Etiology, Clinical Manifestations and Microbiological Profile of Cardiac Device Infections

Aneta Skrzek-Montewka*, Andrzej Wysokinski, Maciej Montewka
Chair, Department of Cardiology, Medical University of Lublin, Aleje Radlewicke 1, 20-059 Lublin, Poland

*Corresponding author: Aneta Skrzek-Montewka, Chair, Department of Cardiology, Medical University of Lublin, Aleje Radlewicke 1, 20-059 Lublin, Poland, E-mail: skrzek.a@wp.pl

Received date: Jul 13, 2016; Accepted date: Aug 25, 2016; Published date: Aug 29 2016

Etiology, Clinical Manifestations and Microbiological Profile of Cardiac Device Infections

Introduction

Infections developing in patients with cardiac implantable electronic devices including permanent pacemakers (PMs), implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy devices (CRT) are causing considerable clinical problems. Lead dependent infective endocarditis (LDIE) is considered the most serious complication. LDIE symptoms are similar to clinical features of respiratory tract infective disease and so some diagnostic difficulties may arise. Cardiovascular implantable electronic device infections as reported by the world registries range between 0.13% and 19.9% for PMs and 0.8% for ICDs and roughly 10% to 25% of these patients develop LDIE [1-14].

Background

The background of the study was to analyse the parameters of clinical features, etiology and microbiological profile of the infections. We also aimed at evaluating the role of echocardiography in detecting LDIE in 767 implantable electronic device patients undergoing transvenous lead extraction (TLE).

Material and Methods

Retrospective examination was conducted at clinical cardiology centre in Lublin, a referral centre in Poland, which deals with implantable electronic device infections. The study group comprised 767 infective and non-infective patients who between 2009 and 2014 underwent transcutaneous extraction of PMs/ICDs/CRT. The group consisted of 382 patients with infections (49.8%) and 385 without infections (50.2%). LDIE patients were found to suffer from concomitant infections. LDIE group comprised significantly more patients with hs-CRP>50 mg/L. Analysis of microbiological data showed that the most common cause of the infective complications were Staphylococcus epidermidis and Staphylococcus aureus. Echocardiography examination revealed the presence of vegetation in 78.26% of LDIE patients in TEE and in 63.48% in TTE.

Conclusions: Fever and concomitant infections predominated in the clinical picture of LDIE. Hs-CRP value proved to be essential for diagnostic procedures. TEE examination proved to be more effective in revealing vegetation than TTE. The most common cause of infective complications was S. epidermidis and S. aureus which points out to the endogenic source of infections.

Keywords: Cardiovascular electronic device infections; Lead dependent infective endocarditis; Pocket infection; Biofilm; Vegetation

Abstract

Introduction: Cardiovascular implantable electronic device infections (CIEDIs) cause a lot of serious clinical problems among which lead dependent infective endocarditis (LDIE) is considered to be the worst.

Background: The background of the study was to analyze the parameters of clinical manifestations, determine the etiology and microbiological profile of the infections as well as evaluate the role of echocardiography in diagnosing LDIE.

Methods: Retrospective examinations were carried out in Reference Clinical Cardiology Centre in Lublin, Poland. The study group comprised 767 patients who between 2009 and 2014 underwent transvenous lead extraction (TLE) for infective and non-infective reasons.

Results: The study group comprised 382 patients with infective complications and 385 without infection. CIEDI group included 30.1% LDIE patients, 38.48% pocket infection patients (PI) and 31.41% mixed LDIE and PI patients. Fever was most frequently reported in LDIE patients. Significantly more LDIE patients were found to suffer from concomitant infections. LDIE group comprised significantly more patients with hs-CRP>50 mg/L. Analysis of microbiological data showed that the most common cause of the infective complications were Staphylococcus epidermidis and Staphylococcus aureus. Echocardiography examination revealed the presence of vegetation in 78.26% of LDIE patients in TEE and in 63.48% in TTE.

Conclusions: Fever and concomitant infections predominated in the clinical picture of LDIE. Hs-CRP value proved to be essential for diagnostic procedures. TEE examination proved to be more effective in revealing vegetation than TTE. The most common cause of infective complications was S. epidermidis and S. aureus which points out to the endogenic source of infections.
most frequent localization in cardiovascular system). Taking all this into consideration we were able to identify major factors leading to proper diagnosis.

