Impact of Intraprocedural Pressor Use on Catheter Ablation for Ventricular Tachycardia

Amneet Sandhu MD, MSc[1,2]; Jeffery Graham MD[4]; Michael Rosenberg, MD[1]; Matthew M. Zipse, MD[1]; Alexis Z. Tumolo, MD[1]; Jose Sanchez, MD[1]; Jason West, MD[1]; Ryan Aleong, MD[1]; Ryan T. Borne, MD[1]; Paul D. Varosy, MD[1,2] ; William H. Sauer, MD[5]; Wendy S. Tzou, MD[1]; and Duy T. Nguyen, MD[3]

[1] Section of Electrophysiology, Division of Cardiology, University of Colorado

[2] Section of Cardiology, Denver VA Medical Center

[3] Section of Electrophysiology, Division of Cardiology, Stanford University

[4] Department of Medicine, University of Colorado

[5] Section of Electrophysiology, Division of Cardiology, Brigham and Women's Hospital

Address for Correspondence:

Duy T Nguyen, MD
Room H2152
300 Pasteur Dr
Stanford School of Medicine
Stanford, CA 94305-5233
Email: duy.t.nguyen@stanford.edu

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Abstract

Background: Ventricular tachycardia (VT) remains a leading cause of morbidity and sudden death. Improvements in catheter ablation have significantly advanced this option as a treatment method for refractory VT. Despite advances, use and impact of inotrope and vasodepressor medicines as part of intraprodcedural management during VT ablation have been understudied.

Methods: We conducted a exploratory, retrospective analysis of consecutive patients undergoing VT ablation. Patient, intra and peri-procedural data, focusing on pressor use and hemodynamics through ablation, and procedural endpoint data were collected.

Results: From 2014-2017, 149 patients underwent VT ablation of which 67% exhibited cardiomyopathy (53% ischemic). Most procedures (71%) were conducted under general anesthesia. In those with cardiomyopathy, steady-state use of dobutamine and dopamine was more common though substantial use of phenylephrine was noted. In adjusted analyses, (1) dobutamine was associated with increased procedure time (402.5±18.8 vs 347.2±14.0 min, $p = 0.03$), (2) dopamine was associated with increased number of distinct VTs (2.8 vs. 2.2, $p<0.001$) while both dopamine and dobutamined resulted in increased intra-procedural cardioversions (1.3 vs. 0.6, $p<0.001$ and 1.34 vs. 0.66, $p=0.001$, respectively) and (3) dobutamine dose exhibited a linear correlation with post-ablation length of stay.

Conclusions: In this exploratory work, we sought to understand effects of hemodynamic drug use on short-term, procedural outcomes of VT ablation. Salient findings include: (1) arrhythmogenic nature of inotropes resulting in an increase in intraprocedural cardioversions, (2) greater

propensity for induction of non-clinical VTs with use of intraprocedural dopamine and (3) substantial use of phenylephrine in those with underlying cardiomyopathy.

Introduction

Ventricular tachycardia (VT) remains a leading cause of sudden death, heart failure and recurrent shocks in those with implantable cardioverter-defibrillators (ICDs) [1, 2]. With substantial increases in catheter ablation of VT across the United States [3], ablation of ventricular arrhythmias has dramatically evolved in the past decade [4-7]. Improvements in mapping techniques, approaches to catheter ablation, epicardial access and advances in ability to address deep substrate have proved promising [5-8]. Yet, despite these advances, use and impact of inotrope and vasopressor medications as part of intraprocedural management during VT ablation procedures has been understudied.

Prior data has shown ischemic substrates tend toward better outcomes compared to non-ischemic substrates [9, 10]. In addition, induction of non-clinical VTs have been associated increased rates of VT recurrence over a 2-year follow-up period [11, 12]. The impact of intraprocedural hemodynamic medication management on such findings, in addition to the safety and success of VT ablation, remains undefined. Given wide heterogeneity in approaches to VT ablation, understanding the effect of hemodynamic medication use to support VT ablation may prove valuable in further refining catheter ablation as a treatment option for VT.

