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Review

Central Venous Stenosis after Hemodialysis: Case Reports and Relationships to Catheters and Cardiac Implantable Devices

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Keywords
Central venous catheters · Hemodialysis catheters · Pacemaker, artificial · Implantable defibrillators · Central venous stenosis

Abstract
The appropriate vascular access for hemodialysis in patients with cardiac implantable electronic devices (CIED) is undefined. We describe two cases of end-stage renal disease patients with CIED and tunneled central venous catheter (CVC) who developed venous cava stenosis: (1) a 70-year-old man with sinus node disease and pacemaker in 2013, CVC, and a Brescia-Cimino forearm fistula in 2015; (2) a 75-year-old woman with previous ventricular arrhythmia with implanted defibrillator in 2014 and CVC in 2016. In either case, after about 1 year from CVC insertion, patients developed superior vena cava (SVC) syndrome due to stenosis diagnosed by axial computerized tomography. In case 1, the patient was not treated by angioplasty of SVC and removed CVC with partial resolving of symptoms. In case 2, a percutaneous transluminal angioplasty with placement of a new CVC was required. To analyze these reports in the context of available literature, we systematically reviewed studies that have analyzed the presence of central venous stenosis associated with the simultaneous presence of CIED and CVC. Five studies were found; two indicated an increased incidence of central venous stenosis, while three did not find any association. While more studies are definitely needed, we suggest that these patients may benefit from epicardial cardiac devices and the insertion of devices directly into the ventriculus. If the new devices are unavailable or contraindicated, peritoneal dialysis or intensive conservative treatment in older patients may be proposed as alternative options.

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Introduction

Nearly half a million patients in the United States are affected by end-stage renal disease (ESRD) and more than 400,000 are treated by chronic hemodialysis (HD). Approximately 20% of these patients use a tunneled central venous catheter (CVC) as vascular access [1]. The first cause of death of these patients is related to heart failure and/or cardiac rhythm disorders [1]. Therefore, an increasing number of elderly ESRD patients need a permanent pacemaker or implantable cardioverter-defibrillator (ICD), collectively known as cardiac implantable electronic devices (CIED) [2]. Recent studies have reported a potential risk of central venous stenosis (CVS) associated with the combined insertion of tunneled CVC and CIED [3]. CVS often occurs with vena cava syndrome defined as the constellation of signs and symptoms due to the obstruction of blood flow in the superior vena cava (SVC); the most frequent are face/neck swelling (82%), upper extremity swelling (68%), dyspnea (66%), cough (50%), and dilated chest vein collaterals (38%). Computed tomography (CT) scan of the chest with intravenous contrast helps to confirm the diagnosis and to provide information regarding the underlying cause [4]. We here describe two cases of patients with vena cava syndrome due to CVS in the concomitant presence of tunneled CVC for HD and CIED. The cases are discussed in the context of information derived from a systematic review of the studies that have analyzed the presence of CVS associated with the dual implantation. This analysis could enrich the knowledge on the best strategy in the growing patient population at risk of complications attributable to this combination.

Case Reports

Patient 1

The first patient is a Caucasian man born in 1948, with type 2 diabetes mellitus and hypertension diagnosed in 1998. After 2 years, the patient was referred to a nephrologist because of chronic kidney disease (CKD) onset (1 g/24 h proteinuria and low estimated glomerular filtration rate, eGFR: 38 mL/min/1.73 m^2). In 2013, asymptomatic bradyarrhythmia was found, occasionally, and the cardiologist indicated a pacemaker implant; a bicameral pacemaker was therefore implanted a few weeks later. In 2015, the patients developed weight gain and increased blood pressure refractory to medical treatment with an eGFR of 10 mL/min/1.73 m^2 and 24-hour urinary protein excretion of 3.5 g/day. Considering the remarkable overload, to allow immediate HD start, a Palindrome™ Precision Symmetric Tip Dialysis Catheter (insertion length 19 cm) was placed in the right internal jugular vein. After that, a right forearm Brescia-Cimino arteriovenous fistula (AVF) was surgically prepared. Due to patient preference, the AVF was not used for the dialysis. After 1 year, he presented with cough and dyspnea and could not lie down due to severe bilateral pleural effusion. Upon physical examination, extensive venous involvement was noted in the chest. The chest CT venography demonstrated an occlusion of the SVC between the segment above the azygos venous orifice and the right atrium (Fig. 1 and 2). The right jugular vein was present, and the left innominate vein was patent and moderately enlarged. There were massive collaterals throughout the chest, shoulder, and mediastinum. Based on this patient's symptoms and examination, SVC syndrome was diagnosed. An endovascular intervention was considered as a possible treatment, which, however, the patient refused. Therefore, CVC was removed and AVF was used as HD access. After 14 days, improvement of signs and symptoms was observed.

