Management of Ventricular Tachycardia in the Setting of a Dedicated Unit for the Treatment of Complex Ventricular Arrhythmias: Long Term Outcome after Ablation

Running title: Della Bella et al.; Impact of ventricular tachycardia ablation

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Abstract:

Background—We investigated the impact of catheter ablation on ventricular tachycardia (VT) recurrences and survival in a large number of patients with structural heart disease treated in the setting of a dedicated multi-skilled unit.

Methods and Results—Since January 2007, we have implemented a multidisciplinary model, aiming for a comprehensive management of VT patients. Programmed Ventricular Stimulation (PVS) was used to assess acute outcome. Primary end-points were VT recurrence and the occurrence of cardiac and sudden cardiac death. Overall, 528 patients were treated by ablation (634 procedures, range 1-4); Among 482 tested with PVS after the last procedure, a Class A result (non-inducibility of any VT) was obtained in 371 pts (77%), class B (inducibility of non-documented VT) in 12.4% and class C (inducibility of index VT) in 10.6%. After a median follow-up time of 26 months VT recurred in 164 among 472 (34.1%) patients. VT recurrence was documented in 28.6% of patients with Class A result vs. 39.6% of patients with Class B and 66.7% with Class C result (log-rank p<0.001). The incidence of cardiac mortality was lower in Class A patients compared to those with Class B and Class C (8.4% vs. 18.5% vs. 22%, respectively, log-rank p=0.002). Based on multivariate analysis post-procedural inducibility of index VT was independently associated both with VT recurrence (HR=4.030, p<0.001) and cardiac mortality (HR=2.099, p=0.04).

Conclusions—Within a dedicated VT unit, catheter ablation prevents long-term VT recurrences which may favourably affect survival in a large number of patients suffering from VT.

Key words: ventricular tachycardia, catheter ablation, heart failure, death
Introduction

In patients with Ventricular Tachycardia (VT) and structural heart disease, the Implanted Cardioverter Defibrillator (ICD), provides a significant protection against the risk of sudden death, however it does not prevent arrhythmia recurrences and the occurrence of electrical storm (ES), which has been shown to be an independent predictor of cardiac mortality.1-7 A curative strategy is therefore required for the care of patients with recurrent ventricular arrhythmias.4-7

The hospital admission and treatment of VT patients requires the management of a broad spectrum of clinical patterns, ranging from paroxysmal episodes, to incessant VT and ES8, leading to acute cardiac failure9 and cardiogenic shock10; Catheter ablation (CA) plays a relevant role in the treatment of drug-refractory VT episodes, recurrent ICD shocks and ES, lowering VT recurrence and improving quality of life.11-13

Data about the effects of CA on survival are controversial. In the VTACH study no survival benefit was observed in ischemic patients treated by CA before ICD implantation while in SMASH trial there was a trend toward decreased mortality in the ablation group, although not statistically significant.11,12 Recently, Sauer reported a beneficial effect of CA on survival in patients according to CA result.13 Based on the complex nature of VT patients, we have implemented a multidisciplinary model and within this expert environment, we investigated the impact of CA on VT recurrences, hospitalization and survival in a large number of patients with structural heart disease.

Methods

Study design

We have implemented a dedicated unit, focused on the management of patients with VT and
structural heart disease, with the purpose of providing assistance to patients, from hospital admission to discharge and follow up, linking the Electrophysiology Laboratory to the Emergency Area and Intensive Care Unit (ICU), in close co-operation with the Heart Failure Unit and Cardiac Surgery. The VT Unit (VTU) became operative in January 2007 in the Arrhythmia Unit at Centro Cardiologico Monzino in Milan, Italy and has been operational at San Raffaele Hospital, Milan since January 2010. To the best of our knowledge, nowadays this strategy still represents a unique experience of a Unit dedicated to VT.

Physicians, hospitals and ICUs throughout the country referred patients to our VTU staff for admission, using a priority phone line, available 24 hours, 7 days a week. A heliport situated nearby the hospital made the emergency transfer of unstable patients possible. A 24-hour continuous service of care was provided by the arrhythmia staff, able to perform CA at any time during day and night.

Study protocol
Risk classification

Upon admission, patients underwent clinical examination, blood gas analysis, ECG, chest x-ray and echocardiography. Arrhythmia pattern was classified as paroxysmal episodes of VT, incessant VT or ES (≥3 episodes of VT separated by >5 minutes during a 24-hour period). Hemodynamic state was evaluated regarding both VT tolerance as well as the circulatory state during sinus rhythm [cardiogenic shock defined by prolonged phases of severe hypotension (<70 mmHg) persisting beyond the temporary resumption of regular rhythm despite continuous infusion of pressor agents].

All patients with cardiogenic shock were considered high risk. Stepwise assessment of arrhythmia pattern, VT tolerance (any VT causing hemodynamic compromise) and presence of
major [left ventricular ejection fraction (LVEF) ≤ 30% and history of chronic kidney disease (CKD) defined as serum creatinine ≥ 1.5 mg/dl] and minor comorbidities (chronically occluded left anterior descending artery and severe pulmonary disease based on the presence of pCO2 > 50 mmHg) were used to classify patients into those with high and low risk (Figure 1). All high risk patients were subsequently treated in ICU and underwent a CA either at the same time or after correcting metabolic, respiratory and circulatory imbalances. Low risk patients underwent an electrophysiologic evaluation and according to this evaluation were electively considered for CA.

