

# Venous Stenosis After Transvenous Lead Placement: A Study of Outcomes and Risk Factors in 212 Consecutive Patients

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**Background**—Venous stenosis is a common complication of transvenous lead implantation, but the risk factors for venous stenosis have not been well defined to date. This study was designed to evaluate the incidence of and risk factors for venous stenosis in a large consecutive cohort.

**Methods and Results**—A total of 212 consecutive patients (136 male, 76 female; mean age 69 years) with existing pacing or implantable cardioverter-defibrillator systems presented for generator replacement, lead revision, or device upgrade with a mean time since implantation of 6.2 years. Venograms were performed and percentage of stenosis was determined. Variables studied included age, sex, number of leads, lead diameter, implant duration, insulation material, side of implant, and anticoagulant use. Overall, 56 of 212 patients had total occlusion of the subclavian or innominate vein (26%). There was a significant association between the number of leads implanted and percentage of venous stenosis ( $P=0.012$ ). Lead diameter, as an independent variable, was not a risk factor; however, greater sum of the lead diameters implanted was a predictor of subsequent venous stenosis ( $P=0.009$ ). Multiple lead implant procedures may be associated with venous stenosis ( $P=0.057$ ). No other variables approached statistical significance.

**Conclusions**—A significant association exists between venous stenosis and the number of implanted leads and also the sum of the lead diameters. When combined with multiple implant procedures, the incidence of venous stenosis is increased. (*J Am Heart Assoc.* 2015;4:e001878 doi: 10.1161/JAHA.115.001878)

**Key Words:** implant techniques • pacing leads • venous stenosis

Since the introduction of transvenous pacing leads in the 1960s, the management of arrhythmias and heart failure has advanced significantly.<sup>1,2</sup> Transvenous implantable cardioverter-defibrillator (ICD) leads were introduced in the early 1980s.<sup>3</sup> Cardiac resynchronization therapy using transvenous left ventricular leads followed in the late 1990s. As new therapies have been developed, more patients with these implanted devices have had procedures for lead revisions or upgrades to ICDs and/or dual and biventricular pacing

systems. The patency of the access veins is a critical factor for procedural success.

Venous stenosis is a recognized complication following the implantation of an ICD or a pacemaker.<sup>4–6</sup> Data on venous occlusion following device implantation are limited, and the risk factors for the development of this complication are not well defined. In more than one study, it was shown that various degrees of venous stenosis occur in 20% to 50% of patients following device implantation.<sup>4,6–9</sup> Lead size was thought to be a risk factor until recent small studies showed no effect of lead size on the incidence of venous stenosis.<sup>3–5</sup> Those studies included only a small number of patients. Other potential factors, such as the number of leads and the use of anticoagulation or antiplatelet therapy, have not been evaluated to date.

Early transvenous leads were as large as 3.95 mm in diameter (13.2 French). The trend toward using smaller leads accelerated in the 1990s, with a potential benefit of decreasing the incidence of venous stenosis with smaller caliber leads; however, downsizing leads to as small as 4.1 French, which can be delivered through a guiding catheter,<sup>1</sup> did not show a decrease in the rate of venous stenosis following device placement.

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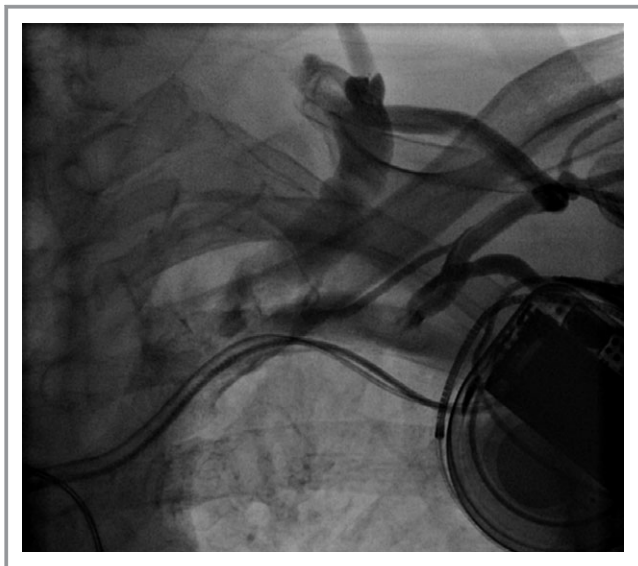
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The purpose of our study was to evaluate the incidence of and the risk factors for venous stenosis following pacemaker or ICD implantation in a large cohort of patients who presented for another elective procedure. The lead diameter, number of leads, sum of lead diameters, type of insulation, implant duration, number of previous procedures, age, sex, side of implant, and anticoagulant use were evaluated in 212 consecutive patients.

