MATERIALE PLASTICE
https://revmaterialeplastice.ro
https://doi.org/10.37358/Mat.Plast.1964

Advantages of Intra-cardiac Polymer Coated Electrodes Leads in Patients with Diabetes Mellitus and Cardiovascular Implantable Electronic Devices

SILVIUS ALEXANDRU PESCARIU, CRISTINA TUDORAN*, MARIANA TUDORAN*, GHEORGHE NICUSOR POP, SORIN PESCARIU, ROMULUS TIMAR, BOGDAN ANDOR
University of Medicine and Pharmacy "Victor Babes", 2 Eftimie Murgu Sq., 300041, Timisoara, Romania

Abstract: *Diabetes mellitus (DM) and cardiovascular diseases (CVD) represent worldwide, major health problems. Frequently, diabetic patients may require therapy with implantable intra-cardiac electronic devices. In this article, we analysed the complications related to the presence of polymer-coated electrodes leads occurred among 351 patients, carriers of implantable electronic intra-cardiac devices: permanent pacemakers (PPM), cardiac resynchronisation therapy (CRT) or implantable cardioverter-defibrillators (ICD). Of all these patients, 99 (28.20%) had type 2 DM (p=0.022), double than the prevalence of DM in the general population (11%). Only two patients with PPM and DM had fractures of electrodes leads and one was diagnosed with right heart infective endocarditis, but no non-diabetic patient developed any complications related to the presence of polymer coated electrodes leads.*

Keywords*: Type 2 diabetes mellitus 1, polymer coated electrodes leads 2, permanent pacemakers 3, resynchronisation therapy 4, cardioverter-defibrillators 5*

1. Introduction

Type 2 diabetes mellitus (DM) represents a major risk factor for ischemic heart disease (IHD), dilated cardiomyopathy (DCM) and chronic heart failure (CHF) being associated with increased cardiovascular morbidity and mortality [1]. Patients with DM are exposed to an elevated risk of arrhythmias, including atrial fibrillation, conduction disturbances and ventricular arrhythmias triggering an increased predisposition for stroke and sudden cardiac death (SCD) [2,3]. For the treatment of these pathologies, cardiac implantable electronic devices (CIED) like permanent pacemakers (PPM), resynchronization therapy (CRT) or cardioverter-defibrillators (ICD) are often required in diabetic patients to save their lives and/or to improve the quality of life. It has been shown that CRTs and ICDs, effectively reduce SCD and cardiovascular mortality in this population with advanced heart disease [4]. As a consequence of the growing number of CIED, complications related to the presence of batteries or of the connecting electrode leads have occurred [5].

The "epoch" of the implantable device therapy begun in the second half of the last century in Sweden with the pioneering work of a group of scientists [6]. They used transvenous leads consisting of twinned stainless steel conductors surrounded by polyethelene, but this material was stiff and degenerated in in vivo conditions, reason why it was rapidly replaced by silicone, initiating the modern era of transvenous leads [5]. Although devices and leads designs have undergone major progresses the highly reliable lead insulators remained a central objective. The most required proprieties were good electrical conductibility, flexibility and durability, biostability and compatibility. Thus, some complications related to the presence of electrodes leads like fractures or infections grafted on right heart structures seem to be more frequent in patients with DM [2,5].

In this article we debate over the complications associated to transvenous implantation of polymer coated electrodes leads in a group of 351 patients admitted during 01 January 2018 – 31 December 2019 in a tertiary cardiovascular center for the implantation of an electronic intra-cardiac device or being carriers of a dysfunctional device or required hospitalization for another medical reason. Their medical records were analyzed in order to evidence any complications associated to the presence of intra-cardiac

**email:cristina13.tudoran@gmail.com, mariana.tudoran@gmail.com*

polymer coated electrodes leads as well as for the type of device implanted, the main indication for this therapy, the concomitance of type 2DM, and their outcomes.