**Catheter ablation procedure**

All procedures were performed under general anaesthesia and mechanical ventilation, with continuous monitoring of invasive arterial pressure and oxygen saturation. In selected cases of patients with incessant VT, CA was performed without general anaesthesia. Written informed consent was obtained from all patients. Patients with BB reentry, focally triggered arrhythmias and fascicular VTs were excluded from the present analysis.

In the absence of contraindications, the LV was accessed by transeptal and retrograde routes in all cases. A first line combined epicardial and endocardial mapping was routinely undertaken in patients with VT and non-ischemic aetiologies: idiopathic dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, previous myocarditis or when pre-procedural imaging suggested the epicardial origin of the re-entrant circuit. Epicardial ablation was the second treatment choice in case of clinical VT recurrence following a previous endocardial ablation. Surgical ablation was undertaken in case of co-existing cardiac surgery indication or in presence of VT that proved to be resistant to endo-epicardial CA.

In all cases we have systematically implemented an ablation strategy of substrate
modification, independently from the VT inducibility, focused on abolition of late and fragmented activity. Specifically, all patients underwent precise electroanatomical mapping in sinus rhythm using the standard definition of scar and border zone. This was the case even after termination of incessant VTs through activation mapping. Programmed ventricular stimulation (PVS) with up to 4 extrastimuli from the right ventricular apex and multiple LV sites (in case of VTs originating from LV) was performed and tolerated VTs were ablated through activation mapping. If non-tolerated VTs were induced, ablation was performed in sinus rhythm only. RF current was delivered with an irrigated-tip catheter aiming to completely abolish abnormal activity at an initial power setting of 30–50W, with a temperature limit of 43°C. Based on the above, general anesthesia was preferred due to enhanced patient comfort, minimized patient movement and most importantly because it aids close monitoring and facilitated adjustment of metabolic, respiratory and circulatory imbalances.

PVS up to four extrastimuli was used to assess acute outcome. Prevention of inducibility of any VT was defined as complete success (Class A); ablation of all previously documented VT(s) with persistent inducibility of any non-documented sustained VTs or ventricular fibrillation was defined as partial success (Class B). The inability to prevent re-induction of one or more previously documented VT(s) was considered as a failure (Class C). In cases of early in-hospital VT recurrence, CA was repeated and the long-term results refer to the period after the last procedure.

**Follow up**

Following the procedure all patients underwent a 5-7 day constant 12-lead ECG telemetry monitoring period in the VTU to assess for possible early VT recurrence. In cases with complete ablation success and an absence of VT recurrence, patients were discharged with therapy
optimization discontinuing amiodarone administration.

Before discharge, all patients were scheduled for regular follow-up visits (at three month intervals) in the VT outpatient clinic or whenever any symptom occurred. All patients who underwent ICD implantation after 2010 at our centre were additionally followed up using remote monitoring.

Primary end-points of the study were the recurrence of sustained VT as documented by regular ICD interrogation or clinical events as well as occurrence of cardiac death and sudden cardiac death (SCD; defined as death resulting from malignant ventricular arrhythmias occurring within 1 hour of the onset of symptoms). Secondary end-points were hospitalization for VT documented recurrence, cardiac decompensation or major eventual medical treatments and interventions.

Statistical analysis
Continuous variables are presented as either means (±SD) or medians (with interquartile ranges), and categorical variables as numbers and percentages. Comparisons between groups were done by unpaired t-test for continuous variables and by Fisher exact test or $\chi^2$ test for proportions, as indicated. Event-free survival was estimated by the Kaplan-Meier method, and curves were compared with the log-rank test. Univariate and multivariate Cox proportional hazards analyses were used to assess the relationship between CA result and study end-points. Differences were considered statistically significant at the 2-sided $p<0.05$ level. All statistical analyses were performed using the SPSS version 15.0 statistical software (SPSS Inc, Texas, Ill, USA).

Results

Study population
Between 2007 and 2011, 616 consecutive patients (548 males, mean age 61±14 years), suffering
from VT episodes due to scar related substrate were referred to the VT Unit. An ICD had previously been implanted in 480 pts; 31 underwent ICD implantation post ablation, 105 were treated by ablation and did not receive an ICD. At the time of admission 58 patients (9.4%) were in incessant VT, 151 (24.5%) had experienced an ES and 407 patients had recurrent paroxysmal VT, (88/407 were at their first VT episode). Catheter ablation was performed in 528 out of these 616 patients. Tolerated VT was present in 62.9% of ablated patients (Table 1).

Among patients with a first onset VT, an ICD was implanted in 35 and CA was offered in 19 of them as a further option due to the inducibility of tolerated VTs under anti-arrhythmic treatment. Moreover, 16 out of 88 patients with a first onset VT underwent ventricular mapping but they were not treated by ablation because of the absence of pathological substrate and VT inducibility, while in the remaining 37 VT was not inducible and they were treated with medical therapy.

One hundred and eight patients (20%) were referred from other ICUs; mean hospital stay was 15±10 days. Four hundred and twenty one pts (79%) had already experienced at least one hospitalization for VT in a different hospital (210 patients in the preceding 6 months); an attempt of CA had been performed in 56 of them (13%).

