Results of Ventricular Tachycardia Induction Protocol in Structural Heart Disease – Relation to Long Term Patient Outcomes

PROJECT REPORT
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DECLARATION

I, Dr. Gurbhej Singh, hereby declare that the project in this book, titled “Results of Ventricular Tachycardia Induction Protocol in Structural Heart Disease – Relation to Long Term Patient Outcomes” was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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<tr>
<td>AICD</td>
<td>Automatic implantable cardioverter-defibrillator</td>
</tr>
<tr>
<td>ARVD</td>
<td>Arrhythmogenic right ventricular dysplasia</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>CAG</td>
<td>Coronary angiogram</td>
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<tr>
<td>CRT</td>
<td>Cardiac resynchronization device</td>
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<tr>
<td>CRT-D</td>
<td>Cardiac resynchronization device-defibrillator</td>
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<tr>
<td>DCMP</td>
<td>Dilated cardiomyopathy</td>
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<td>EMF</td>
<td>Endomyocardial fibrosis</td>
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<td>F/U</td>
<td>Follow up</td>
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<td>HF</td>
<td>Heart failure</td>
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<td>HOCM</td>
<td>Hypertrophic obstructive cardiomyopathy</td>
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<td>DVD</td>
<td>Double vessel disease</td>
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<tr>
<td>LBBB</td>
<td>Left bundle branch block</td>
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<tr>
<td>MACE</td>
<td>Major adverse cardiac events</td>
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<tr>
<td>MVP</td>
<td>Mitral valve prolapse</td>
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<td>LV</td>
<td>Left ventricle</td>
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<tr>
<td>RBBB</td>
<td>Right bundle branch block</td>
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<tr>
<td>RV</td>
<td>Right ventricle</td>
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<tr>
<td>RVOT</td>
<td>Right ventricle outflow</td>
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<td>SC Arrest</td>
<td>Sudden cardiac arrest</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
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<tr>
<td>SHD</td>
<td>Structural heart disease</td>
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<tr>
<td>SVD</td>
<td>Single vessel disease</td>
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<tr>
<td>TVD</td>
<td>Triple vessel disease</td>
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<tr>
<td>TCL</td>
<td>Tachycardia cycle length</td>
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<tr>
<td>VF</td>
<td>Ventricular fibrillation</td>
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<td>VT</td>
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INTRODUCTION

Ventricular tachyarrhythmia is one of the most dreaded cardiac event to occur for both the patient and the clinical cardiologist. The risk involved with the occurrence of this arrhythmia is of sudden cardiac death. Hence it is of utmost importance to characterise and risk stratify the patient for any future arrhythmic event, so as to implement measures of prevention. Risk of sudden cardiac arrest is dependent on many factors including the presence of structural heart disease, ventricular function, presence of ischemia, status of autonomic nervous system and the presence of substrate for arrhythmia in the ventricles. The risk stratification of ventricular arrhythmias includes non-invasive evaluation and electrophysiological evaluation. This risk stratification is vital to plan further management as arrhythmias may have varying prognosis. For example, idiopathic monomorphic sustained ventricular tachycardia with hemodynamic stability will have a different prognosis when compared with a monomorphic ventricular tachycardia with a structural heart disease in the presence of left ventricular dysfunction. With the advent of intensive care unit monitoring, long-term ambulatory electrocardiographic (ECG) recordings and implantable cardioverter defibrillators (ICDs), ventricular arrhythmias have been diagnosed more frequently, especially in patients with structural heart disease. Re-entry, triggered activity, or abnormal automaticity are three major categories of arrhythmia mechanisms thought to be responsible for the generation of ventricular
arrhythmias. The contribution of a particular mechanism depends on the type of cardiac disease as well as dynamic factors such as coronary ischemia, medications, electrolyte disturbances, and autonomic influences.

Measures of prevention include drugs, substrate modification or implantation of devices in the form of implantable defibrillators. Drugs form the mainstay of management in the absence of other treatment modalities but needs a careful attention to the adverse effects and the pro-arrhythmic nature of certain classes of drugs. Also VT may be refractory to drugs and may need additional treatment modalities like radiofrequency ablation or an implantation of an ICD. For a successful radiofrequency ablation procedure, it is necessary to understand the mechanism of origin of tachycardia. Ventricular tachycardia may have a focal origin, the mechanism being either automaticity, triggered activity or a micro re-entry. In most of the cases of non-focal ventricular tachycardia, the mechanism is re-entrant.

Wellen’s et al [1] in 1972 first described the induction and termination of ventricular tachycardia with timed extra stimuli suggesting a re-entrant mechanism.

Over the years VT induction protocol as part of evaluation of syncope or risk of SCD has evolved in significance. There are multiple variables affecting the results of this study and the eventual outcomes depend on nature of structural heart disease, functional class and drug treatment as well as the nature of response.
elicited by the study. While currently available data gives some credence to the utility of VT induction studies in patients with stable ischemic cardiomyopathy, there are some unresolved questions – a) is there a sufficiently sensitive threshold for a result derived from VT induction studies to classify the patient as low risk? b) does ‘non-specific’ or ill sustained tachycardia have relevance to prognosis? The relevance of the results can be assumed to be different for different substrates but can be confirmed only by a long term follow up of patients who have undergone these studies. Further, the relevance of VT induction studies would have changed in the current era since most of the patients in this group would be on class III anti arrhythmic agents (amiodarone). In the ICD era we know that patents with more stable VT has more number of appropriate treatments. It is possible that the type of arrhythmic event may be determined by nature of induced VT in induction studies.

In this study, we evaluated the potential ability of EP inducibility to predict the likelihood of subsequent arrhythmic or adverse cardiac events in structural heart disease patients.
REVIEW OF LITERATURE
In majority of sudden cardiac death (SCD) cases ventricular tachyarrhythmia are the precipitating cause. Holter recordings during such events have shown that the most commonly ventricular tachyarrhythmia is the underlying event rather than brady-arrhythmia. It has been seen that patients who had a sudden cardiac death while on holter recording most often have been found to have a VT (ventricular tachycardia) that degenerated to VF (ventricular fibrillation). \[2\]

Resuscitated cardiac arrest survivors or patients who have had a ventricular tachycardia with hemodynamic compromise have a death rate of 20% in the first year post event. \[3\]

Electrophysiological testing results in supraventricular tachycardia induction in 4-5% of cardiac arrest survivors, which might have been the cause of sudden cardiac arrest. \[4\]

The use of electrophysiological studies with programmed stimulation has been demonstrated to be a valuable approach to the identification of patients at risk of sudden death and/or ventricular arrhythmias or to the evaluation of symptoms such as palpitation, dizziness, or syncope or to guide therapy of chronic tachy-arrhythmias. While induction of VT indicates a specific arrhythmogenic anatomic substrate, induction of VF increases greatly with the aggressiveness of the
stimulation protocol and therefore may be an unspecific response. The induction of VF in patients without prior documentation of sustained ventricular tachyarrhythmia and with preserved left ventricular function, even when induced with one or two extra stimuli, is not useful in the prediction of clinically relevant tachyarrhythmia.

However, the value of induced VF during programmed stimulation in patients at high risk for arrhythmogenic sudden cardiac death is controversial.

**MECHANISM OF VENTRICULAR TACHYCARDIA:**

Mechanism of arrhythmia can be: automaticity, triggered activity, or re-entry.

**AUTOMATICITY:**

Automaticity also called the spontaneous impulse formation is the spontaneous depolarization to reach the threshold potential resulting in propagation of action-potential. It can be enhanced normal automaticity or abnormal automaticity.

Enhanced normal automaticity is a property of normal pacemaker tissue or latent pacemakers where they can start acting like a functional pacemaker. Abnormal automaticity can occur anywhere in the heart where there are abnormal transmembrane potentials, particularly in the steady state depolarization of the membrane potential. In the ventricles the purkinje fibres have spontaneous diastolic depolarization property whereas myocardial cells do not exhibit this property. Also purkinje fibre automaticity may be increased with myocardial
infarction. There is role of autonomic system in regulation of automaticity in the normal or latent pacemakers.

Automaticity may be the underlying cause for atrial tachycardia, accelerated idioventricular rhythms, and ventricular tachycardia secondary to ischemia and also reperfusion.

**TRIGGERED ACTIVITY:**

Triggered activity is the impulse formation in cardiac fibres secondary to afterdepolarization following a preceding impulse or a series of impulses. After-depolarization can be early or delayed, and when this reaches the threshold potential a new action potential is generated. This always occurs as a result of previous impulse in contrast to automaticity which can occur in the absence of such preceding impulse.

**RE-ENTRY:**

The presence of a scar in myocardium suggests fibrosis with surviving myocardial bundles which traverses and thus forms the channels which acts as limb of activation of a re-entry circuit. Additional cell to cell coupling is seen to be reduced. Thus there is slow conduction through these created channels and the substrate for re-entry is set for arrhythmia to occur. There is multiple channel involvement in structural heart disease patients as seen by the multiple morphologies of induced arrhythmias.\(^5\)\(^6\)
VT IN STRUCTURAL HEART DISEASE:

Structural heart disease patients have a substrate for arrhythmogenesis due to structural changes in the ventricles. Scar due to ischemic heart disease is most commonly the substrate for ventricular arrhythmias and is seen in approximately 60% of the patients. Also patients with dilated cardiomyopathy, ARVC (arrhythmogenic right ventricular dysplasia), HCM (hypertrophic cardiomyopathy), prior cardiac surgery, sarcoidosis can also have substrate in the form of a scar. [7]

Non sustained VT or premature ventricular complexes may also be seen in structural heart disease patients with the mechanism being focal automaticity or triggered activity, or scar related re-entry. [8] Studies initially had suggested the association of presence of ventricular ectopy and reduced LVEF to the risk of sudden cardiac death. [9] But recent data has shown that this increased mortality is as a result of the structural heart disease. [10] Also ambulatory monitoring of the heart failure patients has shown NSVT does not predict an increased risk of sudden death. [11]

VT INDUCTION STUDY:

After first reported in 1972 VT induction study has been used as a method to predict, prognosticate, guide management and as a part of VT ablation procedures. However, its importance in patient with LVEF < 30% was questioned after the MADIT II trial showed the benefit of AICD implantation in all patients
with LVEF< 30% without being guided by EP testing. However, VT induction study stills holds a value in guiding management in patients with documented arrhythmias and structural heart disease. It was also seen in the MADIT II trial that patients who had undergone VT induction and had VT induced had higher recurrence on follow up.