2. Materials and methods

2.1. Material

Implantable electronic devices are connected to intra-cardiac structures through electrode leads which are elongated conductive coils containing a stainless steel body, surrounded by a polymer material in contact with the lead body. In certain embodiments, the conductive polymer is a polymer (e.g., silicone) implanted with a conductive filler (e.g., carbon black). The conductive polymer material is generally isodiametric with an outer diameter of the individual coils of the elongated conductive coil [5,7]. A medical electrical electrode is fabricated by sliding an elongated conductive coil over a length of a lead body, dispersing a conductive polymer on the helical coil, inserting a tubing over the elongated conductive coil, distributing the polymer material between individual turns of the elongated conductive coil, heating the tubing so the tubing shrinks around the elongated conductive coil, and removing the tubing (Figure 1 and 2). Silicone is generally considered the best polymer for electrode coating [5,8]. Carbon black provides good conductivity, superior polymeric (flexible and strong) mechanical properties, and proper adhesion to metal. Also, carbon black filled silicone is solid, which makes it different from other porous conductive materials e.g. ETFE (Ethylene-Tetrafluoroethylene) porous tubing [5,8].

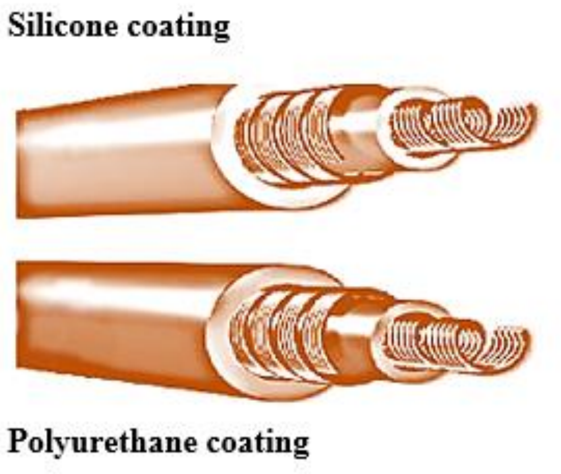

Figure 1. MP35N types Conductor Coils

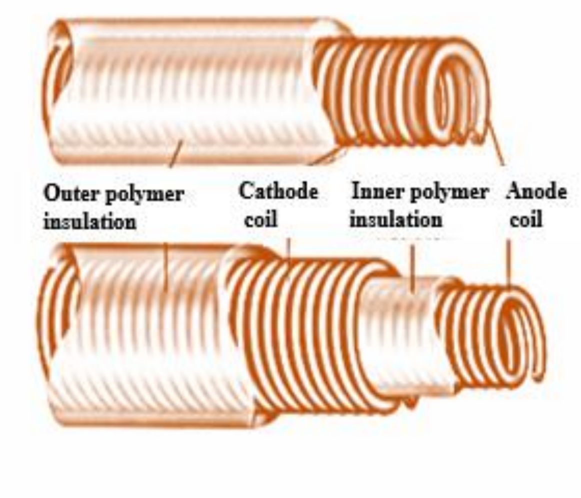

Figure 2. Structure of electrode leads

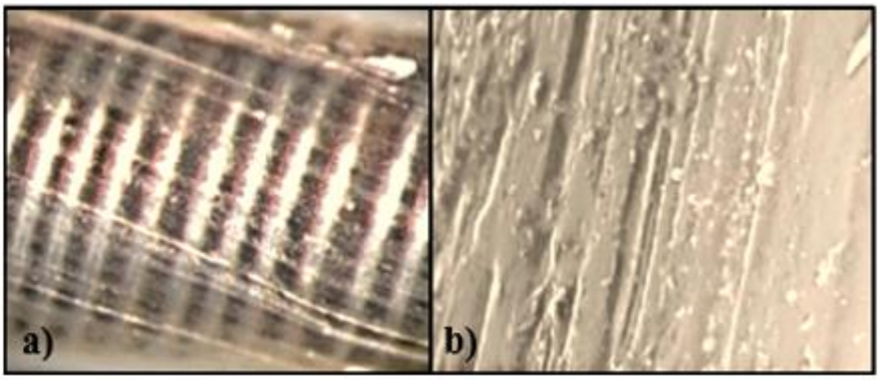

Figure 3. Aspect of abrasion marks on the surface of a polymer coated electrode lead in optic (a) and electronic (b) microscopy predisposing the electrode failure or even fracture