Statistical analysis

Statistical analysis was performed with “Statistics” software. Qualitative variables were compared by means of Chi-square test, whereas quantitative parameters were calculated with mean value standard deviation (± SD) and median (Me). In case of normal distribution of variables and homogenous P-value Student’s T-test was used to evaluate the differences between particular groups. The variables were compared using the mean value and standard deviation whereas quantitative parameters were calculated with mean value standard deviation (± SD). However, when the distribution was different from the normal the differences between groups were calculated with U-Mann-Whitney test for two independent groups. The variables were compared using median (Me). Shapiro-Wilk test was used to check the conformity of the evaluated groups with the standard distribution. 5% error was accepted and two-tailed P-value<0.05 was considered statistically significant.

Results

The study group comprised 382 patients with infective complications (49.8%) and 385 without infection (50.2%). Among patients with infection there were 115 LDIE (30.1%), 147 PI (38.48%) and 120 LDIE+PI patients (31.41%). Fever was reported most often in LDIE patients (37.4°C vs. 37°C). Most PI patients had either proper or slightly increased temperature. LDIE group comprised significantly more patients with concomitant infections of urinary, respiratory, dermal and neurological systems than PI group (22.61% vs. 10.2%; p=0.006, whereas no significant differences were noted between LDIE and LDIE+PI patients (22.61% vs. 18.55%; p=0.41). Analysis of laboratory parameters showed that leukocytosis (WBC>10 × 10^3/µl) was much more common in LDIE patients than PI patients (29.57% vs. 12.93%; p=0.002). Median for WBC value in LDIE patients was within standard; however, it was higher than in PI patients (8.57 × 10^3/µl vs. 7.5 × 10^3/µl) and in LDIE+PI patients (8.57 × 10^3/µl vs. 8.21 × 10^3/µl). It was also noted that significantly more LDIE patients than PI patients had WBC between 10 and 20 × 10^3/µl and most PI patients had WBC between 5 and 10 × 10^3/µl. The above differences were statistically significant (p=0.0006). The highest concentration of CRP was found in LDIE patients. There were significantly more LDIE patients with CRP>50 mg/dl than in the other two groups (p=0.0001 for LDIE vs. PI and p=0.0002 for LDIE vs. LDIE+PI). CRP mean value for LDIE was higher than in the other two groups (33.2 mg/dl vs. 6.7 mg/dl for LDIE vs. PI and 33.2 mg/dl vs. 11.73 mg/dl for LDIE vs. LDIE+PI). Among LDIE patients higher than normal procalcitonin concentration (PCT) was reported most often (p=0.0001 for LDIE vs. PI and p=0.0001 for LDIE vs. LDIE+PI). Mean PCT value in this group was higher than in the other two groups (33.2 mg/dl vs. 6.7 mg/dl for LDIE vs. PI and 33.2 mg/dl vs. 11.73 mg/dl for LDIE vs. LDIE+PI). Most PI patients had mean body temperature higher than PI (37.4°C vs. 36.8°C) and LDIE+PI (37.4°C vs. 37°C). Most PI patients had either proper or slightly elevated temperature. LDIE group comprised significantly more patients with concomitant infections of urinary, respiratory, dermal and neurological systems than PI group (22.61% vs. 10.2%; p=0.006, whereas no significant differences were noted between LDIE and LDIE+PI patients (22.61% vs. 18.55%; p=0.41). Analysis of laboratory parameters showed that leukocytosis (WBC>10 × 10^3/µl) was much more common in LDIE patients than PI patients (29.57% vs. 12.93%; p=0.002). Median for WBC value in LDIE patients was within standard; however, it was higher than in PI patients (8.57 × 10^3/µl vs. 7.5 × 10^3/µl) and in LDIE+PI patients (8.57 × 10^3/µl vs. 8.21 × 10^3/µl). It was also noted that significantly more LDIE patients than PI patients had WBC between 10 and 20 × 10^3/µl and most PI patients had WBC between 5 and 10 × 10^3/µl. The above differences were statistically significant (p=0.0006). The highest concentration of CRP was found in LDIE patients. There were significantly more LDIE patients with CRP>50 mg/dl than in the other two groups (p=0.0001 for LDIE vs. PI and p=0.0002 for LDIE vs. LDIE+PI). CRP mean value for LDIE was higher than in the other two groups (33.2 mg/dl vs. 6.7 mg/dl for LDIE vs. PI and 33.2 mg/dl vs. 11.73 mg/dl for LDIE vs. LDIE+PI). Among LDIE patients higher than normal procalcitonin concentration (PCT) was reported most often (p=0.0001 for LDIE vs. PI and p=0.0001 for LDIE vs. LDIE+PI). Mean PCT value in this group was higher than in the other two, but it was still within standard (0.14 ng/ml vs 0.075 ng/ml for LDIE vs. LDIE+PI). LDIE patients were found to have the lowest Hb concentration. The group comprised significantly more patients with Hb below 10 mg/dl compared to PI patients (p=0.0001) and more patients with Hb below 9 mg/dl compared to LDIE+PI patients (p=0.0002). Hb mean value was lower in LDIE patients compared to PI (12.1 mg/dl vs 13.5 ± 1.78 mg/dl) and slightly lower than in LDIE+PI (11.86 ± 2.2 mg/dl vs 12.68 ± 1.87 mg/dl). The differences were statistically significant (Table 1).