**Buxton et al** analysed patients with non-sustained ventricular tachycardia (n=62) with chronic coronary artery disease. 28 (45%) patients had a sustained VT induced. 44 patients had their therapy guided with electrophysiological study: 19 patients with no inducible sustained VT did not receive antiarrhythmic therapy, and 25 patients with inducible sustained or symptomatic non-sustained VT received therapy guided by the results of electrophysiological studies. The results of electrophysiological studies were ignored by physicians for a second group of 18 patients: four had inducible sustained VT but received no antiarrhythmic therapy, and 14 had inducible sustained or non-sustained VT and received antiarrhythmic therapy not guided by results of electrophysiology testing. At mean 28 months follow up, 11 patients had sudden death. 7/11 patients who died suddenly had inducible sustained VT. 3 out of 44 patients in the group receiving therapy guided by electrophysiological studies died suddenly versus 8/18 in the group receiving therapy not guided by electrophysiological studies (p = .001). Multivariate analysis of the relationship of induced arrhythmias, left ventricular ejection fraction, site of myocardial infarction, history of syncope, or type of antiarrhythmic therapy to outcome revealed a greater than twofold
increased risk for sudden cardiac death in patients whose therapy was not guided by results of electrophysiological study. Patients with inducible sustained VT are at a significantly increased risk for sudden cardiac death, and in this group therapy that prevents induction of sustained VT is associated with a lower rate of sudden cardiac death than empiric therapy.\textsuperscript{12}

**SIGNIFICANCE OF INDUCED VT:**

There is data to suggest that induction of VT during EP testing is associated with higher incidence of events on follow up.

Daubert et al\textsuperscript{13} studied the patients included in MADIT II trial and found that 593 underwent electrophysiology study out of 720 patients. The patients who were inducible had greater number of ICD shocks as compared to the non-inducible arm. ICD therapy for spontaneous VF was less common in inducible group as compared to the non-inducible. 2 year event rate (Kaplan Meier) for VT/VF, in the inducible group was 29.4% and 25.5 % for the non-inducible group. They further found that induction of polymorphic VT/VF even with double extra-stimulus was less relevant as compared to the induction of monomorphic VT.

MUSTT\textsuperscript{14} (Multicentre Un-Sustained Tachycardia trial) sub-study had shown a significant risk of mortality in EP inducible patients when compared with non-inducible group. 2-year mortality was 1.33 fold higher than non-inducible patients in these post MI patients.
**Sausa J et al** studied 56 patients with coronary artery disease who presented with aborted sudden cardiac death unrelated to myocardial infarction. Mean LVEF was 0.34±16. During EP testing sustained monomorphic VT was inducible in 22 patients who subsequently underwent a electrophysiological pharmacological testing. 11 patients had suppression of VT induction, 10 did not have and underwent AICD implantation. Among the 34 patients who did not have VT induction, the precipitant of arrhythmia was identified and corrected in 9 out of 34. An AICD was recommended in the remaining 25 patients. It was seen that 2-year incidence of sudden death was 31 % in patients on drugs after EP testing, 26 % in patients on drugs empirically, 0 % in correctable causes and 9 % in AICD group. At 3-years cumulative incidence of sudden death in patients on drugs was 53 % as compared to 9 % in the AICD group which was statistically significant. [15]

**Swerdlow et al** [16] prospectively studied 196 consecutive survivors of out-of-hospital ventricular fibrillation (VF) not associated with acute myocardial infarction and 46 consecutive, control patients without prior ventricular arrhythmias. Programmed stimulation included two extra stimuli (S3 protocol) in all patients and three extra stimuli (S4 protocol) in the last 140 study patients and in all control patients. In study patients, logistic regression identified two independent predictors of induced, sustained VT for both S3 and S4 protocols: prior spontaneous, sustained VT (37 patients; p .001) and prior myocardial infarction (113 patients; p = .005). With the S3 protocol, sustained VT was
induced in 54% of patients with both prior myocardial infarction and prior sustained VT vs 4% without either; with the S4 protocol, sustained VT was induced in 91% vs 13%, respectively. Eighty-three percent of induced VT episodes had a cycle length less than 300 msec, and all required termination by cardioversion or pacing. VF was induced only in survivors of out-of-hospital VF without prior, spontaneous, sustained VT (S3 protocol, 9%; S4 protocol, 24%) but not in study patients with prior sustained VT (S3, p = .10; S4, p = .05) or control patients (S3, p = .06; S4, p = .01). The mean coupling intervals of extra stimuli that induced VF were not significantly different from the intervals that induced sustained VT. These data indicate that prospective analysis of clinical variables can identify survivors of out-of-hospital VF with a very high and very low probability of induced sustained VT and that there is a significant correlation between induced VF and spontaneous out-of-hospital VF as the only clinical arrhythmia.

Elder et al [17] analysed clinical, electrophysiological and follow-up data for 108 patients with aborted sudden death. The mean follow-up interval was 2 years. All patients underwent baseline drug-free invasive electrophysiology studies. Seventy-five patients (group I) had inducible ventricular arrhythmias (including non-sustained and sustained ventricular tachycardia and ventricular fibrillation) and 33 patients (group II) had no inducible arrhythmias. Non inducibility was not predictive of a favourable outcome, because the incidence of both sudden death and recurrent ventricular tachycardia was similar in the two
groups. Treatment guided by electrophysiology testing was used in 17 patients; in 13 (17%) in group [arrhythmias became non-inducible, and in 4 (5%) sustained ventricular arrhythmias became non-sustained after administration of conventional drugs. There was a significantly higher incidence of sudden death and recurrent ventricular tachycardia in the 4 patients with inducible arrhythmias (n =3, 75%) compared with the 13 patients whose arrhythmias were non-inducible (n =2, 15%) (p < 0.05). For the group as a whole, 11% died suddenly and 15% had recurrence of ventricular tachycardia. Sixty-four patients were treated with amiodarone and, of these, four (6%) died suddenly during the follow-up period and nine (14%) had recurrent ventricular tachycardia. Ventricular arrhythmias could be induced in 69% of patients with aborted sudden death but inducibility could be suppressed in only 20% of them. The role of therapy guided by electrophysiology testing could therefore not be fully assessed. The findings reveal a significant recurrence rate of symptomatic, potentially life-threatening ventricular arrhythmias in medically treated patients with aborted sudden death.

Also it has been seen that non inducibility at the end of VT ablation is a marker of better long term outcomes.

**RISK STRATIFICATION:**

MADIT [18] (Multicentre Automatic Defibrillator Implantation Trial) showed the benefit of programmed stimulation to risk stratify the patients with prior MI, LVEF ≤ 35%, NYHA class I, II or III and having a documented asymptomatic
non-sustained VT and who had inducible, non-suppressible ventricular tachyarrhythmia. 196 patients were randomly assigned to receive an implanted defibrillator (n = 95) or conventional medical therapy (n = 101). Mean follow up of 27 months showed 15 deaths in the defibrillator group (11 from cardiac causes) and 39 deaths in the conventional-therapy group (27 from cardiac causes) (HR overall mortality, 0.46; 95% CI, 0.26 to 0.82; p < 0.009). There was no evidence that amiodarone, beta-blockers, or any other anti-arrhythmic therapy had a significant influence on the observed hazard ratio.

The MADIT II [19] was designed to evaluate the potential survival benefit of a prophylactically implanted defibrillator (in the absence of electrophysiological testing to induce arrhythmias) in patients with a prior myocardial infarction and a left ventricular ejection fraction of 0.30 or less. During an average follow-up of 20 months, the mortality rates were 19.8 percent in the conventional-therapy group and 14.2 percent in the defibrillator group. The hazard ratio for the risk of death from any cause in the defibrillator group as compared with the conventional-therapy group was 0.69 (95 percent confidence interval, 0.51 to 0.93; P = 0.016). The effect of defibrillator therapy on survival was similar in subgroup analyses stratified according to age, sex, ejection fraction, New York Heart Association class, and the QRS interval.

Vanderpol et al [20] studied five hundred twenty-nine patients with programmed ventricular stimulation for evaluation of supraventricular and ventricular tachy-arrhythmias. Eighty-six patients had clinical ventricular
tachycardia. Sustained ventricular tachycardia was induced in 91% of the 57 patients with a sustained form of the arrhythmia clinically, non-sustained ventricular tachycardia was induced in 62 percent of 29 patients with a symptomatic non-sustained form clinically, in 4 percent of 57 patients with a sustained form and in 0.7 percent of the 443 patients with no documented spontaneous ventricular tachycardia. All 52 patients with induced sustained ventricular tachycardia had the sustained form clinically. The morphologic features, axis and cycle length of 54 of 62 episodes of induced ventricular tachycardia in 43 patients were similar to those of the clinically observed arrhythmia. They concluded that VT resembling the clinical variety can be induced in the laboratory in almost all patients with sustained VT clinically, in the majority of those with symptomatic NSVT clinically, and only rarely in patients with no previously documented VT.

VT INDUCTION- METHOD OF INDUCTION:

S. Zaman et al compared the VT induction with ≤3 extra-stimuli versus four extra-stimuli in 432 patients. 164 had induction of VT, with less than or equal to two, three, and four ES in 24% (n - 39), 46% (n - 75), and 30% (n - 50). When compared VT induced with 4th extra-stimulus was faster (shorter CL (218 vs. 256 msec, P - 0.01) and more haemodynamically unstable requiring DC version (77 vs. 55%, P - 0.05). It was found that at the end of 3 years these patients were at equal risk of events on follow up. [21]
Also multiple studies have shown previously that induction of VT/VF increases with the number of the extra-stimulus are used.\textsuperscript{[22]} VT can be induced in a significant proportion of patients with the fourth ES. These patients are at comparable risk of arrhythmia to patients with inducible VT with less than or equal to three ES.

**VT INDUCTION IN CORONARY ARTERY DISEASE:**

In coronary artery disease and left ventricular (LV) dysfunction induction of ventricular tachycardia is seen to predict the occurrence of spontaneous arrhythmia on follow up\textsuperscript{[23]}.

