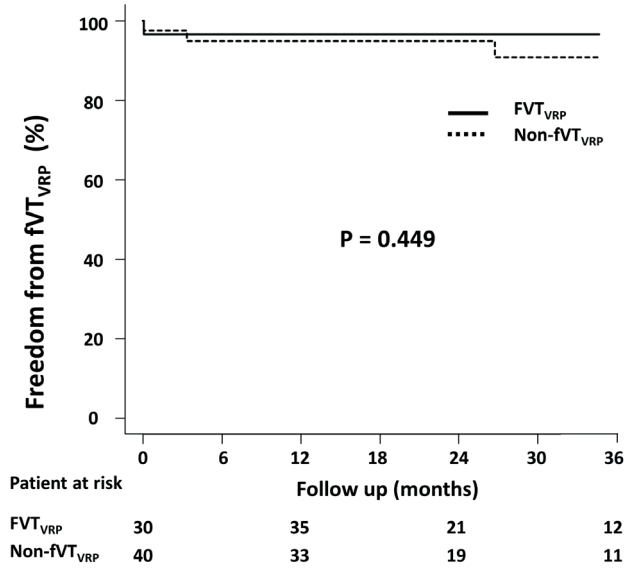


NICM indicates nonischemic cardiomyopathy; LVEF, left ventricular ejection fraction; AAD, anti-arrhythmic drug; and LBBB, left bundle branch block.

Complications

There was no procedure-related mortality. Four patients had complications of the vascular access. One patient with a basoseptal central isthmus developed predicted complete atrioventricular block after ablation. Pericardial bleeding requiring percutaneous drainage occurred in 2 of 19 patients undergoing pericardial access.

Figure 4.
FVT_{VRP} free survival according to groups



fVT_{VRP} indicates fast ventricular tachycadia based on the individual ventricular refractory period; VT ventricular tachycardia.

Mortality

Thirteen patients died during follow-up (4 [13%] in fVT_{VRP} and 9 [23%]) in non-fVT_{VRP} group; P=0.329). Cardiac death occurred in 9 patients (70%). No patient died suddenly. Heart failure was the leading cause of death in both groups (3 and 4 patients in fVT_{VRP} and non-fVT_{VRP} group, respectively). There was no difference in the incidence of cardiac death between groups (HR 1.53: 95% CI 0.40–7.24: P=0.543).

DISCUSSION

In the present study, we propose a patient-specific definition for 'fast VT' based on the individual ventricular refractory period (fVT_{VRP}) and evaluate the clinical relevance of persistent inducibility of nonclinical 'fVT_{VRP}' after ablation.

Patients with SHD who remained exclusively inducible for fVT_{VRP}, defined as a VT with CL ≤ individual VRP_{400} (+30ms) had a better VT-free survival compared to patients who remained inducible for any slower nonclinical VT. Inducibility of only fVT_{VRP} was associated with lower VT recurrence on multivariate analysis after adjusting for confounding factors. These nonclinical fVT_{VRP} were typically inducible with multiple short coupled

extrastimuli and occurred rarely spontaneously questioning the need for targeting them by ablation.

A proposal for an individualized definition of fast VT

The prognostic impact of inducibility of previously undocumented VTs after ablation, in particular of fast VTs, remains unclear[2-8]. Accordingly, many electrophysiology laboratories employ noninducibility of VTs with similar or longer CL than clinical VT as one procedural endpoint and accept persistent inducibility of faster VTs[1]. However, an important limitation for data comparison and endpoint recommendation is that a CL cutoff value to define a fast VT has not been established. Previously applied arbitrary definitions are based on ICD zones rates (typically<320ms)[18], hemodynamic tolerance, indeterminate VT-QRS morphology (former ventricular flutter) or comparison with the CL of clinically documented VTs[2].

The most common mechanism of VT in patients with SHD is reentry facilitated by slow conducting regions and fixed or functional conduction (-pseudo)block within scar tissue[9, 10]. This has been demonstrated by activation and entrainment mapping for slow tolerated VTs[19]. Substrate-based ablation approaches targeting electrograms consistent with slow conduction or poor coupling during sinus rhythm are based on the assumption that all induced VTs are dependent on regions of slow conduction[11-13]. However, fast VTs may remain inducible even after complete scar homogenization suggesting the presence of a different underlying substrate[13, 14].