Table 1. Clinical and laboratory parameters in patients with CDI who underwent TLE between 2009 and 2014.

| Clinical and laboratory parameters | LDIE (n=115) | PI (n=147) | LDIE+PI (n=120) |
|-----------------------------------|-------------|------------|----------------|
| Fever (temp>38 °C)%               | 36.52       | 5.44       | 16.67          |
| Concomitant infections of other systems % | 22.61 | 10.2 | 18.33 |
| Leukocytosis (>10.5 × 10^3/µl) %  | 29.57       | 12.93      | 20             |
| WBC (x 10^3/µl)                   | x ± SD      | 9.65 ± 4.83| 7.99 ± 2.56    |
|                                  | Me          | 8.57       | 7.5            |
| CRP ≥ 5.0 mg/dl%                 | x ± SD      | 83.48      | 57.14          |
|                                  | Me          | 55.68      | 15.74          |
| CRP (mg/dl)                      | x ± SD      | 33.2       | 6.7            |
|                                  | Me          | 33.2       | 6.7            |
| PCT ≥ 0.5 ng/ml %                | x ± SD      | 15.91      | 2.94           |
| PCT (ng/ml)                      | Mean value ± SD | 3.06 | 0.13          |
|                                  | Me          | 0.14       | 0.075          |
| Hb (K: Hb<12 g/dl; M: Hb<14 g/dl)%| x ± SD      | 68.7       | 52.38          |
|                                  | Me          | 12.1       | 13.5           |

Citation: Skrzek-Montewka A, Wysokinski A, Montewka M (2016) Etiology, Clinical Manifestations and Microbiological Profile of Cardiac Device Infections. Clin Microbiol 5: 258. doi:10.4172/2327-5073.1000258
The present study showed that the most common cause of infective complications were CoNS bacteria out of which S. epidermidis was a prevailing one. The second most frequently isolated pathogen was S. aureus. The other pathogens occurred rarely were: S. hemolyticus, Enterobacter cloacae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Streptococcus mitis.

Positive blood culture results were obtained in 15.16% of patients with infections. The most commonly isolated pathogens were CoNS (40.43%) and S. aureus (29.79%, MRSA-8.51%, MSSA-21.28%). CoNS contained 20.36% MRCONS and 20.1% MSCNS. S. epidermidis proved to be most frequent pathogen, which was isolated in 21.28% cases (MRSE–10.64%, MSSE-10.64%). Other CoNS bacteria were isolated in 19.15% cases and included S. haemolyticus, S. capitis, S. hominis and S. saprophyticus (Figure 1).

Figure 1: Distribution of microorganisms in blood cultures of CDI patients.