MADIT I and II were also done in CAD patients both had shown that induction of VT predicts the recurrence of ventricular arrhythmia on follow up.\textsuperscript{[17,18]}

Kadish et al\textsuperscript{[24]} concluded from a study done in 280 patients with Non sustained VT that VT is most often inducible in patients with coronary artery disease and least often in patients without structural heart disease. With the exception of patients with idiopathic dilated cardiomyopathy, management of patients with non-sustained ventricular tachycardia guided by electrophysiological testing appears to resulted in low incidence of sudden cardiac death although effects on total mortality were less impressive. Patients with idiopathic dilated cardiomyopathy and patients with other heart diseases who continue to have inducible ventricular tachycardia despite antiarrhythmic drug therapy are at substantial risk of sudden cardiac death.
VT INDUCTION IN DILATED CARDIOMYOPATHY:
Milner, P.G. et al \[25\] studied the value of EP testing and VT induction in 19 patients of idiopathic dilated cardiomyopathy who had symptomatic ventricular tachycardia (VT) or ventricular fibrillation (VF). 13(68\%) patients had clinical ventricular tachy-arrhythmias induced. 9(69\%) patients had suppression of VT induction following drug testing. On \(17\pm11\) months follow up no significant difference was seen among the patients with or without inducible ventricular arrhythmia. These data indicate that the sensitivity of programmed ventricular stimulation in these was approximately 70\%, and that non-inducibility during control EPS or prevention of arrhythmia induction with antiarrhythmic therapy does not confer long-term protection against recurrent arrhythmias.

REPRODUCIBILITY OF VT
Brembilla et al\[26\] evaluated the reproducibility of arrhythmia induction in patients of CAD without spontaneous documented VT, not on anti-arrhythmic drugs and depressed LV function in 30 patients which were divided into 2 groups after VT induction, group I (17)as having inducible and group 2(13) as having non inducible. On follow up during PVS second time it was seen that all patients except one had inducible VT in group I but there was change in cycle length. In group 2 five patients had inducible VT with a reproducibility of 61.5 \%. They
concluded that in CAD patients with VT non inducible and later with new onset of symptoms, require PVS again to decide for management.

Many previous studies have demonstrated a reproducibility of 76-96% varying in duration from hours, days to weeks after the first PVS. [27]

**SIGNIFICANCE OF PATTERN OF ARYRHYTHMIA INDUCED:**

Meyborg et al [28] did a prospective study on 102 patients at high risk for arrhythmogenic sudden cardiac death who received an automated implantable cardioverter-defibrillator (AICD). 56 patients received the AICD for primary prevention and 46 for secondary prevention. 58 patients had induction of a monomorphic VT (VT group) and 44 had induction of a polymorphic VT, ventricular flutter, or ventricular fibrillation (VF group) during programmed electrical stimulation. Average follow up was 20 months in both groups. In patients who received the AICD for primary prevention, 16 of 32 patients in the VT group, compared with only four of 24 patients in the VF group, received an appropriate AICD protocol (p = 0.02). In the entire study population, 479 appropriate AICD protocols were recorded in 28 (48%) patients in the VT group and 28 appropriate protocols in 11 (25%) patients in the VF group. Cumulative Kaplan-Meier event-free survival curves were significantly different (p = 0.02).

Kou et al performed 206 programmed ventricular stimulations in 130 patients with either a documented VT or syncope. Non sustained polymorphic VT was induced in 111, and with continuation of stimulation sustained monomorphic VT
in 48, and sustained polymorphic VT in 13. Overall sustained monomorphic VT was induced in 110 and polymorphic VT in 18. The incidence of non-sustained polymorphic VT preceding the induction of sustained monomorphic VT was significantly greater than sustained polymorphic VT. Hence they concluded that non sustained VT induction is not a predictor of outcome of programmed ventricular stimulation and use of non-sustained polymorphic VT as end point will increase specificity of the study by limiting the number of non-clinical arrhythmias at the cost of significantly impairing the yield of monomorphic VT induction. [29]

LONG TERM OUTCOMES:
Daubert et al [30] did a DEFINITE (Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation) sub study where patients randomized to the ICD arm, but not the conventional arm, underwent non-invasive EP testing via the ICD shortly after ICD implantation using up to three extra stimuli at three cycle lengths plus burst pacing. Inducibility was defined as monomorphic or polymorphic VT or VF lasting 15 seconds. Patients were followed for a median of 29+ months (interquartile range = 2–41). An independent committee, blinded to inducibility status, characterized the rhythm triggering ICD shocks. In follow-up, 34.5% of the inducible group (10 of 29) experienced ICD therapy for VT or VF or arrhythmic death versus 12.0% (21 of 175) non-inducible patients (hazard ratio = 2.60, P = 0.014).
MANAGEMENT OF PATIENTS WITH VT IN STRUCTURAL HEART DISEASE:

**ICD**

ICD implantation as such is not seen to prevent occurrence of VT and patients require drugs in 39–70% of patients to reduce the arrhythmic events. [31]

The SCDHeFT trial included patients with both ischemic and non-ischemic cardiomyopathies, an LVEF of ≤35%, and NYHA class ii or iii heart failure. Patients were randomly assigned to receive an ICD, amiodarone, or conventional therapy. although no difference in survival was found between the amiodarone therapy and conventional therapy groups, ICD use reduced mortality by 7.2% over 5 years compared with conventional therapy, which corresponds to a relative risk reduction of 23%. [32]

**VT ABLATION**

It has been seen that induction of VT on EPS is related to higher sudden cardiac arrest or spontaneous VT/VF on follow up as compared to non-inducible group. Also cardiac mortality has been seen to be higher in patients in the inducible group. No VT/VF induction at EP study has been seen to have improved survival on long term. [33]

Most of the data for VT ablation comes from ischemic cardiomyopathy patients. The success rate is reported from 50-80%, with up to 10 % incidence of major complications. [34] In cases of dilated cardiomyopathies and ARVC scars are mid-
myocardial or epicardial and access may be a challenge. Epicardial approach under fluoroscopic guidance is helpful to reach potential spaces for radiofrequency ablation.\textsuperscript{[35]}

Reddy et al. performed catheter ablation in patients who had a AICD implanted for secondary prevention of ventricular arrhythmias and compared with the conventional group. It was found that ablation group had significant reduction of IID therapy from 33\% to 12 \% (p=0.007). Although the trial was powered enough for assessment of mortality but a trend towards reduction in mortality was seen.\textsuperscript{[36]}

**DRUGS:**

It is seen that patients with heart failure are at risk of VT, the incidence of sudden cardiac death is reduced with beta blockers and angiotensin converting enzyme inhibitors.\textsuperscript{[37],[38]}

Amiodarone and sotalol have been shown to reduce the number of device therapies but not the mortality.\textsuperscript{[39],[40]}

Connolly et al studied patients with LVEF \(\leq 40\%\), with a history of a sustained ventricular arrhythmia and received a AICD, and randomly assigned them to receive a \(\beta\) blocker, sotalol, or amiodarone plus a \(\beta\) blocker. At 12 month follow up it was seen that patients on beta blockers had AICD shocks in 39\%, 24\% in the sotalol group and 10 \% in the amiodarone and the beta blocker group. The discontinuation rates were high in the sotalol and amiodarone groups.\textsuperscript{[41]}

Amiodarone the most widely used drug has been studied and the markers such as inducibility on amiodarone, QT prolongation, reverse T3, and ventricular
effective refractory period have been studied to predict efficacy, effect or absorption. [42] [43] Fisher et al[44] reviewed the value of programmed electrical stimulation (PES) and Holter monitoring in the assessment of amiodarone efficacy. Non-inducibility was associated with a favourable prognosis among 366 VT patients. 88 (24%) were found to be non-inducible on amiodarone, and 10% of these had recurrences. 39% patients were inducible on amiodarone therapy. Further, increased difficulty of induction with PES or induction of a slower or better tolerated VT may indicate a favourable outlook, and add to the value of PES. It was seen that suppression of previously frequent arrhythmias meant excellent protection for patients with benign arrhythmias and moderate protection with malignant arrhythmias. Holter assessment was done in 186 VT patients. It was found that in 114 (61%) patient’s arrhythmias were suppressed, and recurrences were seen in 18% whereas in 50% patient’s arrhythmias were not suppressed. It was also found that arrhythmias on amiodarone had lower rate.

Krafchek, J, et al studied prospectively 45 patients with ischemic heart disease and inducible sustained monomorphic ventricular tachycardia to see whether slower onset of action of amiodarone is seen to have effect on inducibility of arrhythmias. They defined “non-inducible” on medication as absence of induction of arrhythmia and change from a sustained to a non-sustained type. They found that early testing for inducibility at 2-3 weeks resulted in non-inducibility at 2-3 weeks and further additional 18 % had non inducibility at 6 weeks. Hence they
concluded testing for VT induction at a later date correctly predicts the recurrence rate. [45]

**ROLE OF ELECTROPHYSIOLOGICAL TESTING IN SELECTING ANTI ARRYTHMIC DRUGS:**

EP testing is useful to guide anti-arrhythmia by studying the effect of drug to inhibit inducibility. Horowitz et al studied 20 patients having recurrent sustained ventricular tachycardia for the predictive value of electrophysiological testing (EPS) and therapeutic efficacy of antiarrhythmic drugs. After initial control EPS the effects of drugs like lidocaine, procainamide, quinidine, disopyramide and diphenylhydantoin on the ability to initiate VT were assessed. Procainamide prevented the initiation of sustained VT in 9 of 20 patients (8 patients when administered orally), Quinidine prevented 3 of 12 patients. In only one patient were procainamide and quinidine both successful. Disopyramide was successful in one of five patients in whom it was used. One of these drugs was successful in preventing the initiation of VT in 11 of the 20 patients. [46]

Several studies have examined the role of ejection fraction, Holter monitoring, the signal averaged electrocardiogram, and electrophysiological testing in defining prognosis in patients with ventricular tachycardia. However, the use of these diagnostic tests and the most appropriate form of therapy in patients with various types of heart disease and ventricular tachycardia are as yet unclear. The purpose of this study is to describe the outcome in a large cohort of patients with
various types of structural heart disease who had ventricular tachycardia and whose management was guided by electrophysiological testing.
AIM AND HYPOTHESIS
AIM

1) To identify the electrophysiological information derived from VT induction studies and correlate it to long term outcomes in patients with structural heart disease.

2) To study prognostic value of induced monomorphic ventricular tachycardia (VT) and ventricular flutter or fibrillation (VF) during programmed electrical stimulation in patients with structural heart disease.

