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Incidence and Risk Factors of Subclavian Vein Stenosis after Permanent Transvenous Pacemaker in Pediatric Population

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ABSTRACT

Background: Subclavian venous (SCV) stenosis due to a permanent transvenous pacemaker has been described as the most common complication associated with this procedure however, the incidence and risk factors of venous obstruction and occlusion due to endocardial leads in a small group of infants and young children were not fully assessed.

Objective: The aim of the current work was to evaluate the incidence and degree of subclavian stenosis and risk factors for stenosis in the pediatric population after transvenous pacemaker insertion.

Patients and Methods: This is a cross-sectional study conducted on children who had transvenous pacing leads implanted between 2010 and 2018 at the cardiology clinic of Cairo university children's Hospital with pre-implantation subclavian venography and evaluated after the duration of implantation ranged from 1-5 years. Subclavian venography was done to all patients.

Results: The incidence of mild to moderate stenosis in cases at time of assessment was 88.3 % of the cases, while the incidence of severe angiographic stenosis was only 11.7 % of cases with development of venous collaterals in patients of severe stenosis. Risk of subclavian stenosis increased with lower weight at time of implantation.

Conclusion: It could be concluded that subclavian vein stenosis is a common complication after transvenous pacemaker insertion in the pediatric population, but it occurs at mild to moderate degrees, while severe stenosis is rare, usually asymptomatic, and subclinical and correlated with the weight of the patient at the time of implantation of pacemaker. So, transvenous pacing in children can be done safely with favorable results and minor complications.

Keywords: Incidence, Risk Factors, Subclavian vein Stenosis, Transvenous Pacemaker, Pediatric Population

INTRODUCTION

The most frequent complications related to permanent transvenous pacemaker have been characterized as venous stenosis and thrombosis [1] .

In the literature, there are many different estimates of the incidence of subclavian vein stenosis following device installation, ranging from 30% to 50% [2].

More than a month after the insertion of the device, patients with chronic lead-related subclavian vein stenosis/occlusion typically have excruciating arm swelling that may be accompanied by cyanosis and apparent venous collaterals over the ipsilateral chest and upper extremity. Due to the establishment of venous collaterals, the majority of patients continue to be asymptomatic. Symptoms may be brought on by a minor venous stenosis that already exists but has not yet developed collaterals, an ipsilateral arteriovenous fistula in dialysis patients, insufficient collaterals, or their sudden occlusion [3].

The complicated inflammatory and fibrotic changes that take place at the endocardial lead interface have received most of the attention in histopathologic research.

Similar inflammatory and fibrotic alterations have been found in autopsy studies near the vein where the device leads are inserted. When lead removal is required, dense fibrotic adhesions are frequently found, which is how excimer laser lead extraction was created. At recognizable anatomic locations such the lead insertion point, venous bifurcation sites, and the costoclavicular area, this fibrosis may manifest itself more frequently. Although the reason why some anatomical sites are more likely to develop stenosis is not fully understood, the explanation is probably complex and connected to endothelial damage from insertion as well as repetitive mechanical trauma at bifurcation sites or where bone compression may happen [4].

The incidence of venous blockage and occlusion due to endocardial leads in a small group of neonates and infants was not thoroughly evaluated [5] and risk factors for the development of subclavian vein stenosis have been described but are not clearly characterized.

Therefore, the purpose of our study was to assess the prevalence, severity, and risk factors for subclavian

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stenosis in the pediatric population, which has not yet been thoroughly identified.

PATIENTS AND METHODS

This is a cross-sectional study conducted on 60 children who had transvenous pacing leads implanted between 2010 and 2018 at the Cardiology Clinic, Cairo university children's Hospital with pre-implantation subclavian venography with the exclusion of children with vasculitis or congenital systemic venous abnormalities.

The mean age of the study population was 82.03± 43.999 months with 50 % being males and 50% being females.

All children were subjected to the following:

A. **Detailed history taking including** age (at the time of implantation and at the time of assessment), sex, duration from pacing till the time of assessment, history of the cause of pacing, history of associated congenital heart diseases, history of systemic lupus in the mother and the pacing details including type of pacemaker and lead, site of entry to the subclavian vein.