Independent of the VT ablation strategy taken by the electrophysiology team, we hypothesized that differences in intraprocedural hemodynamic support drugs may alter procedure times, number of non-clinical VTs induced, VT recurrence and measures of procedural success. In this manuscript, we sought to evaluate the impact of use of intraprocedural hemodynamic

medications – in particular dobutamine, dopamine and phenylephrine on VT ablation. Understanding this relationship may impact the collective approach taken by EP and Anesthesia teams in providing optimal conditions for complex procedures such as VT ablation.

Methods

From 2013-2017, a retrospective analysis from one hundred and forty-nine consecutive patients that underwent VT ablation at University of Colorado Hospital was conducted. All patients with VT, referred for catheter ablation, were included with underlying substrate representative of ischemic and non-ischemic heart disease. Patients undergoing VT ablation with left ventricular assist devices (LVAD) were included in this analysis. Indications for VT ablation comprised of: (1) recurrent VT despite anti-arrhythmic therapy, (2) new onset sustained or non-sustained VT, (3) VT storm, (4) symptoms, predominantly syncope, resultant from ventricular dysrhythmias, and (5) ICD discharges. All patients analyzed in this study were treated by radiofrequency catheter ablation.

Demographic data, patient history, and intra-procedural data were reviewed through clinic, pre-procedural, intra-procedural (anesthesia records and catheter ablation data) as well as post-procedure documentation. Total length of procedure, number of cardioversions required, number of VTs induced and procedural success, as measured by inducibility of clinical or non-clinical VT, were recorded. The number of inducible ventricular dysrhythmias was determined at the discretion of the electrophysiologist and per description of the procedural report. Fluid management was conducted at the discretion of the treatment team (electrophysiologist(s), anesthesia team) with goal to maintain a near net even fluid status. Procedural success was stratified into complete (no inducible VT at end of procedure), partial or incomplete (non-clinical

VT inducible at end of procedure) and failure (clinical VT inducible at end of procedure). During the steady-state phase of each VT ablation procedure (ie. post-induction and initiation of anesthesia), the cumulative infusion and bolus doses, as well as the time exposed to dopamine, dobutamine and phenylephrine were calculated and analyzed.

Cardiomyopathy was identified by clinical history and reported ejection fraction was obtained from the most recent echocardiogram preceding the VT ablation procedure. The following classifications were used to stratify level of cardiomyopathy and severity of systolic dysfunction: >50% normal, 40-49% mild, 30-39% moderate and <29% severe.

Follow-up included all patients that continued care through the University of Colorado Health System or as obtainable through medical records. Recurrent ventricular tachycardia was defined as all occurrences of appropriate ICD shock or anti-tachycardia pacing (ATP) or clinically documented recurrence of VT or concern for VT recurrence requiring antiarrhythmic modifications. All recurrent VT episodes were included in analysis if repeat catheter ablation of VT was undertaken. Length of follow-up was determined as the last encounter documented in the medical record.

Statistical analysis

Data analysis was performed with STATA 13.2 (StataCorp, College Station, Tx). All categorical variables are listed as percentages. Comparisons between categorical variables were completed using the χ^2 test. Continuous variables were evaluated using linear (procedural time, number of VTs), logistic (induced VTs at case completion) and poisson (number of cardioversions, length of stay) regression models and are reported as mean ± SD or as median

with inter-quartile ranges. Multivariate Cox regression models were used to evaluate VT recurrence among dependent variables. P-values of <0.05 were considered significant.

Results

One hundred and forty-nine patients underwent VT radiofrequency catheter ablation (RFCA) between 2013-2017 at University of Colorado. Demographic, co-morbid conditions and medication data for the study cohort are shown in Table 1. Sixty-seven percent of patients had cardiomyopathy, defined as an EF <50%, of which 53% were primarily ischemic in origin with an average ejection fraction (EF) of 29.1% (CI 26.7%- 31.4%). Of all cases, 71% were conducted with use of general endotracheal anesthesia. Of all patients, only those with cardiomyopathy (EF <50%) received dobutamine intra-procedurally. Furthermore, patients with cardiomyopathy received dopamine (55% vs. 22%, p<0.05) more often than those without cardiomyopathy. Patients without cardiomyopathy received more total phenylephrine (2798 mcg vs. 1137 mcg, p = 0.02) than those with cardiomyopathy.

