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A road map to epicardial approach for catheter ablation of ventricular tachycardia in structural heart disease: results from a 10-year tertiary-center experience

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Abstract

Background: Epicardial approach in VT ablation is still regarded as a second-step strategy, due to the risk of complications. In a large, single-center cohort of patients with structural heart disease, we evaluated an operative model indicating epicardial approach in different etiologies, even at the first VT ablation attempt, and report the safety of epicardial procedures with the management of procedure-related complications.

Methods: All VT ablation procedures including epicardial approach over a 10-years period were included. First-line epicardial approach (First-Epi) was indicated in ARVC and post-myocarditis VT; in IDCM and post-MI patients, indications resulted from available imaging techniques or 12-lead VT morphology. REDO procedures were set up according to previous mapping findings. The appropriateness of epicardial approach was evaluated considering the rate of effective epicardial ablation. Feasibility, complications and long-term outcome were reported.

Results: Four hundred and eighty-eight subjects with a median age of 60 years (IQR 47-65) and of LVEF 41% (IQR 30-55) underwent 626 epicardial VT ablations. Percutaneous access had a success rate of 92.2% and a complication rate of 3.6%. The appropriateness of first-line epicardial approach was 85.4% in ischemic heart disease (IHD), 66.3% in idiopathic dilated cardiomyopathy (IDCM), 93.5% in myocarditis and 92.4% in arrhythmogenic right ventricular cardiomyopathy (ARVC). IDCM independently predicted ineffective epicardial approach (OR 2.8; 1.83-4.3; $p<0.001$). After a follow-up of 41 months (IQR 19-64), IDCM patients experienced higher rate of recurrences and mortality compared to other etiologies.

Conclusions: In patients with VT in the context of structural heart disease epicardial approach is integral part of ablation armamentarium regardless of the etiology with high feasibility and low complication rate in experienced centers. Our data support its use at first ablation attempt in VTs related to ARVC and myocarditis.

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What is known?

- The three-dimensional nature of reentry circuits determining the substrate for ventricular tachycardias in patients with structural heart disease is nowadays widely recognized among the different etiologies.
- Even if epicardial approach has gained in the last decades increasing relevance in the catheter ablation of ventricular tachycardia (VT), contemporary consensus documents regard it as a second-step strategy mainly in non-ischemic patients.

What the study adds?

- In patients with ventricular tachycardia in the setting of structural heart disease, percutaneous and surgical epicardial approach are integral part of ablation armamentarium, with high feasibility and low complication rate in experienced centers.
- A first line epicardial approach of ventricular tachycardia in the setting of previous myocarditis or arrhythmogenic right ventricular cardiomyopathy seems to be justified by the presence of epicardial ablation targets in more than 90% of subjects.

Non-standard abbreviations and acronyms

AAD: antiarrhythmic drugs

ARVC: arrhythmogenic right ventricular cardiomyopathy

CA: coronary artery

EGM: electrograms

EPS: electrophysiology study

IDCM: idiopathic dilated cardiomyopathy

IQR: interquartile range

LVEF: left ventricle ejection fraction

MI: myocardial infarction

MRI: magnetic resonance imaging

PN: phrenic nerve

SHD: structural heart disease

VT: ventricular tachycardia

Background.

Since its introduction late in ‘90, epicardial mapping and ablation has become a well-established technique to treat epicardial ventricular tachycardia (VT), mainly in non-ischemic etiologies, but also in post-MI VTs refractory to endocardial ablation (1,2).

ECG and imaging criteria have been reported to potentially identify epicardial involvement in ischemic and non-ischemic etiologies (3–6), but the best definition of epicardial substrates has been provided by ablation series and studies of simultaneous endo-epicardial VT mapping (7–9).

In the absence of strong predictors of deep/epicardial VT substrate at pre-procedure assessment, current guidelines do not provide definitive indications to a first-line epicardial approach. In daily practice, the perception of a risky technique often goes beyond the indication to the approach itself. The expertise of the physician to perform the access (2), and the availability of a multiskilled team to treat complications (10-12) are factors that greatly influence the decision; as a consequence, epicardial approach is generally a second-step strategy.

The recurrence of VT after failure of endocardial ablation, because the epicardial location of a reentry circuit has been overlooked, however, may be also a major complication. Prompt identification of the need of epicardial approach, at the time of the index procedure, is desirable when setting the mapping and ablation strategy.

In a large cohort of patients with SHD undergoing VT ablation, we aim to provide: 1) solid data on the appropriateness and feasibility of our decisional algorithm to define first-line or REDO indications to epicardial approach; 2) complications related to the epicardial procedure (either percutaneous and surgical), and institutional facilities required to manage them.

Methods.

Study Population

Of the 1608 VT ablations performed at San Raffaele Arrhythmia Department (Milan, Italy) in the period between January 2010 and October 2020, we considered in the present study all the 626 (38.9%) procedures in which an epicardial access (either percutaneous or surgical) was indicated according to our operative model.

All patients gave informed consent to the procedure and to the utilization of their anonymized clinical data for research purposes. The study was in accordance with good clinical practice and the principles of the Declaration of Helsinki of clinical research involving human patients. This study and collection of data was approved by local ethical committee.

Operative Model for the Indication to Epicardial Access at the first procedure.

First-Epi group included patients at their first ablation attempt for whom an epicardial approach was planned. The indications for the 4 most represented VT etiologies were defined; other etiologies were evaluated on a case-by-case basis. In ARVC and post-myocarditis VTs, epicardial approach was straightaway indicated at the first ablation attempt. In a small ARVC subgroup, epicardial puncture was performed after endocardial mapping findings confirmed the “early form” ARVC (14). In IDCM, 12 lead ECG findings, during SR (15) or, if available, during VT (16) were considered to identify septal or anterior basal locations of the VT substrate, where epicardial approach was not performed.

In post-MI VT indications were: 1) 12 lead ECG (4) or image-based (5-6) criteria for suspected epicardial substrate, according to the previously published literature (pseudo delta wave≥34 ms and duration of intrinsicoid deflection in V2 >85 ms; wall-thinning <5 mm at multidetector computed tomography; hyperenhancement ≥75% of the wall thickness at contrast-enhanced-CMR); 2) intra-operative switch (adjuvant access), if the index procedure was scheduled endocardial, but failed to prevent inducibility of the clinical VT and the entire diastolic activity during VT was not recorded (17). The decision algorithm graph is available in the supplementary materials. REDO-epi included patients with previous attempted ablation, regardless of the previous procedure setting or the center that performed it.

Mapping and Ablation Procedure

Antiarrhythmic drugs were discontinued at least 5 half-lives before catheter ablation. Under general anesthesia, percutaneous epicardial approach was attempted at first by subxiphoid inferior puncture (1). A deflectable Agilis-epi sheathTM was used to facilitate catheter handling at mapping and enhance stability during ablation. Epicardial mapping, either via ablation or multielectrode catheters, included bipolar/unipolar voltage map, LAT/ILAM during baseline rhythm with identification and annotation of abnormal EGMs/ areas of slow conduction. VT inducibility was tested from RV apex, left ventricle or epicardial space, with up to four extrastimuli. Hemodynamically tolerated VTs underwent activation mapping to identify reentry critical sites; substrate-based strategies were employed in the remaining cases. Coronary angiogram was performed to avoid close proximity of epicardial vessels to the ablation targets; inflatable balloons were advanced in epicardial space if PN lied on the ablation target to displace its course (18). Point-by-point ablation was performed by means of open-irrigated ablation catheters, in a temperature-controlled mode and power setting up to 50 Watt.

Surgical cryo-ablation (AtriCure Cryo2® probe) applications of 3 minutes at -70° C were delivered, until the abolition of local EGMs was documented.

Endocardial mapping was performed afterwards, aiming at the characterization and subsequent abolition of abnormal EGMs or endocardial VT morphologies. Anticoagulation was started immediately after the access to the left chambers was achieved. If intra-operative switch was considered during endocardial procedures, transeptal sheath was pulled back from the left atrium, then protamine sulphate was administered, until ATC dropped to 180 sec to carry out the puncture. During epicardial mapping and ablation, no anticoagulation was indicated.

Surgical access to the pericardium was indicated in case of previous cardiac surgery, failed percutaneous access because of adhesions or failure of previous endo-epicardial ablation to provide cryoablation.

Endo-epi remap was carried out to confirm substrate abolition. Acute ablation efficacy was assessed at post-procedure electrophysiological study (EPS), according to our standard practice (19,20).