Leads are subjected yearly to millions of mechanical stress/strain cycles generated by cardiac, respiratory, and other body motions. They must confront with problems of blood compatibility, platelet adhesion, leukocyte activation, thrombosis, and chemical attack from trace-metal catalyzed oxidative reactions [9,10]. Consequently, they can be associated to several complications like lead failure, lead displacement or fracture and bacterial graft leading to endocarditis [8,10].

2.2. Methods

Of all patients, carriers of an CIED admitted between 1 Jan 2018 – 31 Dec 2019 in a cardiovascular tertiary center, we selected those with complications related to the presence of CIED and especially of the intra-cardiac polymer coated electrodes lead. By using the International classification and statistic of diseases (ICD-10-AM) - code Z95, from hospital’s database, of all 351 subjects admitted for the implantation of a CIED for rhythm control or for resynchronization therapy or who were already carriers of a dysfunctional device or who required hospitalization for other reasons, we identified 19 patients with issues related to the presence of CIED. Five of them, all diabetics had complications attributed to the presence of electrode leads.

2.3. Data analysis

It was performed using SPSS v.25.0 (Statistical Package for the Social Sciences, Chicago, IL, USA) for Linux Mint 19. Continuous variables were presented as a mean and standard deviation (SD) or median and associated quartiles (Q1-25 percentage quartile, Q3-75 percentage quartile) and categorical data were presented as counts (percentages). The bias-corrected and accelerated (BCa) bootstrap interval (1000 bootstrap samples) was used to calculate the 95% confidence interval. We performed descriptive and inferential statistics analysis to summarize the characteristics of the study population. The results of the Shapiro-Wilk normality test showed a non-Gaussian distribution, which is why we continued to use nonparametric tests. To evaluate the prevalence of DM, implantation and complications related to CIED and/or their intra-cardiac electrodes leads in groups, we applied the chi-squared test ($\chi 2$) and Fisher exact test (Freeman-Halton extension). A p value of less than 0.05 was considered to indicate a statistical significance. All patients' personal data were anonymized and the Ethics Committee of our hospital approved this study.

3. Results and discussions

For this study, we selected from hospital’s database, 351 patients, 221 men and 130 women, aged between 35 and 86 years, mean age 68.91+11.65, admitted during 2018-2019 in a tertiary cardiovascular center with CIED related pathology. Of all, 265 patients had PPM related pathology: 109 suffered the implantation of a new PPM, 83 had complications related to the existing one – mostly depleted battery needing replacement – and 73 were PPM carriers hospitalized for another cardiovascular reason. Other 58 patients required CRT implantation for dilated cardiomyopathies or/and chronic heart failure with reduced ejection fraction: 21 had new implantations and 37 were carriers, 12 of them with depleted battery and 25 with other cardiovascular problems – mostly decompensated heart failure. The remaining 28 patients had implantable ICDs for ventricular arrhythmias or were survivors of SCD: 7 new cases and 21 carriers (Table 1, Figure 1).