Positive lead cultures were detected in 55.08% cases. The most common pathogens were CoNS (69.27%) and S. aureus (19.27%, MRSA-3.65%, MSSA-15.63%). CoNS comprised 38.86% MRCNS and 38.29% MSCNS. Prevailing S. epidermidis was detected in 52.08% cases (MRSE-29.17%, MSSE-22.92%). Other CoNS pathogens were isolated in 17.19% cases and included S. haemolyticus, S. capitis, S. simulans, S. cohnii, S. hominis, S. saprophyticus, S. warneri and S. xylosus. In 11.46% of cases less common bacteria were detected. They included E. coli, E. faecalis, E. cloacae, E. aerogenes, A. baumanii, K. pneumonia, K. Kristinae, P. aeruginosa, P. mirabilis, Str. mitis, Str. agalactiae (Figure 2).

Positive cultures of pocket were revealed in 59.41% infective patients. Most frequently isolated pathogens were CoNS (63.16%) and S. aureus (21.05%, MRSA-6.02%, MSSA-15.04%). CoNS comprised 37.7% MRCNS and 31.15% MSCNS. Dominating S. epidermidis was isolated in 48.87% of cases (MRSE–26.32%, MSSE-22.56%) other CoNS pathogens were detected in 14.29% of cases and included S. haemolyticus, S. hominis, S. saprophyticus and S. schleiferi (0.75%). In 13.53% of cases less common bacteria were isolated E. coli, E. faecalis, E. cloacae, C. freundii, A. baumanii, P. aeruginosa, P. mirabilis. Fungi were found in 1.5% of cases and included Candida albicans and Aspergillus fumigatus.

Blood culture results showed that S. epidermidis was isolated more often in infections developing after 12 months of device implantation and S. aureus within 12 months. Culture results in leads represented similar values but the differences were not statistically significant. Pocket cultures results suggested that S. epidermidis and S. aureus alike were responsible for developing site infection within or after 12 months (Table 2). It was also observed that CoNS occurred more frequently than S. aureus in patients with inactive leads (36.84% vs. 7.14%), but the differences were not statistically significant. Additionally, CoNS were more frequent than S.aureus in patients with at least 3 leads (36.84% vs. 7.14%), but the differences were not statistically significant.

Table 2: Comparison of the number of S. epidermidis and S. aureus related infections depending on the time from implantation to the onset of symptoms.

| Positive culture (+) | S. epidermidis | S. aureus |
|---------------------|---------------|-----------|
| ≤ 12 month          | 17.65         | 23.33     |
| >12 month           | 47.06         | 20        |
| Blood culture %     | 48.57         | 54.1      |
| Lead culture %      | 48.05         | 23.21     |
| Pocket culture %    | 19.48         | 19.48     |

Figure 2: Distribution of microorganisms in explanted lead cultures in patients with CDIs.
LDIE vs. LDIE+IM). Right atrium appeared to be most common location for vegetation in both groups (53.91% vs. 40%). The second most common was superior vena caval orifice (15.65% vs. 5.83%), then came right ventricle (10.43% vs. 11.67%), tricuspid valve (12.17% vs. 2.5%) and some single locations in left atrium and left ventricle (2.6% vs. 0%) (Table 3).

| Vegetation %       | LDIE   | LDIE+IM |
|--------------------|--------|---------|
| Vegetation revealed in TTE % | 63.48  | 35.83   |
| Vegetation revealed in TEE %  | 78.26  | 50.83   |
| Vegetation %       |        |         |
| Small (<1 cm)      | 25.22  | 30      |
| Medium (1-2 cm)    | 35.65  | 17.5    |
| Large (>2 cm)      | 17.39  | 5       |
| Right atrium       | 53.91  | 40      |
| Superior vena cava orifice | 15.65 | 5.83 |
| Right ventricle    | 10.43  | 11.67   |
| Tricuspid valve    | 12.17  | 2.5     |

| Location %         |        |         |
|--------------------|--------|---------|
| Mitral valve       | 2.6    | 0       |

Table 3: Echocardiography results (presence, size and location of vegetation in the heart) in patients undergoing TLE between 2009 and 2014.