Major complications were defined as adverse events that required the end of the ablation session or another procedure (or surgery) to manage it or prolonged a patient's hospitalization. Minor complications were those that did not require to interrupt the procedure or any additional measurements.

Appropriateness of epicardial approach.

Epicardial approach was considered appropriate (effective) whenever an epicardial substrate was targeted for the ablation. This included: 1) isolated diastolic EGMs during VT or full epicardial imaging of VT reentry, according to our previous experience (17); 2) epicardial abnormal EGMs/LAVAs or slow conduction areas during SR (19-22).

If endocardial ablation only or no ablation were performed, the epicardial approach was considered to be pointless (inappropriate) and substrate distribution was analyzed.

The prevalence of epicardial substrate was reported according to the main etiologies and analyzed according to First-Epi and REDO-epi group in specific subgroups.

In-hospital clinical course

Triamcinolone 2 mg/Kg was injected in the epicardial space at the end of the procedure, and non-traumatic pig-tail catheter was advanced to prevent myocardial damage. The sheath was removed after 2 hours if no effusion was documented. The drainage system was maintained for at least 12 hours if self-limiting bleeding occurred. Patients were monitored for at least 3 days after the procedure and indometacin was administered for 3 weeks in those with clinical evidence of pericarditis.

Whenever in-hospital VT recurrences indicated a further ablation attempt, the procedure approach was based upon previous mapping findings and documented 12 lead VT morphology.

Long-term Outcome

Clinical follow-up visits and ICD interrogations were scheduled at 3, 6, and 12 months after the procedure; phone calls were performed thereafter or in unavailable patients. VT recurrences, defined as any sustained VT terminated either from implanted device or AADs, and death related to any cause were reported.

Statistics

Continuous variables were expressed as mean value ± standard deviation when normally distributed and as median value with interquartile range (25°–75°) when 1-sample Kolmogorov-Smirnov test showed not normal distribution. The categorical variables were presented as number and percentages and their proportion was compared using a Chi-square analysis or Fisher's exact test, as appropriate. Yates correction was applied when indicated. Continuous variables which were normally distributed were compared using the Student t-test for independent samples, in case of non-normally distributed variables, Mann-Whitney U test was used.

Univariate logistic regression analysis was used to calculate estimated and 95% confidence intervals odds ratios for variables available before the procedure and associated with ineffective epicardial puncture. Variables with $p<0.05$ on univariate analysis were entered into a multivariable logistic regression model to identify independent risk factors for ineffective puncture.

Kaplan–Meier curve and log-rank test were used to assess survival function at follow-up. Univariate and multivariate analyses were performed with the Cox proportional hazard regression model to identify variables associated to long-term VT recurrences and all-causes mortality. Variables with $p<0.05$ on univariate analysis were entered into the multivariable logistic regression model. Data were analyzed with SPSS software version 26.0 (SPSS Inc., Chicago, Illinois).

Results.

Overall study population.

In the study period, 626 procedures including an epicardial approach were performed in 488 patients (1,28 procedure per patient; range 1-5 procedures). Median age was 60 years (IQR 47-65) years; 440 pts (90,2%) were male. Median LVEF was 41% (IQR 30-55%).

VT etiologies were: IDCM in 162 pts (33.2%), ARVC in 102 cases (20.9%); infarct-related in 92 pts (18.9%) and 86 post-myocarditis pts (17.6%). Baseline characteristics of the study population are shown in **Table 1**.

Procedure characteristics.

First-line Epi group included 317 (50.6%) procedures and 309 (49.4%) were REDO procedures (REDO-Epi). Percutaneous combined endo-epicardial approach was performed in 524 out of the 626 procedures (83.7%), 49 procedures had percutaneous epicardial approach only (7.8%) and 53 (8.5%) procedures were performed by means of surgical access.

The distribution of First Epi vs REDO-epi procedures according to VT etiologies and indications to epicardial approach are shown in **Table 2**.

Feasibility of the percutaneous epicardial access and ablation.

Overall, out of the total of 575 attempted, there were 45 (7.8%) failed percutaneous epicardial punctures. No difference between First-Epi group versus REDO-group was observed (23/309, 7.4% vs. 22/264, 8.3%; p=0.71). In 2 pts of First-epi group, the surgical subxiphoid window was successfully carried out during the same procedure, so they had both accesses in the same session.

A significant difference was observed when comparing the rate of failed epi access among each etiology subgroup: 12/117 IHD (10.3%); IDCM 22/196 (11.2%); ARVC 4/120 (3.3%); Myocarditis 3/94 (3.2%); 2/46 in other etiologies (4.3%) [X^2 (2, N = 573) = 9.8562, p =0.042].

In 63 procedures (10.8%) the presence of CA or PN was documented on the target ablation site; inflatable balloons were used in 21 cases to dislodge the PN course. CA pathway was integrated on the map in 19 cases, to guide the ablation. Complete ablation of the target area was prevented in 15/63 (23.8%) because of safety concerns.

In 8 procedures of REDO-group, surgical access to perform epicardial cryoablation was performed.

Efficacy of the decisional model for epicardial approach.

Out of the 583 procedures with ultimate epicardial mapping (either percutaneous or surgical), epicardial ablation was performed in 468 (80.6%).

When considering First-Epi and REDO-Epi procedures with ultimate epicardial mapping, a similar rate of procedures included epicardial ablation: 241/296 (81.4%) and 227/287 (79,1%), respectively (**Table 3**).

The rate of appropriateness of epicardial approach among different etiologies in the First-Epi group was: 35/41 IHD (85.4%); 61/92 in IDCM (66.3%); 58/62 in Myocarditis (93.6%); 61/66 in ARVC (92,4%) and 25/34 in Others (73.5%), χ^2=26,24; p<0.0001 **(Fig. 2).** According to our operative model for first-line epicardial approach, the highest odds for epicardial ablation were found in ARVC (OR 4.057; 95% CI:1.299-8.937; p=0.007) and Myocarditis (OR 3.971; 95% CI: 1.376-11.465; p=0.005) while a statistically significant negative odd was in IDCM etiology (OR 0.27; 95% CI: 0.147-0.494; p=0.0001) (**Figure 3**).

In First-epi group, epicardial ablation only occurred in 95/583 procedures (16,2%). It was significantly higher in post-myocarditis VT [41/62 (67.2%)], as compared to other VT etiologies, namely ARVC (21/66; 31.8 %; $\chi^{2=}$14.5098; p<.0001), IHD (11/41; 26.8%; χ2=14.4261 p< .0001) and IDCM [22/92; 23.7%; χ2=26.6329; p<.00001]. In Post-MI pts, indication to First-epi was appropriate in 16/19 imaging-guided procedures (85.4%), 6/8 ECG-guided procedures (75%) and in 14/15 of adjuvant accesses (93.3%).

Inappropriate epicardial access.

Overall, epicardial access was ineffective in 115/583 cases (19.7%). Endocardial ablation only [111/583 (19%)] or no ablation [4/583 (0,7%)] was performed because of the lack of any epicardial ablation target. The rate did not differ between first and REDO procedures, [55/296 procedures (18.6%) in First-Epi vs 60/287 (20.9%) in REDO-Epi, p=0.6].

In First-epi group, the highest rate of ineffective approach occurred IDCM pts (31/92; 33.7%) as compared to 6/41 IHD (14.6%); 4/62 Myocarditis (6.4%); 5/66 ARVC (7,6%) and 9/34 in Others (26.4%), p<0.001.

Septal substrates with healthy epicardium were documented in 19/55 First-epi procedures (34.5%); absence of LAVAs/LPs despite epicardial bipolar scar occurred in 36/55 cases (65.5%) (**Figure 4**).

Among REDO-Epi with ineffective epicardial access, indications had been previous failed endocardial approach (39/60, 65%); failed epicardial ablation (16/60; 26,7%); VT morphology (3/60; 5%) and intraoperative switch (2/60, 3.3%). When considering pointless epicardial approach, IDCM was the most frequent etiology both in First-Epi (31/55 (56.4%) and REDO-Epi group (32/60, 53.3%; p=0.8). IDCM etiology (OR: 2.8; 95% CI: 1.83 to 4.3; p < 0.001) and age> 65 years (OR: 1.82; 95% CI: 1.19 to 2.79; p = 0.006) emerged as independent risk-factors for ineffective epicardial access **(Table 4, supplemental materials)** at multivariate analysis.