In our study, we have defined fast VT for an individual patient (fVT_{VRP}) as a VT with a CL close to the VRP measured with a CL of 400ms, which derived from the rationale that the possible shortest CL of a reentrant VT is regulated by VRP in conjunction with the myocardial conduction velocity[15]. Determination of the VRP at the RV apex with a CL of 400ms cannot account for regional variations and the potential shortening of VRP at shorter CL. However, despite the complexity of rate-dependency and regional differences in VRP, our suggested cut-off may be clinically useful as an easily applicable surrogate for the shortest CL of inducible VT in an individual patient.

Clinical relevance of persistent inducibility of fVT_{VRP}. Do they need to be targeted?

Current expert consensus on VT ablation recommends elimination of clinical VT as the minimum endpoint for scar-related VT ablation[1]. However, spontaneous occurrence of non-targeted nonclinical VTs has been reported[7, 8]. In addition, persistent inducibility of any VT has been associated with an increased risk of VT recurrence favouring non-inducibility of any VT as ablation endpoint[5, 20]. Of note, highly variable acute success

results have been reported across studies (noninducibility of any VT in 38-77%) despite similar recurrence rates during follow-up (34-53%[2-4, 8, 13, 21]. This may be partly explained by the variation of PES protocols which are not standardized and not always (entirely) performed after ablation. Particularly, fast VT induction may depend on the application of the entire protocol including triple extrastimuli down to the refractory period. Of importance, in our study, triple extrastimulation and short coupled extrastimuli (mean CL: 224±30ms) were required for fVT_{VRP} induction in the majority of the patients. In addition, although a large range of remaining VTCL has been reported in patients with partial success (230-545ms)[7], data on its impact on VT recurrence are scarce.

To the best of our knowledge, our study is the first to systematically evaluate the influence of remaining VTCL on VT recurrence in patients in whom clinical VTs have been successfully abolished by ablation. Patients who remained exclusively inducible for fVT_{VRP} had a lower incidence of VT recurrence compared to those inducible for any slower VT. Patients with remaining slower VTs had lower LVEF, more often an impaired renal function, were more often on amiodarone and had a higher number of induced VTs, probably representing a more diseased population. However, inducibility of only fVT_{VRP} remained associated with lower VT recurrence after adjusting for baseline patient characteristics. Of importance, 3-year VT-free survival in patients rendered noninducible for any VT (complete success group) was comparable with those in fVT_{VRP} group (74%, CI95% 58-84% vs. 63%, CI95% 47-78%; P=0.156).

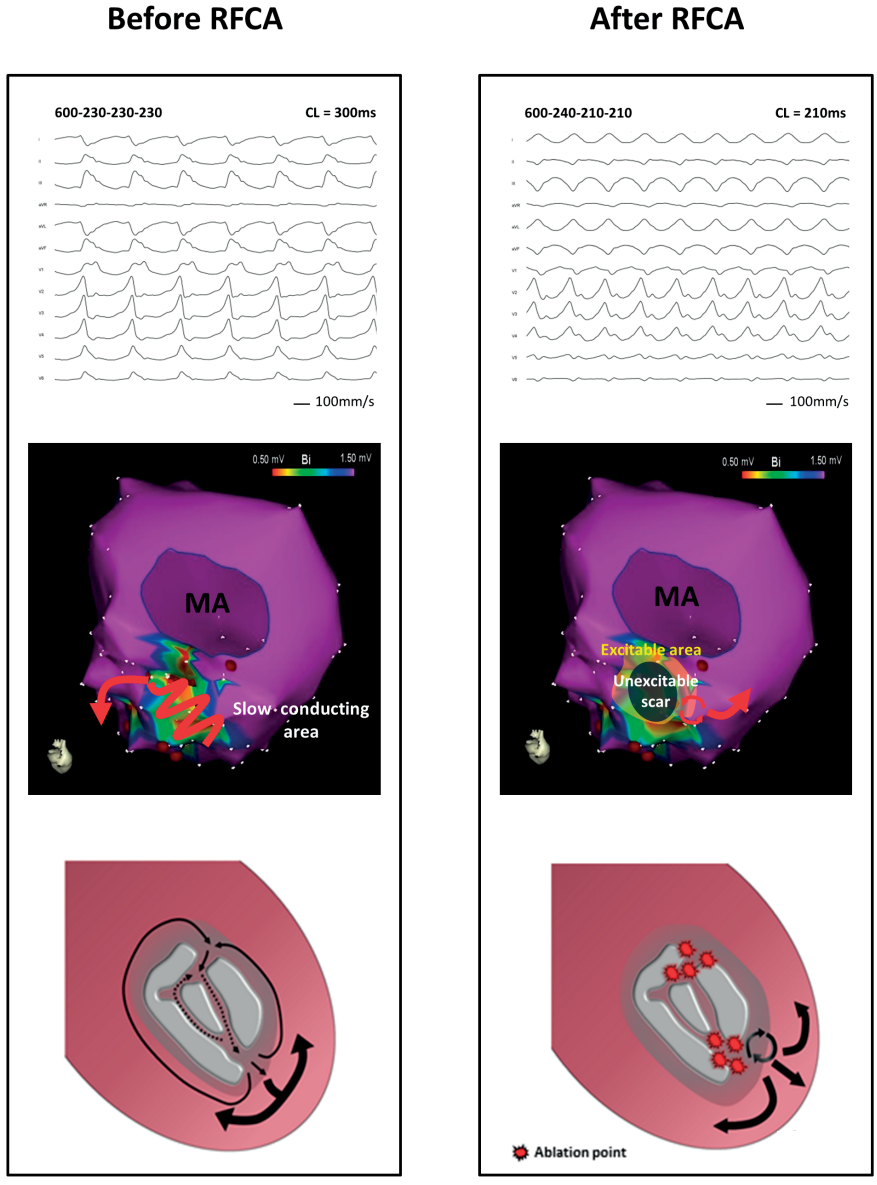
In addition, fVT_{VRP} occurred rarely spontaneously. No clinical VT before ablation fulfilled the criteria for fVT_{VRP} and only 4 out of 70 patients (6%) had a spontaneous fVT_{VRP} after the procedure. Of note, only 5 of the 70 patients (7%) were on an AAD at VT recurrence that was not present during VT induction and may therefore have prolonged the CL of the recurrent VT.