Discussion

Clinical manifestations of infections, especially LDIE in patients with implanted cardiac devices, are nonspecific and as such, often detected too late. It necessitates more thorough examination of a variety of clinical and laboratory parameters which will help identify and distinguish this condition from other infections of similar clinical symptoms.

Analysis of clinical and laboratory data suggested that body temperature level and infective parameters in patients referred for TLE were significantly elevated compared to control group. Fever and accompanying infections of other organs could be observed mostly in LDIE patients. This group of patients represented elevated infective parameters of WBC, CRP, PCT and the lowest Hb concentration. CRP appeared to be the most sensitive indicator for LDIE. CRP concentration was elevated in 83.48% of LDIE patients, with median of 33.2 mg/dl. CRP parameters of WBC, CRP, PCT and the lowest Hb concentration. CRP appeared to be most sensitive indicator for LDIE. CRP concentration and distinguish this condition from other infections of similar clinical parameters. Infective complications appear to be in strict correlation with higher inflammatory parameters, mostly CRP and OB. WBC values are variated, which suggests that it is not an indicator sensitive enough to identify these diseases and its variability in CIED infective complications has not been fully accounted for. The present study showed that CRP appeared to be the most sensitive indicator of infection especially LDIE. Although high WBC concentrations were stated in considerably more LDIE patients than PI or LDIE+PI patients, median was about the norm.

One of the most common diagnostic methods for LDIE is TEE and TTE. TTE method has its weak points owing to problems with visualization which are caused by reverberations i.e. multiple reflections of ultrasound waves from endocardiac leads. Additionally, vegetation is often located in right atrium, tricuspid valve or superior vena caval orifice-the sites which are inaccessible for TTE [18,19]. TTE sensitivity is often not high enough to detect LDIE (23 to 26% efficacies). TEE offers better visualization of the above mentioned sites and consequently the detection of vegetation is higher (59 to 63%), which results in more effective diagnosis compared to TTE [18,20]. Thus, TEE is commonly chosen to diagnose LDIE and to monitor the course of treatment after endocardiac leads removal [13,15,21-23]. Our study confirmed the advantage of TEE over TTE in identifying vegetation. Among LDIE patients, vegetations were found in 78.26% and LDIE+PI in 50.83% of cases. In LDIE group vegetation was detected in 63.48% of patients with TTE and in 78.26% with TEE examination. In LDIE+PI group the proportions were more or less the same, for TTE-35.83% and for TEE-50.83%. In both groups vegetations were mostly found in right atrium (53.91% vs 40%), but in a lot of LDIE patients vegetations were located in the superior vena caval orifice (15.65%) and in the right ventricle (10.43%). There were patients with several concomitant vegetations developed in different parts of the heart. Golzio et al. [15] examined 293 patients including 136 patients with CDI. TEE examination revealed vegetation in 62.2% patients with LDIE and 21.9% with PI. This gave rise to the assumption than TEE examination should be performed when LDIE is suspected and accompanied by pocket infection but no systemic symptoms or major abnormalities in laboratory parameters are reported. Polecwycz [30] presented similar analysis. She estimated the efficacy of TEE and TTE examinations in detecting vegetations (30.3% and 60.9%, respectively). Additionally, right atrium and superior vena caval orifice proved to be the most common vegetation site (81.8% and 27%, respectively).