Complications.

Overall, major complications related to epicardial approach occurred in 24/626 (3.8%) procedures; 3 of which in pts undergoing surgical access. The rate of complications was comparable between the First-epi group and the REDO-epi group [12 vs 12 procedures (p=0.9), respectively].

There were 9 pericardial tamponades related to the puncture and ablation; persistent drainage (after 3 hrs of observation) prevented endocardial mapping and led to cardiac surgery in 6 patients (2 First-epi vs. 4 REDO-Epi); 3 patients had a late tamponade (within 72 hours), managed by means of percutaneous pericardiocentesis.

Sub-diaphragm hematoma was documented late after 4 procedures (range 1-4 days): 3 First-Epi and 1 REDO-Epi**,** respectively. Two patients had undergone surgical repair of the tear of the left lobe of the liver, and urgent percutaneous chemoembolization of a parietal branch of the internal mammal artery, respectively. In the last 2 cases, no active bleeding was documented at the time of diagnosis and a conservative strategy with blood transfusion, daily check of hemoglobin level and CT scan of the abdomen before discharge was maintained.

Emergency percutaneous CA angioplasty was performed in 4 procedures (2 First-Epi vs 2 REDO-Epi) because of the acute occlusion of CA (marginal branch in 3 pts, diagonal branch in 1 pt) during ablation. In two cases coronary angiogram was performed before ablation and estimated a 5 mm distance of the ablation catheter to the vessel.

Long-persistent phrenic nerve damage with left hemidiaphragm elevation was documented after the procedure in 1 patient, who developed symptoms of mild restrictive ventilatory pattern due to basal left lung atelectasis. No specific therapy but respiratory rehabilitation has been indicated.

Post-operative course was characterized by a major complication, related to the surgical approach in 3 procedures (2 wound infections requiring surgical revision and 1 sub-diaphragmatic hematoma; 0.4%).

Nineteen procedures (3%) required post-operative monitoring in intensive care-unit (ICU); mean stay was 10±7.2 days (range 1-21 days). Overall, there were 11 in-hospital deaths (2.5%), in two patients (0,3%) related to a cardiogenic shock following cardiac tamponade. Nine pts with advanced heart failure died after the procedure, because of progressive hemodynamic decompensation, refractory to mechanical hemodynamic support and high-dose inotropic drugs. Minor complications were: self-limited bleeding in 11 procedures (1.7%) and pericarditis in 13 pts (2%).

Long-term outcome after epicardial VT ablation.

At discharge, 352 patients (72.1%) were on beta-blockers; 78 pts on amiodarone (15.9%), 72 (14.7%) on sotalol and 20 (4.1%) on class-1 AADs; 22 patients were lost at follow-up. On a median follow-up period of 41 months (IQR 19-64 months), 126 experienced VT recurrence (27.0%) and 90 patients died (19.3%). After the last procedure, (**Figure 5**) cumulative VT free-survival were 76.4% at 20 months and 61.5% at 40 months; the overall survival rate were 85.5% and 73.7% at the same time frames.

Etiology significantly stratified outcome, both when analyzing VT-recurrence and all-cause deaths **(Fig. 6)**. IDCM patients experienced higher recurrence rate and mortality compared to patients with ARVC and Myocarditis (log-rank $p=0.014$ and $p<0.0001$): being 35,5% and 36,6% after a median follow-up of 33 (IQR 11-55) months compared to 17,2% and 4.1% for ARVC (median follow-up of 51 (IQR 29-73) months) and 23,3 and 5,8% (median follow-up of 44 (19-69) months) for myocarditis, respectively.

NYHA III-IV (HR: 2.24; 95% CI: 1.46 to 3.44; $p<0.0001$) and VT inducibility at the end of the procedure (HR: 1.63; 95% CI: 1.10 to 2.41; $p=0.016$) were independent predictors of VT recurrence **(tables 5, supplemental materials)**.

Independent predictors for all-causes mortality included NYHA III-IV (HR: 4.34; 95% CI: 2.68 to 7.03; p<0.0001), LVEF<35% (HR: 2.48; 95% CI: 1.45 to 4.23; p<0.0001), IDCM etiology (HR: 1,89; 95% CI: 1.22 to 2.93; p=0.004), history of AF (HR: 1.57; 95% CI: 1.02 to 2.41; p=0.04) and chronic kidney disease (HR: 1.72; 95% CI: 1.09 to 2.69; p=0.019) **(Table 6, supplemental materials)**

Discussion.

This is the first experience to report the appropriateness of distinctive criteria to the epicardial approach in a large, single-Center cohort of patients referred for catheter ablation of ventricular arrhythmias. As qualifying aspects, we included a consistent number of endo-epicardial first ablation procedures, long-term ablation outcome and procedure safety. Indications may be used as a road map in daily practice, to bring forward the detection and treatment of epicardial VT substrates. We tested the strength of indication, primarily based on VT etiology and modulated by specific imaging and ECG findings.

Main findings of our study can be summarized as follows:

1) In non-ischemic VT etiologies, namely post-myocarditis and ARVC, the likelihood of epicardial ablation is very high (93.5% and 92.4% respectively).
2) IDCM pts and antero-septal substrates show the highest rate of useless approach.
3) A considerable number of patients with post-MI VT need an epicardial ablation and the decision should be made according to endocardial mapping findings.
4) In our experience, a subxiphoid inferior puncture was successfully achieved in 92.2% of cases; surgical access was performed in case of failure, with an overall complication rate of 3.8%.

Epicardial approach as a first ablation attempt: ARVC and Myocarditis-related VTs.

High density epicardial mapping revealed the presence of suitable targets for RF ablation in 92.4% ARVC patients, either during SR (abnormal EGMs) or during VT activation mapping, leading to a very high long term success rate (82% at 5 ys follow-up). VT recurrence free survival in the present study is higher as compared to other series, on a comparable FU period (23-25).

The need for epicardial approach appears even more striking in post-myocarditis VTs, as these patients showed the highest likelihood (93.5%) of epicardial substrate, according to the present experience and previous data (26,27). Moreover, in this subgroup we observed the highest rate of epicardial ablation only, because of the absence of any endocardial substrate or in the presence of a consistent epicardial, single-layer reentry (67.2%) **(Fig 7).**

Current data confirm and strengthen previous reports about the epicardial substrate distribution and long-term outcome of ablation in patients affected by VT in the setting of ARVC or myocarditis (19).

Epicardial approach in IDCM: a heterogeneous arrhythmic substrate.

Non-ischemic dilated cardiomyopathy, instead, appeared to be the main source of mistaken indications both at first approach (54.8%) and REDO procedures (53.3%), and emerged as independent risk factor for inappropriate epicardial access.

The inability to anticipate the substrate at pre-operative assessment could partially explain the failure rate. From an operative standpoint, EPS before the procedure and imaging data (28,29) should be routinely pursue in IDCM pts, to refine the procedure setting.

Alternatively, the presence of LBBB or AV block with pacing dependency might indicate septal substrate (16). A septal VT origin should address the need for biventricular mapping or alternative ablation sources (30), instead of early epicardial access.

Intramural layers participate extensively in the reentry circuit, particularly in non-ischemic cardiomyopathies (31,32). As a consequence, ablation may not address all the critical components, or might not be able to treat deep substrates even if delivered at high power. In both cases, the ablation success is negatively affected (18) and epicardial cryoablation can be considered (33).

It can be speculated that this heterogeneous substrate, with variable localization and depth, made IDCM the strongest independent predictor of inappropriate indication for epicardial approach and the less favourable long-term FU.

Epicardial components of post-MI VT circuits.

Only 45 post-MI procedures were included in First-Epi group, with the highest difference compared to REDO-Epi (Tab.2). Overall, a consistent epicardial ablation target was found in 85% of First- epi cases, but the role of a single criterion cannot be determined.

Pre-procedure imaging has shown to be efficient in selecting a first-line endo-epicardial approach (5); it was available in a limited number of patients in our series. A first-line endocardial ablation seems to be reasonable in post-MI pts, according to scar biology.

Adjuvant epicardial puncture because of persistent VT inducibility, after abolition of endocardial substrate, might be appropriate; it was the most efficient criterion in the present study. This approach poses some technical challenges, related to anticoagulation reversal. In such cases, abolition of endocardial substrate should be carefully checked before proceeding to the puncture.