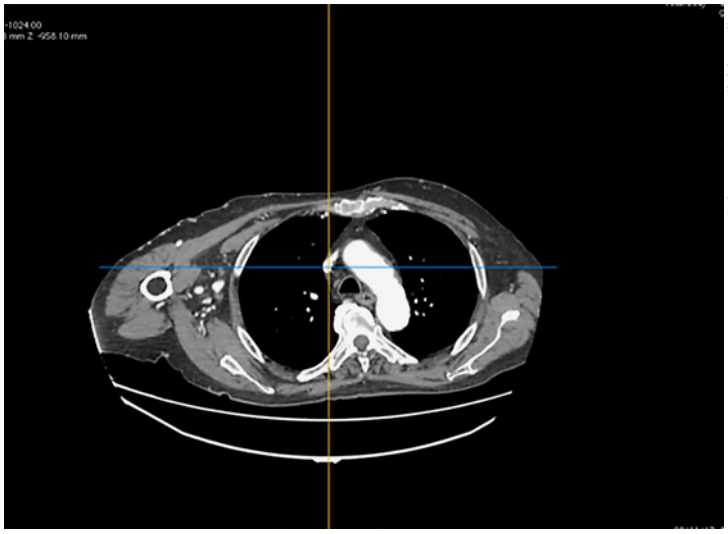

Fig. 1. Transversal section of the superior vena cava stenosis (case 1).

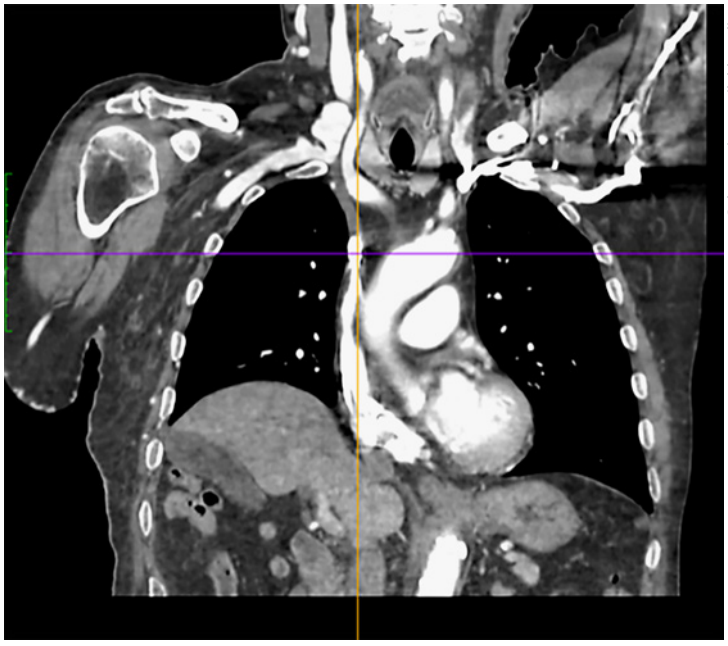

Fig. 2. Longitudinal section of the superior vena cava stenosis (case 1).

Patient 2

The second patient is a 75-year-old Caucasian woman, followed in outpatient renal clinic because of CKD, diagnosed in 1995, secondary to autosomal dominant polycystic kidney disease. In 1995, eGFR was 28 mL/min/1.73 m^2. At the ultrasound control, the right kidney was enlarged (length: 15 cm) and showed 5 cysts; the left kidney was 14 cm long with 7 cysts. In 2014, the patient had a syncope due to ventricular tachycardia immediately treated by defibrillation. An ICD was therefore placed after this episode. In 2016, eGFR was 7 mL/min/1.73 m^2 with uremia, therefore requiring initiation of dialytic treatment. AVF was not prepared because of the absence of suitable superficial venous bed of the arm. A dialysis catheter (insertion length 19 cm) was therefore positioned in the right internal jugular vein. After 16 months, the patient developed dilated chest vein collaterals without other symptoms;