## Methods

A total of 212 consecutive patients with existing pacing or ICD systems were included in this study. Patients presented for generator replacement, lead revision, or upgrade to ICD or cardiac resynchronization therapy between October 2006 and February 2014. Overall, 136 patients were male and 76 were female, mean age was 69 years (range 25 to 95 years), and the mean time since implantation was 6.24 years (range 0.12 to 28.66 years). The study was approved by our institutional review board, and participants gave informed consent. All patients underwent venography through an ipsilateral intravenous line using 10 to 15 mL of contrast at the beginning of the procedure.

Venous stenosis was categorized as absent-0%; mild<50%; moderate-50% to 74%; severe-75% to 99%; and totally occluded if 100% stenosis was found. The degree of venous stenosis was adjudicated by 2 experienced clinicians (Figure). Variables examined for association with venous stenosis were age, sex, number of leads, cephalic versus subclavian vein, right- versus left-sided implant, lead diameter, silicone versus polyurethane insulation, time since implant, multiple lead-



**Figure.** Venogram demonstrating venous occlusion in a patient presenting for another procedure related to the device.

insertion procedures, and the use of anticoagulant or antiplatelet therapy.

Data on anticoagulation and antiplatelet use was not available for the entire cohort. We were able to obtain the medication history for 139 patients. Of those patients, 38% were on warfarin, 59% were receiving aspirin, and 8% were receiving clopidogrel. A subgroup analysis regarding those medications was done for this group.

## Statistical Analysis

Data were analyzed using the Pearson chi-square test, the Jonckheere–Terpstra test, the Cochran–Armitage test, and the

**Table 1.** Demographic and Clinical Variables (n=212)

Variable	Descriptive Statistics
<b>Age</b>	
Mean (SD)	69.0 (14.3)
Range	25 to 95
Sex (male), n (%)	137 (65%)
Implant date range	01/1985 to 08/2013
Procedure date range	10/2006 to 02/2014
<b>Implant duration (years)</b>	
Median (IQR)	6.24 (4.52 to 9.08)
Range	0.12 to 28.66
<b>Lead access (side; n=211), n (%)</b>	
Left	162 (77)
Right	49 (23)
<b>Lead access (n=211), n (%)</b>	
Axillary	11 (5)
Cephalic	16 (8)
Subclavian	184 (87)
<b>Number of leads, n (%)</b>	
1	29 (14)
2	145 (68)
3	38 (18)
<b>Insulation, n (%)</b>	
Polyurethane only	7 (3)
Silicone only	173 (82)
Polyurethane and silicone	32 (15)
<b>Lead diameter, n (%)</b>	
4.1 to 5.5	28 (13)
5.6 to 7.5 only	60 (28)
5.6 to 7.5 and >7.5	50 (24)
>7.5 only	74 (35)
<b>Multiple lead implant procedures, n (%)</b>	
	24 (11)

**Table 2.** Venous Stenosis (n=212)

Variable	n (%)
Venous stenosis	130 (61)
Percentage stenosis	
0%	82 (39)
20% to 49%	21 (10)
50% to 74%	33 (16)
75% to 99%	20 (9)
100%	56 (26)

Wilcoxon rank-sum test. A nominal 2-sided *P* value <0.05 defined statistical significance. Multivariate logistic regression analysis was performed to determine predictors of venous stenosis by entering all predictors with *P* values <0.10 in univariate analysis into a forward stepwise model.

### Results

Lead diameter ranged from 4.1 to 11.8 French. Overall, 82% had silicone insulation, 3% had polyurethane insulation, and 15% had both silicone and polyurethane insulation (Table 1).

A total of 29 patients (14%) had 1 lead, 145 (68%) had 2 leads, and 38 (18%) had 3 leads at the time of evaluation; 77% were on the left side, and 23% were on the right. There were 92% in the subclavian/axillary vein and 8% in the cephalic vein (Table 1).

Of the 212 patients evaluated, 82 (39%) were judged to have 0% stenosis, 21 (10%) had mild (<50%) stenosis, 33 (16%) of patients had 50% to 74% stenosis, 20 (9%) had 75% to 99% stenosis, and 56 (26%) had a total occlusion (100%) of the vein with the development of collateral circulation (Table 2).

In univariate analysis, the number of leads had a significant association with venous stenosis (Cochran–Armitage trend test *P*=0.008). The number with venous stenosis was 12 (42%) among patients with 1 lead, 90 (62%) among patients with 2 leads, and 28 (74%) among patients with 3 leads (Table 3).