**Risk stratification and initial management**

On the basis of the abovementioned method (Figure 1), patients were classified into high (n=221, 36%) and low risk (n=395, 64%). Among high risk patients, 53 were directly admitted to the ICU due to the extreme instability of the arrhythmia pattern (ongoing ES in 40, incessant VT in 13) and 18 due to cardiogenic shock during sinus rhythm requiring circulatory support (either Intra-Aortic balloon counterpulsation or Extracorporeal Membrane Oxygenation); concomitant ventilatory support was provided in 10 patients with respiratory failure and haemodialysis in 3
for acute renal failures. Hemodynamic stabilization was achieved in all patients. All high risk patients underwent CA as well as 307 out of 395 (77.7%) low risk ones.

**CA acute results**

Overall, among 528 patients treated by ablation, 634 procedures were performed (range 1-4); Mean duration of the procedure was 220±75 min, mean fluoroscopy time was 36±13 min and mean RF time was 1320±470 sec. The first procedure was endocardial in 348 (66%), endo-epicardial in 156 (29.5%) and surgical in 21 (4.3%). In three patients the epicardium was accessed in the electrophysiology laboratories through a surgical subxyphoid window. In 69 pts ablation was repeated due to in-hospital recurrence of VT during the same hospitalization.

At the end of the last ablation procedure 482 patients underwent post ablation PVS while inducibility was not tested in 46 pts (8.7%) because of absence of VT inducibility at baseline PVS (n=39) or severe acute complications (n=7). A Class A result was obtained in 371 patients (77%), class B in 60 patients (12.4%), class C in 51 patients (10.6%). Class A acute results were more prevalent in low compared to high risk patients (81.1% vs. 71.1%, p=0.01) while the prevalence of a Class B (10.3% vs. 15.4%, p=0.09) and Class C (8.5% vs. 13.4%, p=0.08) result was marginally but not statistically different between low and high risk patients.

Among 60 Class B patients, polymorphic VT degrading to VF was induced in 22 patients, a VT with a different morphology was induced in 28 patients with a previously available ECG of the index VT while a VT with a difference in cycle length ≥50ms was defined as a Class B result in 10 patients with previously available stored ICD electrograms and correspondent cycle length of the initially induced VT. Inducibility of VF was more prevalent in high compared to low risk patients with a Class B result (48.4% vs. 24.1%, p=0.05).

Regarding patients with acute VT recurrence and a second ablation procedure in the same
hospitalization (n=69), a Class A acute result had been registered after the first ablation in 32 patients, Class B in 21 patients and Class C in 16 patients. Accordingly, after the second procedure Class A was achieved in 41 patients, Class B in 10 and Class C in 14 patients, while VT inducibility was not tested in 4 patients.

Amiodarone was maintained in 167 patients (31.6%) after discharge due to ablation failure, in-hospital VT recurrence, or atrial fibrillation; 357 pts (67.6%) were under beta-blocker therapy at the highest tolerated dose.

Complications

Intraprocedural electromechanical dissociation was observed in 3 patients: 2 were supported by ECMO and treated by ablation recovering uneventfully, 1 patient died. Three patients suffered from intra-procedural acute heart decompensation, one had transient total atrioventricular block and one permanent LBBB.

Major vascular complications (arterio-venous fistula/pseudoaneurysm) requiring surgical repair occurred in 23 patients (4%) and minor vascular complications in 38 patients (7%).

Pericardial effusion occurred in 17 patients (3%), requiring drainage due to tamponade in 11 patients (2%). Late tamponade after the pericardial sheath removal (24h after the procedure) occurred in only 2 cases of endo-epicardial CA.

Retro-peritoneal hematoma was evident in one patient due to acute anaemia and treated by surgical repair of the hypogastric artery (endocardial procedure). One patient underwent peri-procedural percutaneous coronary intervention due to acute myocardial ischemia (endocardial procedure). An abdominal hematoma, due to the puncture of a small diaphragmatic artery occurred in 2 patients during subxiphoid puncture, requiring surgical repair in one patient; both recovered uneventfully.
In Hospital follow up

Mean hospitalization time in the VTU was 8±3 days (ranging 5-16). Nine patients died because of refractory heart failure. In 3 patients a Left Ventricular Assist Device was implanted. In-hospital recurrence of paroxysmal VT was experienced by 96 pts (18%).

VT Recurrence

After a median follow-up time of 26 months (interquartile range 13-46), follow up of arrhythmia recurrences was available in 472 patients (47 lost to follow up and 9 experienced in-hospital death without experiencing VT recurrence in this short post-ablation period). No difference was observed between patients lost to follow up and the final study population in any of the assessed clinical characteristics, while CA acute results seemed to be more favorable in patients lost at follow up (Class A 83.7 vs. 76.7%, Class B 14 vs. 12.2% and Class C 2.3 vs. 11.1%), although not reaching statistical significance.

VT recurred in 164 patients (34.1%) and median recurrence survival time was 44.2 months (CI 95% 41.5-46.9). Forty patients experienced at least one hospitalization due to VT during the first 6 months after ablation (comparison to 210 hospital admissions for VT in the preceding 6 months: p<0.001). VT recurrence was documented in 95/332 patients with Class A result in the last ablation procedure (28.6%) vs. 21/53 of patients with Class B (39.6%) and 32/48 Class C (66.7%) result (log-rank p<0.001), as well in 13/39 not tested pts (33%) (Figure 2).