Our study aimed at determining microbiological profile of the infections and their sources. Analysis of the group with infections revealed 15.6% of cases with positive blood culture results out of which 27% were LDIE and 13.33% were LDIE+PI patients. In PI patients, positive blood cultures results were non-diagnostic (one out of minimum two cultures was positive) and affected by impurities found on patients’ skin. CoNS especially S.epidermidis was the pathogen most often found in blood cultures. The second most frequent was S. aureus. In patients with isolated LDIE there were 33.33% CoNS out of which 18.52% were S. epidermidis (MRSE-11.11%) and 29.93% S. aureus (MRSA- 7.41%). In LDIE+PI patients there were 28.57% CoNS out of which 7.14% were S. epidermidis and the remaining 21.43% constituted other types of staphylococcus including S. haemolyticus, S. capitis and S. hominis, S. aureus was isolated in 50% of cases.
carried out on a group of 100 patients, methicillin resistant CoNS was than S. epidermidis [29,30]. It has been observed that 45% patients months to develop. It was also stated that in pocket infection cultures, epidermidis (10-68%) and S. aureus (24-59%). Additionally, in studies taking this into account, it has been recommended that the moment S. aureus occurred as rods were isolated in 1-17% cases, Enterococcus in 5-6% cases and CoNS and S. aureus (10-68%) and S. aureus (24-59%). One of the reports pointed out that after implantation (71.43% vs. 36.84%), but the incidence of S. aureus related infections was 18.8/100 thousand cases out of which 9% were strains resistant to methicillin. Gram negative rods were isolated in 1-17% cases, Enterococcus in 5-6% cases and S. epidermidis in 4-6% cases. Fungi were found in 2% of cases. One of the studies presents reports from 12 countries where infections were diagnosed on the basis of clinical manifestations and points out that in 12-49% cases negative blood culture results were obtained [17]. Other reports present similar results [2,5,14,24-28].

In our studies we have observed that patients with S. aureus dominating in blood and lead end cultures developed infection within 12 months of implantation whereas S. epidermidis took over 12 months to develop. It was also stated that in pocket infection cultures, S. aureus occurred as often as S. epidermidis, independent of the time between implantation and infection onset. However, some reports confirm that S. aureus takes shorter time to develop after implantation than S. epidermidis [29,30]. It has been observed that 45% patients with S. aureus in their blood cultures developed infection in a year. After a year, S. aureus related infections were scarcely reported [31]. Taking this into account, it has been recommended that the moment S. aureus is detected the whole PM/ICD/CRT device be removed instantly, irrespective of clinical manifestations or vegetations found in echocardiographic examination.

Another problem is connected with the results received from cultures from extracted lead ends. Currently researchers are of different opinions some claim that positive blood culture is a major Duke criterion for LDIE, others do not consider them to be relevant diagnostic signs as there is a possibility that the lead might have been contaminated with bacteria from infected pocket during extraction [32]. According to different sources, positive cultures of lead ends in case of pocket infection are found in 79.3%- 87.5% [14,18]. It has been suggested that positive lead cultures might indicate that the infection is spreading to endocardium and consequently, patients with PI should be referred for TLE just after it was diagnosed [12,33]. Mayo Clinic does not recognize lead culture results as a diagnostic criterion for LDIE. They claim that positive lead cultures may be decisive in diagnosing LDIE only in case of lack of pocket infection when the device was extracted far from the pocket or in the case of surgical device extraction [13,14,18]. In our study, we obtained 43.62%, of positive culture results of extracted leads in patients with LDIE, 77.16% in patients with LDIE+PI and 54.76% in patients with PI. This is quite a big amount, taking into account the fact that lead extraction was performed with particular attention so as to prevent lead contamination with skin physiological flora or with pocket bacteria. The above observations suggest that lead cultures should be taken into consideration while diagnosing LDIE but the possibility of lead contamination during TLE cannot be excluded. Analysis of the microbiological studies of the lead showed that CoNS (69.27%) and S. aureus (19.27%) were most often isolated pathogens. Other microorganism was found in 11.76% cases. Among them were E. coli, E. faecalis, E. cloacae, E. aerogenes, Ac. baumanni, K. pneumoniae, K. Kristinae, Ps. aeruginosa, Pr. mirabilis, Str. mitis, Str. agalactiae.