Our findings suggest that induction of fVT_{VRP} after ablation may not be prognostically relevant, questioning the need for targeting them by ablation. Prospective studies to confirm our hypothesis are warranted.

Potential underlying mechanisms and substrate for fVT_{VRP}

FVT_{VRP} have a CL close to the individual VRP, induction requires the application of multiple short coupled extrastimuli and they are typically inducible after slow conducting areas within the scar have been ablated. These fVT_{VRP} may have a different underlying substrate than macroreentrant VTs with an area of slow conduction identifiable during VT or stable sinus rhythm (**Figure 5**).

Figure 5.



Representative case of a patient with a prior inferoposterior MI. VT 12-lead ECGs (top), LV endocardial bipolar voltage maps (middle) in posteroanterior view color-coded according to the bar and schematic representations of the presumed VT mechanisms (bottom) before (left panel) and after RFCA (right panel) are shown. Before ablation, the clinical VT (CL=300ms, left top) was induced with triple extrastimulation. Ablation on the exit site of the slow conducting area terminated the VT (left middle, bottom). After rendering the scar core unexcitable (dark grey area, right middle) by RF, a nonclinical fVT_{VRP} (CL=210ms, VRP_{400}=200, right top) was induced with triple extrastimulation but shorter coupling intervals. According to its morphology, the fVT_{VRP} exit site was assumed at the septal edge of the scar (right middle). The myocardium in the scar border zone (grey shaded area) remained excitable and may have been involved in the maintenance of a small reentrant circuit giving rise to the fast fVT_{VRP} (right bottom). MA indicates mitral annulus; PA, posteroanterior

Functional reentry is a mechanism of reentrant excitation with an unexcitable gap in its center, and could represent itself as a scroll wave in the affected ventricles. Although this concept is often used to explain the mechanism of meandering reentrant circuits giving rise to fibrillatory activity, the presence of more stationary, yet functional, reentrant circuits have been demonstrated in a prior experimental study[22] and in human ventricle[23] and atria, where its source was localized near fibrotic areas. In addition, a scroll wave as source of monomorphic VT has been case reported[24]. Even after eliminating slow conducting regions, the border to normal myocardium may still serve as a source for scroll wave stabilization, thereby creating the conditions favoring monomorphic VT in which the CL would indeed be determined by VRP. More experimental approaches, including animal experiments, might be needed to elucidate the potential substrate and mechanism for fVT_{VRP}.

Limitations

The main limitation of this study is its retrospective observational nature. The VRP for definition of fVT_{VRP} was always determined from the RV apex at a basic drive CL of 400ms. We can therefore not exclude that regional variations in the VRP (RV vs LV ERP, VRP in infarcted vs non-infarcted myocardium) as well as variations in the VRP related to the VTCL (namely during fast VTs, the VRP is expected to be shorter) could have impacted our results. Inducibility of fVT_{VRP} in the non-fVT_{VRP} group might be underestimated because reinduction was stopped when any sustained VT was induced with less aggressive induction protocols. Reproducibility of fVT_{VRP} induction after ablation was generally not performed. The anti-arrhythmic regimen after ablation was left at the discretion of the referring cardiologist and it might have influenced the incidence of VT recurrence in some patients.