After adjusting for cardiomyopathy, dobutamine was the only medication associated with increased procedural time (402.5±18.8 min with dobutamine vs 347.2±14.0 min without dobutamine, p = 0.03; 371.2±17.0 min with dopamine vs 363.8±14.6 min without dopamine, p = 0.98; ±18.5 min with phenylephrine vs 347.5±21.6 min without phenylephrine, p = 0.75). After adjusting for severity of cardiomyopathy and procedural time, the use of dopamine, but not phenylephrine or dobutamine, was associated with a greater number of induced VTs (p = 0.02; Figure 1). In multivariable poisson regression models adjusted for severity of cardiomyopathy and procedure time, the use of dopamine (1.3±0.2 CVs with vs 0.6±0.1 CVs without, p = 0.001) and dobutamine (1.3±0.2 CVs with vs 0.7±0.1 CVs without, p = 0.006), but not phenylephrine

(1.0±0.1 CVs with vs 0.7±0.1 CVs without, p = 0.092), were significantly associated with the number of cardioversions performed (Figure 2).

The median length of stay was 5 days (mean 7.0 days, range 1 – 59 days, IQR 2 – 9 days). In multivariate Poisson regression, severity of cardiomyopathy was significantly associated with length of stay and procedure time ($p < 0.0001$). In multivariable poisson regression models, adjusted for procedure time and severity of cardiomyopathy, there was a significant increase in the length of stay for patients requiring treatment with dobutamine ($p = 0.0014$). There was no effect of phenylephrine or dopamine use on length of stay.

Non-inducibility at case completion was also associated with shorter length of stay after adjustment for severity of cardiomyopathy and procedure time (5.5±0.4 vs. 9.8±0.5 days, $p < 0.001$). After adjustment for inducibility, procedure time, and severity of cardiomyopathy, there was a significant increase in the length of hospital stay for individuals receiving dobutamine during the case ($p < 0.0001$, Figure 3). Individuals receiving dopamine had shorter hospital stays than those without, after adjustment for procedure length, severity of cardiomyopathy, and inducibility ($p < 0.0001$). Phenylephrine did not have a significant effect on length of stay. The dose rate for dobutamine, but not dopamine or phenylephrine, received during the case was also associated with an increase in the length of stay ($p < 0.001$, Figure 4).

Of the 149 subjects recorded, 15 patients were lost to follow up while 134 were monitored for VT recurrence after the procedure for a median of 5 months (mean 98.3 months, range 0.03 – 38 months) or 1112.8 person-months, during which time 71 subjects had recurrence. Of all covariates, both number of VT morphologies (HR 1.22 per VT morphology, 95%CI 1.11-1.34, $p < 0.001$) and lack of complete procedural success (HR 0.59, 95%CI 0.36 - 0.95, $p = 0.031$) were significantly associated with VT recurrence.

Discussion

To our knowledge, this is the first study seeking to understand the effect of hemodynamic drug use on short-term, procedural outcomes of VT ablation. As VT ablation is a complex, multi-disciplinary undertaking – evaluation of variables that may impact outcomes of VT ablation may improve catheter ablation as a treatment method. Salient findings of this work include: (1) arrhythmogenic nature of inotropes resulting in an increase in intraprocedural cardioversions, (2) greater propensity for induction of non-clinical VTs with use of intraprocedural dopamine and (3) substantial use of phenylephrine in those with underlying cardiomyopathy.

Compared to phenylephrine, we observed an increase in intraprocedural cardioversions with the use of dobutamine and dopamine after correcting for severity of cardiomyopathy and procedural time. Multiple prior studies have described the trade-off between hemodynamic support, particularly for patients with left ventricular systolic dysfunction and potential for arrhythmogenicity, with inotropic medicines [13, 14]. Intraprocedural cardioversions could reflect a propensity for induction of unstable ventricular dysrhythmias with use of inotropes or the sympathetic stimulation from these inotropes rendered VTs less amenable to pace termination.

