Left Ventricular Outflow Tract Arrhythmias: Clinical Characteristics and Site of Origin

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ABSTRACT: **Background:** Left ventricular outflow tract (LVOT) arrhythmias are increasingly recognized. Data regarding the distribution of the sites of origin (SOO) of the arrhythmias are sparse.

Objectives: To describe the clinical characteristics of patients with LVOT arrhythmias and the distribution of their SOO.

Methods: All 42 consecutive patients with LVOT arrhythmias who underwent radiofrequency (RF) ablation during the period 2000–2014 were included. SOO identification was based on mapping activation, pace mapping and a 3D mapping system in eight patients.

Results: The study group comprised 28 males (66.7%) and 14 females, the mean age was 55 ± 15.4 years. Most patients (76%) were symptomatic. All suffered from high grade ventricular arrhythmias. Left ventricular (LV) dysfunction (ejection fraction ≤ 50%) was observed in 15 patients (35.7%), of whom 14 (93.3%) were males. The left coronary cusp (LCC) was the most common arrhythmia SOO (64.3%). Other locations were the right coronary cusp (RCC), the junction of the RCC-LCC commissure, aortic-mitral continuity, endocardial-LVOT, and a coronary sinus branch. Acute successful ablation was achieved in 29 patients (69%) and transient arrhythmia abolition in 40 (95.2%). There was a trend for a higher success rate using cooled tip ablation catheters as compared to standard catheters. The ablation procedure significantly improved LV function in all patients with tachycardiomyopathy.

Conclusions: LVOT arrhythmias mostly originate from the LCC and are associated with LV dysfunction in 36% of patients. Knowledge regarding the prevalence of the anatomic origin of the LVOT arrhythmias may help achieve successful ablation. The use of cooled tip ablation catheters might have beneficial effects on the success rate of the procedure.

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KEY WORDS: left ventricular outflow tract (LVOT), arrhythmia, ablation, site of origin, tachycardiomyopathy

Outflow tract (OT) tachycardia is a subtype of idiopathic ventricular tachycardia (VT) that occurs without an apparent structural heart disease and accounts for 10% of all patients presenting with VT [1]. The mechanism of OT tachycardia is thought to be c-AMP-mediated triggered activity due to delayed after-depolarization determined by intracellular calcium overload [2]. The majority of OT arrhythmias arise from the right OT (RVOT), while 15–25% of arrhythmias arise from the left ventricular OT (LVOT), including the aortic coronary cusps [1,3]. The typical arrhythmic presentation of OT arrhythmias ranges from repetitive uniform premature ventricular extrasystoles and non-sustained VT to repetitive monomorphic VT and exercise-induced sustained VT. Their prognosis is generally benign [4] with only a few reports of a malignant variant resulting in life-threatening arrhythmias [5].

The LVOT is an anatomically complex region with close proximity to structures in the RVOT, which explains the difficulty of accurately localizing and ablating these arrhythmias. The latter are generally characterized by a left or right bundle branch block morphology with inferior QRS axis. Several sites of origin (SOO) have been described in the LVOT region [3,6]. The identification of the SOO based on electrocardiographic (ECG) features was evaluated in several studies [7-10]. Medical therapy with beta-blockers, verapamil or class IC antiarrhythmic drugs is effective in only 25–50% of patients [4,11]. Radiofrequency (RF) ablation is an alternative therapy reported to be successful [12]. The aim of this study was to describe the clinical characteristics, LV function, and distribution of the SOO in patients with LVOT arrhythmias who underwent RF ablation at our center.

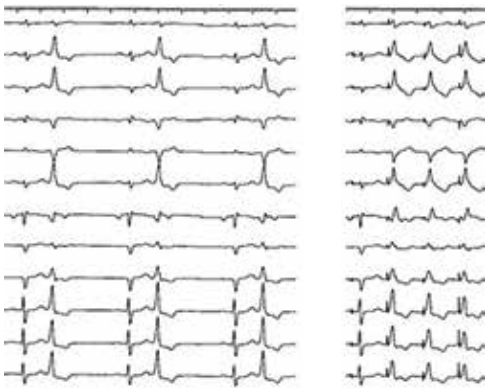
PATIENTS AND METHODS

This was a single-center retrospective cohort study. All 42 consecutive patients with LVOT arrhythmias who underwent RF ablation (46 procedures) between May 2000 and December 2014 were included. The case of the first study patient was published previously [13]. The clinical and procedural data were collected from the procedural report and patient records.