Interestingly, among 61 REDO-Epi procedures in which epicardial approach was indicated because of a previous failed endocardial ablation (Table 3, supplemental material), VT substrate was still endocardial in 26,2 % of cases; this finding demands a careful assessment of ablation efficacy, to avoid that incomplete endocardial ablation leads to unnecessary epicardial punctures.

Feasibility and complications of epicardial access.

In the present cohort the overall rate of failed access was low (7.8%), and comparable to the previous literature (1,11-13,34). The main reason preventing from successful percutaneous access was the inability to advance the guidewire despite multiple punctures of fibrous pericardium due to adhesions. Interestingly, multiple epicardial procedures were not associated with higher failure rates; the routinary use of corticosteroids before epicardial sheath removal is, in our opinion, the predominant reason for this observation.

The availability of a surgical equipe was fundamental to overcome the issue of inaccessible space. Surgical dissection of pericardial adhesions can be safely performed, whereas attempts to crawl the ablation catheter carry the risk of late tamponade. If intramural substrates are refractory to RF epicardial ablation, the cryoablation offers the advantages of larger and deeper lesions (41).

Recently, a trend toward higher complication rate with percutaneous inferior approach as compared to the anterior one has been described (10.1% vs 4.9%) (42). In our experience of inferior-only oriented punctures, the rate of epicardial-related complications was very low as compared to previously reported data (3.6% vs 10.1%), on a considerable larger number of procedures (575 vs 189). Starting from 2014, tools and approaches were routinely implemented in the need to treat substrates minimizing the risks of damaging epicardial structures, like CA e PN. Deaths related to a complication were extremely rare; nevertheless, in view of potential gravity of the complications, and the risk of acute heart failure, adequate operator training and the presence of a multi-disciplinary team are recommended to prevent adverse outcome.

Long-term outcome of epicardial ablation.

Including repeated procedures, the cumulative VT free-survival in our study was 76.4% at 20 months, which is higher compared to the 71% reported by a previous multicenter safety study by Sacher and colleagues in a comparable follow-up (11), and was still good on a longer FU period (61.5% at 40 months).

The results from the VT-International Collaborative Group reported one-year freedom from recurrence of 70% on a large population of SHD patients and 69% in a large population of non-ischemic etiologies (37-38). The relative contribution of epicardial approach against the overall strategy cannot be determined in the present study, but we observed an excellent prognosis in ARVC e post-myocarditis pts. In our opinion, this is a major indicator to perform epicardial approach at the first attempt in these etiologies. All the results are also to be interpreted in view of the significant proportion of patients withdrawing amiodarone therapy after the procedure (15.9% vs 96.9%). The clinical impact of the outcome is, in our view, extremely important in ARVC and myocarditis pts, who are typically younger, as well as for advanced HF patients, for whom a detrimental effect of amiodarone is still questioned.

Limitations.

The main limitation of this study is the absence of randomization to prove the efficacy of our decisional model to warrant epicardial approach at the first ablation procedure. Neverthless, our findings are in line with previous reports, and eventually empower the indications to anticipate epicardial approach in the clinical history of the patient.

Imaging techniques (cardiac tomography scan or MRI) have not routinely used pre-operatively to detect scar location and extension, so they were available in a limited number of patients. As our standard approach, however, detection of the VT substrate was based on the careful evaluation of abnormal local EGMs, and VT activation mapping whenever possible, to prove the participation of a specific substrate into the VT reentry mechanism. This is the report of a high-volume, tertiary Center with highly skilled operators (at least 20 epicardial procedures/year), so the results and complications rate might not be routinely applicable on a large scale and not comparable to other approaches. In the large timeframe of patient enrollment, technological improvements might have contributed to the ablation outcome, in addition to the epicardial approach per se.

Conclusions

The access to the epicardial space, with percutaneous or surgical techniques, has become a cornerstone in VT ablation. In the present study, we showed that high prevalence of epicardial substrate, and low complications rates, may justify an epicardial approach even at the first ablation attempt in etiologies like post-myocarditis and ARVC.

In our opinion, the benefits far outweigh the risks in these subgroups.

IDCM patients with antero-septal substrate show the highest rate of inappropriate approach; the inability to characterize or to treat intramural VT components endo-epicardially might be responsible for the worse outcome in this subgroup and the futility of routinary epicardial approach in these patients. A considerable number of patients with post-MI VT need an epicardial ablation, and the decision should be based on endocardial mapping findings, either in single or staged procedure.

Bibliography

1. Sosa E, Scanavacca M, d'Avila A, Pilleggi F. A new technique to perform epicardial mapping in the electrophysiology laboratory. J Cardiovasc Electrophysiol. June 1996;7(6):531–6.

2. Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, et al. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias: executive summary. Europace. Mar 2020;22(3):450–95.

3. Vallès E, Bazan V, Marchlinski FE. ECG criteria to identify epicardial ventricular achycardia in nonischemic cardiomyopathy. Circ Arrhythm Electrophysiol. Feb 2010;3(1):63–71.

4. Berruezo A, Mont L, Nava S, Chueca E, Bartholomay E, Brugada J. Electrocardiographic recognition of the epicardial origin of ventricular tachycardias. Circulation 2004;109:1842-7A

5. Acosta J, Fernández-Armenta J, Penela D, Andreu D, Borras R, Vassanelli F, Korshunov V, Perea RJ, de Caralt TM, Ortiz JT, Fita G, Sitges M, Brugada J, Mont L, Berruezo A. Infarct ransmurality as a criterion for first-line endo-epicardial substrate-guided ventricular tachycardia ablation in ischemic cardiomyopathy. Heart Rhythm. 2016 Jan;13(1):85-95

6. Komatsu Y, Cochet H, Jadidi A, Sacher F, Shah A, Derval N, Scherr D, Pascale P, Roten L, Denis A, Ramoul K, Miyazaki S, Daly M, Riffaud M, Sermesant M, Relan J, Ayache N, Kim S, Montaudon M, Laurent F, Hocini M, Haïssaguerre M, Jaïs P. Regional myocardial wall thinning at multidetector computed tomography correlates to arrhythmogenic substrate in postinfarction ventricular tachycardia: assessment of structural and electrical substrate. Circ Arrhythm Electrophysiol. 2013 Apr;6(2):342-50. doi: 10.1161/CIRCEP.112.000191. Epub 2013 Mar 10. PMID: 23476043.

7. Darma A, Bertagnolli L, Weber A, Dinov B, Torri F, Lurz JA, et al. Epicardial ablation of ventricular tachycardia in patients with structural heart disease: a single-centre experience over 12 years. Europace. Dec 2021;23(12):1980–8.

8. Frontera A, Hadjis A, Calore F, Della Bella P. Simultaneous endo-epicardial-high density mapping of ventricular tachycardia with the use of multi-electrode mapping catheters. J Interv Card Electrophysiol. Sept 2020;58(3):365–7.

9. Tung R, Raiman M, Liao H, Zhan X, Chung FP, Nagel R, et al. Simultaneous Endocardial and Epicardial Delineation of 3D Reentrant Ventricular Tachycardia. J Am Coll Cardiol. Mar 2020;75(8):884–97.

10. Katja Zeppenfeld and others, 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by 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 the Association for European Paediatric and Congenital Cardiology (AEPC), European Heart Journal, Volume 43, Issue 40, 21 October 2022, Pages 3997–4126

11. Sacher F, Roberts-Thomson K, Maury P, Tedrow U, Nault I, Steven D, et al. Epicardial ventricular tachycardia ablation a multicenter safety study. J Am Coll Cardiol. May 2010;55(21):2366–72.

12. Romero J, Patel K, Lakkireddy D, Alviz I, Velasco A, Rodriguez D, et al. Epicardial access complications during electrophysiology procedures. J Cardiovasc Electrophysiol. July 2021;32(7):1985–94.

13. Della Bella P, Brugada J, Zeppenfeld K, Merino J, Neuzil P, Maury P, et al. Epicardial ablation for ventricular tachycardia: a European multicenter study. Circ Arrhythm Electrophysiol. Oct 2011;4(5):653–9.

14. Kirubakaran S, Bisceglia C, et al. Characterization of the arrhythmogenic substrate in patients with arrhythmogenic right ventricular cardiomyopathy undergoing ventricular tachycardia ablation. Europace. 2017 Jun 1;19(6):1049-1062

15. Oloriz T, Wellens HJJ, Santagostino G, Trevisi N, Silberbauer J, Peretto G, et al. The value of the 12-lead electrocardiogram in localizing the scar in non-ischaemic cardiomyopathy. Europace. Dec 2016;18(12):1850–9.