In our study, 99 patients were diagnosed with type 2 DM, in opposition to 252 subjects without diabetes, thus a consistent higher percent than the general prevalence of type 2 DM reported for our country (11%) in Predatorr study. Patients without DM, but carriers of a CIED (252 -71.79%) significantly outnumbered those with diabetes (99 – 28.20%, p=0.017). Although, the prevalence of PPM implantation was higher in the first category (78.57% versus 67.67%, p<0.001), but with a higher indication for dual-chamber devices. Due to the increased prevalence of DCM in diabetic population, they had a significantly higher indication for CRT implantation (26.26% versus 12.69%, p=0.002). There was no statistically significant difference concerning ICDs between diabetic and non-diabetic patients (p=0.406), (Table 1).

Numerous studies in the medical literature debate over the increased prevalence of cardiovascular diseases in the diabetic population [4,11,12,13]. Especially, poorly controlled type 2 DM together with its co-morbidities are responsible for higher incidence of arrhythmias and/or conduction disturbances, probably due to associated IHD, diabetic microangiopathy or increased cholinergic sensitivity [14,15,16]. Taking into account this high risk of arrhythmias and the increased prevalence of DCM in diabetic patients, they require the implantation of CIED more frequently and at a younger age. The prevalence of intra-cardiac devices is more than double in patients with type 2 DM and they are twice as likely to need resynchronization therapy compared to the nondiabetic population. In a recent study, Dalgaard et al analyzed several Danish medical data-bases for patients with PPM implantation during 2001 and 2012 and evidenced an increased prevalence of DM among them (16.8% - p <0.001) [16].

Table 1. Complications diagnosed in patients with CIED

Characteristics	**Patients with type 2 DM - 99**	**Patients without DM - 252**	**p**
Male gender	63 – 63.63%	158 – 62.69%	NS
Mean age (years)	66.65 ± 9.76	69.8 ± 12.22	0.022
Permanent pacemakers	67 – 67.67%	198 – 78.57%	<0.001
Complications related to PPM	26 – 38.80%	57 – 28.78%	0.469
-Depleted battery	18 – 69.23%	52 – 91.22%	0.604
-Pocket infection	1 – 3.84%	2 – 3.50%	0.193
-Pocket erosion	2 – 7.69%	3 – 5.26%	0.623
Complications related to lead	5 – 19.23%	0	0.0017
-Lead displacement	2 – 7.69%	0	0.079
-Lead fracture	2 – 7.69%	0	0.079
-Endocarditis	1 – 3.84%	0	0.282
Resynchronisation therapy - CRT:	26 – 26.26%	32 – 12.69%	0.002
Dysfunctions: depleted battery	7 – 26.92%	5 – 15.62%	NS
Implantable cardioverter - ICD:	6 – 6.06%	22 – 8.73%	NS
Dysfunctions: depleted battery	1 – 16.66%	2 – 9.09%	NS

Legend**:** diabetes mellitus –DM; cardiac implantable electronic devices -CIED; permanent pacemaker –PPM; resynchronization therapy –CRT; cardioverter-defibrillators –ICD; Statistical methods: Chi-square test, Fisher exact test (Freeman-Halton extension).

Of the whole group of 351 patients with CIED, 102 (29.05%) were admitted for various complications associated to devices. In the majority of cases, 97 (95.02%), there were issues related to the battery (depleted – needing replacement) or to the pocket (erosion or infection). Of the 26 patients with diabetes mellitus and PPM, 5 (19.23%) carriers of PPM for more than 5 years, had complications associated with the presence of polymer coated electrode leads, with a statistically significant difference (p=0.0017) compared to patients with PPM, but without DM. Of all these patients, 2 had displacements of the electrode lead, only 3 having complications that could be attributed to a failure of the coil and/or of the polymer coating (2 fractures and 1 infection) see table 1, significantly higher (p=0.0219) than in non-diabetic subjects. It is possible that the higher prevalence of complications related to the presence of polymer coated electrode leads in patients with DM could be explained by supplementary biochemical stress or/and depressed immunity in these patients [5,11,17,18].

It is intriguing that there were no events related to polymer coated electrode leads in patients with CRT or ICD, possibly explained by different design, these leads being thicker, more compact and with more inner coils and a smoother outer surface that can prevent tissue ingrowth and may facilitate lead extraction [5,8,10,19].