B. **Full clinical examination.** Weight, height, body surface area, and clinical signs of subclavian obstruction including upper limb edema or dilated upper limb veins.

C. **Venography of a subclavian vein:** venography was done on the patients by inserting a peripheral venous cannula, injection of radio-opaque dye, and imaging the subclavian vein in catheterization lab then measurement of subclavian vein diameter ***proximally*** from the site of lead insertion to its junction with innominate vein, measurement of diameter of the ***mid-segment*** between the junction of the subclavian vein with innominate vein to its junction with SVC and measurement of diameter at ***distal segment*** between the junction of the innominate vein with SVC and SVC distally to RA.

Mild stenosis was defined as less than 50 % reduction of luminal diameter compared to the diameter of a wide area; **moderate stenosis** was defined as more than 50 % reduction of luminal diameter compared to the diameter of a wide area while **severe stenosis** was defined as 70 % reduction of luminal diameter compared to the diameter of wide-area **(Figure 1).**

All these measurements were taken at the time of implantation from recorded data and at the time of assessment for the studied group and compared to each other.

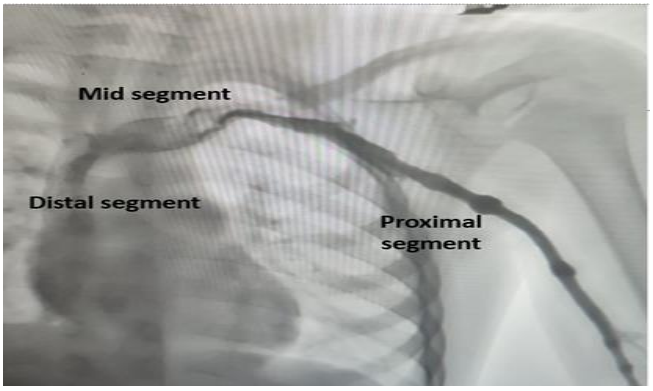

Figure (1): Subclavian Venography with different segments.

Ethical Consideration:

The Institutional Review Board of the Faculty of Medicine at Cairo University gave its ethical approval for this study, which was carried out in accordance with the Declaration of Helsinki, the code of conduct established by the World Medical Association for human study.

According to the policies of the ethics committee of the Faculty of Medicine, Cairo University, informed consent was obtained from the parents or guardians of the children.

Statistical methods

The statistical study was performed using IBM SPSS Statistics for Windows, version 26.0. (IBM Corp.; USA; Armonk, NY). To check whether the numerical variables were normal, we employed the Shapiro-Wilk test. Our numerical data, which were not normally distributed, were shown as a median and range. (Minimum-maximum).

Numbers or percentages have been used to express nominal variables. To compare groups, we utilized the non-parametric Wilcoxson signed rank test for numerical variables. All statistical tests conducted as part of this investigation were performed with a significance threshold of 0.05. If the P value was less than 0.05, it was considered statistically significant.

RESULTS

Table (1) shows comparison between implantation and assessment times as regard to patients' clinical data. There was a statistically significant improvement in weight, height, body surface area after implantation of pacemaker with p value < 0.05.

Mean duration from pacing till assessment was 3.05±1.107 years. The main cause of pacing with postoperative heart block, main subclavian axis was Lt Subclavian vein, most of the cases had abnormal heart structure. Only one case was associated with clinical signs of venous obstruction.

Table (1): Comparison between implantation and assessment times concerning patients' clinical data.

	At the time of implantation (n=60)	At the time of assessment (n=60)	P value
Age (months)	82.03±43.999	109.48±50.256	0.004*
Weight(kg)	22.20±8.117	32.68±14.434	<0.001*
Height(cm)	117.20±15.490	123.62±23.729	0.019*
Body Surface Area	0.81±0.250	0.97±0.363	0.010*
sex			
Male	30 (50 %)		
Female	30 (50 %)		
Duration from pacing till assessment time	3.05±1.107 years		
Cause of pacing	Congenital CHB	13 (21.6 %)	
	Post-operative CHB	47 (78.4 %)	
Associated CHD	Normal Heart		15 (25 %)
	Abnormal Heart (CC-TGA or post-operative repair)		45 (75 %)
Side of subclavian vein	Right	9 (15 %)	
	Left	49 (81.7 %)	
	Bilateral	2 (3.3 %)	
Clinical signs of venous obstruction (Limb edema or upper limb dilated veins)	Absent	59 (98.3%)	
	Present	1 (1.7 %)	

P: p-value for comparing between the two studied groups *: Statistically significant at P <0.05
CC-TGA: Congenitally corrected Transposition of great arteries, CHB: Complete heart block
CHD: Congenital heart disease.