16. Oloriz T, Silberbauer J, Maccabelli G, Mizuno H, Baratto F, Kirubakaran S, et al. Catheter ablation of ventricular arrhythmia in nonischemic cardiomyopathy: anteroseptal versus inferolateral scar sub-types. Circ Arrhythm Electrophysiol. Jun 2014;7(3):Jun 414–23

17. Hadjis A, Frontera A, Limite LR, Bisceglia C, Bognoni L, Foppoli L, et al. Complete Electroanatomic Imaging of the Diastolic Pathway Is Associated With Improved Freedom From Ventricular Tachycardia Recurrence. Circ Arrhythm Electrophysiol. Sept 2020;13(9):e008651.

18. Okubo K, Trevisi N, Foppoli L, Bisceglia C, Baratto F, Gigli L, et al. Phrenic Nerve Limitation During Epicardial Catheter Ablation of Ventricular Tachycardia. JACC Clin Electrophysiol. January 2019;5(1):81–90.

19. Okubo K, Gigli L, Trevisi N, Foppoli L, Radinovic A, Bisceglia C, et al. Long-Term Outcome After Ventricular Tachycardia Ablation in Nonischemic Cardiomyopathy: Late Potential Abolition and VT Noninducibility. Circ Arrhythm Electrophysiol. Aug 2020;13(8):e008307.

20. Silberbauer J, Oloriz T, Maccabelli G, Tsiachris D, Baratto F, Vergara P, et al. Noninducibility and late potential abolition: a novel combined prognostic procedural end point for catheter ablation of postinfarction ventricular tachycardia. Circ Arrhythm Electrophysiol. June 2014;7(3):424–35.

21. Tsiachris D, Silberbauer J, Maccabelli G, Oloriz T, Baratto F, Mizuno H, et al. Electroanatomical voltage and morphology characteristics in postinfarction patients undergoing ventricular tachycardia ablation: pragmatic approach favoring late potentials abolition. Circ Arrhythm Electrophysiol. Aug 2015;8(4):863–73.

22. Irie T, Yu R, Bradfield JS, Vaseghi M,et al. Relationship between sinus rhythm late activation zones and critical sites for scar-related ventricular tachycardia: systematic analysis of isochronal late activation mapping. Circ Arrhythm Electrophysiol. 2015 Apr;8(2):390-9

23.Santangeli P, Zado ES, Supple GE, Haqqani HM, Garcia FC, Tschabrunn CM, et al. Long-Term Outcome With Catheter Ablation of Ventricular Tachycardia in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy. Circ Arrhythm Electrophysiol. Dec 2015;8(6):1413–21.

24. Mathew S, Saguner AM, Schenker N, Kaiser L, Zhang P, Yashuiro Y, et al. Catheter Ablation of Ventricular Tachycardia in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: A Sequential Approach. J Am Heart Assoc. Mar 2019;8(5):e010365.

25. Daimee UA, Assis FR, Murray B, Tichnell C, James CA, Calkins H, et al. Clinical outcomes of catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy: Insights from the Johns Hopkins ARVC Program. Heart Rhythm. Aug 2021;18(8):1369–76.

26. Berte B, Yamashita S, Sacher F, Cochet H, Hooks D, Aljefairi N, et al. Epicardial only mapping and ablation of ventricular tachycardia: a case series. Europace. Feb 2016;18(2):267–73.

27. Maccabelli G, Tsiachris D, Silberbauer J, Esposito A, Bisceglia C, Baratto F, et al. Imaging and epicardial substrate ablation of ventricular tachycardia in patients late after myocarditis. Europace. Sep 2014;16(9):1363–72.

28. Tung R, Kim S, Yagishita D, Vaseghi M, Ennis DB, Ouadah S, et al. Scar voltage threshold determination using ex vivo magnetic resonance imaging integration in a porcine infarct model: Influence of interelectrode distances and three-dimensional spatial effects of scar. Heart Rhythm. Oct 2016;13(10):1993–2002.

29. Stevens SM, Tung R, Rashid S, Gima J, Cote S, Pavez G, et al. Device artifact reduction for magnetic resonance imaging of patients with implantable cardioverter-

defibrillators and ventricular tachycardia: late gadolinium enhancement correlation with electroanatomic mapping. Heart Rhythm. Feb 2014;11(2):289–98

30. Della Bella P, Peretto G, Paglino G, Bisceglia C, et al.. Bipolar radiofrequency ablation for ventricular tachycardias originating from the interventricular septum: safety and efficacy in a pilot cohort study. Heart Rhythm 2020;17:2111–8.

31. Shirai Y, Liang JJ, Santangeli P, Arkles JS, Schaller RD, Supple GE, et al. Comparison of the Ventricular Tachycardia Circuit Between Patients With Ischemic and Nonischemic Cardiomyopathies: Detailed Characterization by Entrainment. Circ Arrhythm Electrophysiol. Jul 2019;12(7):e007249.

32. Bhaskaran A, Nayyar S, Porta-Sánchez A, Jons C, Massé S, Magtibay K, et al. Direct and indirect mapping of intramural space in ventricular tachycardia. Heart Rhythm. Mar 2020;17(3):439–46.

33. Anter E, Hutchinson MD, Deo R, Haqqani HM, et al. Surgical ablation of refractory ventricular tachycardia in patients with nonischemic cardiomyopathy. Circ Arrhythm Electrophysiol. 2011 Aug;4(4):494-500

34. Baldinger SH, Kumar S, Barbhaiya CR, Mahida S, Epstein LM, Michaud GF, John R, Tedrow UB, Stevenson WG. Epicardial Radiofrequency Ablation Failure During Ablation Procedures for Ventricular Arrhythmias: Reasons and Implications for Outcomes. Circ Arrhythm Electrophysiol. 2015 Dec;8(6):1422-32

35. Li A, Hayase J, Boyle NG. Hybrid Surgical Ablation for Ventricular Arrhythmias. Card Electrophysiol Clin. Sept 2020;12(3):383–90.

36. Mathew S, Feickert S, Fink T, Rillig A, Reissmann B, Rottner L, et al. Epicardial access for VT ablation: analysis of two different puncture techniques, incidence of adhesions and complication management. Clin Res Cardiol. Jun 2021;110(6):810–21.

37. Vaseghi M, Hu TY, Tung R, Vergara P, Frankel DS, Di Biase L, et al. Outcomes of Catheter Ablation of Ventricular Tachycardia Based on Etiology in Nonischemic

Heart Disease: An International Ventricular Tachycardia Ablation Center Collaborative Study. JACC Clin Electrophysiol. Sep 2018;4(9):1141–50.

38. Tung R, Vaseghi M, Frankel DS, Vergara P, Di Biase L, Nagashima K, et al. Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: An International VT Ablation Center Collaborative Group study. Heart Rhythm. Sep 2015;12(9):1997–2007.

Table 1. Clinical characteristics of the study population.

Number of subjects	488	
Male	440	90.2
Age, y	60	[47-65]
LVEF, %	41	[30-55]
Etiology		
IDCM	162	33.2
ARVC	102	20.9
IHD	92	18.9
Myocarditis	86	17.6
Others	46	9.4
Hypertension	196	40.2
Diabetes mellitus	59	12.1
CKD	108	22.1
AF	136	27.9
LV aneurysm	28	5.7
LV thrombus	11	2.3
Previous cardiac surgery	16	3.2
Prior VT ablations	243	49.7
1	157	32.2
2	58	11.9
>2	28	5.7
NYHA Class III-IV	96	19.7
ICD	310	63.5
CRT-D	88	18.0
Clinical presentation		

Recurrent VT	334	68.4
Electrical storm	131	26.8
Incessant VT	23	4.7
Previous AADs		
Amiodarone	473	96.9
Beta-blockers	333	68.2
Class I	122	25.0
Sotalol	59	12.1

Data are presented as N. (%) or mean±SD

Abbreviations are AAD=antiarrhythmic drugs; ARVC=arrhythmogenic right ventricular cardiomyopathy; AF=atrial fibrillation; CKD=chronic kidney disease; CRT=cardiac resincronization therapy; ICD=implantable cardioverter defibrillator; IDCM=idiopathic dilated cardiomyopathy; LVEF=left ventricular ejection fraction; MI=myocardial infarction; NYHA=New York Heart Association; VT=ventricular tachycardia.