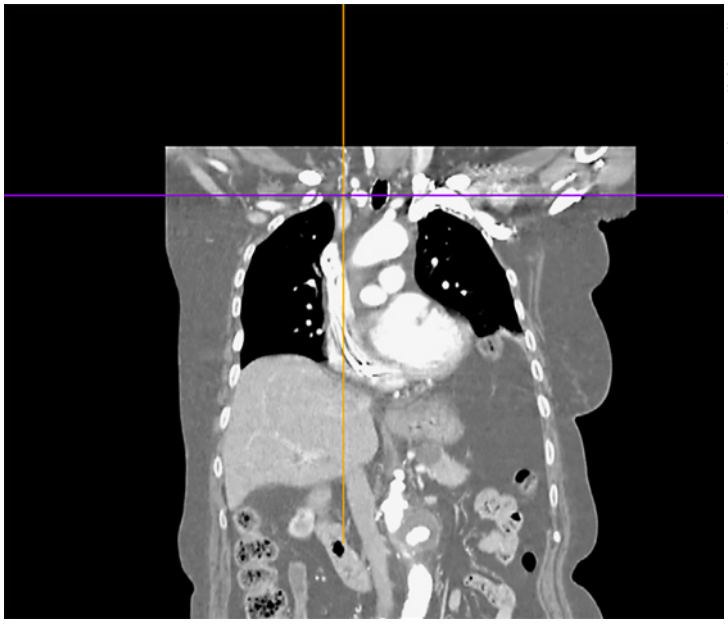

Fig. 3. Longitudinal section of the superior vena cava stenosis (case 2).

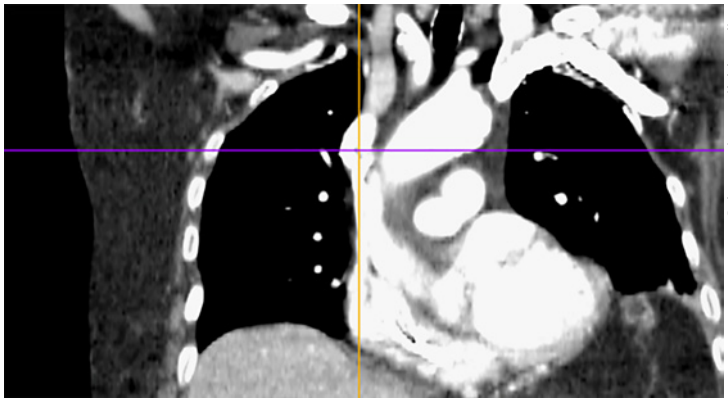

Fig. 4. Longitudinal section of the superior vena cava stenosis (case 2).

a CT scan of the chest with intravenous contrast was performed and a stenosis of SVC upper section was found (Fig. 3 and 4). The diagnosis was SVC syndrome. CVC was removed and replaced by a catheter in the right femoral vein. After 1 month, there was no total resolving of the symptoms and the patient underwent percutaneous transluminal angioplasty without stent. All the symptoms resolved within 3 months.

Materials and Methods of Systematic Review

We searched studies on CVS associated with the presence of HD catheters and intracardiac device catheters. A systematic search of articles published in all languages was performed using PubMed and Scopus databases to identify relevant published studies. We used the following Medical Subject Headings (MeSH) and text words: "central venous catheters," "central venous catheterization," "defibrillators, implantable," "cardiac resynchronization therapy devices," "intra-cardiac devices," "pacemaker artificial," "hemodialysis catheters," "central venous stenosis," "central venous thrombosis." The detailed search syntax is