HYPOTHESIS

VT inducibility during electrophysiological testing can predict recurrence of ventricular arrhythmias and mortality.
MATERIAL AND METHODS
MATERIAL AND METHODS

STUDY DESIGN:

- **Setting:** Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology

- **Study duration:** JULY 2014-DEC 2015

- **Patient inclusion:** Jan 2004- Dec 2014

- **Study design:** Retrospective longitudinal observational follow up study

A retrospective evaluation of all VT induction protocols was done in patients with structural heart disease. Consecutive patients who had undergone VT induction studies in SCTIMST were included in the study. This included VT induction as part of VT ablation procedures before radiofrequency ablation during the said procedure.

**Inclusion criteria:**

All VT induction studies done electively in

1. Patients with documented ventricular tachycardia (including VF) or syncope, and

2. Structural heart disease
Exclusion criteria:

VT induction studies done in patients with the following conditions were excluded from analysis

1. VT storm, during admission for VT storm
2. Acute coronary syndrome.
3. Uncontrolled heart failure

PROCEDURE:

All patients after detailed history, clinical examination and investigations were told to withhold anti arrhythmic drugs for at least five half-lives. Informed consent was taken from all patients before procedure. Pre applied defibrillator pads were applied at the beginning. Arterial line was secured before the beginning of procedure. Most of the patients were catheterized for procedure as the procedure times are long sometimes. Monitoring of all vital parameters were done. Patients who were on anticoagulation were shifted to heparin with monitoring of a PTT.

Baseline measurement included recording of baseline cycle length, and all necessary intervals (Atrial-His, His bundle-ventricular, His potential). As a minimum we used a right atrial electrode, his bundle electrode, coronary sinus electrode and a ventricular electrode to record electro grams.
PROGRAMMED ELECTRICAL STIMULATION:

Cardiac stimulation was carried out through the electrodes placed from a external stimulator and electrograms recorded. Extra-stimulus was delivered after eight paced beats(stimuli) and was labelled as S1……S2. Similarly, for double or triple extra-stimulus we delivered 2 or 3 extra-stimuli after a drive of eight beats. These were given at specific coupling intervals.

This was used to assess the retrograde ventriculo-atrial conduction and also measurement of refractory periods of ventricular, His purkinje and AV node were done as a part of protocol in all patients. The response of extra-stimuli was recorded. Initial extra-stimuli were given through right ventricular apex, followed by RV outflow tract. Number of extra-stimuli and site of extra-stimuli were recorded.

ANALYSIS:

The following records were analysed

1. Outpatient and inpatient medical records
2. Electrocardiograms
3. Echocardiography reports
4. Angiographic information – including presence of aneurysms
5. Holter records
6. Medication information
7. Electrophysiology study information
   a. Basal conduction parameters
   b. Ventricular extra stimulation protocol used
      i. Number of extra-stimuli
      ii. Sites of stimulation
      iii. Ventricular refractory period
      iv. Response to VES testing
         1. Ill sustained monomorphic tachycardia
         2. Polymorphic tachycardia
         3. Sustained monomorphic VT
            a. Hemodynamically stable and lasting > 15 sec
            b. Hemodynamically unstable
            c. Reproducibility
         4. Ventricular fibrillation
         5. No induction of VT/VF
   v. Tachycardia characteristics
      1. VT morphology
      2. VT cycle length
      3. Mode of termination
Definitions of VT induction protocol results

- Sustained monomorphic VT – Monomorphic VT lasting more than 30 sec and cycle length (CL) more than 250 msec.
- Monomorphic fast VT – Monomorphic VT lasting at least 10 seconds (if terminated by DC version) or 15 seconds (if spontaneously terminated) and CL less than 250 msec.
- Polymorphic VT – Polymorphic or unstable QRS morphology with average rate faster than 200 beats/min and requiring DC version or lasting more than 10 secs and not falling into VF category
- Ventricular fibrillation – VT with CL less than 200 msec, regardless of QRS morphology
- Non inducible - A response not fitting into either of the above definitions.
- Inducibility defined by sustained monomorphic VT/polymorphic VT induced with \( \leq 3 \) extrastimuli lasting more than 10 seconds or requiring DC version

Stratification of analysis:

Analysis was stratified for different disease sub classes (Ischemic cardiomyopathy, hypertrophic cardiomyopathy etc) and for treatment status (Medical treatment, Medical treatment plus ICD , Medical treatment plus VT ablation)
Outcomes of study

Primary outcomes

1. Recurrence of ventricular arrhythmia
   i. Documented VT – documented VT will be sub classified for stability, rate and morphologic type
   ii. Arrhythmic syncope
   iii. Appropriate ICD interventions

2. All-cause mortality

3. Sudden death

Secondary outcomes

1. Heart Failure admissions

2. Medication intolerance or adverse effects

3. Inappropriate ICD interventions.

Follow up:

Follow up was till death or last follow up. For each patient, if a primary outcome (arrhythmia) had occurred, the results of further VT induction studies in them were followed and analysed separately. If no further VT induction studies or VT ablation were done on them they were followed within the same cohort for VT burden and other end points.
STATISTICS:

The data was analysed by the principal investigator. Hospital deaths, late deaths, ventricular arrhythmias, device related complications, ICD discharges and procedure related events were recorded. All data was handled with care to maintain patient confidentiality. Records are maintained in both computer and paper formats. Descriptive summaries are presented as frequencies and percentages for categorical data, and as means and standard deviations for continuous variables. Continuous variables were compared using Student’s $t$ test or Mann-Whitney $U$ test as appropriate, Group comparisons were made using $\chi^2$ tests. Kaplan-Meier survival analyses was performed to evaluate differences in freedom from arrhythmic event, ICD shock (if implanted). Univariate and multivariate analysis were done from Cox proportional hazard model. All statistical analyses were performed using the SPSS statistical software package (release 16.0, SPSS Inc.; Chicago, Ill).
RESULTS
RESULTS

In our study we screened 411 consecutive patients who underwent ventricular tachycardia (VT) induction study and included 169 patients in our data analysis. We excluded 242 patients (structurally normal heart, admission with VT storm, acute coronary syndrome). Out of 169 patients we found that 79 (46.74%) patients had an inducible VT and 90 (53.25%) had non inducible VT. 67 (39.64%) patients had a monomorphic VT inducible and 12 (7.10%) had a sustained polymorphic VT induced. In the non-inducible group 20 (11.83%) patients had ill-sustained VT/VF induced and 70 (41.42%) had no VT/VF induced even after aggressive protocols used. We classified the patients for analysis as per the pattern of the VT induced and divided them into 4 groups as per the definitions mentioned previously (Group 1 -monomorphic VT, Group 2- sustained polymorphic VT, group 3- ill sustained VT/VF, group 4- no VT/VF induced). (Figure 1) Inducible group had patients who had either a monomorphic sustained VT or a sustained polymorphic VT. Ill sustained VT/VF and no inducible VT/VF were taken in the non-inducible group.
Figure 1: Study flow – patients were divided into 4 groups. Group 1 - monomorphic VT, Group 2- sustained polymorphic VT, group 3- ill sustained VT/VF, group 4- no VT/VF induced

BASELINE CHARACTERISTICS:
Median age of patients in the study was 53 years with range 11-78 years. Majority of the patients in the study were males (n=142, 84.02%) with M: F ratio 5.25:1. (Table 1). 65.08(n=110) % patients had syncope as the presenting symptom followed by palpitations in 22.48%(n=38). 6(3.55%) patients had history of documented and resuscitated sudden cardiac arrest. Coronary artery disease was seen in 46.75% (n=79) patients, followed by hypertrophic obstructive cardiomyopathy in 12.4%(n=21) and dilated cardiomyopathy in 10.05%(n=17). Arrhythmogenic right ventricular dysplasia and congenital heart disease were 8.2%(n=14) and 8.86%(n=15) respectively. Rheumatic heart disease patients formed a small percentage of 4.14%. Most of the study population was on beta
<table>
<thead>
<tr>
<th>BASELINE CHARACTERISTICS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>GENDER</td>
<td>M 142; F 27</td>
</tr>
<tr>
<td>Median age</td>
<td>53 (range 11 to 78 years)</td>
</tr>
<tr>
<td><strong>Underlying SHD</strong></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>79(46.75%)</td>
</tr>
<tr>
<td>RHD</td>
<td>7(4.14%)</td>
</tr>
<tr>
<td>DCM</td>
<td>17(10.05%)</td>
</tr>
<tr>
<td>ARVD</td>
<td>14(8.2%)</td>
</tr>
<tr>
<td>EMF</td>
<td>5(2.95%)</td>
</tr>
<tr>
<td>MVP</td>
<td>5(2.95%)</td>
</tr>
<tr>
<td>HCM</td>
<td>21(12.4%)</td>
</tr>
<tr>
<td>CHD</td>
<td>15(8.87%)</td>
</tr>
<tr>
<td>RCM</td>
<td>1(0.5%)</td>
</tr>
<tr>
<td>SARCOID</td>
<td>3(1.7%)</td>
</tr>
<tr>
<td>BAV</td>
<td>2(1.18%)</td>
</tr>
<tr>
<td>MYOCARDITIS</td>
<td>1(0.5%)</td>
</tr>
<tr>
<td>Non-compaction</td>
<td>1(0.5%)</td>
</tr>
<tr>
<td><strong>Presenting symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>110(65.08%)</td>
</tr>
<tr>
<td>Pre-syncope</td>
<td>14(8.28%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>38(22.48%)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>5(2.95%)</td>
</tr>
<tr>
<td>SC ARREST</td>
<td>6(3.55%)</td>
</tr>
<tr>
<td><strong>Functional Class(NYHA)</strong></td>
<td>1.98±0.98</td>
</tr>
<tr>
<td><strong>Drugs prior to EPS</strong></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>87(51.47%)</td>
</tr>
<tr>
<td>Betablocker</td>
<td>148(87.57%)</td>
</tr>
<tr>
<td>CCB</td>
<td>12(7.10%)</td>
</tr>
<tr>
<td>A+B</td>
<td>83(49.11%)</td>
</tr>
<tr>
<td>A+C</td>
<td>1(0.5%)</td>
</tr>
<tr>
<td>B+C</td>
<td>2(1.18%)</td>
</tr>
<tr>
<td>All 3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Hemodynamics</strong></td>
<td></td>
</tr>
<tr>
<td>Hemodynamically stable</td>
<td>42(24.85%)</td>
</tr>
<tr>
<td>Hemodynamically Unstable</td>
<td>42(24.85%)</td>
</tr>
<tr>
<td><strong>Documented VT</strong></td>
<td></td>
</tr>
<tr>
<td>Tracing NA</td>
<td>18(10.65%)</td>
</tr>
<tr>
<td>LBBB Morphology</td>
<td>28(16.56%)</td>
</tr>
<tr>
<td>RBBB Morphology</td>
<td>44(26.03%)</td>
</tr>
<tr>
<td>Polymorphic</td>
<td>1(0.59%)</td>
</tr>
<tr>
<td>QRS duration(msec)</td>
<td>142±38</td>
</tr>
<tr>
<td><strong>LV dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Mod-severe (EF &lt;40%)</td>
<td>43(25.44%)</td>
</tr>
<tr>
<td>Normal or Mild LV dysfunction</td>
<td>126(74.56%)</td>
</tr>
</tbody>
</table>
RESULTS

Table 1: Baseline characteristics of all patients.