At univariate analysis, VT recurrence was predicted by both post-procedural inducibility of previously documented VT (Class C vs. A and B, HR=4.485, p<0.001) and Class A (vs. B and C) result (HR=0.418, p<0.001), ES as the presenting pattern, presence of non-tolerated VT, NYHA class, IDCM as the VT substrate, LVEF and post-ablation amiodarone therapy. After
performing multivariate analysis, only failed CA (Class C vs. A and B, HR=4.030, p<0.001), presence of non-tolerated VT (HR=1.553, p=0.012) and post-ablation amiodarone therapy (HR=1.492, p=0.024) predicted VT recurrence (Table 2).

Additionally, we analyzed the characteristics of VT recurrence separately for high and low risk patients. Among 175 high risk patients, VT recurred in 37.4% (46/123) of patients with Class A, in 33.3% (9/27) with Class B and in 84% (21/25) of patients with post-procedural inducibility of index VT (log-rank p<0.001). The incidence of VT recurrence was significantly lower in Class A (23.4%, 49/209) compared to Class B (46.2%, 12/26) and Class C (47.8%, 11/23) in low risk patients (log-rank p<0.001). The absence of any post-procedural inducibility (Class A vs. B and C, HR=0.439, p=0.002), instead of the presence of CA failure was associated with VT recurrence in low risk patients. In contrast, post-procedural inducibility of index VT (Class C vs. A and B, HR=5.880, p<0.001), presence of non-tolerated VT (HR=1.710, p=0.032), presence of DCM (HR=1.747, p=0.035) and post-ablation amiodarone therapy (HR=1.810, p=0.019) predicted VT recurrence in high risk patients (Table 3, Figure 2).

**Heart Failure**

At least one episode of heart failure occurred in 41 patients, leading to death in 12 patients. NYHA class was a strong predictor of acute heart failure episode occurrence (HR=1.874, p=0.002) along with the presence of IDCM (HR=2.234, p=0.028) and ES (HR=2.207, p=0.028).

Among 18 patients admitted with cardiogenic shock, 2 patients had in hospital death due to heart failure and 1 patient experienced in hospital ES recurrence and died; Left Ventricular Assist Device was implanted in 3 patients and 1 died due to graft rejection after heart transplantation; among the 14 alive patients, VT recurred in 1 patient during long term follow-up.
Survival

Seventy five pts died during follow up (15.6%): 22 died due to SCD (13 CAD, 7 IDC, 1 ARVD, 1 HCM), 34 due to heart failure (22 CAD, 10 IDC, 1 Valvular, 1 HCM), 19 due to non-cardiac death. The incidence of the combined end point of cardiac death and SCD was lower in patients with a Class A acute result compared to those with a Class B and Class C result (8.4% vs. 18.5% vs. 22%, respectively, log-rank p=0.002), while it reached up to 18% among non tested patients due to baseline non-inducibility (Figure 3).

Based on multivariate analysis cardiac mortality was strongly associated to NYHA class (HR=2.771, p<0.001), presence of ES on admission (HR=2.624, p=0.002), CKD (HR=2.060, p=0.016) and post-procedural inducibility of index VT (Class C vs. A and B, HR=2.099, p=0.041) (Table 4).

Among low risk patients, the incidence of combined cardiac mortality was significantly lower in patients with a Class A (vs. B and C) acute result (3.4% vs. 10.2%, log-rank p=0.031). Furthermore, in the high risk group the incidence of combined cardiac mortality was significantly increased in patients with a Class C (vs. A and B) acute result (33.4% vs. 18.2%, log-rank p=0.05). Multivariate analysis indicated that NYHA class (HR=2.532, p<0.001), presence of ES on admission (HR=3.532, p=0.009), CKD (HR=2.330, p=0.018) and Class C were also the independent predictors of cardiac mortality in high risk patients (HR=2.284, p=0.045), in contrast to low risk patients where NYHA class only predicted cardiac mortality (Table 5, Figure 3).

Analysis of first ablation procedures

In order to investigate the net predictive value of non-inducibility of any VT after the first procedure, we re-analyzed the data considering as VT recurrences, all cases of in-hospital
recurrence irrespectively of whether VT did not recur during long term follow up after the second procedure. Specifically, we compared a Class A acute result after the first procedure (n=321) with any inducible VT (n=114) or baseline non-inducibility (n=37) as the comparator group (47 were lost at follow up 9 had in-hospital death). Notably, non-inducibility after the first procedure was accompanied by lower incidence of VT recurrence (34.3% vs. 57.6%, log-rank p<0.001). Moreover, non-inducible patients after the first procedure (n=324) compared to inducible (n=120) and those with unknown status (n=37) exhibited decreased incidence of combined cardiac death (8% vs. 18.7%, log-rank p<0.001). In successive multivariate analysis, non-inducibility of any VT was independently associated with a lower incidence of VT recurrence (HR=0.516, p<0.001) and combined cardiac death (HR=0.539, p=0.038) (Figure 4, Table 6).

Discussion
Our study reports the 5-year experience of the VTU, the first model implemented to provide a state of the art, co-operative and 24-hour available service for the admission and treatment of patients with VT. Based on our results, a successful VT ablation procedure based on non-inducibility of any VT decreases arrhythmia recurrence and cardiac mortality in the largest series of VT patients with structural heart disease.