CONCLUSION

In patients with SHD, inducibility after ablation of only fVT_{VRP} is associated with low VT recurrence during follow-up. In addition, fVT_{VRP} occur rarely spontaneously. These findings suggest that eliminating these VTs might not be required, questioning noninducibility of any VT as a prognostically relevant ablation endpoint.

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Supplementary table 1. Baseline characteristics and procedural outcome of the entire population

	All
	(n=191)
Age, years	64±13
Male sex	161 (84%)
LVEF, %	37 ± 13
Prior admission for heart failure	72 (38%)
Hypertension	81 (42%)
Diabetes Mellitus	28 (15%)
History of atrial flutter/fibrillation	60 (31%)
Renal failure	61 (32%)
ICD before ablation	124 (65%)
Prior VT ablation	34 (18%)
Clinical VT CL, ms	371 ± 81
VT clinical presentation	
Electrical storm*	23 (12%)
Incessant VT	27 (14%)
Failed AADs before ablation	
Amiodarone	78 (41%)
Sotalol	53 (28%)
Class 1 AAD	14 (7%)
Epicardial ablation	56 (49%)
Fluoro time, min	38 ± 20
Procedure time, min	213 ± 85
Acute procedural outcome	
Complete success	77 (40%)
Partial success	70 (37%)
Failure	31 (16%)
Undetermined	13 (7%)

MI indicates myocardial infarction; NICM, non-ischemic cardiomyopathy; LVEF, left ventricular ejection fraction; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia; CL, cycle length and AAD, anti-arrhythmic drug *Acute procedural outcome was undetermined because of incomplete PES after RFCA

Supplementary table 2. Electrophysiological and procedural characteristics

	All (n=70)	FVT_{VRP} (n=30)	Non-fVT_{VRP} (n=40)	P
Amiodarone during the procedure	34 (49%)	7 (23%)	27 (68%)	<0.001
VRP drive CL 600ms	264 ± 27	260 ± 31	267 ± 23	0.387
VRP drive CL 400ms	230 ± 25	226 ± 23	234 ± 26	**0.236**
Number of induced VTs	4 (3-5)	3 (2-5)	4 (3-6)	0.005
Induced VT max CL, ms	423 ± 126	356 ± 97	469 ± 124	<0.001
Induced VT min CL, ms	262 ± 43	237 ± 40	281 ± 36	<0.001
Induced VT mean CL, ms	335 ± 71	286 ± 53	370 ± 61	<0.001
Induction of clinical/presumptive clinical VT	65 (94%)	26 (87%)	39 (98%)	0.082
Epicardial ablation	20 (29%)	4(13%)	4(13%)	0.242
Procedure time	204 ± 69	196 ± 60	209 ± 76	0.476
Fluoroscopy time	37 ± 17	34 ± 12	40 ± 20	0.165
Number of remaining VTs	1 (1-1)	1 (1-1)	1 (1-2)	0.100
Remaining VT max CL, ms	271 ± 49	232 ± 25	319 ± 39	<0.001
Remaining VT min CL, ms	282 ± 55	230 ± 26	302 ± 40	<0.001
fVT_{VRP} remaining	36 (51%)	30 (100%)	6 (15%)	<0.001

VT indicates ventricular tachycardia; VRP, ventricular refractory period; max, maximum; CL, cycle length and min, minimum.

Supplementary table 3. Mode of induction and termination of remaining VTs

	All (n=70)	FVT_{VRP} (n=30)	Non-fVT_{VRP} (n=40)	P
Number of remaining VTs	87	34	53	
Mode of induction				
Spontaneous or catheter manipulation	5 (6%)	1 (3%)	4 (8%)	0.368
Single or double extrastimuli	12 (14%)	1 (3%)	11 (21%)	0.010
Triple extrastimuli	70 (80%)	32 (94%)	38 (72%)	0.010
Min coupling interval for induction	244 ± 33	224 ± 30	257 ± 28	<0.001
Mode of termination				
Spontaneous termination	2 (2%)	1 (3%)	1 (2%)	0.690
Immediate ECV due to unstable HD	5 (6%)	2 (6%)	3 (6%)	0.949
Rapid pacing attempt	80 (92%)	31 (91%)	49 (92%)	0.831
Success	36 (45%)	12 (39%)	24 (49%)	0.368
Failure	44 (55%)	19 (61%)	25 (51%)	0.368

VT indicates ventricular tachycardia; ECV, electrical cardioversion and HD, hemodynamic