ABLATION PROCEDURE

All patients gave informed consent. The procedure was performed under conscious sedation with intravenous midazolam or fentanyl. At the beginning of the procedure an attempt was made to record spontaneous ventricular premature beats

Figure 1. Left panel: Baseline ventricular bigeminy of an arrhythmia originating at the aortic mitral continuity. **Right panel:** excellent (11/12) pace mapping match



(VPBs) or VT. These were used as a template for further mapping. A left retrograde arterial approach was used in all patients and a pericardial approach was also performed in one patient. Heparin was administered after catheter placement to maintain an activated clotting time (ACT) ≥ 250 sec. Coronary angiography was obtained during the procedure in some patients. Pace mapping was performed in all patients to compare the 12 lead ECG morphology of the paced QRS with the previously established template [Figure 1]. Identification of the arrhythmia SOO was based on data from mapping activation (site of earliest activation where the longest interval from the local ventricular electrogram to the earliest deflection of the QRS on the surface ECG during tachycardia or VPB was found), pace mapping or both, as well as from a 3D mapping system in eight patients. The latter consisted of either the CARTO™ system (CARTO RMT TM, Biosense Webster, USA) in seven patients or NavX™ (Endocardial Solutions, St. Jude Medical, Inc., St. Paul, MN, USA) in one patient. The use of a 3D mapping system was subject to availability, starting in 2013 with the CARTO system, and the NavX in one patient in 2004. RF energy was delivered mostly through standard 4 mm tip ablation catheters (maximal temperature 55°C). An irrigated cooled tip catheter was used in nine patients using power of 25–45 watts. Ablation was considered an acute success if no clinical arrhythmias occurred or were induced during a waiting period of 30 minutes. Patients were monitored for 24 hours after the procedure.

The arrhythmia SOO in the LVOT region was classified as supra-valvular [left coronary cusp (LCC), right coronary cusp (RCC), and junction of the RCC-LCC commissure)], infra-valvular [aortic-mitral continuity (AMC), endocardial-LVOT] or epicardial (coronary sinus branches).

STATISTICAL ANALYSIS

Continuous variables are expressed as the mean ± standard deviation if normally distributed. Categorical variables are expressed as frequency (percentage) and tested with the Fisher's exact test. Means are compared using Student's *t*-test or the Wilcoxon test. Statistical analyses were performed with SPSS for Windows (release 17.0, SPSS Inc., Chicago, IL, USA).

RESULTS

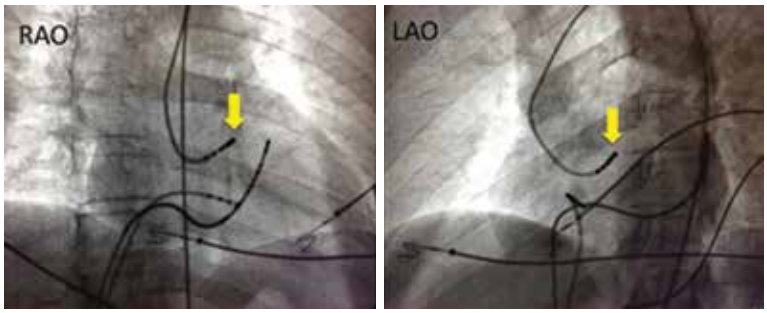
CLINICAL DATA

The study population comprised 42 patients: 28 males and 14 females (66.7% and 33.3% respectively), with a mean age of 55 ± 15.4 years. Four patients (9%) underwent two ablation procedures. Most patients (76%) were symptomatic. Twenty-five patients (60%) experienced palpitations; dizziness, dyspnea and chest pain occurred in two patients (4.8%) each and syncope occurred in one patient (2.4%). Ten patients (24%) were asymptomatic and the arrhythmia was discovered during routine testing. All suffered from high grade ventricular arrhythmias (VAs), including multiple ventricular premature beats (VPBs) in 40 (95.2%), bigeminy in 28 (66.7%), non-sustained VT (NSVT) in 20 (47.6%), and sustained VT in 3 (11.9%). In two of the latter patients the arrhythmia occurred during exercise. The mean VPB burden was 27.2% ± 14.6. Eight (80%) of the asymptomatic patients suffered from NSVT. Mean left ventricular ejection fraction (LVEF) was 51.8 ± 11.8%. LV dysfunction was present in 15 patients (35.7%) (14 males). LV dysfunction was more common in males, with a trend towards statistical significance (93.3% vs. 66.7%, $P = 0.08$). LV dysfunction with EF < 35%, 35–45%, and 50% were observed in 9 (21.6%), 4 (9.5%), and 2 patients (4.8%), respectively. LV dysfunction was found in 6 asymptomatic patients (60%). Seventeen patients (40.5%) had undergone a previous RF ablation procedure (performed in another center in 13 patients). During that procedure, ablation in the RVOT was performed in 12 patients, ablation in the LVOT in 3, and both right and left OT ablation in 1 patient each. In 16 patients (38.1%) several anti-arrhythmic drugs failed to control the arrhythmia.