Utilization of ICDs is consistently being expanded based on the results of randomized clinical trials demonstrating a greater life expectancy in patients with an increased risk or a history of malignant ventricular arrhythmias1-3; however, patients suffering from ICD shocks have a decreased quality of life if >5 shocks per year are delivered, while a pooled analysis of all randomized ICD trials indicating an ICD-unresponsive SCD rate of 5%1-4,6. Catheter ablation has
been shown to reduce arrhythmia recurrence in patients with VT, however no study has been
powered to test whether prevention or a significant reduction of ICD therapies by CA improves
survival.\textsuperscript{14-17} In the early Cooled RF trial, which included only patients with hemodynamically
stable VT, CA was successful, as defined by elimination of all mappable VTs, in 41\%. VT
recurred in 46\% of patients and the mortality rate was 25\% after 1 year.\textsuperscript{15} In the Thermocool
trial, ablation of all inducible VTs was accomplished in 49\%. VT recurred in 53\% after a 6
month follow-up, but the frequency of VT was reduced by >75\% in 67\% of patients.\textsuperscript{16} The 1-
year mortality rate was 18\% with low LVEF and arrhythmia recurrence being among the adverse
predictors.\textsuperscript{16} In the EuroVT study, a successful procedure was defined by termination and non-
inducibility of all clinically relevant VTs (\textgreater cycle length compared to index VT) and it was
accomplished in 81\% of the patients. VT recurrence was 49\% and a significant reduction of ICD
therapies occurred in 79\%.\textsuperscript{17} Of course, in all these studies any beneficial effect of CA may be
influenced by drug therapy. In patients with incessant VT, CA is the only treatment option with a
recurrence of the same clinical pattern in 24\% and of paroxysmal VT in another 24\%.\textsuperscript{16}
Additionally, when the presenting arrhythmia is ES, a frightening event with poor short and
long-term prognosis, we have previously demonstrated the favourable role of a successful CA,
together with pharmacological therapy, on arrhythmia recurrence and overall cardiac mortality.\textsuperscript{8}

Early CA, before or after the first ICD shock, was performed in the SMASH trial leading
to a 73\% reduction of ICD shocks and a trend towards improved survival in ablated patients.\textsuperscript{11} In
the VTACH trial, CA was applied after the first tolerated VT episode prolonging the time to VT
recurrence and reducing its incidence, while no survival benefit was observed in the ablation
group.\textsuperscript{12} Lastly, in a CA study focusing on long-term mortality, Sauer indicated as independent
predictors the presence of renal disease, poor LVEF, advanced age, VT tolerance and VT
inducibility. Notably, VT ablation performed after the year 2003 (implementing electroanatomical mapping and irrigated radiofrequency technologies) was demonstrated to be more effective than previously in achieving a satisfying long term outcome.\textsuperscript{13}

In the current study we present the impact of CA on the largest series of patients with all clinical patterns of VT presentation and all types of structural heart disease. Our study population is characterized by a high proportion of first VT ablation procedures (87\%) and tolerated VT (62.9\%). The latter could be attributed to the different definition used in previous studies, where non-reproducible and pleomorphic VTs were included together with hemodynamically non-tolerated VTs, as well as to the inclusion of multiple aetiologies of structural heart disease.\textsuperscript{13,14,17} The relatively high success rate of CA (90\% of patients with Class A or B) could be attributed to the comprehensive multi-skilled management of the patients and the systematic implementation of an ablation strategy focusing of endo-epicardial substrate modification, independently from VT inducibility and tolerance. This approach enabled us to achieve a prolongation of time to first recurrence and a reduction in short-term hospitalization due to VT. Moreover, a successful CA procedure based on different classifications of non-inducibility of any VT was associated with lower arrhythmia recurrence rate in both high and low risk patients independently from VT pattern, tolerance and type of underlying heart disease while amiodarone, administrated only after failed CA, predicted recurrence predominantly in less successfully ablated high risk patients. The independent predictive value of amiodarone might be considered a surrogate for ablation failure, indicating the inefficacious role of amiodarone in preventing re-entrant VTs. Notably, in low risk patients post procedural non-inducibility, per se, seems to provide a better outcome, whilst in high-risk patients, non-inducibility of the index VT is associated with lower arrhythmia recurrence rate. The presence of more advanced cardiac disease and the use of a more
aggressive stimulation protocol (up to a 4th extrastimulus) may explain the induction of non-specific VT, leading to a Class B result, in our high risk population.\textsuperscript{18}

The salient finding of the present study is the significant reduction of the incidence of the combined end-point of cardiac death and SCD in VT patients with a Class A acute result as compared to those with a Class B and Class C result (8.4\% vs. 18.5\% vs. 22\%); results were similar when we compared non-inducible patients after the first procedure versus inducible ones and those with unknown status. Moreover, post procedural inducibility of a previously documented VT predicted mortality in high risk patients and in the whole study population.\textsuperscript{10}

The predictive value of post-procedure stimulation regarding VT recurrence and mortality has previously been examined in several studies with contradictory results.\textsuperscript{13,15,19} Indeed, the ability to render an inducible VT non-inducible may simply be a marker for better outcomes and characterize baseline healthier patients. However, independently from the classification used regarding post-ablation non-inducibility, this was accompanied by reduced morbidity and mortality. Remarkably, baseline non-inducible patients, presumed to have a healthier status, exhibited a recurrence rate of 33\% and an incidence of cardiac mortality of 18\%.

The study purpose was not to demonstrate the superiority of our multi-skilled approach to the treatment of VT patients (dedicated VTU, risk classification approach, endo-epicardial ablation performed in general anesthesia and based on substrate modification) as compared to other strategies. We consider it extremely important, although, to describe the complexity of patients with VT beyond CA, focusing on the necessity for global management. According to our results, CA might be proposed as the treatment for high risk patients with VT, whom were previously not considered candidates for invasive therapy, (i.e patients with hemodynamic instability, ES, renal disease) since non-inducibility of index VT is not only life-saving acutely
but can also modify the survival curve of this population. Evolution of techniques and expertise, as well as hemodynamic assistance are pivotal to provide safe and effective procedures in this setting.  