The odds ratio of venous stenosis was 3.97 (95% CI 1.41 to 11.15; *P*=0.009) for patients with 3 leads relative to those with 1 lead and 2.32 (95% CI 1.03 to 5.22; *P*=0.042) for patients with 2 leads relative to those with 1 lead (Table 3).

The data also suggested a higher percentage of venous stenosis in patients with multiple lead-implant procedures than in those with a single procedure (79% versus 59%, *P*=0.057) (Table 3).

It is important to note, however, that these 2 variables (multiple procedures and number of leads) were highly correlated because the reason for multiple procedures was usually additional lead implantation.

In addition to the number of leads and multiple procedures, the total lead diameter (TLD)—defined as the sum of the diameters of all implanted leads—was also analyzed. The TLD was significantly higher in patients with venous stenosis than in those with no venous stenosis (15.3±3.9 versus 13.9±3.7, *P*=0.009) (Table 4).

There was no significant association between venous stenosis and sex, age, length of time since implant, type of insulation, individual lead diameter, warfarin use, aspirin use, clopidogrel use, the site of implantation, or the accessed vein (Table 4).

We also performed a multivariate logistic regression analysis to find independent predictors for venous stenosis. We included TLD in the multivariate analysis and excluded number of procedures and number of leads due to high degree of correlation among these 3 variables. We corrected for age by including it in the multivariate model despite a nonsignificant *P* value in univariate analysis because age is usually an important factor for atherosclerosis.

Because total venous occlusion carries procedural challenges that often necessitate alternative venous access, we also compared patients with total venous occlusion with those with partial or no stenosis. We found that TLD and age were independent predictors for 100% stenosis (Table 5, model 1). When we replaced TLD with the number of leads (Table 5, model 2), we found that patients with 3 leads were more likely to have 100% stenosis than patients with 1 lead (odds ratio

**Table 3.** Association of Number of Leads and Multiple Lead Implant Procedures With Venous Occlusion

Variable	Venous Occlusion, n (%)	<i>P</i> Value	Odds Ratio	95% CI	<i>P</i> Value
<b>Number of leads</b>					
1 (n=29)	12 (41)	Cochran-Armitage trend test <i>P</i> =0.008	Reference	—	—
2 (n=145)	90 (62)		2.32	(1.03 to 5.22)	0.042
3 (n=38)	28 (74)		3.97	(1.41 to 11.15)	0.009
<b>Multiple procedures</b>					
Yes (n=24)	19 (79)	Pearson chi-square <i>P</i> =0.057	2.64	(0.94 to 7.36)	—
No (n=188)	111 (59)		Reference	—	—

**Table 4.** Demographic and Clinical Variables by Presence of Venous Occlusion

Variable	With Venous Occlusion n=130	No Venous Occlusion n=82	P Value*
Age			( <i>t</i> test)
Mean (SD)	69.4 (14.3)	68.4 (14.2)	0.645
Range	32 to 95	25 to 92	
Sex (male), n (%)	87 (67)	50 (61)	0.388
Implant duration (years)			(Wilcoxon)
Median (IQR)	6.20 (4.24 to 8.65)	6.30 (4.61 to 9.55)	0.365
Range	0.12 to 28.66	0.25 to 20.09	
		(n=81)	
Lead access (left), n (%)	100 (77)	62 (77)	0.949
Lead access (n=81), n (%)			
Axillary	9 (7)	2 (2)	0.131
Cephalic	7 (5)	9 (11)	
Subclavian	114 (88)	70 (86)	
Insulation, n (%)			
Polyurethane only	3 (2)	4 (5)	0.265
Silicone only	104 (80)	69 (84)	
Polyurethane and Silicone	23 (18)	9 (11)	
Lead diameter, n (%)			
4.0 to 5.5	22 (17)	6 (7)	0.199
5.6 to 7.5 only	36 (28)	24 (29)	
5.6 to ≥7.5	31 (24)	19 (22)	
>7.5 only	41 (32)	33 (40)	
Sum of lead diameters (total French), mean±SD	15.3±3.9	13.9±3.7	0.009
	(n=88)	(n=51)	
Warfarin use, n (%)	37 (42)	16 (31)	0.212
	(n=72)	(n=38)	
Aspirin use, n (%)	43 (60)	22 (58)	0.853
	(n=74)	(n=42)	
Clopidogrel, n (%)	7 (9)	2 (5)	0.484

\*P value from Pearson chi-square test unless indicated.

3.3,  $P=0.04$ ). Whether this was due to multiple procedures or related to the number of leads or TLD is unclear because these 3 variables were highly correlated.