ELECTROPHYSIOLOGIC DATA

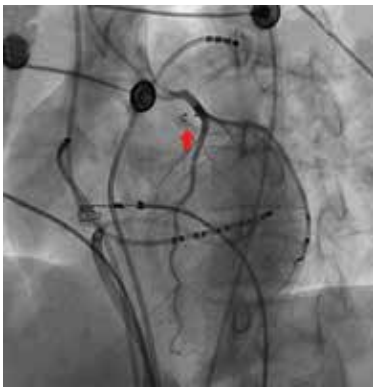
Arrhythmia morphology on ECG was analyzed by expert electrophysiologists, and was compatible with a LVOT origin in all patients (demonstrating inferior QRS axis with early transition on precordial leads ≤ V3). In addition to mapping in the LVOT area, 30 patients (71%) were mapped in the RVOT: 17 (40%) during the same procedure and 13 (31%) during a previous failed RF ablation in the RVOT. In 12 patients (29%) when the ECG was strongly suggestive of LVOT origin, RVOT mapping was not performed. The LCC was the most common SOO of LVOT arrhythmia in 27 patients (64.3%) [Figure 2]. The SOO was found at the junction of the RCC-LCC commissure and the RCC in 4 patients each (9.5%), the AMC in 3 (7.1%), the endocardial-LVOT in 2 (4.8%) and in a coronary sinus branch

Figure 2. RAO and LAO fluoroscopy images, respectively, with an arrow pointing to the ablation catheter in the left coronary cusp. This represents the conventional manual approach with fluoroscopy and ablation signal-guided ablation



LAO = left anterior oblique, RAO = right anterior oblique

Figure 3. Epicardial arrhythmia site of origin at the anterior interventricular great vein. Arrow is pointing to a Cardima quadripolar catheter (Cardima Inc., Fremont, CA, USA) advanced in the anterior interventricular great vein. During coronary angiography, the close proximity to the proximal left anterior descending artery is shown in LAO view, which limited the ability to ablate at this site.



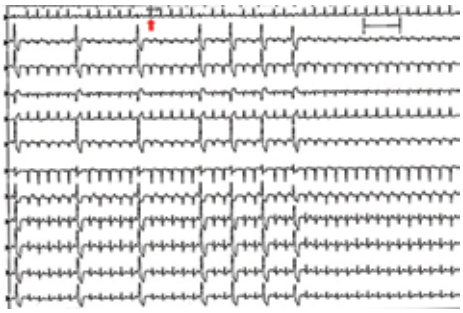
LAO = left anterior oblique

in 1 patient (2.4%) [Figure 3]. In one patient (2.4%), data on the exact SOO in the LVOT were not available. Earliest activation was average -30.7 ± 15, median -27. The average pace mapping concordance was 10.8 ± 1.3 (median 11).

ACUTE RESULTS OF ABLATION

Acute successful ablation was achieved in 29 patients (69%) [Figure 4]. The procedure failed in five (11.9%). Reasons for procedure failure were true failure in three patients, multiple SOOs in one, and an epicardial SOO in the proximal anterior interventricular great vein very close to the left anterior descending artery in one patient [Figure 3]. The procedure was discontinued in 5 patients (11.9%). Reasons for discontinuation were technical problems in two patients, few VPBs that prevented accurate mapping in one patient, patient agitation in one, and a SOO located just beneath the LCC in one patient. The result was unclear in 3 patients (7.1%): in two due to infrequent spontaneous arrhythmia and in one due to pleomorphic VPBs originating from both right and left OT areas. The mean number of RF pulses used was 4.6 ± 4.6, median 3 (1–19). In

Figure 4. 12 lead ECG during first radiofrequency ablation delivered at the left coronary cusp. Acute successful abolition of the arrhythmia is achieved at relatively low power (17 watts) and temperature (44°C) administered through a standard ablation catheter



acute successful ablations the mean number of RF pulses was 3.7 ± 4.1, median 2 (1–19).