Table 2. Characteristics of the VT ablations including an epicardial access.

		FIRST-Epi	REDO-Epi	*P* value
Total	626	317 (50.6)	309 (49.4)	
		Epicardial Access		
Epicardial only	49 (7.8)	25 (7.9)	24 (7.8)	0.8820
Endo-epicardial	524 (83.7)	285 (89.9)	239 (77.3)	0.0001
Surgical	53 (8.5)	7 (2.2) §	46 (14.9)	0.0001
		Etiology		
IHD	135 (21.6)	45 (14.2)	90 (29.1)	0.0001
IDCM	216 (34.5)	105 (33.1)	111 (35.9)	0.5013
Myocarditis	101 (16.1)	63 (19.9)	38 (12.3)	0.0122
ARVC	120 (19.2)	68 (21.5)	52 (16.8)	0.1556
Others	54 (8.6)	36 (11.4)	18 (5.8)	0.0153
		Indications		
Non-ischemic etiology	213 (34.0)	213 (67.2)	0 (0)	-
Imaging	25 (3.9)	21 (6.6)	4 (1.3)	0.0007
ECG criteria	40 (60.6)	33 (10.4)	7 (2.3)	0.0001
Prior epi	76 (12.1)	0 (0)	76 (24.6)	-
Prior failed endo	199 (31.8)	0 (0)	199 (64.4)	-
Intra-operative switch	44 (7.0)	27 (8.5)	17 (5.5)	0.1603
Transmural scar / aneurysm	14 (2.2)	13 (4.1)	1 (0.3)	0.0017
Apical thrombus	3 (0.4)	1 (0.3)	2 (0.6)	0.6196
Concomitant surgery	10 (1.6)	7 (2.2)	3 (1)	0.3402
Double prosthetic valve	1 (0.2)	1 (0.3)	0 (0)	1.0000
Failed percutaneous epicardial access *	45 (7.8)	23 (7.4)	22 (8.3)	1.0000
		Procedures data		
VT inducibility	388 (61.9)	197 (62.1)	191 (61.8)	0.9346
Haemodynamic support (ECMO)	32 (5.1)	11 (3.5)	21 (6.8)	0.0697
Endo-epi RF**	468 (80.3)	241 (81.3)	227 (79.1)	0.5331
RF endo only**	111 (19.0)	51 (17.3)	60 (20.9)	0.2924
No ablation**	4 (0.7)	4 (1.4)	0 (0)	0.1238
		Ablation outcome		
VT-noninducible	420 (67.1)	221 (69.7)	199 (64.4)	0.1736
Non-clinical VT inducible	81 (12.9)	37 (11.7)	44 (14.2)	0.3439
Clinical VT inducible	16 (2.6)	6 (1.9)	10 (3.2)	0.3206

EPS contraindicated	109 (17.4)	53 (16.7)	56 (18.1)	0.6740
In-hospital recurrence	127 (20.3)	56 (17.7)	71 (23)	0.0920
		Major Complications		
Overall	21 (3.3)	11 (3.4)	10 (3.2)	1.0000
Tamponade (surgery)	6	2 (0.6)	4 (1.3)	0.4454
Late tamponade (drainage)	3	3 (0.9)	0 (0)	0.2489
Sub-diaphragmatic lesion	4	3 (0.9)	1 (0.3)	0.6239
CA damage (PCI)	4	2 (0.6)	2 (0.6)	1.0000
PN lesion (permanent)	1	1 (0.3)	0 (0)	1.0000
Surgery related complications	3	1 (0.3)	2 (0.6)	0.2433
In hospital death	11 (1.7)	6 (1.9)	5 (1.6)	1.0000

Data are reported as number (%) or SD.

*Percentage is calculated on the number of the attempted percutaneous epicardial punctures.

**percentages are calculated on the total effective epicardial accesses.

° surgical epicardial access

§in 2 pts immediate surgical access was performed during the same procedure.

Abbreviations are ARVC= arrhythmogenic right ventricular cardiomyopathy; CA= coronary artery; ECMO=extra-corporeal membrane oxygenation; EPS=electrophysiological study; IDCM=idiopathic dilated; IHD=ischemic heart disease; cardiomyopathy; PN=phrenic nerve; RF=radiofrequency; VT=ventricular tachycardia.

Table 3. Characteristics of patients according to effectiveness of epicardial access in First-Epi vs REDO-Epi group.

	First-Epi			REDO-Epi		
	Effective	Ineffective	P-value	Effective	Ineffective	P-value
N.	240	55		228	60	0.6
Male sex	221 (92.1)	48 (87.3)	0.28	203 (89.0)	54 (90.0)	1.0
Age	54±15	61±13	0.002	57±15	62±12	0.04
CKD	40 (16.6)	17 (30.9)	0.02	56 (24.6)	24 (40.0)	0.001
LVEF	44±15	39±12	0.03	40±12	36±13	0.04
NYHA III-IV	38 (15.8)	13 (23.6)	0.95	54 (23.7)	17 (28.4)	0.57
Etiologies						
IHD	35 (14.6)	6 (10.9)	0.6656	64 (28.2)	18 (30)	0.8724
IDCM	61 (25.5)	31 (56.4)	0.0001	70 (30.7)	32 (53.3)	0.0013
Myocarditis	58 (24.2)	4 (7.3)	0.0052	34 (14.9)	2 (3.3)	0.0146
ARVC	61 (25.4)	5 (9.1)	0.0070	48 (21.1)	2 (3.3)	0.0005
Others	25 (10.4)	9 (16.4)	0.2421	12 (5.3)	6 (10)	0.2269
Indications						
First intention	166 (69.2)	34 (61.8)	0.3374	nd	nd	
Imaging	16 (6.7)	5 (9.1)	0.5607	3 (1.3)	1 (1.7)	1.0000
ECG criteria	23 (9.6)	9 (16.4)	0.1525	5 (2.2)	3 (5.0)	0.6384
Prior epi	nd	nd	-	55 (24.1)	16 (26.7)	0.7368
Prior failed endo	nd	nd	-	146 (64)	39 (65)	1.0000
Intra-operative switch	20 (8.3)	3 (5.5)	0.5875	13 (5.7)	2 (3.3)	0.7442
Apical thrombus	1 (0.4)	0 (0)	1.0000	2 (0.9)	0 (0)	1.0000
Concomitant to surgery	5 (2.1)	0 (0)	0.5879	3 (1.3)	0 (0)	1.0000
Transmural scar/aneurysm	8 (3.3)	3 (5.5)	0.4357	1 (0.4)	0 (0)	1.0000
Double prosthetic valve	1 (0.4)	0 (0)	1.0000	0 (0)	0 (0)	1.0000
Ablation outcome						
VT-noninducible	170 (71.1)	39 (70.9)	1.0000	150 (66.1)	36 (60)	0.4474
Non-clinical VT inducible	27 (11.3)	6 (10.9)	1.0000	35 (15.4)	7 (11.7)	0.5429

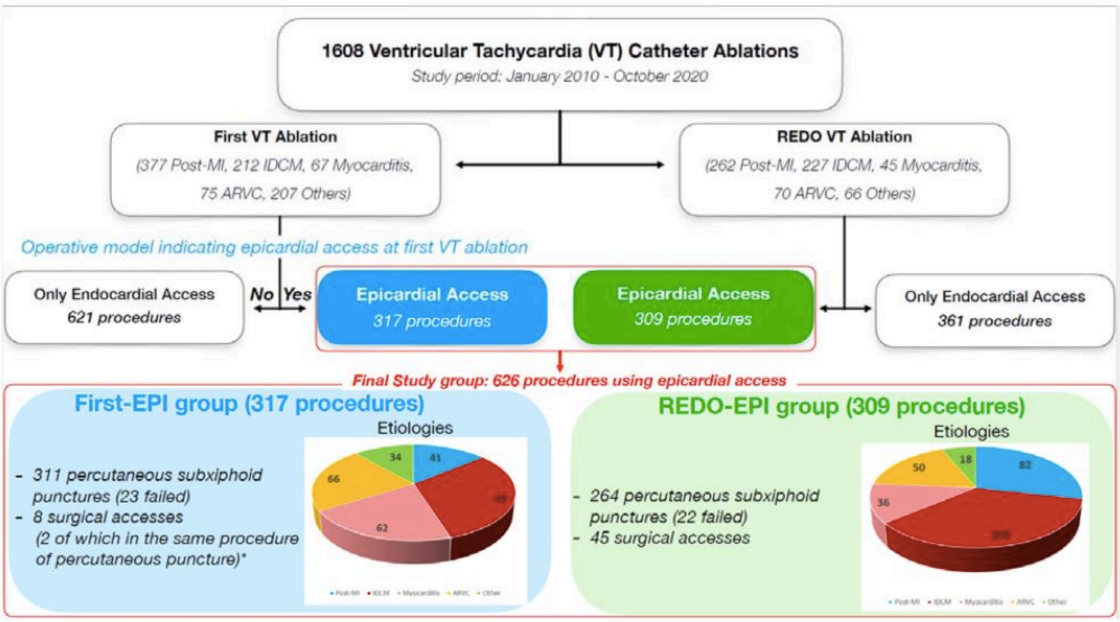
Clinical VT inducible	2 (0.8)	1 (1.8)	0.4640	7 (3.1)	2 (3.3)	1.0000
EPS contraindicated	40 (16.7)	9 (16.4)	1.0000	35 (15.4)	15 (25)	0.0878
In-hospital recurrence	39 (16.3)	10 (18.2)	0.6931	41 (18.1)	21 (35)	0.0076
Complications	6 (2.5)	5 (9.1)	0.02	4 (1.7)	4 (6.7)	0.03