Subsequent hospitalization rate was also markedly decreased as compared to the pre-ablation period. One may suggest that the centralized management of progressively increasing number of VT patients may reduce the public health costs for VT treatment in the long term.

Complications

The reported acute mortality rate in the 2 US multicenter trials and in the EURO-VT trial ranged from 0% to 3%. In our cohort, only one patient (0.2%) expired during the procedure due to electromechanical dissociation, while observed in-hospital mortality was 1.7%. Major complications occurred in 9 patients (2%), while late tamponade occurred only in 2 cases after the pericardial sheath removal. Compared to previous reports (from 0 to 7.3%), our complication rate shows that in an experienced unit focused on VT treatment, CA (including epicardial) is a safe procedure. Moreover, in case of hemodynamic instability, acute hemodynamic support was instituted and no procedures were aborted; substrate modification during sinus rhythm also allowed effective and safe ablation in these patients.

Limitations

This study was a prospective analysis of the short- and long-term outcome in patients with VT treated by CA, not a controlled randomized trial comparing CA with other forms of treatment for VT or a control group. Moreover, 9% of patients were lost to follow-up including a disproportionately high number of patients who were initially found to be rendered non-inducible during ablation. On the other hand, the large size of study population, the prolonged follow up period with a significant incidence of events and the discontinuation of amiodarone in successfully ablated patients constitutes the strengths of our study.
Conclusion

This is the largest clinical experience evaluating the potential benefit of CA for the treatment of VT in patients with any type of structural heart disease, independently from the arrhythmia pattern and VT tolerance. We have implemented a dedicated unit, focused on the treatment and care of these patients from patients’ admittance to electrophysiological procedure, therapy optimization and close follow up, linking the electrophysiology procedure to the Emergency Area and Intensive Care Unit (ICU), in close co-operation with the Heart Failure Unit and Cardiac Surgery. Within this expert environment our results indicate that CA affects favourably VT recurrences, hospitalization and survival in a large cohort of patients suffering from VT. This study supports the implementation of a multidisciplinary unit dedicated to the treatment of VT.

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Conflict of Interest Disclosures: Dr. Della Bella is a consultant for St. Jude Medical and has received honoraria for lectures from Biosense Webster, St. Jude Medical and Biotronik.

References:


Table 1. Baseline clinical characteristics of patients who underwent ablation of ventricular tachycardia.

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<thead>
<tr>
<th>Underlying heart disease</th>
<th>N, %</th>
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<tr>
<td>Ischemic heart disease</td>
<td>290 (54.9%)</td>
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<tr>
<td>Idiopathic dilated cardiomyopathy</td>
<td>109 (20.6%)</td>
</tr>
<tr>
<td>Arrhythmogenic right ventricular cardiomyopathy</td>
<td>34 (6.4%)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>8 (1.5%)</td>
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<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>24 (4.5%)</td>
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<tr>
<td>Previous myocarditis</td>
<td>9 (1.7%)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Myocardial benign tumors</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Storage diseases</td>
<td>33 (6.3%)</td>
</tr>
<tr>
<td>Other diseases</td>
<td></td>
</tr>
</tbody>
</table>

| Age, Mean ± SD, Years                     | 62.1±14 |
| Males/Females                            | 473/55  |
| Left ventricular ejection fraction        | 38.5±13 |
| Left ventricular ejection fraction ≤ 30%, N, % | 190 (36%) |

| New York Heart Association, N, %         |        |
| Class I                                  | 183 (34.7%) |
| Class II                                 | 194 (36.7%) |
| Class III                                | 129 (24.4%) |
| Class IV                                 | 22 (4.2%)  |
| Prior amiodarone therapy, N, %           | 410 (77.7%) |
| Amiodarone adverse reaction, N, %        | 79 (15%)  |
| Renal Disease, N, %                      | 117 (22.2%) |
| Atrial Fibrillation, N, %                | 124 (23.5%) |
| Implantable Cardioverter Defibrillator, N, % | 432 (81.8%) |
| Non-tolerated VT, N, %                   | 196 (37.1%) |
| Electrical Storm, N, %                   | 151 (28.6%) |
| Incessant VT, N, %                       | 58 (11%)  |
| High risk/Low risk                       | 221/307  |

VT=ventricular tachycardia
### Table 2. Univariate and multivariate Cox Regression analysis of VT Recurrences