Transient abolition of the arrhythmia was achieved in 40 patients (95.2%), including 4 of 5 patients in whom the procedure failed and 4 of 5 patients in whom the procedure was discontinued. In nine patients (21.4%) a cooled tip catheter was used without any complication. Acute success was achieved in 8 of the 9 patients in whom cooled tip catheters were used compared with 20 of 31 patients in whom standard catheters were used (88.9% vs. 64.5%, $P = 0.23$). In two patients data regarding the type of catheter used were unavailable.

Two patients (4.8%) experienced a complication. One patient had a pseudoaneurysm of the femoral artery, which resolved spontaneously. The second patient developed chest pain and ischemic changes in lateral ECG leads, after one RF pulse at the LCC. Coronary angiography demonstrated isolated mid-diagonal lesion that did not require any intervention. All patients were monitored for 24 hours after the procedure and were discharged in good condition.

Follow-up data regarding LV function after the ablation procedure were available in 14 of 15 patients with LV dysfunction. One patient died 5 years after the ablation procedure due to an unknown cause and the data regarding LV function were unavailable for this patient. Of the 15 patients, acute success was achieved in 13 (86.7%); the procedure failed in 2 (including the patient who died during follow-up). Assessment of LV function was performed at a median of 315 days (1–3650) after the ablation procedure. Mean LV function increased significantly from 37.4% ± 8.2 before to 54.3% ± 6.8 after the ablation procedure ($P = 0.0001$). LV function improved in all patients following the ablation procedure, and normalized (EF ≥ 55%) in 9 (64.2%).

DISCUSSION

The aim of this study was to describe the clinical and electrophysiologic characteristics of patients who underwent an ablation procedure for LVOT arrhythmias at our center.

CLINICAL FINDINGS

Consistent with the results of previous studies the majority of patients suffering from LVOT arrhythmias in our study population were male [3,14]. Most presented with palpitations, and syncope occurred in only one patient. The most common arrhythmias were multiple VPBs, bigeminy and NSVT, while sustained VT was rare [15,16].

It has been established that frequent VPBs can result in "tachycardiomyopathy" [17,18]. Several studies reported LV function in RVOT arrhythmias, which ranged from 39% to 61.6% at baseline [19], but data regarding LVOT arrhythmias are sparse. Other than case reports, there is a large series of 265 patients with OT arrhythmias originating in coronary cusps and LVOT in 44 and 10 patients, respectively, in which only 2 cases of LVOT arrhythmias associated with LV dysfunction were observed [20]. In our study 35.7% of the patients suffered from LV dysfunction that could be attributed to the arrhythmia. We found a trend toward gender differences in the rates of LV dysfunction, which was more common in males. In addition, LV dysfunction was the main reason for performing RF ablation in our asymptomatic patients (60%). LV function significantly improved after the ablation procedure in all patients, establishing the diagnosis of tachycardiomyopathy as the cause of their LV dysfunction, as well as the reversibility of LV dysfunction after successful elimination of the arrhythmia. Interestingly, in the one patient whose ablation failed, yet transient abolition was achieved, LV function improved from 35% to 50%, perhaps due to lowering of the arrhythmia burden. Therefore, we believe that LVOT arrhythmias share the same potential as RVOT arrhythmias for leading to "tachycardiomyopathy," supporting our recommendation for ablation in young asymptomatic patients (20%), especially males, to avoid long-term medical therapy and further possible LV dysfunction.

A recent study found RF ablation to be more effective than anti-arrhythmic drug therapy for decreasing VPB frequency and improving LV function [21]. Subgroup analysis showed that the increase in LVEF was greater after RF ablation of LVOT and LV VT (non-OT) as compared with those originating from the RVOT [21]. Therefore, considering the high prevalence of LV dysfunction that we observed in LVOT arrhythmias, we suggest that RF ablation be preferred to medical therapy for treating arrhythmias originating from the LVOT.