Data are presented as N. (%) or mean±SD.

Abbreviations are ARVC=arrhythmogenic right ventricular cardiomyopathy; CKD=chronic kidney disease; EPS=electrophysiological study; IDCM=idiopathic dilated cardiomyopathy; LVEF=left ventricular ejection fraction; MI=myocardial infarction; NYHA=New York Heart Association; VT=ventricular tachycardia.

Figures and Legends

Figure 1. Study design and patient enrollment. Between January 2010 and October 2020, 1608 VT ablations were performed at the San Raffaele Hospital, of which 938 were first ablation attempts and 670 were REDO procedures. The application of the decision algorithm to the first ablation indicated the epicardial approach in 317 procedures; the indication in REDO patients considered etiology and data from previous ablation procedures. Overall, 626 procedures including epicardial approach were included in the study group.



*2 procedures required both percutaneous and surgical epicardial access.

Figure 2. Left: rate of epicardial vs endocardial procedures according to VT etiologies at first procedure (A) and REDO procedure (B). Right: appropriateness of epicardial approach among different etiologies, respectively in First-Epi (C) and REDO-epi group (D). The absolute numbers are expressed in the boxes.

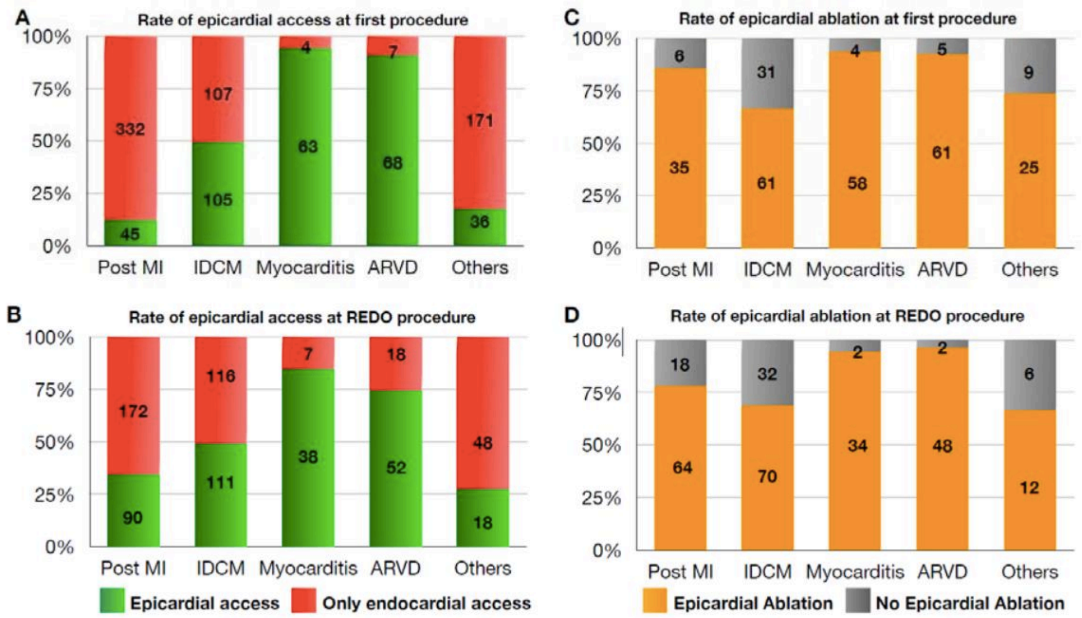
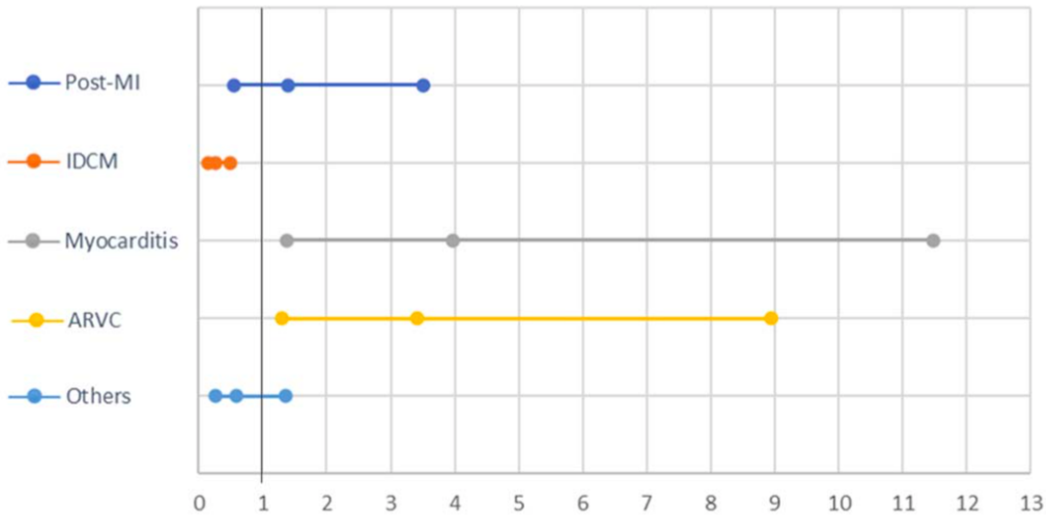


Figure 3. Odds for appropriate epicardial approach of our operative model according to etiologies. Plot of unadjusted OR for the risk of epicardial ablation according to VT etiology in First-Epi group with ultimate epicardial mapping. OR, 95% CI and p-values are reported in the table below. MI: myocardial infarction; IDCM: idiopathic dilated cardiomyopathy; ARVC: arrhythmogenic right ventricular cardiomyopathy; CI: confidence interval; LL: lower limit; UL: upper limit



	OR	CI 95%		p=
		LL	UL	
Post-MI	1,39	0,555	3,501	.665
IDCM	0,27	0,147	0,494	.0001
Myocarditis	3,971	1,376	11,465	.005
ARVC	3,408	1,299	8,937	.007
Others	0,594	0,261	1,357	.24

Figure 4. Inappropriate epicardial approach in IDCM patient with antero-septal substrate at the first ablation attempt. **Left** (from top to the bottom): endocardial bipolar voltage, unipolar voltage and LAT maps. A large septal unipolar scar area encompasses a linear bipolar low-voltage zone. No late potentials were recorded. **Right**: Epicardial bipolar voltage map (top) with patchy low-voltage areas, and LAT map (bottom), showing no late potentials. **Middle**: extensive septal endocardial ablations were delivered (pink dots) targeting endocardial exit sites of the inducible VT morphologies (bottom). No ablations were delivered epicardially, because of the absence of any ablation target.