## Discussion

Our study found that more than half of patients (130 of 212) developed various degrees of venous stenosis after ICD or pacemaker implantation. Overall, 51% of our patients had >50% stenosis. Our results are comparable to previous smaller studies.<sup>3–5,10,11</sup>

The prophylactic use of anticoagulant or antiplatelet medications to prevent the development of venous stenosis has

been studied with conflicting results. More than one study, for example, showed that anticoagulant or antiplatelet use was not associated with a decreased incidence of venous stenosis or thrombosis.<sup>7</sup> On the contrary, Van Rooden et al evaluated 145 consecutive patients for the presence of venous thrombosis and found that the absence of anticoagulant therapy was associated with an increased risk of venous thrombosis.<sup>12</sup> In that study, however, they used Doppler ultrasound to evaluate for venous stenosis, and that technology is not as sensitive as contrast venography for detection of stenosis. Our study showed no association between antiplatelet or anticoagulant use for the development of venous stenosis, and that finding is in agreement with most other studies.

**Table 5.** Multivariate Analysis to Predict Total Vein Occlusion

Clinical Predictor	Model 1			Model 2		
	OR	P Value	CI	OR	P Value	CI
Age	1.0370	0.004	1.01 to 1.06	1.038	0.004	1.01 to 1.06
Total lead diameter	1.11	0.014	1.02 to 1.2			
<b>Number of leads</b>						
2 vs 1				1.36	0.5	0.47 to 3.9
3 vs 1				3.32	0.046	1.02 to 10.8

OR indicates odds ratio.

We conjecture that venous stenosis may be induced by endothelial trauma during the procedure. This would explain why anticoagulant or antiplatelet administration does not alter the clinical course. Supporting this hypothesis is the finding of an increased risk of venous stenosis in patients who had multiple implant procedures. Multiple entries into the venous system causes repetitive trauma to the endothelium that may promote an inflammatory reaction and the cascade of events that may lead to venous stenosis. The study by Da Costa et al<sup>9</sup> supports this hypothesis. They found that patients with previous use of transvenous temporary leads had higher incidence of venous stenosis.

The association of venous stenosis and the number of leads has also been an area of controversy. Goto et al, Oginosawa et al, and Bracke et al found no association between venous stenosis and the number of leads present.<sup>7,8,13</sup> Other investigators disagreed with this finding. Van Rooden et al and Bulur et al both found a significant association between venous stenosis and having multiple leads in their series.<sup>12,14</sup> Our results are consistent with their results. Patients with multiple leads implanted more commonly had multiple procedures, and this also supports the repetitive trauma hypothesis. Likewise, multiple leads result in a greater total sum of lead diameters, which correlated with greater incidence of venous stenosis.

**Limitations**

The major limitation of our study is the absence of a control group. Our venograms were performed in patients with previous device implant procedures. Although unprovoked venous stenosis should be extremely rare, we do not have data regarding existing venous stenosis due to other factors such as chronic indwelling ports or frequent central venous catheterizations. In addition, the absence of a prospective randomized design limits the application of our conclusions to some degree. Another limitation of our study is that information regarding anticoagulation use was available for only approximately two-thirds of the study population. Data

were gathered at 2 different institutions, and we were unable to obtain medication history for approximately one-third of the patients who had their procedures at the first institution.

**Conclusion**

Complete occlusion of the subclavian/axillary or innominate vein occurred in 26% of patients in our series. These patients were all asymptomatic and had good collateral venous flow. This tended to occur regardless of individual lead size, age, sex, lead insulation, side of implant, time since implant, or use of anticoagulant or antiplatelet therapy.

Our study has implications for both lead manufacturers and lead implanters. Smaller diameter leads have, as a group, resulted in greater risk of significant complications such as perforation<sup>15-17</sup> or lead failure,<sup>6,7</sup> with a decrease in venous stenosis as a potential benefit. With that in mind, implanters need to consider whether an individual patient would benefit from a larger lead with proven durability at initial implant. Likewise, device manufacturers may wish to focus on lead longevity rather than size. A recent study by Steckman et al<sup>18</sup> showed a significant increase in in-hospital complications when device reoperations necessitated a lead procedure as opposed to a generator change alone.

Likewise, because venous stenosis tended to increase with multiple leads, multiple procedures, and the sum of lead diameters implanted, physicians may wish to consider single-chamber or single-lead VDD devices in patients with good sinus node function. Having said that, if an implanter views a patient as borderline for needing an atrial or ventricular lead, it may be better to add it at the initial implant than to expose the patient to a second procedure 1 or 2 years later.

Our data suggest that if a patient with an existing system requires the addition of a lead, then selecting a smaller lead diameter would be beneficial because we noted that in patients with multiple leads and multiple procedures, TLD affects the incidence of venous stenosis.

## Disclosures

None.

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