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CIs)</th>
<th>p</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>1.004 (0.992-1.015)</td>
<td>0.532</td>
<td>1.192 (0.904-1.572)</td>
<td>0.214</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.013 (0.604-1.698)</td>
<td>0.962</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA Class</td>
<td>1.367 (1.146-1.631)</td>
<td>0.001</td>
<td>1.192 (0.904-1.572)</td>
<td>0.214</td>
</tr>
<tr>
<td>Class A (vs. B &amp; C)</td>
<td>0.418 (0.298-0.585)</td>
<td>&lt;0.001</td>
<td>0.920 (0.569-1.489)</td>
<td>0.735</td>
</tr>
<tr>
<td><strong>Class C (vs. A &amp; B)</strong></td>
<td><strong>4.485 (3.002-6.703)</strong></td>
<td>&lt;0.001</td>
<td><strong>4.030 (2.277-7.134)</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>0.978 (0.966-0.991)</td>
<td>0.001</td>
<td>1.000 (0.980-1.020)</td>
<td>0.982</td>
</tr>
<tr>
<td>Non-tolerated VT</td>
<td>1.541 (1.122-2.117)</td>
<td>0.008</td>
<td><strong>1.553 (1.100-2.193)</strong></td>
<td><strong>0.012</strong></td>
</tr>
<tr>
<td>Electrical Storm</td>
<td>1.690 (1.226-2.331)</td>
<td>0.001</td>
<td>1.315 (0.916-1.888)</td>
<td>0.138</td>
</tr>
<tr>
<td>Incessant VT</td>
<td>0.927 (0.544-1.578)</td>
<td>0.779</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Disease</td>
<td>1.209 (0.834-1.752)</td>
<td>0.317</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.102 (0.770-1.577)</td>
<td>0.594</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic Dilated Cardiomyopathy</td>
<td>1.737 (1.230-2.454)</td>
<td>0.002</td>
<td>1.396 (0.960-2.031)</td>
<td>0.081</td>
</tr>
<tr>
<td><strong>Amiodarone Therapy</strong></td>
<td><strong>1.619 (1.183-2.216)</strong></td>
<td>0.003</td>
<td><strong>1.492 (1.055-2.112)</strong></td>
<td><strong>0.024</strong></td>
</tr>
</tbody>
</table>

NYHA=New York Heart Association, VT=ventricular tachycardia

### Table 3. Multivariate Cox Regression analysis of VT Recurrences for low and high risk patients.

<table>
<thead>
<tr>
<th></th>
<th>Low risk patients</th>
<th>HR (95% CIs)</th>
<th>p</th>
<th>High Risk patients</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A (vs. B &amp; C)</td>
<td></td>
<td>0.439 (0.260-0.742)</td>
<td>0.002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class C (vs. A &amp; B)</td>
<td></td>
<td>5.880 (3.375-10.242)</td>
<td>&lt;0.001</td>
<td>Non tolerated VT</td>
<td>1.710 (1.048-2.791)</td>
<td>0.032</td>
</tr>
<tr>
<td>Idiopathic Dilated Cardiomyopathy</td>
<td>1.747 (1.039-2.939)</td>
<td>0.035</td>
<td>Amiodarone Therapy</td>
<td>1.810 (1.101-2.974)</td>
<td>0.019</td>
<td></td>
</tr>
</tbody>
</table>

VT=ventricular tachycardia
Table 4. Univariate and multivariate Cox Regression analysis of Cardiac Mortality

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CIs)</th>
<th>p</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>1.055 (1.027-1.084)</td>
<td>&lt;0.001</td>
<td>1.019 (0.988-1.051)</td>
<td>0.24</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.897 (0.358-2.249)</td>
<td>0.816</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA Class</td>
<td>3.770 (2.747-5.173)</td>
<td>&lt;0.001</td>
<td><strong>2.771 (1.733-4.430)</strong></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Class A</td>
<td>0.389 (0.221-0.686)</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Class C</strong></td>
<td><strong>2.565 (1.310-5.022)</strong></td>
<td>0.005</td>
<td><strong>2.099 (1.032-4.270)</strong></td>
<td><strong>0.041</strong></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>0.926 (0.900-0.952)</td>
<td>&lt;0.001</td>
<td>1.006 (0.969-1.044)</td>
<td>0.768</td>
</tr>
<tr>
<td>Non tolerated VT</td>
<td>1.272 (0.743-2.175)</td>
<td>0.380</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Electrical Storm</strong></td>
<td><strong>5.305 (3.049-9.232)</strong></td>
<td>&lt;0.001</td>
<td><strong>2.624 (1.433-4.805)</strong></td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Incessant VT</td>
<td>1.308 (0.592-2.889)</td>
<td>0.507</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Disease</td>
<td>3.590 (2.119-6.081)</td>
<td>&lt;0.001</td>
<td><strong>2.060 (1.146-3.703)</strong></td>
<td><strong>0.016</strong></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.842 (1.066-3.185)</td>
<td>0.029</td>
<td>1.125 (0.603-2.102)</td>
<td>0.711</td>
</tr>
<tr>
<td>Idiopathic Dilated Cardiomyopathy</td>
<td>1.696 (0.959-2.999)</td>
<td>0.069</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NYHA=New York Heart Association, VT=ventricular tachycardia

Table 5. Multivariate Cox Regression analysis of cardiac mortality for low and high risk patients.

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class</td>
<td>4.000 (1.305-12.265)</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.532 (1.507-4.253)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Electrical Storm</td>
<td>3.532 (1.362-9.163)</td>
<td>0.009</td>
</tr>
<tr>
<td>Renal disease</td>
<td>2.330 (1.155-4.698)</td>
<td>0.018</td>
</tr>
<tr>
<td>Class C (vs. A &amp; B)</td>
<td>2.284 (1.020-5.117)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

NYHA=New York Heart Association, VT=ventricular tachycardia
Table 6. Multivariate Cox Regression analysis of VT Recurrences and Cardiac Mortality according to baseline non-inducibility after the first ablation procedure.