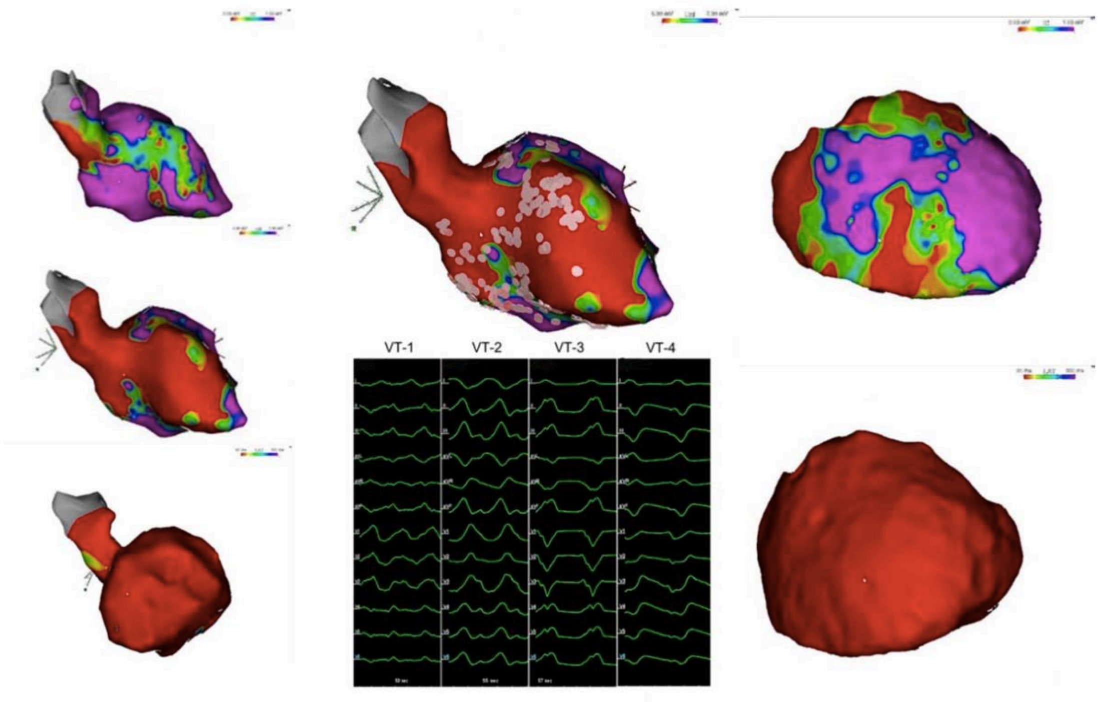


Figure 5. Kaplan-Meier estimates of survival free from VT-recurrences (left) and overall survival (right) in the overall population.

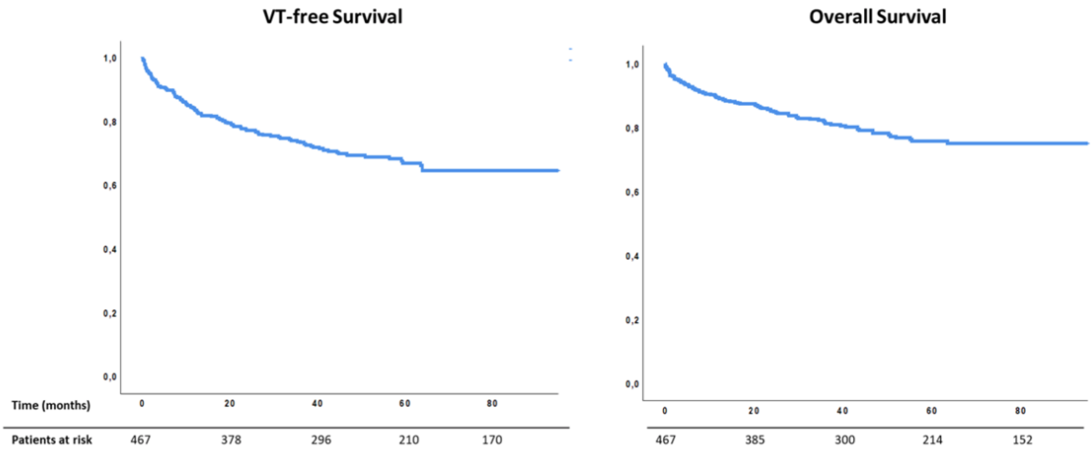


Figure 6. Kaplan-Meier estimates of survival free from VT-recurrences and all-cause of death in the population stratified for etiology (top) and acute procedure outcome (bottom).

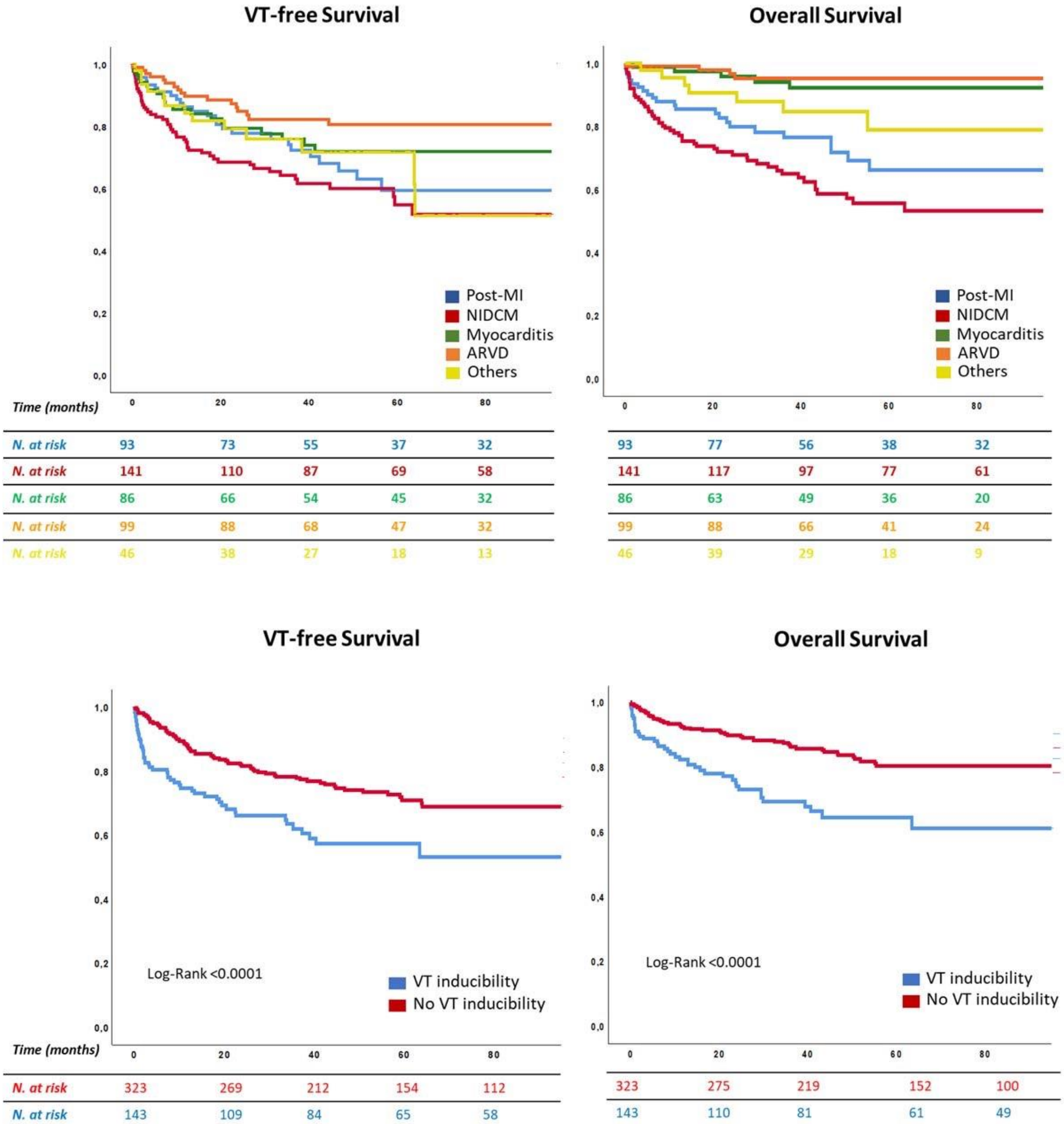


Figure 7. A case of epicardial ablation in a patient with previous myocarditis. Top: Clinical VT showed RBBB morphology, superior axis, CL 277 msec (on the left). Epicardial activation map during VT (middle) tracked the overall diastolic activity (right) by means of multielectrode catheter: entrance of VT isthmus (orange-yellow), mid-isthmus (green) and exit site (light blue). Bottom: ablation set on epicardial infero-lateral wall. Red shadow marks the pathway of a coronary branch.