<table>
<thead>
<tr>
<th>CAG (n=129)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>49(28.99%)</td>
</tr>
<tr>
<td>Mild CAD</td>
<td>21(12.42%)</td>
</tr>
<tr>
<td>SVD</td>
<td>29(17.15%)</td>
</tr>
<tr>
<td>DVD</td>
<td>20(11.83%)</td>
</tr>
<tr>
<td>TVD</td>
<td>10(5.91%)</td>
</tr>
</tbody>
</table>

blocker 87.57%(n=148) followed by amiodarone in 51.47%(n=87). Small number of patients were on calcium channel blockers. The patients with documented history of hemodynamically stable arrhythmias were 42(24.85%) and hemodynamically unstable arrhythmias were also 42%(24.85%). VT was documented in 53.84%(n=91) patients and majority had RBBB morphology (26.03%, n=44). Left ventricular dysfunction was seen in 43(25.44%) patients. 49(28.99%) patients had normal coronaries.
<table>
<thead>
<tr>
<th>Demographics</th>
<th>INDUCIBLE VT (n=79)</th>
<th>NON INDUCIBLE(n=90)</th>
<th>p value (INDUCIBLE VERSUS NON INDUCIBLE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>M =59 ; F =8</td>
<td>M=10;F=2</td>
<td>M=73;F=17</td>
</tr>
<tr>
<td>Median age (Range)</td>
<td>54 (19-76 years)</td>
<td>57.6(28-82 years)</td>
<td>41.07(17-78years)</td>
</tr>
<tr>
<td><strong>Underlying SHD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n(%)</td>
<td>CAD</td>
<td>RHD</td>
<td>ARVD</td>
</tr>
<tr>
<td></td>
<td>44(65.67%)</td>
<td>2(2.98%)</td>
<td>6(8.95%)</td>
</tr>
<tr>
<td></td>
<td>5(41.67%)</td>
<td>0</td>
<td>1(8.33%)</td>
</tr>
<tr>
<td></td>
<td>30(33.33%)</td>
<td>5(5.56%)</td>
<td>8(8.89%)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.0001</td>
<td>0.454</td>
<td>0.788</td>
</tr>
<tr>
<td></td>
<td>RHD</td>
<td>DCM</td>
<td>ARVD</td>
</tr>
<tr>
<td>n(%)</td>
<td>2(2.98%)</td>
<td>7(10.44%)</td>
<td>6(8.95%)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>2(16.67%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>5(5.56%)</td>
<td>8(8.89%)</td>
<td>4(4.44%)</td>
</tr>
<tr>
<td></td>
<td>0.454</td>
<td>0.612</td>
<td>0.788</td>
</tr>
<tr>
<td></td>
<td>HCM</td>
<td>CHD</td>
<td>RCM</td>
</tr>
<tr>
<td>n(%)</td>
<td>4(5.97%)</td>
<td>3(4.47%)</td>
<td>1(1.49%)</td>
</tr>
<tr>
<td></td>
<td>3(25%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>14(15.56%)</td>
<td>12(13.33%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0.244</td>
<td>0.032</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td>ARVD</td>
<td>CHD</td>
<td>RCM</td>
</tr>
<tr>
<td>n(%)</td>
<td>7(10.44%)</td>
<td>3(4.47%)</td>
<td>1(1.49%)</td>
</tr>
<tr>
<td></td>
<td>2(16.67%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8(8.89%)</td>
<td>12(13.33%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0.612</td>
<td>0.032</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td>MYOCARDITIS</td>
<td>NON COMPACTION</td>
<td></td>
</tr>
<tr>
<td>n(%)</td>
<td>6(8.95%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>8(8.89%)</td>
<td>2(2.22%)</td>
<td>0</td>
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<tr>
<td></td>
<td>0.788</td>
<td>1.000</td>
<td>0.467</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Syncope</td>
<td>Pre-syncope</td>
<td>Palpitations</td>
</tr>
<tr>
<td>n(%)</td>
<td>44(65.67%)</td>
<td>3(4.47%)</td>
<td>20(29.87%)</td>
</tr>
<tr>
<td></td>
<td>7(58.33%)</td>
<td>3(25%)</td>
<td>2(16.67%)</td>
</tr>
<tr>
<td></td>
<td>59(65.56%)</td>
<td>8(8.89%)</td>
<td>16(17.78%)</td>
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<tr>
<td></td>
<td>1.000</td>
<td>0.788</td>
<td>1408</td>
</tr>
<tr>
<td></td>
<td>MYOCARDITIS</td>
<td>NON COMPACTION</td>
<td></td>
</tr>
<tr>
<td>n(%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0.467</td>
<td>0.467</td>
<td>0.467</td>
</tr>
</tbody>
</table>

Table 2: Baseline characteristics of all patients as per inducibility/pattern of VT induced.
### Baseline characteristics of patients according to the pattern of VT induced.

<table>
<thead>
<tr>
<th></th>
<th>INDUCIBLE (n=79)</th>
<th>NON INDUCIBLE (n=90)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>INDUCIBLE MONOMORPHIC VT (n=67)</td>
<td>SUSTAINED POLYMORPHIC VT (n=12)</td>
<td>(INDUCIBLE VERSUS NON INDUCIBLE)</td>
</tr>
<tr>
<td>Drugs prior to EPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone(A)</td>
<td>53(79.10%)</td>
<td>3(25%)</td>
<td>31(34.44%)</td>
</tr>
<tr>
<td>Beta-blocker(B)</td>
<td>65(97.01%)</td>
<td>11(91.67%)</td>
<td>72(80%)</td>
</tr>
<tr>
<td>CCB(C)</td>
<td>6(8.95%)</td>
<td>2(16.67%)</td>
<td>4(44.44%)</td>
</tr>
<tr>
<td>A+B</td>
<td>50(74.62%)</td>
<td>5(41.67%)</td>
<td>28(31.11%)</td>
</tr>
<tr>
<td>A+C</td>
<td>0</td>
<td>0</td>
<td>1(1.11%)</td>
</tr>
<tr>
<td>B+C</td>
<td>0</td>
<td>0</td>
<td>2(2.22%)</td>
</tr>
<tr>
<td>All 3</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>32(47.76%)</td>
<td>3(25%)</td>
<td>7(7.78%)</td>
</tr>
<tr>
<td>Unstable</td>
<td>21(31.34%)</td>
<td>3(25%)</td>
<td>18(20%)</td>
</tr>
<tr>
<td>Documented VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tracing NA</td>
<td>7(10.44%)</td>
<td>2(16.67%)</td>
<td>9(10%)</td>
</tr>
<tr>
<td>LBBB Morphology</td>
<td>15(22.38%)</td>
<td>1(8.33%)</td>
<td>12(13.33%)</td>
</tr>
<tr>
<td>RBBB Morphology</td>
<td>31(46.26%)</td>
<td>0</td>
<td>13(14.44%)</td>
</tr>
<tr>
<td>Polymorphic</td>
<td>0</td>
<td>0</td>
<td>1(1.11%)</td>
</tr>
<tr>
<td>QRS duration</td>
<td>142</td>
<td>141</td>
<td>144</td>
</tr>
<tr>
<td>LV dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mod-severe (EF &lt;40%)</td>
<td>24(35.82%)</td>
<td>6(50%)</td>
<td>13(14.44%)</td>
</tr>
<tr>
<td>Normal or Mild LV dysfunction</td>
<td>43(64.17%)</td>
<td>6(50%)</td>
<td>77(85.56%)</td>
</tr>
</tbody>
</table>

Table 2(continued): Baseline characteristics of patients according to the pattern of VT induced.

Baseline characteristics of patients in inducible versus non inducible group showed a significantly higher number of coronary artery disease patients in the inducible group (49,28.99%) p=<0.001. There was no difference with respect to
the presenting symptoms. Significantly higher number of patients were on amiodarone (56.70.09%) in the inducible group as compared to non-inducible group((p<0.001), however there was no difference in the usage of beta blockers (p-0.21). Significantly higher number of patients were on combination of beta blocker and amiodarone in the inducible arm(p<0.0001). More patients in the inducible arm had hemodynamically stable arrhythmia as compared to non-inducible arm(p<0.0001). However, there was no difference in the hemodynamically unstable arrhythmias. History of documented VT was seen in a higher number of inducible VT group patients as compared to non-inducible group(p<0.0001). RBBB morphology was documented more in the inducible arm, n=31(18.34%) compared to non-inducible, n=13(7.69%), p -0.004.

Patients with inducible VT had more number of patients (n=30,17.75%) with left ventricular dysfunction as compared to non-inducible group (n=13,7.69%). (p=0.007)

**ELECTROPHYSIOLOGY STUDY CHARACTERSTICS**

As a protocol VT induction was done after studying all the basic parameters in EP catheterization laboratory with defibrillator and all resuscitation drugs stand-by. VT induction was attempted from right ventricular apex in majority of the patients, 59(34.91%) in the inducible group and 88(52.07%) in the non-inducible group. (Figure 2)
Figure 2: Electrophysiological characteristics of patients. A) Site of extra-stimulus B) Induction of Ventricular tachycardia method C) Response after VT induction; D) Morphology of VT induced (RV-Right Ventricle, LV-Left ventricle, VF-Ventricular fibrillation, VT-Ventricular tachycardia, LBBB-Left bundle branch block, RBBB Right bundle branch block)

5 (2.9%) patients each had induction done from right ventricular outflow tract (RVOT). Both RV apex and RVOT was used in 2 (1.18%) patients in inducible group and 8 (4.73%) patients in non-inducible group. VT was induced with burst pacing in 18% patients, single extra stimulus in 17%, double extra
stimulus in 27% and triple extra stimuli in 38% patients. (Figure 2B & C). RBBB was the most commonly monomorphic VT morphology induced seen in 43% patients followed by LBBB morphology in 26%. 31% patients had morphology more than 1 morphology.