<table>
<thead>
<tr>
<th>VT Recurrences</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA Class</td>
<td>1.323 (1.042-1.681)</td>
<td>0.022</td>
</tr>
<tr>
<td>Non inducibility</td>
<td>0.516 (0.387-0.688)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>1.002 (0.985-1.019)</td>
<td>0.812</td>
</tr>
<tr>
<td>Non-tolerated VT</td>
<td>1.089 (0.808-1.468)</td>
<td>0.575</td>
</tr>
<tr>
<td>Electrical Storm</td>
<td>1.227 (0.895-1.681)</td>
<td>0.203</td>
</tr>
<tr>
<td>Idiopathic Dilated Cardiomyopathy</td>
<td>1.512 (1.098-2.082)</td>
<td>0.011</td>
</tr>
<tr>
<td>Amiodarone Therapy</td>
<td>1.311 (0.976-1.761)</td>
<td>0.072</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac Mortality</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>1.023 (0.990-1.056)</td>
<td>0.177</td>
</tr>
<tr>
<td>NYHA Class</td>
<td>2.875 (1.845-4.481)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non inducibility</td>
<td>0.539 (0.301-0.966)</td>
<td>0.038</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>0.994 (0.958-1.031)</td>
<td>0.749</td>
</tr>
<tr>
<td>Electrical Storm</td>
<td>2.735 (1.529-4.894)</td>
<td>0.001</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>2.013 (1.165-3.476)</td>
<td>0.012</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.030 (0.585-1.813)</td>
<td>0.920</td>
</tr>
</tbody>
</table>

VT=ventricular tachycardia

Figure Legends:

Figure 1. Proposed algorithm for risk stratification of patients presenting with VT based on arrhythmia pattern, VT tolerance and presence of major (chronically occluded LAD and history of CKD defined as serum creatinine ≥1.5 mg/dl) and minor comorbidities (LVEF≤30% and severe pulmonary disease based on the presence of pCO₂ >50mmHg). VT=Ventricular Tachycardia, LVEF=Left Ventricular Ejection Fraction, LAD=Left Anterior Descending Artery, CKD=Chronic Kidney Disease
**Figure 2.** Kaplan-Meier curves of freedom from VT recurrence according to catheter ablation acute result adjusted for arrhythmia pattern, Ventricular Tachycardia tolerance, Ejection Fraction, functional class, type of cardiomyopathy and administration of amiodarone at discharge in the whole study population (**Panel A**), in low (**Panel B**) and in high risk patients (**Panel C**).

**Figure 3.** Kaplan-Meier curves of survival from cardiac and sudden cardiac death according to catheter ablation acute result adjusted for arrhythmia pattern, Ejection Fraction, functional class, age, type of cardiomyopathy, Chronic Kidney Disease and atrial fibrillation in the whole study population (**Panel A**), in low (**Panel B**) and in high risk patients (**Panel C**). Note: Among low risk patients, those without ventricular tachycardia inducibility exhibited significantly improved survival as compared to those with post procedural inducibility (unadjusted log-rank p=0.031).

**Figure 4.** Kaplan-Meier curves of freedom from VT recurrence (right panel) and survival from cardiac and sudden cardiac death (left panel) according to non-inducibility after the first ablation procedure adjusted for covariates.
1. ARRHYTHMIA PRESENTATION PATTERN

ES
INCESSANT VT
PAROXYSMAL VT

2. ASSESS HAEMODYNAMIC TOLERANCE

HYPOTENSIVE VT
TOLERATED VT
HYPOTENSIVE VT
TOLERATED VT
HYPOTENSIVE VT
TOLERATED VT

3. CO-MORBIDITIES EVALUATION

If any
If none
If any
If none
≥1 major or 2 minor
Any other case
2 major or 1 major + ≥1 minor
Any other case
2 major or 1 major + 2 minors
Any other case

MAJOR COMORBIDITIES:
- Chronically occluded Left Anterior Descending Coronary Artery
- History of Chronic Kidney Disease

MINOR COMORBIDITIES:
- LVEF ≤30%
- Severe pulmonary disease

HIGH RISK
LOW RISK

Figure 1
Figure 2

Panel A

- Class A
- Class B
- Class C

p < 0.001

Panel B

- Low risk
- No VT inducible
- VT inducible

p = 0.002

Panel C

- High risk
- Index VT non inducible
- Index VT Inducible

p < 0.001

Freedom from VT recurrence vs Months
Figure 3
Figure 4

The figure shows two Kaplan-Meier survival curves. The left panel depicts the freedom from VT inducible events over time, with two curves representing 'No VT inducible' and 'VT inducible or unknown status'. The p-value for this comparison is less than 0.001.

The right panel illustrates survival from cardiac death, with curves for 'No VT inducible' and 'VT inducible or unknown status'. The p-value for this comparison is 0.038.
Management of Ventricular Tachycardia in the Setting of a Dedicated Unit for the Treatment of Complex Ventricular Arrhythmias: Long Term Outcome after Ablation
Paolo Della Bella, Francesca Baratto, Dimitris Tsiachris, Nicola Trevisi, Pasquale Vergara, Caterina Bisceglia, Francesco Petracca, Corrado Carbucicchio, Stefano Benussi, Francesco Maisano, Ottavio Paolo Della Bella, Francesca Baratto, Dimitris Tsiachris, Nicola Trevisi, Pasquale Vergara, Caterina Bisceglia, Francesco Petracca, Corrado Carbucicchio, Stefano Benussi, Francesco Maisano, Ottavio Alfieri, Federico Pappalardo, Alberto Zangrillo and Giuseppe Maccabelli

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