Table 2 shows comparison between implantation and assessment times as regard to patient ‘s subclavian venography, showing significant subclavian stenosis at proximal, mid and distal segments with p value < 0.05. 50 % of cases had mild stenosis, 38.3 % of cases had moderate stenosis and only 11.7 % of cases had severe stenosis and only 7 cases have venous collaterals due to significant subclavian stenosis.

Table 2: Comparison between implantation and assessment times as regards to patient's subclavian venography

Subclavian Venography	At the time of implantation (n=60)	At the time of assessment (n=60)	P value
Proximal segment	0.8±0.2133	0.53±0.2937	0.001*
Midsegment	0.78±0.1903	0.49±0.1714	<0.001*
Distal segment	0.87±0.2162	0.594±0.2861	0.004*
Degree of Stenosis	Mild Stenosis	30 (50 %)	
	Moderate Stenosis	23 (38.3 %)	
	Severe stenosis	7 (11.7 %)	
Presence of venous collaterals	Absent	53 (88.3%)	
	Present	7 (11.7 %)	

P: p-value for comparing between the two studied groups *: Statistically significant at P <0.05

Table (3) shows correlation between subclavian vein venography at time of assessment and weight at time of implantation, showing significant correlation between proximal and distal segments stenosis and weight and non-significant correlation with type of lead and type of device.

Table (3): Correlation between subclavian vein venography at the time of assessment and weight at the time of implantation

Subclavian Venography	Correlation (r)	P value
Proximal segment	0.44	<0.001*
Midsegment	0.17	0.187
Distal segment	0.396	0.002 *
Type of device	0.2	0.7
Lead type	0.15	0.8

P: p-value for comparing between the two studied groups *: Statistically significant at P <0.05

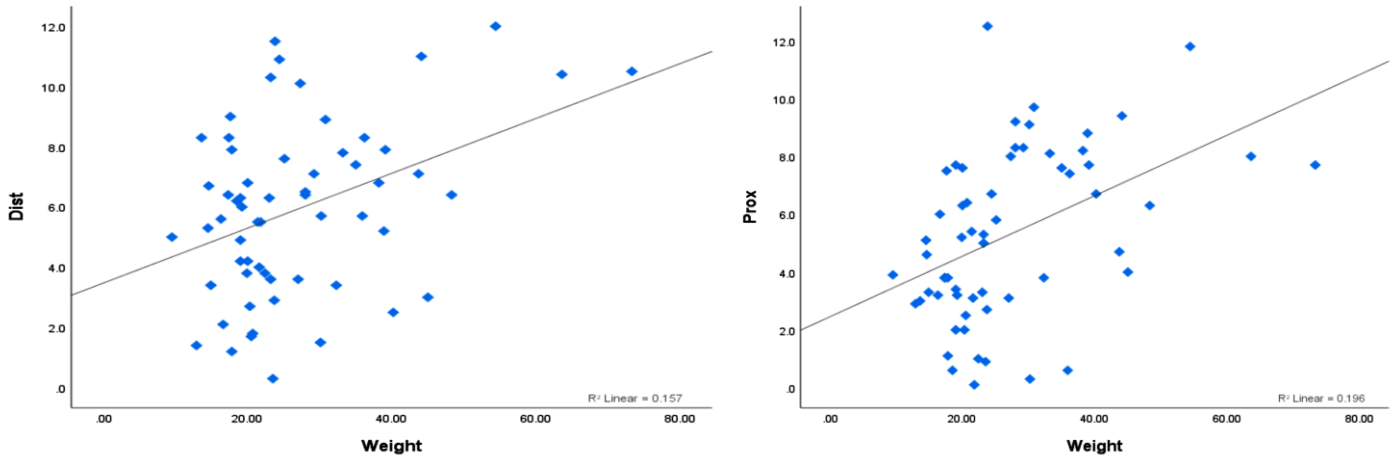

Figure (2): Correlation between subclavian vein stenosis at proximal and distal segments and weight