The most serious complications related to CIED are those concerning the electrode leads which represent the "weak link" of these devices. Because they are exposed to a huge mechanical stress, biochemical offensives due to platelet adhesion, leukocyte activation, thrombosis, chemical attacks exerted by free radicals and trace-metal catalyzed oxidative reactions, their design represents a crucial challenge [8,10,14]. In this sense, their external coating plays an important role. The ideal polymer coatings are those with: a) good electrical conductivity; b) flexibility and resistance; c) a smooth structure to prevent cell ingrowth and d) biostability and compatibility. In certain embodiments, such material is a polymer filled with a conductive material [8,10].

In the recent past, use of new insulators, polyether urethanes (Pellethane 80A) in particular, accounted for many lead failures. In the new millennium, nearly four decades after its introduction, silicone rubbers for lead insulation remain a dominant material. However, innovative lead designs using combinations of insulating materials have received promising clinical evaluation [8,10].

4. Conclusions

Patients with type 2 DM require the implantation of an electronic intra-cardiac device more frequently and at a younger age than those without diabetes. In our study, diabetic subjects were exposed to an increased risk of complications, especially related to polymer coated electrode leads.

References

1. AGARWAL, G., SINGH, S.K., Arrhythmias in Type 2 Diabetes Mellitus, Indian J Endocrinol Metab., **21**(5), 2017, 715–718.
2. SHAHREYAR, M., MUPPIDI, V., CHOUDHURI, I., SRA, J., TAJIK, A.J., JAHANGIR, A., Implantable cardioverter defibrillators in diabetics: efficacy and safety in patients at risk of sudden cardiac death, Expert Rev Cardiovasc Ther., **13**(8), 2015, 897–906.
3. TUDORAN, M., TUDORAN, C., CIOCARLIE, T., POP, G.N., BERCEANU-VADUVA, M.M., VELIMIROVICI, D.E., ABU AWWAD, A., BERCEANU-VADUVA, D.M., Aspects of Heart Failure in Patients with Ischemic Heart Disease after Percutaneous Coronary Revascularization with Polymer-coated Drug-Eluting Stents versus Bare-Metal Stents, *Mater. Plast.*, **56**(1), 2019, 37-40.
4. STEINER, H., GEIST, M., GOLDENBERG, I., SULEIMAN, M., GLIKSON, M., TENENBAUM, A., SWISSA, M., FISMANN, E.Z., GOLOVCHINER, G., STRASBERG, B., BARSHESHET, A., Characteristics and outcomes of diabetic patients with an implantable cardioverter defibrillator in a real world setting: results from the Israeli ICD registry and On behalf of the Israeli Working Group of Pacing and EP, Cardiovasc Diabetol., **15**, 2016, 160.
5. BONGIOMI, M.G., BURRI, H., DEHARO, J.C., STARCK, C., KENNERGREN, C., SAGHY, L., RAO, A., TASCINI, C., LEVER, N., KUTARSKI, A., LOZANO, I.F., STRATHMORE, N., COSTA, R., EPSTEIN, L., LOVE, C., BLOMSTROM-LUNDQVIST, C., ESC Scientific Document Group, 2018 EHRA expert consensus statement on lead extraction: recommendations on definitions, endpoints, research trial design, and data collection requirements for clinical scientific studies and registries: endorsed by APHRS/HRS/LAHRS, *EP Europace*, **7**(20), 2018, 1217.
6. GADLER, F., VALZANIA, C., LINDE, C., Current use of implantable electrical devices in Sweden: data from the Swedish pacemaker and implantable cardioverter-defibrillator registry. Europace., **17**(1), 2015, 69-77.
7. TUDORAN, M., TUDORAN, C., High-risk pulmonary embolism in a patient with acute dissecting aneurysm: case report. Nigerian Jornal of Clinical Practice, **19**(6), 2016, 831-833.
8. ELLENBOGEN, K.A., WILKOFF, B.L., G. KAY, N., Chu Pak LAU, C.P., AURICCHIO, A., Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy, Elservier, fifth edition, 2016, ISBN-13: 9780323378048.
9. TUDORAN, M., TUDORAN, C., VLAD, M., BALAS, M., ABU-AWWAD, A., POP, G.N., Impact of Therapy with L-Thyroxine on the Evolution of Arterial and Aortic Stiffness in Female Patients with Overt and Subclinical Hypothyroidism, *Rev. Chim*., **70**(4), 2019, 1372 – 1376.
10. HAYES, D.L., ASIRVATHAM, S.J, FRIEDMAN, P.A., Cardiac Pacing, Defibrillation and Resynchronization: A Clinical Approach, Wiley, third edition, 2013, ISBN-13: 9780470658338
11. LEAR, J.T., LAWRENCE, I.G., BURDEN, A.C., Prevalence of diabetes in elderly patients requiring permanent cardiac pacemaker insertion. Acta Diabetol., **33**(2), 1996, 169-170.
12. MOVAHED M.R., HASHEMZADEH M., JAMAL M.M., Increased Prevalence of Third-Degree Atrioventricular Block in Patients With Type II Diabetes Mellitus, Chest, **128**(4), 2005, 2611–2614.