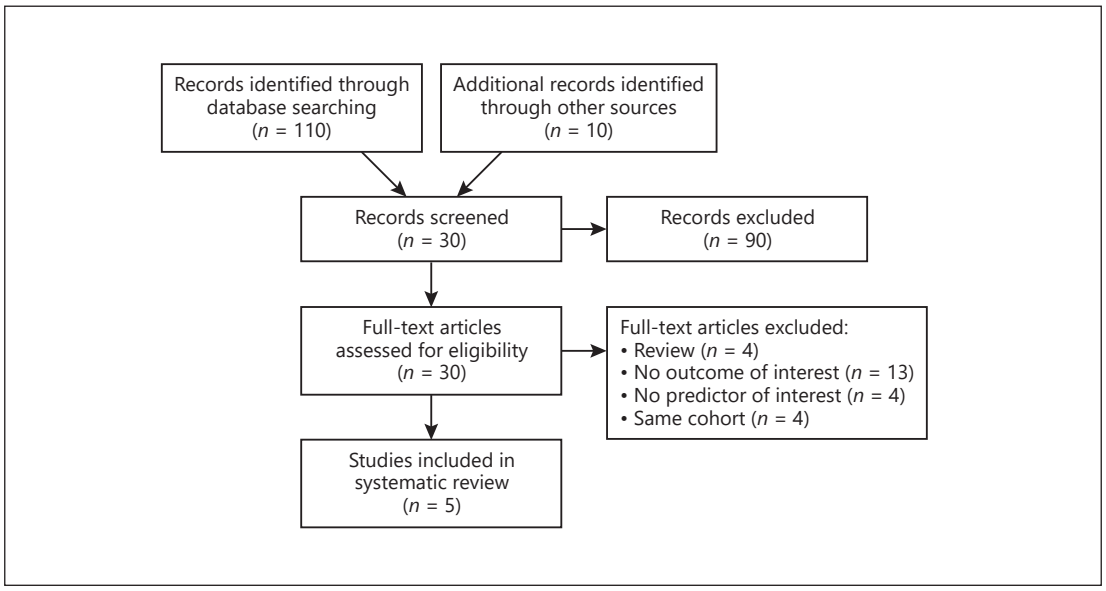

Fig. 5. Flow diagram of the literature selection process.

reported in the Appendix. Bibliographies of relevant articles and reviews were also manually screened for additional studies. Original observational studies evaluating stenosis and thrombosis in patients with intracardiac devices and HD catheters were retained. The search was designed and performed by two authors (M.Pa. and C.G.).

Results

The flow diagram of the selection process is described in Figure 5. Five observational studies on the risks of combined CVC and CIED were examined (Table 1). Saad et al. [5] showed 1.3% of combination of tunneled venous catheter and CIED in their cohort with no case of symptomatic SVC stenosis. Bhadauria et al. [3] demonstrated in five patients with coexisting CVC and pacemaker no immediate or delayed complications. Only one patient had a tunneled catheter and could be followed up for 2 years, and he did not have any leads-related complication or CVS, while the other patients had uncuffed catheters with a total duration of coexistence ranging from 9 to 33 days [3]. A Greek study published in 2009 showed two cases of patients with CIED and CVC who developed CVS. The authors hypothesized, on the basis of patient characteristics, that platelet abnormalities, alteration in clotting factors, elevated levels of inflammation molecules (cytokines, C-reactive protein, homocysteine), and elevated venous pressure during HD concurred to vascular damage and constituted a prerequisite for the steno-thrombosis in the presence of catheter-induced trauma [6]. Furthermore, the risk of developing SVC syndrome was higher in the presence of multiple catheter placements over time. An Italian study showed the case of a 65-year-old man who underwent multiple placements of CVC in the right subclavian and jugular vein because of the absence of an adequate vascular heritage for the creation of AVF in his upper limbs. The patient had a pacemaker implanted for a symptomatic atrioventricular block. After 2 years, the patient was admitted for signs of SVC syndrome. Chest contrast enhanced CT angiography showed a severe obstruction of the SVC with significant reduction in the luminal diameter of the vessel, due to the presence

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Table 1. Studies that have compared outcomes of patients with CIED and CVC

First author [ref.], year	Design/setting	Outcome	Sample, *n*	Age, years	eGFR	CVD, %	DM, %	FU, months	Main findings
Saad [5], 2015	Retrospective; MHD patients with vascular access and CIED. Symptomatic vein stenosis onset	Failure of vascular access, removal of CIED, patient lost for all cause	129	70.4	NA	NA	69	12	No case of symptomatic vein stenosis
Bhadauria [3], 2017	Retrospective; patients with CIED and CVC	Onset of CVS, infections, catheter-related complications	5	65.4±4.8	NA	NA	NA	23.5	No immediate or delayed complications
Pipili [6], 2009	Case report; CKD patients with multiple catheterization and CVS	CVS due to catheterization in CKD patients	2	75±3	NA 28	100	0	NA	Platelet abnormalities, clotting factors, inflammation molecules, venous pressure during HD associated with catheter-induced trauma may predispose to SVC
Santoro [7], 2011	Case report; MHD patient with CVC, CIED, and CVS	CVS	1	65	NA	NA	NA	NA	Multiple catheterizations and CIED increase the risk of SVC syndrome
Aurshina [8], 2018	Retrospective; patients with HD catheter. Evaluation for presence of preexisting pacemakers and central lines	Onset of CVS, infections, catheter-related complications	600	73.6±12	NA	NA	75	6	In a cohort of 600 patients with HD catheter, only 29 had CIED or central lines. No complications during the follow-up