DISCUSSION

Third-degree atrioventricular (AV) block, either congenital or post-surgical, and sporadic symptomatic sinus node dysfunction are the most frequent indications for permanent pacemaker installation in children [6]. In the past, surgical epicardial pacing by a thoracotomy has been considered the main therapy option for children, especially those under 10 kg, however it is not preferred because of how intrusive it is. There is high morbidity, increased perioperative mortality, and a lengthy hospital stay of 4-5 days even with minimally invasive surgery. In comparison to transvenous leads, epicardial leads had higher pacing thresholds and a higher frequency of lead fractures [7]. Therefore, a number of studies [8-10] described their success with transvenous pacing in kids under 10 kg while reporting only mild side effects.

Patients undergoing device insertion or revision frequently develop venous occlusion or thrombosis. De novo implants are expected to have a 13.7% incidence, whereas system improvements will have a 26–64% one. Vein occlusions in patients having their first pacemaker implanted are typically related to past central line instrumentation for hemodialysis and long-term infusion therapy [11]. This study's primary objective was to assess pediatric patients who had subclavian venous access following pacemaker placement. The main aim of this study was to evaluate subclavian venous access after pacemaker implantation in pediatrics. The cardiology clinic at Cairo University Children's Hospital conducted a cross-sectional study involving sixty kids who had transvenous pacing leads inserted between 2010 and 2018. There were 30 males and 30 females in the study group at the time of implantation, with a mean age and standard deviation of 82.03 and 43.999 months, 117.20 and 15.490 cm in height, 22.20 and 8.117 kg in weight, and a mean BSA of 0.81 and 0.250. The time from pacing to assessment ranged from 1.08 to 5.0 years, with a mean value of 3.05 and 1.107 years. Age, weight, and BSA considerably increased in our study's participants at the time of assessment compared to the time of pacemaker implantation, indicating enhanced growth parameters.

The Minimum Age of our studied group was 11 months at the time of implantation and the minimum weight of our studied group was 8 kg at the time of implantation these results coincide with several studies which reported early transvenous pacemaker insertion in the pediatric population as an alternative therapeutic modality to epicardial pacemaker insertion as **Konta *et al.*** [12], that reported that the median age was 6.7 months (range, 1 day to 3 years) with a median weight of 4.6 (range, 2.7–10) kg at the time of pacemaker implantation. Additionally, **Lotfy *et al.*** [13] showed that the youngest patient without an endocardial PM was 56 days old and 3.2 kg, while the youngest patient with one was 16 days old and 3.5 kg.

As regards the cause of pacing of the studied group, 13(21.6%) the cause of pacing was congenital CHB, and 47(78.4%) the cause of pacing was post-operative CHB.

15(25%) with normal heart and 45(75.0%) with abnormal heart. The study by **Lotfy *et al.*** [13], which found that postoperative total cardiac block occurred in 54 (52.4%) of the study group, provided evidence in favor of our findings. Congenital heart block (33.2%, n = 31), congenital sinus node dysfunction (3.8%, n = 4), inappropriate sinus bradycardia (0.9%), and postoperative sinus node dysfunction (0.9%) were some of the other explanations. The final 11 surgeries were replacements for PMs. Similar to this, **Celiker *et al.*** [14] shown that postoperative conditions were more frequently the reason for PM implantation than congenital ones. According to **Welisch *et al.*** [15], high-grade AV block (Mobitz II or total AV block) was a factor in the need for pacing in 65% of their patients, 55% of whom had undergone surgery or had an intervention. Others, like **Kumor *et al.*** [16], have reported more congenital than postoperative justifications for pacing.