<table>
<thead>
<tr>
<th>INDUCIBLE VT (n=79)</th>
<th>NON INDUCIBLE(n=90)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIFICIBLE MONOMORPHIC VT (n=67)</td>
<td>SUSTAINED POLYMORPHIC VT(n=12)</td>
<td>(INDUCIBLE VERSUS NON INDUCIBLE)</td>
</tr>
<tr>
<td>CAG (n=129)</td>
<td>Normal 16(23.89%) 2(16.67%) 31934.44%</td>
<td>0.126</td>
</tr>
<tr>
<td>Mild CAD 9(13.43%) 5(41.67%) 7(7.78%)</td>
<td>0.0625</td>
<td></td>
</tr>
<tr>
<td>SVD 18(26.87%) 39(25%) 8(8.89%)</td>
<td>0.0037</td>
<td></td>
</tr>
<tr>
<td>DVD 12(17.91%) 1(8.33%) 7(7.78%)</td>
<td>0.0975</td>
<td></td>
</tr>
<tr>
<td>TVD 3(4.47%) 1(8.33%) 6(6.67%)</td>
<td>0.741</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>ICD 33(49.25%) 5(41.67%) 20(22.22%)</td>
<td>0.0006</td>
</tr>
<tr>
<td>CRT D 3(4.47%) 1(8.33%) 1(1.11%)</td>
<td>0.186</td>
<td></td>
</tr>
<tr>
<td>VT ablation 20(29.85%) 0 0</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Procedural characteristics for patients- Intervention

**PROCEDURAL DATA**

Coronary angiographic data was available in 129 patients (76.33%). In the inducible group 18(10.65%) patients had normal coronaries as compared to 31(18.34%) in the inducible group, p – 0.126. Single vessel disease was seen more commonly in the inducible group as compared to the non-inducible group. A total of 42 patients (24.85% of total) had intra-cardiac defibrillator (ICD) implanted in the inducible group, the decision guided by the inducibility, whereas
in the non-inducible group 21 patients underwent ICD implantation (p=0.0006). CRT was implanted in 3 patients in the inducible versus 1 in the non-inducible group p=0.1864. VT ablation was done in the inducible group in 20 patients (11.83%).

**FOLLOW UP**

Mean follow up duration of the inducible group was 3.5 years (range 4 months to 9.5 years) in the monomorphic arm and 3 years (range 3 months to 9.4 years) in the sustained polymorphic arm as compared to 3 years (range 3 months to 9 years) in the non-inducible arm.

Patients who were lost to follow up were excluded from the analysis at the onset. There were 20 patients who had incomplete follow up and were excluded from the study analysis.

**EVENTS ON FOLLOW UP**

Events were defined as recurrence of VT, AICD shock, all-cause mortality, sudden death and heart failure admissions. Significantly higher number of patients in the inducible arm had events on follow up. (Table 3). As a whole there were 86 events in 79 patients in the inducible group as compared to 35 events in the non-inducible group which was statistically significant.
Table 3: Follow up data of all the groups as per the pattern of the VT induced after VT induction study.

<table>
<thead>
<tr>
<th></th>
<th>INDUCIBLE VT (n=79)</th>
<th>NON INDUCIBLE(n=90)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MONOMORPHIC VT (n=67)</td>
<td>POLYMORPHIC VT(n=12)</td>
<td>(INDUCIBLE VERSUS NON INDUCIBLE)</td>
</tr>
<tr>
<td>Mean Follow-up days(years)</td>
<td>1294 (~3yr 6mon)</td>
<td>1108 (~3 yrs)</td>
<td>1123 (~3 yrs)</td>
</tr>
<tr>
<td>Lost to f/u</td>
<td>4</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Event on F/U(n)</td>
<td>76</td>
<td>5</td>
<td>35</td>
</tr>
<tr>
<td>Sudden death n (%)</td>
<td>9(13.43%)</td>
<td>2(16.67%)</td>
<td>5(5.56%)</td>
</tr>
<tr>
<td>Mortality n (%)</td>
<td>13(19.40%)</td>
<td>2(16.67%)</td>
<td>10(11.11%)</td>
</tr>
<tr>
<td>Recurrent VT (n, %)</td>
<td>34(50.74%)</td>
<td>1(8.33%)</td>
<td>12(13.33%)</td>
</tr>
<tr>
<td>ICD shock n (%)</td>
<td>19(28.35%)</td>
<td>1(8.33%)</td>
<td>5(5.56%)</td>
</tr>
<tr>
<td>Average number of shock</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>De novo ICD/ upgradation to CRT-D- n (%)</td>
<td>4(5.97%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>VT ablation (Re or native)- n (%)</td>
<td>5(7.46%)</td>
<td>2(16.67%)</td>
<td>3(3.33%)</td>
</tr>
<tr>
<td>HF admission n (%)</td>
<td>19(28.35%)</td>
<td>2(16.67%)</td>
<td>9(10%)</td>
</tr>
</tbody>
</table>

**RECURRENCE OF VT/AICD SHOCK:**

Recurrence of VT was significantly in the inducible group as compared to the non-inducible group (p=<0.0001). This suggests that the patients who had a inducible VT at EPS had a higher chance of recurrence of VT on follow up. Maximum number of VT recurrences was documented in the monomorphic
group attributable to the higher detection rate as this was the group which had maximum numbers of ICD implantation and termination of lethal arrhythmias with therapy. AICD shock therapy as expected was higher in the group which had either a monomorphic VT or a sustained polymorphic VT induced, p=0.0001. One patient had recurrence of VT in the polymorphic sustained group.

HEART FAILURE ADMISSIONS:

21 patients in the inducible group had heart failure admissions as compared to 9 in the non-inducible group (p=0.008). This was expected as significantly higher number of patients in the inducible group had LV dysfunction as compared to the non-inducible group.

NEW ICD IMPLANTATION/UPGRADATION TO CRT-D:

4 patients in the inducible group underwent a de novo AICD implantation/CRT D upgradation. (p=0.0458)

MORTALITY:

There was no significant difference in the mortality among both the inducible and non-inducible subgroups(p=0.1932), and sudden deaths also were not significant when compared between both the groups however showed a trend towards significance(p=0.071).
MACE:

When total adverse cardiac events were compared then there was a significantly higher number of MACE in the inducible group as compared to the non-inducible group. \( p=0.004 \) (Figure 4) This difference was mainly driven by the recurrence of VT and AICD shocks in the inducible group.

STUDY END POINTS:

Arrhythmic syncope, AICD shocks, recurrence VT and heart failure admissions were higher in the inducible group when compared to the non-inducible group. However, there was statistically no significant difference with respect to sudden death and medication side effects (Figure 3)

SURVIVAL ACCORDING TO PATTERN OF VT INDUCED:

We did analysis of these patients according to the pattern of VT induced at VT induction study and then studied the follow up events. We found that monomorphic VT group had a significantly higher MACE as compared to all other patterns induced \( p=0.001 \). Sustained polymorphic, ill sustained VT/VF or no VT/VF induced did not differ significantly from other groups (Figure 5)
Figure 3: Study end points- Arrhythmic syncope, recurrence of VT, AICD shock, heart failure admissions were significantly higher in the induced group as compared to non-inducible group.

For evaluating the long term implication of the pattern of VT induced we divided the patients into 4 groups. Group 1- Monomorphic VT; Group 2 – Sustained polymorphic VT; Group 3- Ill sustained VF/VT; Group 4; No VT/VF.
RESULTS

A) Mortality – Inducible group does not have any significant difference from non-inducible group (p=0.342)

B) MACE total: Inducible group has a significant higher number of MACE events as compared to non-inducible group (p=0.004)

MONOMORPHIC VERSUS NO VT/VF:
When there was a monomorphic VT induced on EP study there were higher major adverse cardiac events when compared to no inducible VT/VF group. (p=0.001)
A) Mortality – as per morphology of VT induced. None of induced has a significant difference when compared to rest.

B) MACE Total: as per morphology of VT induced. Monomorphic VT induction has a significant difference when compared to all other morphologies induced or no VT / VF induced (p < 0.001)
RESULTS

A) Sustained monomorphic VT/VF versus no VT/VF induced (p = 0.717)

B) Sustained polymorphic VT versus no VT/VF induced (p = 0.670)

C) Ill sustained VT/VF versus no VT/VF induced (p = 0.096)

There was no difference in the mortality when monomorphic VT was compared with Group 4 that is no VT/VF induced. (p = 0.717).

**SUSTAINED POLYMORPHIC VT/VF VERSUS NO VT/VF:**

There was no difference in both mortality and MACE when sustained polymorphic VT was compared to no VT/VF group (Figure 6 & 7)
RESULTS

A) Sustained monomorphic VT/VF versus no VT/VF induced (p = 0.001)
B) Sustained polymorphic VT versus no VT/VF induced (p = 0.665)
C) Ill sustained VT/VF versus no VT/VF induced (p = 0.262)

Figure 7: Kaplan Meier survival curve comparing total MACE in each group versus no inducible VT/VF (log rank p value)

ILL SUSTAINED VT/VF VERSUS NO VT/VF:
Ill sustained VT/VF induction also did not show any significant difference when compared to no VT/VF induced on EP study. (Figure 6 & 7)

PREDICTORS OF EVENTS:
Multivariate analysis showed that induced monomorphic VT on EP study was a predictor of recurrence of VT (HR 0.379, 95% CI, 0.174-0.583, p = 0.016) and also AICD shock (HR 0.554, 95% CI, 0.136-0.964, p = 0.012).
Table 4: Multivariate analysis: Induced monomorphic VT was seen to be a predictor of recurrence of VT and AICD shock. LVEF < 30% was a predictor of heart failure.

Induction of monomorphic VT was not seen to predict occurrence of mortality, however showed a trend towards significance (HR-0.212, 95% CI-0.002-0.426, p- 0.053). (Table 4).

Also LV ejection fraction less than 30% was a predictor of heart failure admission. (HR 0.244, 95% CI, 0.059-0.430, p- 0.010). LVEF 30-40% was a predictor of AICD shock (HR-0.844, 95% CI- 0.469-1.22, p – 0.001).