All studies are observational studies. Age is mean±SE or median. eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2) at start of follow-up for endpoint analysis; CVD, cardiovascular disease including (a) peripheral and cerebral vascular disease and ischemic heart disease or (b) coronary artery disease and cerebrovascular disease; DM, diabetes mellitus; FU, months of follow-up (median); MHD, maintenance hemodialysis; CIED, cardiac implantable electronic devices; CVC, central venous catheter; CKD, chronic kidney disease; CVS, central venous stenosis; HD, hemodialysis; NA, not available; SVC, superior vena cava.

of the tunneled CVC and wire leads of the pacemaker. A venography revealed obstruction of the SVC at the junction of the left brachiocephalic vein with a collateral circulation. Therefore, the patient underwent endovascular angioplasty of the stenotic vascular segment, with placement of a metallic stent [7]. A recent retrospective study was conducted in HD patients with CVC placed over a period of 10 years. For each catheter that was placed, perioperative chest X-ray was used to evaluate for preexisting pacemakers and central lines. The position and laterality of placement of the HD catheter along with AVF presence with functional capacity for access was noted. A total of 600 HD catheters were placed over the decade. The authors found 20 pacemakers or automatic ICDs and 19 central lines on the same side of the neck as the HD catheter that was placed in the ipsilateral jugular vein. No patient exhibited malfunction or dislodgment of the central line, pacemaker, or ICD or evidence of upper extremity venous obstruction based upon signs, symptoms, or duplex exams. The authors therefore suggested that placement of HD catheter in the internal jugular vein ipsilateral to the preexisting catheter/leads is safe and spares the contralateral limb for AVF creation [8].

Discussion/Conclusion

We systematically reviewed, for the first time, the few studies evaluating the association of the concomitant use of CIED and HD CVC with the onset of CVS. A higher risk to develop CVS was reported in some studies [6, 7] but not in others [3, 5, 8]. However, these results must be interpreted considering the study design and the small sample size of available studies. Moreover, in our case reports, we observed the onset of CVS in two patients with concomitant use of CIED and CVC with a resolution of syndrome after CVC removal. During the past decade, the number of ESRD patients with an ICD or cardiac resynchronization therapy with a defibrillator within a year of initiating dialysis therapy has increased more than ten-fold, from 0.06% in 1995 to 0.75% in 2005 [9]. Moreover, Saad et al. [5] reported that in one center in the United States, among 1,235 patients on chronic HD, a CIED was present in 129 patients (10.5%). The most common method of CIED insertion is the transvenous placement of the electrical leads, and the left subclavian or cephalic vein approach is preferred by many implanting physicians for CIED lead insertion, due to favorable venous anatomy and optimal shock vectors for ICD therapy. When a vascular access is required, the presence of electrical leads in the central veins could be associated with vascular and infectious complications, which demands an individual approach in access creation [10]. Patients with a pacemaker or an ICD show a similar risk of venous obstruction. Furthermore, neither the hardware (lead duration, lead size, insulation material) nor the operative technique (cephalic versus subclavian approach or right versus left pectoral implantation) appear to modify the rate of venous complications [11]. On the other hand, studies in non-ESRD patients have demonstrated CVS in patients with CIED, ranging from 26% to 64% [12, 13]. CVS is generally asymptomatic in most patients, but this may not be the case in HD patients. Indeed, HD patients with upper extremity AVF and ipsilateral transvenous CIED leads are prone to develop clinically significant venous hypertension due to the high rate of venous blood return, which may overwhelm the capacity of the obstructed central veins, manifesting as SVC syndrome with or without associated dialysis access dysfunction. In a series of 14 ESRD patients with a pacemaker on the same side as AVF [11], 10 patients (71%) developed symptomatic venous hypertension and demonstrated subclavian vein stenosis or occlusion on angiography. Venous hypertension due to AVF and ipsilateral CIED leads has been in fact described in numerous other reports [14–18]. A possible explanation for SVC