Venous occlusion is a recognized complication of transvenous endocardial pacing [17]. In the current study there was statistically significant stenosis of proximal, mid, and distal segments after subclavian angiography in cases at the time of assessment compared to their diameter at the time of implantation with p value less than 0.05. The incidence of mild to moderate stenosis in cases at the time of assessment was 88.3 % of the cases, while the incidence of severe angiographic stenosis was only 11.7 % of cases with development of venous collaterals in in patients of severe stenosis, despite angiographic stenosis evident by subclavian angiography, only 1 patient (1.7 % of cases) developed clinical signs of venous obstruction with edema and dilated veins of upper limb which in agree with study done **by Wei-Da and Ju-Yi** [18] which showed that small fraction of patients develops severe stenosis or occlusion of subclavian vein after pacemaker insertion . The incidence of venous obstruction was variable in different studies but agreed with our study in that symptomatic clinical occlusion was rare after pacemaker insertion which can be explained by the development of collateral venous circulation as the stenosis gradually worsens and chronic occlusion nature which had been validated by a study conducted by **Jeong and Na** [3], who reported possible causes of symptoms included the absence of sufficient collaterals or their sudden obstruction, an acute thrombotic event on a pre-existing moderate venous stenosis where collaterals had not yet formed, or the onset of an ipsilateral arteriovenous fistula in dialysis patients.

Numerous studies that routinely performed post-implant venography showed high stenosis rates. The majority of studies have classified stenosis as mild in 70% of cases. At a mean post-procedure follow-up of 4 months, **Antonelli *et al.'s*** [19] consecutive venography of 40 patients revealed substantial venous stenosis in 23% of them. Rates as high as 50% have been recorded in studies with extended follow-ups [20]. In 202 patients, **Da Costa *et al.*** prospectively examined venography at 6 months after implant. 51% of patients had stenosis that was more severe than mild. Due to collateral venous circulation, which appears as the stenosis gradually increases, the majority of the patients in these investigations were asymptomatic [1]. According to studies done on adult patients, the incidence of blockage can range from 30 to 45 percent, whereas the typical full occlusion rate is 12 percent, and the symptomatic occlusion rate is 1 to 3 percent [21]. Furthermore, **Lelakowski *et al.*** **[11]** and **Konta *et al.*** [12] demonstrated that 3.7% of the research group had symptomatic venous obstruction but no clinical evidence of SCV occlusion. According to **Stojanov *et al.*** [7], transvenous pacing was applied to 12 children weighing 2.25 to 10 kg between 1986 and 2003. The outcome was excellent with no lead malfunction, infection, or clinical venous blockage across a time span of 3 months to 13 years. The use of transvenous pacing in 12 patients weighing less than 10 kg (5 individuals weighing less than 5 kg) was described by **Robledo-Nolasco *et al***. between 2001 and 2007 [10]. Only one lead became loose over the 4.6 years of follow-up, and there was no clinical venous obstruction.

Although they have been identified, risk factors for subclavian vein stenosis remain poorly understood. In Our study, the risk of subclavian stenosis increased with lower weight at the time of implantation with a correlation of 0.44 and p-value <0.001 for the proximal segment and p-value of 0.002 for the distal segment, but not correlated to the type of device or lead type or other patient clinical data. This result was consistent with a study by **Konta *et al.*** [12], which discovered that SCV occlusion after numerous surgeries during long-term follow-up occurred more frequently in patients who weighed less than 5 kg at the time of pacemaker implantation. Of the 13 patients, 10 (77%) were under 5 kg and 2 (15%) were over 5 kg. Although patient age, body size, and lead parameters at implantation do not predict venous occlusion, **Bar-Cohen *et al.*** [22] have shown that the frequency of venous occlusion in young children is comparable to that reported in adults.

The rate of SCV occlusion in patients weighing 5 to 10 kg was comparable to that in patients who were noticeably older. The degree of vein damage at implantation or lead diameter did not correlate with any of the patient- and device-specific factors, according to **Boczar *et al.'s*** [20] findings. These included the type of lead (silicone or polyurethane), the length of time after the lead was implanted, the age, sex, pacemaker or defibrillator, and the entrance site. According to study done by **Peter *et al.*** [1] the most risk factors associated with venous obstruction are the presence of multiple

leads, history of multiple procedures, reduced left ventricular function, pocket infection , absence of anticoagulation and previous transvenous temporary pacing leads.

CONCLUSION

It could be concluded that subclavian vein stenosis is a common complication after transvenous pacemaker insertion in the pediatric population, but it occurs at mild to moderate degrees, while severe stenosis is rare, usually asymptomatic, and subclinical and correlated with the weight of the patient at the time of implantation of pacemaker. So, transvenous pacing in children can be done safely with favorable results and minor complications.

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