**PROCEDURE OUTCOMES:**
Out of 79 patients in the inducible group 42 patients had a ICD implanted, 16 had ablation done, and 3 patients had both ablation and ICD implantation within 1 month hence considered in ICD group, and 21 were on medical follow up.
Table 5: Procedure outcomes—Follow up data of groups—None of the adverse events were different amongst the AICD /Ablation and the medical follow up group.

The patients who underwent intervention either in the form of AICD implantation were compared with the medical follow up group. Sudden death was significantly lower in the AICD group as compared with the medical follow up group (p=0.012). Also all-cause mortality was higher in the medical group patients as compared to patients who underwent AICD /radiofrequency ablation (p=0.022).
Figure 8: Study flow – events according to the procedural outcome.
DISCUSSION

VT induction study also called programmed ventricular stimulation first reported in 1972\cite{1} has been used as a method to predict, risk stratify, prognosticate and also guide various treatment modalities available.

We did this study to show that induction of VT predicts the recurrence of subsequent arrhythmias on follow up and VT induction study guided management decision is helpful to prevent sudden cardiac death. We wanted to study the outcomes in each of the pattern induced so as to know the significance of each pattern induced during a VT induction study. Our study we included all consecutive patients with structural heart disease who had presented with syncope and underwent a VT induction study. Most of the previous studies have included coronary artery disease patients.

CHARACTERISTICS OF STUDY POPULATION:

Majority of the patients had syncope as the presenting symptom (65.08\%) followed by palpitations in 22.48\%. 3.55\% patients had history of documented and resuscitated sudden cardiac arrest. There was no difference with respect to the presenting symptoms in the inducible or the non-inducible group. More patients in the inducible arm had hemodynamically stable arrhythmia as compared to non-inducible arm. However, there was no difference in the hemodynamically unstable arrhythmias.
STRUCTURAL HEART DISEASE:

Amongst the structural heart diseases most of our study population had coronary artery disease in 46.75% patients, followed by hypertrophic obstructive cardiomyopathy in 12.4% and dilated cardiomyopathy in 10.05%, arrhythmogenic right ventricular dysplasia and congenital heart disease were 8.2% and 8.86% respectively. So effectively, we had a heterogeneous population with respect to the structural heart disease, but it is to be noted that the mechanism of ventricular arrhythmias in majority of these patients involves scar or fibrosis as a substrate leading to re-entry. Kadish et al [24] also had concluded from a study done in 280 patients with non-sustained VT that VT is most often inducible in patients with coronary artery disease and least often in patients without structural heart disease.

DRUGS:

Higher drug usage in the population was evident from 87.57 % patients being on beta blockers and 51.47 % patients on amiodarone. Drugs do have impact on the inducibility of VT during EP study. Fisher et al [43] had reviewed the value of programmed electrical stimulation (PES) and Holter monitoring in the assessment of amiodarone efficacy and found that non-inducibility was associated with a favourable prognosis among 366 VT patients.

In our study significantly higher number of patients were on amiodarone (70.09%) in the inducible group as compared to non-inducible
group((p<0.001), however there was no difference in the usage of beta blockers (p-0.21). However, all patients planned for EP testing were asked to withhold amiodarone for 5 half-lives prior to procedure. Significantly higher number of patients were on combination of beta blocker and amiodarone in the inducible arm(p<-0.0001). This was as expected as more patients in the inducible group had documented VT as compared to the non-inducible group and hence patients with documented VT will have higher number of patients on drugs.

MADIT [18] study had shown that there was no evidence that amiodarone, beta-blockers, or any other anti-arrhythmic therapy had a significant influence on the observed hazard ratio of overall mortality in the AICD group versus conventional medical therapy.

DOCUMENTED ARYTHMIA:

VT was documented in 53.84%(n=91) patients and majority had RBBB morphology (26.03%, n=44). As seen in many previous studies history of documented VT was seen in a higher number of inducible VT group patients as compared to non-inducible group.

VENTRICULAR DYSFUNCTION:

As a whole left ventricular dysfunction was seen in 43(25.44%) patients. Patients with inducible VT had more number of patients with left ventricular dysfunction as compared to non-inducible group(p=0.007). Inducibility might have been
contributed with the left ventricular dysfunction, presence of more fibrosis. We although did not measure the scar burden with MRI. Presence of LV dysfunction was seen by echocardiography.

MADIT I\textsuperscript{[18]} had shown that patients with LVEF\textless;35\% and inducible VT/VF were more benefitted from prophylactic AICD implantation. MADIT II\textsuperscript{[18]} whereas had shown that in the presence of significant LV dysfunction, additional EP testing has limited role.

**CORONARY ARTERY DISEASE:**

Overall 49(28.99\%) patients had normal coronaries. In the inducible group there were significantly higher number of coronary artery disease patients (49,28.99\%) \(p<0.001\) thereby suggesting the presence of substrate for arrhythmogenesis. Single vessel disease was seen more commonly in the inducible group as compared to the non-inducible group. In coronary artery disease and left ventricular (LV) dysfunction induction of ventricular tachycardia is seen to predict the occurrence of spontaneous arrhythmia on follow up.\textsuperscript{[23],[24]}

CARISMA study had found that induction of VT after 6 weeks of acute MI predicted the occurrence of future life threatening arrhythmias.\textsuperscript{[47]}

**ELECTROPHYSIOLOGY STUDY CHARACTERISTICS**

Majority of patients underwent VT induction from RV apex followed by RVOT. VT was induced with burst pacing in 18 \% patients, single extra stimulus in 17 \%, double extra stimulus in 27\% and triple extra stimuli in 38 \% patients. We did
not very aggressive protocol of more than 3 extra-stimuli as it is known that
induction of VT/VF increases as the number of extra-stimuli increases. We had
used upto 3 extra-stimulus for VT induction but S. Zaman et al\cite{21} had compared
the VT induction with ≤ 3 extra-stimuli versus four extra-stimuli in 432 patients.
At the end of 3 years follow up they found that these patients were at equal risk
of events.

RBBB was the most commonly monomorphic VT morphology induced seen in
43% patients followed by LBBB morphology in 26%. 31% patients had
morphology more than 1 morphology.

**PROCEDURAL DATA**

All of our study population did not undergo a coronary angiogram. Coronary
angiographic data was available in 129 patients (76.33%).

46.74% of our patients had inducible VT as per definition and 39.64% of total
patients had a monomorphic VT inducible and 7.10% had a sustained
polymorphic VT induced.

Our results of inducibility are similar as seen by Buxton et al\cite{12} who
had studied 62 patients with CAD and non-sustained VT had found 45% inducibility and also found that EP study guided therapy had less chance of
sudden cardiac death as compared to the other group. Also MUSTT\cite{13} trial sub
study had shown a significant risk of mortality in patients who were EP inducible
when compared with non-inducible group. 2-year mortality was 1.33 fold higher than non-inducible patients in these post MI patients.

**AICD:**

AICD implantation decision was made after a detailed history, examination of all records, presence of documented records of VT in the past, echocardiographic parameters, EP study and VT induction result.

A total of 42 patients (24.85%) had intra-cardiac defibrillator (ICD) implanted in the inducible group, the decision guided by the inducibility, whereas in the non-inducible group 21 patients underwent ICD implantation \( (p=0.0006) \). The decision to implant a AICD in the non-inducible group was based on documented arrhythmia, syncope, LV function in the absence of induction of a significant arrhythmia at VT induction. CRT was implanted in 3 patients in the inducible versus 1 in the non-inducible group. VT ablation was done in the inducible group in 20 patients (11.83%). Our results are similar to a study by Daubert et al \(^{[12]} \) where they studied 593 patients included in MADIT II trial and found that inducible patients had greater number of ICD shocks as compared to the non-inducible arm. ICD therapy for spontaneous VF was less common in inducible group as compared to the non-inducible. They had also noted that induction of polymorphic VT/VF even with double extra-stimulus was less relevant as compared to the induction of monomorphic VT.
EVENTS ON FOLLOW UP:

MORTALITY:

There was no significant difference in the mortality among both the inducible and non-inducible subgroups (p=0.1932), possibly explained by the fact that although there was no difference with respect to mortality, there were higher number of events in inducible group which were adequately treated and thus the mortality free survival was equivalent to the non-inducible group. Also sudden death was higher in the medical treatment arm of the inducible group as compared to AICD arm. When inducible group was compared with the non-inducible arm there was no significant difference in the sudden death, thereby signifying the importance of AICD implantation leading to prevention of sudden cardiac death. When we compared various groups of VT induced, they did not differ in mortality on follow-up.

VT RECURRENCE/AICD SHOCK:

Inducible group had higher number of events on follow up as compared to the non-inducible arm. The presence of induction of a monomorphic VT was a predictor of recurrence of arrhythmia on follow up. Also patients who received a AICD in the inducible group had higher number of AICD shocks as compared to the non-inducible group. This signifies the importance of prevention of mortality by adequate intervention.
When this was analysed as per the pattern of VT induced then it was seen induction of monomorphic VT had maximum number of VT recurrences, attributable to the higher detection rate as this was the group which had maximum numbers of ICD implantation and termination of lethal arrhythmias with therapy.

Our results are similar to MADIT II trial which also had shown that inducible VT in LVEF < 30% did correlate with the recurrence of VT on follow up the contrast from our study being that we had patients with normal ejection fraction also. However, this study showed inverse relationship to the occurrence of VF on follow-up, which we did not analyse. Additionally, all patients in MADIT II trial had not undergone EP study.

HEART FAILURE ADMISSIONS:

As expected more patients with inducible group had LV dysfunction hence the heart failure admissions were higher in the inducible group.

MAJOR ADVERSE CARDIAC EVENTS:

Major adverse cardiac events included recurrence VT, AICD shock, mortality, heart failure admission. Composite of adverse cardiac events was higher in the inducible group as compared to the non-inducible group. (p=0.004), driven mainly by the recurrence of VT and AICD shocks in the inducible group.

Only induction of monomorphic VT during EPS showed higher MACE on follow up as compared to no VT/VF induction. Sustained polymorphic VT induction or
ill sustained induction did not show any significance when compared to no VT/VF group. Our results are similar to MADIT II trial which showed that monomorphic VT induction was a strong predictor of recurrence of arrhythmias on follow up.

We found that arrhythmic syncope, AICD shocks, recurrence VT and heart failure admissions were higher in the inducible group when compared to the non-inducible group. However, there was statistically no significant difference with respect to sudden death and medication side effects.

Sudden death did not differ much in inducible group versus non inducible because of prevention of sudden cardiac death by ICD therapy.