13. TUDORAN, C., TUDORAN, M., PARV, F., POP, G.N., BALAS, M., VLAD, M. Association between impaired arterial and aortic stiffness and diastolic dysfunction in female patients with overt and subclinical hypothyroidism, Acta Medica Mediterranea, **35**, 2019, 2843.

14. STEINER, H., GEIST, M., GOLDENBERG, I., SULEIMAN, M., GLIKSON, M., TENENBAUM, A., SWISSA, M., FISMANN, E.Z., GOLOVCHINER, G., STRASBERG, B., BARSHESHET, A., Characteristics and outcomes of diabetic patients with an implantable cardioverter defibrillator in a real world setting: results from the Israeli ICD registry and On behalf of the Israeli Working Group of Pacing and EP, Cardiovasc Diabetol., **15**, 2016, 160.

15. TUDORAN, C., ABU-AWWAD, A., GIURGI-ONCU, C., CIOCARLIE, T., RADA, M., TUDORAN, M., Influences of Thyroid Hormones on the Alteration of Autonomic Nervous System in Female Patients with Overt Hyperthyroidism, *Rev. Chim.,* **70**(7), 2019, 2552-2555.

16. DALGAARD, F., RUWALD, M.H., LINDHART, T.B., GISLASON, G.H., TORP-PEDERSEN, C., PALLISGAARD, J.L., Patients with atrial fibrillation and permanent pacemaker: Temporal changes in patient characteristics and pharmacotherapy, PLoS One., **13**(3), 2018.

17.ROMAN - PINTOS, L.M., VILLEGAS - RIVERA,G., RODRIGUEZ - CARRIZALEZ, A.D., MIRANDA-DIAZ, A.G., CARDONA-MUNOZ, E.G., Diabetic Polyneuropathy in Type 2 Diabetes Mellitus: Inflammation, Oxidative Stress, and Mitochondrial Function, J Diabetes Res., 2016.

18. MOHAMMAD-REZA, M., Diabetes as a risk factor for cardiac conduction defects: a review, Diabetes, Obesity, Metabolism, **9**(3), 2007, 209-446.

19. SHAHREYAR, M., MUPPIDI, V., CHOUDHURI, I., SRA, J., TAJIK, A.J., JAHANGIR, A., Implantable cardioverter defibrillators in diabetics: efficacy and safety in patients at risk of sudden cardiac death, Expert Rev Cardiovasc Ther., **13**(8), 2015, 897–906.

Manuscript received: 3.04.2020