Compared to dobutamine or phenylephrine, dopamine was also found to be associated with an increased number of intraprocedural VTs. Dopaminergic stimulation has been correlated with cardiac arrhythmogenicity [15]. Pharmacologic differences between dobutamine and dopamine could, in part, explain this finding, though this correlation needs to be evaluated in further studies. Analogously, we correlated non-complete procedural success (partial success or failure) with use of dobutamine. These findings indicate impact of inotropes on intra-procedural

inducibility. Given prior descriptions of clinical and non-clinical intraprocedural VT morphologies on short and long-term outcomes [16, 17], intraprocedural inotrope use may affect short and long-term success rates.

Our data introduces questions regarding whether (1) treatment of all inducible VTs versus clinically relevant ventricular dysrhythmias may depend on inotrope use and exposure, (2) how intraprocedural pressors may impact VT cycle length and hemodynamic stability of VTs and (3) whether inotropic use may affect hospitalization and long-term outcomes. In comparison to dopamine and phenylephrine, dobutamine was correlated with increased procedural time and length of stay. Likely a reflection of patient acuity and procedural complexity, no such relationship was noted with dopamine, which was also used in a similar patient cohort. An independent relationship between these variables and dobutamine remains to be further studied.

Another important finding from this study was the fact that a substantial number of patients with cardiomyopathy received phenylephrine to support hemodynamics during VT ablation. Though this medication is often used to counteract the distributive features of anesthesia during induction, we found that this pure alpha agonist is often used throughout the VT ablation procedure. Use of alpha agonists in the setting of underlying LV systolic dysfunction may adversely impact LV pressure, dilation and stretch [18], thereby potentially impacting both short and long-term results of catheter ablation.

Our data shows an increased number of cardioversions and non-clinical VTs with use of inotropes compared to phenylephrine. Though this could be related to greater use of these medications in sicker patients (ie. those with cardiomyopathy referred for catheter ablation of VT), this finding provides further support that these medications correlate with increased arrhythmogenicity and likely affect complex catheter ablation procedures. Further work,

including larger scale analyses and real-time physiological measurements during VT ablation, may help elucidate optimal titration of inotropes that are routinely used to support hemodynamics through complex procedures.

This exploratory work should be considered with multiple limitations. First, our cohort was not stratified between etiologies of LV systolic dysfunction or cause of underlying cardiomyopathy. Given the differences in these populations and its influence on mechanisms or arrhythmogenesis, this may impact the analysis reported above. The intent of our work was to explore the impact of hemodynamic medications used to support VT ablation procedures on aggregate findings during the procedure (ie. number of VTs induced and cardioversions performed). This exploratory work may help guide future, prospective, systematic analyses looking to evaluate the impact of exposure of inotropic medicines to support VT ablation. Specifically, further work could look to characterize individual VTs induced, corresponding cycle lengths and the effect of hemodynamic drugs. Information regarding each induced VT was not collected or evaluated for this study.

Conclusion

In comparison to phenylephrine, intraprocedural use of beta-agonist inotropes to support catheter ablation of VT resulted in a greater number of non-clinical VTs induced and cardioversions performed. Given their near ubiquitous use during VT RFCA and arrhythmogenic nature of these medications, strategies to optimize use of these medications may influence the effectiveness and outcomes of catheter ablation for VT.

Figure and Table Legend:

Table 1: Demographic, comorbid conditions, medication and number of prior procedures for the study cohort.

Figure 1: Number of VTs induced by use of intraprocedural pressor adjusted for severity of cardiomyopathy and procedural time.

Figure 2: Intraprocedural cardioversions during VT ablation by pressor type adjusted for severity of cardiomyopathy and procedure time.

Figure 3: Hospital length of stay (adjusted for inducibility at end of case, severity of cardiomyopathy and procedural time) by maximum, intraprocedural dose rate of dobutamine.

Figure 4: Hospital length of stay by inducibility status (adjusted for severity of cardiomyopathy and procedural time) by maximum, intraprocedural dose of dobutamine.

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