**SURVIVAL ACCORDING TO PATTERN OF VT INDUCED:**

There was no significant difference with respect to the pattern induced during EPS and long term mortality free survival. This difference was mitigated by the AICD implantation to prevent mortality.

**MONOMORPHIC VERSUS NO VT/VF:**

When there was a monomorphic VT induced on EP study there were higher major adverse cardiac events when compared to no inducible VT/VF group. This difference was mainly driven by the recurrence of VT and ICD shocks. There was no difference in the mortality when monomorphic VT was compared with Group 4 that is no VT/VF induced. Our results are similar to a prospective study done by Meyborg et al in which he had compared the monomorphic VT induction as
compared to VF induction and had found that patients who had monomorphic VT had appropriate AICD protocols in significantly more patients than compared to the VF group. \cite{28}

**SUSTAINED POLYMORPHIC VT/VF VERSUS NO VT/VF:**

There was no difference in both mortality and MACE when sustained polymorphic VT was compared to no VT/VF group.

**ILL SUSTAINED VT/VF VERSUS NO VT/VF:**

Ill sustained VT/VF induction also did not show any significant difference when compared to no VT/VF induced on EP study.

**PREDICTORS OF EVENTS:**

Induction of monomorphic VT on EP study was a predictor of recurrence of VT and also AICD shock. Induction of monomorphic VT was not seen to predict occurrence of mortality, however showed a trend towards significance. Daubert et al \cite{29} had done DEFINITE (Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation) sub study where patients randomized to the ICD arm underwent non-invasive EP testing via the ICD. On follow-up, they found that inducible group experienced ICD therapy for VT or VF or arrhythmic death more commonly than non-inducible patients. A study by Richards et al had found that
induction of VT is the single best predictor for VT occurrence after myocardial infarction.\cite{48}

We also found that LV ejection fraction less than 30 % was a predictor of heart failure admission and LVEF 30-40 % was a predictor of AICD shock.

**PROCEDURE OUTCOMES:**

The patients who underwent intervention either in the form of AICD implantation or ablation were compared with the medical follow up group. Sudden death was significantly lower in the AICD group as compared with the medical follow up group. Also all-cause mortality was higher in the medical group patients as compared to patients who underwent AICD /radiofrequency ablation (p=0.019). Our results are similar to SCD HefT trial, which had included both ischemic and non-ischemic patients and found that ICD use reduced mortality by 7.2% over 5 years compared with conventional therapy, which corresponds to a relative risk reduction of 23\% .\cite{32}

**SUMMARY:**

Patients who had a inducible monomorphic VT at EP study had a higher chance of recurrence of arrhythmic events and a higher chance of getting a ICD therapy. The mortality was not different in patients who underwent a AICD implantation after a positive VT induction study versus the group who had no VT/VF induced
on EP study, thereby indicating that these patients who had a AICD implanted had adequately treated arrhythmias by AICD intervention thus preventing mortality. Additionally, the patients in the inducible group had lower incidence of sudden death and all-cause mortality, thereby indicating that these patients were prevented from mortality with adequate intervention in the form of AICD shock.
LIMITATIONS
LIMITATIONS

The limitations of our study include a retrospective non-randomized design. It is also a single centre study but there are not many centres in the country which do this procedure routinely. Another limitation is that scar quantification has not been taken into account. We included all structural heart disease patients, which may seem heterogeneous but the mechanism in majority of structural heart disease patients is re-entry secondary to a scar.
CONCLUSION

VT induction study helps guide the management of patients with syncope or documented arrhythmia.

Induction of monomorphic VT/polymorphic VT with ≤ 3 extra-stimuli is associated with higher number of events on follow-up (recurrence VT, AICD shock, heart failure, all-cause mortality).

Induction of monomorphic VT is a predictor of recurrence of VT and ICD shock.

Mortality is not different in patients receiving AICD guided by VT induction as compared to non-inducible patients.

AICD implantation guided by VT induction study prevents sudden death.
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PATIENT INFORMATION SHEET

TITLE OF THE STUDY: *Results Of Ventricular Tachycardia Induction Protocol In Structural Heart Disease - Relation To Long Term Patient Outcomes.*

**Study number:**
You are being requested to participate in a study to see if the test which was conducted on you as a part of your management known as Electrophysiology testing - ventricular tachycardia induction study, can predict future ventricular arrythmias and mortality. We hope to include about 150 – 200 people from this hospital in this study.

**What role Electrophysiological testing play ?**
The use of electrophysiological studies with programmed stimulation has been demonstrated to be a valuable approach to the identification of patients at risk of sudden death and/or ventricular arrhythmias or to the evaluation symptoms such as palpitation, dizziness, or syncope or to guide therapy of chronic tachyarrhythmias.

**Any additional test will be conducted?**
No. Only the records will be studied of people who undergo this testing as a part of their management.

**If you take part what will you have to do?**
If you agree to participate in this study, your records will be studied. You may be contacted by telephone the doctors in this study who will ask you about any symptoms you are experiencing.

**Can you withdraw from this study after it starts?**
Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

**Will you have to pay for the study ?**
No. This study is a observational study and you will not have to pay for participating in the study.

**What happens after the study is over?**
You may or may not benefit from the study that you are participating. Once the study is over, in future it may be of help in deciding management of patients who have or are at risk of arrhythmias.

**Will your personal details be kept confidential?**
The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Gurbhej Singh, (tel: 09567601557) or email: nuts229dm@@sctimst.ac.in
CONSENT

Participant’s name: 
Date of Birth / Age (in years):

I ………………………………………………………………………………………………

(Please tick boxes)

- Declare that I have read the above information provide to me regarding the study: *Results Of Ventricular Tachycardia Induction Protocol In Structural Heart Disease - Relation To Long Term Patient Outcomes.* and have clarified any doubts that I had. [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights. [ ]
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. [ ]
- I understand that my identity will not be revealed in any information released to third parties or published. [ ]
- I voluntarily agree to take part in this study. [ ]
- I received a copy of this signed consent form. [ ]

Name:
Signature:
Date:
Name of witness:
Relation to participant:
Date:

(Person Obtaining Consent): I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

____________________________________________________________
Name and Signature of Person Obtaining Consent

Principal Investigator.
APPENDIX


(അവസാനം)

എന്നിങ്ങനെ…………………………………… (അവന്ത്) / അനുയോജ്യതയാണ്………………ഉപയോഗിക്കുന്ന ഇന്ത്യൻ ഭാഷാ പ്രവൃത്തിയുടെ അനുകൂലതയാണ് അനുഭവപ്പെട്ടത്.

(അവസാനം പ്രവാചനം (V) അനുഭവാനുശീലനം)

അനുഭവം എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത്, അനുഭവസംയന്ത്രം പലപ്പോഴും നിലനിൽന്നു പോലെ നിലനിൽന്നു കാണുന്ന അനുഭവം എന്നാണ് പ്രവാചനം.

• അനുഭവഫലമായിട്ടാണ് പ്രവാചകനുമായി ഇനിയെ കാണുന്ന അനുഭവം എന്നാണ് പ്രവാചനം.

• അനുഭവം എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത്, ഇനി നിലവിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം.

• യു അനുഭവം എന്നർത്ഥത്തിൽ അനുഭവമാണ് കാണുന്ന അനുഭവമാണ് എന്നാണ് പ്രവാചനം നിലவിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം.

• അനുഭവം എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം.

• അനുഭവം എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം.

• അനുഭവം എന്നാണ് പ്രവാചനം നിലവിൽ കാണുന്നത് എന്നാണ് പ്രവാചനം.

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• അനുഭавഫലമായിട്ടാണ് പ്രവാചകനുമായി ഇനിയെ കാണുന്ന അനുഭവം എന്നാണ് പ്രവാചനം.

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PROFORMA

Hospital No.: CATH NO.

Age/Sex:

Contact No.

Address:

Weight: Height: BSA:

BMI:

DIAGNOSIS:

PRESENTING COMPLAINTS:

NYHA CLASS

HISTORY OF PRESENT ILLNESS:

DRUG HISTORY:

GENERAL PHYSICAL EXAMINATION:

BP- PULSE- JVP-

CARDIOVASCULAR:

SYSTEMIC EXAMINATION:

INVESTIGATIONS:

Blood Urea Nitrogen: S. Creatinine: Na/K/Cl:

TROP T (If done): PRO BNP(If done):

1. Electrocardiogram

2. Echocardiography -

3. CAG + LV ANGIOGRAM

<table>
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<td>LCX</td>
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<td>RAMUS</td>
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<td>LV ANGIO</td>
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4. Holter:

5. Electrophysiology study information
   a. Basal conduction parameter - SCL
      
      $\text{SCL}$
      $\text{AH}$
      $\text{HV}$
   b. Ventricular extra stimulation protocol used
      i. Number of extrastimuli
      ii. Sites of stimulation
      iii. Ventricular refractory period
      iv. Response to VES testing

| 1. Ill sustained monomorphic tachycardia |
| 2. Polymorphic tachycardia |
| 3. Sustained monomorphic VT |
| a) Hemodynamically stable and lasting > 15 sec |
| b) Hemodynamically unstable |
| c) Reproducibility |
| 4. Ventricular fibrillation |
| 5. No induction of VT /VF |

v. Tachycardia characteristics

| 1. VT morphology |
| 2. VT cycle length |
| 3. Mode of termination |

FOLLOW UP:

ALIVE (YES/NO):

NYHA CLASS:

ARYRTHMIAS:

HEMODYNAMICALLY

STABLE/UNSTABLE:

SHOCKS(ICD):
**ECHO:**

**ELECTROPHYSIOLOGIC STUDY:**

a. Basal conduction parameter

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</table>

b. Ventricular extra stimulation protocol used

i. Number of extrastimuli

ii. Sites of stimulation

iii. Ventricular refractory period

iv. Response to VES testing

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</tr>
<tr>
<td>3. Sustained monomorphic VT</td>
<td></td>
</tr>
<tr>
<td>b) Hemodynamically stable and lasting &gt; 15 sec</td>
<td></td>
</tr>
<tr>
<td>c) Reproducibility</td>
<td></td>
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</tbody>
</table>

4. Ventricular fibrillation

5. No induction of VT /VF

v. Tachycardia characteristics

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<td>Mode of termination</td>
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<td>ALAN KADISH. &quot;Management of Nonsustained Ventricular Tachycardia Guided By Electrophysiologic Testing&quot;, Pacing and Clinical Electrophysiology, 5/1993</td>
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