development beside vein injury during implantation is that repeated traumatization by leads in the vein wall is responsible for the progressive fibrotic stenosis just above the right atrium. Endothelialization of pacing leads can further reduce the luminal diameter of the vessel, leading to a clinically significant CVS [7]. The current recommendations for the placement of the CIED suggest avoiding the association between transvenous CIED and HD catheters for the risk related to infections [2]; however, no specific indications on the risk of the SVC stenosis have been provided. Our literature revision confirms the absence of a clear consensus. However, the described case reports, while confirming a potential risk, also highlight the need of new safer strategies. New approaches may be therefore considered. First, transvenous access for CIED should be avoided in patients likely needing HD in the short term, that is, those with rapid CKD progression and/or eGFR <20 mL/min/1.73 m^2. If transvenous CIED must be placed, the best strategy in the pre-dialysis patient will be AVF placement on the contralateral arm to CIED and avoidance of CVC if possible [10]. Second, the use of epicardial devices that traverse through the subcutaneous tissue and do not require vascular puncture, as the leads are inserted directly into the epicardium, could be implemented. Most studies comparing the value of epicardial versus transvenous CIED lead placement have been conducted in patients from the general population in whom transvenous leads had been removed because of infection. Efficacy and mortality were usually equal in both groups [19, 20]. However, placement requires cardiothoracic surgery, which is an expensive procedure. An additional option is the use of the transcatheter pacemaker. This device sits in a steerable catheter delivery system. The catheter is placed into the right ventricle, and the device is affixed to the myocardium through four electrically inactive nitinol tines located at the distal end of the device. After verification of device fixation and adequate electrical measurements, the catheter is cut, and the delivery system removed [21]. The problem is that the current generation of leadless pacemakers is not intended to replace all rhythm management therapy; however, these pacemakers represent an alternative for ventricular-only pacing. Third, in order to preserve the vascular asset, it is possible to use peritoneal dialysis. A Canadian study of more than 38,000 patients starting dialysis therapy between 2001 and 2008 found that in the 5 years after dialysis therapy initiation, risk of death was 20% higher in patients who started HD therapy with CVC, compared with those treated with peritoneal dialysis [22]. Therefore, considering the risk of CVS, we think that the patients with CIED could benefit from this renal replacement therapy. Fourth, in particular for elderly CIED patients, careful attempts of maintaining dialysis-free patients should be pursued. An Italian case report describes a case of a CKD patient who remained for 15 years in stage 5 despite severe disease [23]. Although this case may be considered extreme, it is not an isolated case; the Diet Or Dialysis in the Elderly (DODE) was a multicenter trial in Italy showing that a supplemented very low protein diet (0.3 g/kg body weight) safely postpones dialysis treatment for about 1 year in elderly patients (>70 years of age) with very low GFR (5–7 mL/min/1.73 m^2) [24]. A limitation that we can find in the evaluation of our case reports and in the literature review is the unavailability of echocardiographic right heart function assessment, usually related to vascular access and which could be useful to correctly evaluate the uremic patient [25]. In conclusion, nephrologists and surgeons should avoid placing CVC on the same side of a CIED, and the same holds true when preparing an AVF. Potential therapeutic alternatives in uremic patients, as in those with advanced CKD, are the use of epicardial devices or transcatheter pacemakers as the management of uremia by treatment other than HD such as peritoneal dialysis and intensive conservative therapy. We definitely need further studies with more appropriate design, longer follow-up, and, particularly, larger sample size to gain adequate insights into this (improperly) underestimated issue.

Appendix

Literature Search Strategy for PubMed

#1 ("central venous catheters" OR "hemodialysis catheters" OR "catheterization central venous")

#2 ((("pacemaker artificial" OR "Defibrillators, Implantable" OR "cardiac resynchronization therapy devices" OR "intra-cardiac devices")))

#3 #1 AND #2

humans NOT animals

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization, C.G., S.B., M.Pa., M.Pr., A.M., G.B., P.V., V.D.F., L.D.N., R.M., and G.C. Methodology, C.G., S.B., M.Pr., and M.Pa. Formal analysis, C.G., S.B., M.Pr., L.D.N, R.M., and G.C. Investigation, C.G., S.B., M.Pa., M.Pr., A.M., G.B., P.V., V.D.F., L.D.N., R.M., and G.C. Resources, C.G., S.B., M.Pa., M.Pr., A.M., G.B., P.V., V.D.F., L.D.N., R.M., and G.C. Data curation, C.G., S.B., M.Pa., M.Pr., A.M., G.B., P.V., V.D.F., L.D.N., R.M., and G.C. Writing – original draft preparation, C.G., S.B., M.Pa. Writing – review and editing, C.G., S.B., M.Pa., M.Pr., A.M., G.B., P.V., V.D.F., L.D.N., R.M., and G.C.

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