ARRHYTHMIA ORIGIN

In our patient population, which presented with ECG compatible with a SOO in the LVOT (inferior QRS axis with early transition on precordial leads), a supra-valvular SOO was identified in 35 patients (74%). The LCC was the most common SOO of LVOT arrhythmia in 64.3% of the patients while the junction of the RCC-LCC commissure and the RCC were the SOO in 9.5% each. A SOO in the infra-valvular LVOT area (the AMC and the endocardial-LVOT) was rare (11.9% of the patients). The fact that an epicardial SOO was identified only in one patient (2.4%) should be interpreted with caution. Actually such localization frequently results in a typical ECG pattern (prominent R in V1) that could result in a priori non-indication for ablation due to the presumed close relationship of the arrhythmia SOO with the coronary vessels.

An anatomic distribution of arrhythmia SOO similar to that in our study was also found by Kumagai et al. [8] in a series of 45 patients with LVOT VAs. They found that 71% of the arrhythmias originated from the coronary cusps (LCC 66.6% and RCC 4%). No SOO were identified in the junction of the RCC-LCC commissure. Other SOO were the anterior mitral annulus (MA) in 18%, AMC in 7%, and an epicardial SOO in 4% [8]. Bala and fellow-authors [22] described 37 patients with coronary cusp VAs, in whom 51% originated at the RCC-LCC commissure. In that study intracardiac echocardiography was used to analyze coronary cusp anatomy and catheter position. This can explain the different incidence rates reported when identifying that SOO. With regard to ablation of the epicardial SOO, we have encountered considerable difficulty in ablation, as reported recently by Nagashima at al. [23].

ABLATION RESULTS

Acute ablation success was achieved in 69% of our patients; the procedure failed in 11.9%, and was discontinued in 11.9%, while the result was unclear in 7.1%. Reported success rates of RF ablation of LVOT arrhythmia range from 58% to 100% [16,20,22,24]. This wide range of results can be explained by the different definitions of success used in different studies. In our study transient abolition of the arrhythmia was achieved in 95.2% of patients, suggesting that SOO was very close to the ablation pulse site. Although not statistically significant, we found a trend to higher success rates when using cooled tip catheters. The latter allows higher energy to be transmitted to the tissue with creation of deeper and wider lesions, and less charring and risk of coagulum formation by cooling of the tip/tissue interface.

Irrigated RF catheter ablation proved to be more efficient in VT ablation in patients with prior myocardial infarction [25], yet data on the use of various types of ablation catheters in OT ablation are sparse. Bala at al. [22] reported on 3 of 19 patients in whom an irrigated-tip catheter was used because of inadequate power delivery at the RCC–LCC commissure. In a recent study by Zhong and team [21] all ablation procedures of OT and non-OT VTs were performed using irrigated tip catheters. Considering that in our study transient abolition of OT arrhythmias was achieved in 95.2% of patients, it is tempting to speculate that failed ablation might have resulted from lack of sufficient power delivered during ablation. This problem might be addressed with the more systematic use of cooled tip ablation catheters for LVOT arrhythmias.

STUDY LIMITATIONS

This is a single-center retrospective cohort study. Selection bias may influence the results since our center is a tertiary referral center. The procedures were performed over a period of 14 years, during which the methods of ablation evolved in a way that could influence the success of the procedures. The SOO was identified using fluoroscopy, and a 3D mapping system when available, without using intracardiac ultrasound, limiting the ability to define the exact location of SOOs. Long-term follow-up was limited to a subgroup of patients with tachycardiomyopathy, prohibiting analysis of long-term success in the whole cohort.

CONCLUSIONS

In our experience, LVOT arrhythmias mostly originate from the LCC and are associated with LV dysfunction in 35.7% of patients. Ablation significantly improved LV function in all patients with tachycardiomyopathy and should be preferred to medical therapy. As catheter ablation is being used more frequently in the treatment of LVOT arrhythmias, knowledge on the prevalence of the different SOO may assist in planning the approach to the ablation procedure. The use of irrigated ablation catheters may be critical for increasing procedural success rate.

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"An artist should never be a prisoner of himself, prisoner of style, prisoner of reputation, prisoner of success, etc."

Henri Matisse (1869-1954), French artist, known for his use of color and his fluid and original draughtsmanship. Along with Pablo Picasso and Marcel Duchamp, Matisse is regarded as one of the three artists who helped define the revolutionary developments in the plastic arts, painting and sculpture