Some researchers reported that despite very thorough skin disinfection, positive culture results were obtained in 48% of pockets right after their dissection and in 37% of cases right before the wound suture, whereas in cultures taken before the skin was disinfected, positive results were reported in 88.3% of cases [34]. Our study detected positive pocket cultures in 50.41% of patients with infections. Most of these patients had site symptoms including redness, warmth, swelling and pus discharge from the wound. Positive pocket cultures were found in 53.57% of PI patients and in 58.02% of LDIE+PI patients who made up 31.41% of all cases. Positive pocket cultures were found in 32.08% of LDIE patients who did not show any signs of infection in this site. These cultures were also dominated by CoN (63.16%) and S. epidermidis (48.87%, MRSE- 26.32%) as well as S. aureus (21.05%, MRSA-6.02%). One of the reports pointed out that CoNS, more than any other pathogen was responsible for pocket infections. It has been emphasized that CoNS was predominating in patients who underwent further repair procedures or had more leads, including infective ones, implanted in cardiovascular system. Present study showed that CoNS, more often than S.aureus was found in patients with leads left in their hearts (36.84% vs. 7.14%). The same applies to patients with at least three leads (31.58% vs. 14.29%) and to those who underwent at least three surgeries (including implantation) (36.84% vs. 14.29%). However, more S.aureus related infections were detected after implantation (71.43% vs. 36.84%), but the differences were not statistically significant. Present study remains in compliance with other world reports and confirms the assumption that staphylococcus bacteria are mostly responsible for developing infections. Microorganisms which in normal circumstances constitute physiological bacterial flora of the skin lead to infections during implantation or device exchange or when the lead or generator box get outside as a result of skin injury and consequently the infection spread along the lead down to the right endocardium giving rise to lead related endocarditis. Sometimes those pathogenic microorganisms happen to be transmitted through blood vessels to the device pocket where they form biofilm on PM/ICD/CRT elements. Biofilm consist of individual bacteria accumulating and making up dense cultures which form multilcellular structure covering biomaterials. It may originate from bacteria triggering infections coming from other systems which as the infection spreads through blood vessels finally reach the heart. Our study shows that patients with concomitant infections of skin, respiratory or urinary systems or neuroinfections are more susceptible to infective complications, especially to LDIE. Similar results were reported by other studies [35].

The reason why so many infections are caused by CoNS is that cardio-implants get easily contaminated during the surgery. These bacteria are most often found in operative area and adhere more easily than S.aureus to biomaterials. S. aureus tends to occur more often in patients undergoing a single surgical procedure when infection
developing within 12 months of the surgery. Similar results were reported by other researchers who also underlined that *S. aureus* was detected mainly in patients with concomitant disorders. Immune deficiency prompts the development of *S. aureus* infections, and this is why these infections tend to have much more severe course [18,36–38].

**Conclusions**

1. Fever and concomitant infections predominated in the clinical picture of LDIE.

2. In patients with infections, especially LDIE, CRP appeared critical to diagnostic results.

3. Transesophageal echocardiography proved more efficient at diagnosing LDIE than transthoracic examination.

4. *Staphylococcus epidermidis* and *Staphylococcus aureus* seem to be most often causes of infective complications. They normally make up physiological flora of the skin and mucous membranes, which points out that infections are of endogenic origin.

5. *S. epidermidis* infections developed after more than 12 months of the surgery whereas *S. aureus* took less than 12 months.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

**References**

1. Baddour LM, Bettmann MA, Bolger AF, Epstein AE, Ferrieri P, et al. (2009) Nonvalvular cardiovascular device-related infections. Circulation 108: 2015–2031.

2. Baddour LM, Wilson WR, Bayer AS, Fowler VG, Tleyjeh IM, et al. (2015) Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. A scientific statement for healthcare professionals from the American heart association. Circulation. 132:1435–1486.

3. Raman TS, Gupta SK, Valle JA, Yamada E (2009) Risk factors for mortality in patients with cardiac device-related infection. Circ Arrhythm Electrophysiol 2: 129-134.

4. Cacoub P, Leprince P, Nataf P, Hausfater P, Dorent R, et al. (1998) Pacemaker infective endocarditis. Am J Cardiol 82: 480–484.

5. Carrasco F, Anguita M, Ruiz M, Castillo JC, Delgado M, et al. (2016) Clinical features and changes in epidemiology of infective endocarditis on pacemaker devices over a 27-year period (1987-2013). Europace 18: 836-841.

6. Di Monaco A, Pelargonio G, Narducci ML, Manzoli L, Boccia S, et al. (2014) Safety of transvenous lead extraction according to centre volume: a systematic review and meta-analysis. Europace 16: 1496-1507.

7. Chua JD, Wilkoff BL, Lee I, Juratli N, Longworth DL, et al. (2000) Diagnosis and management of infections involving implantable electrophysiologic cardiac devices. Ann Intern Med 133: 604-608.

8. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, et al. (2009) Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J 30: 2369-2413.

9. Kane AD, Ndiaye MB, Pessinaba S, Mbaye A, Bodian M, et al. (2012) Infections secondary to pacemaker implantation: a synopsis of six cases. Cardiovasc J Afr 23: e1-4.

10. Kim DH, Tate J, Dresen WF, Papa FC, Bloch KC, et al. (2014) Cardiac Implanted Electronic Device-Related Infective Endocarditis: Clinical Features, Management, and Outcomes of 80 Consecutive Patients. PACE 37:978-985.

11. Klug D, Balde M, Pavin D, Hidden-Lucet F, Clementy J, et al. (2007) Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: result of a large prospective study. Circulation 116:1349-1355.

12. Klug D, Wallet F, Lacroix D, Marquié C, Kouakam C, et al. (2004) Local symptoms at the site of pacemaker implantation indicate latent systemic infection. Heart 90:882-886.

13. Koutentakis M, Siminelakis S, Korantzeopoulos P, Petrou A, Priavali H, et al. (2014) Surgical management of cardiac implantable electronic device infections. J Thorac Dis 6 Suppl 1: S173-179.

14. Sohail M, Hussain S, Le K, Le KY, Dib C, et al. (2011) Risk factor associated with early versus late onset implantable cardioverter-defibrillator infections. J Interv Card Electrophysiol 31: 12-19.

15. Golzio PG, Fanelli AL, Vinci M, Pelissero E, Morello M, et al. (2013) Lead vegetations in patients with local and systemic cardiac device infections: prevalence, risk factors, and therapeutic effects. Europace 15:89-100.

16. Ipek EG, Guray U, Demirkan B, Guray Y, Aksoy T (2012) Infections of implantable cardiac rhythm devices: predisposing factors and outcome. Acta Cardiol 67: 303-310.

17. Michalkiewicz D, Kutaraski A (2004) Pacjent po odelektrodowym zapaleniu wserdzia z usunietymi elektrodami-co dalej…?.Folia Cardiologica Excerpta 2:132-135.

18. Rap MI, Chacko A (2015) Optimising the use of transoesophageal echocardiography in diagnosing suspected infective endocarditis. Acta Cardiol 70: 487–491.

19. Greenspon AJ, Prutkin JM, Sohail MR, et al. (2012) Timing of the most recent device procedure influences the clinical outcome of lead-associated endocarditis: result of the MEDIC [Multicenter Electrophysiologic Device Infection Cohort]. J Am Coll Cardiol 7:681-897.

20. Greenspon AJ, Le KY, Prutkin JM, Sohail MR, Vikram HR, et al. (2014) Influence of vegetation size on the clinical presentation and outcome of lead-associated endocarditis: results from the MEDIC registry. JACC Cardiovasc Imaging 7: 541-549.

21. Le Dolley Y, Thuny F, Mancini J, Casalta JP, Riberi A, et al. (2010) Diagnosis of cardiac device-related infective endocarditis after device removal. JACC Cardiovasc Imaging 3: 673-681.

22. Obeid KM, Szpunar S, Khatri B, Khatri R (2012) Long-term outcomes of cardiovascular implantable electronic devices in patients with *Staphylococcus aureus* bacteremia. Pacing Clin Electrophysiol 8:961-5.

23. Bongiorni MG, Tascini C, Tagliabue E, Di Cori A, Soldati E, et al. (2012) Microbiology of cardiac implantable electronic device infections. Europace 14: 1334-1339.

24. Deharo JC, Quatre A, Mancini J, Khairy P, Dolley YL, et al. (2012) Long-term outcomes following infection of cardiac implantable electronic devices: a prospective matched cohort study. Heart 98:724-3.

25. Massoure PL, Reuter S, Lafitte S, Laborde J, Bordachard P, et al. (2007) Pacemaker endocarditis: clinical features and management of 60 consecutive cases. Pacing Clin Electrophysiol 30: 1171-183.

26. Bluhm G (1985) Pacemaker infections. A clinical study with special reference to prophylactic use of some isoxazolyl penicillins Acta Med Scand 699: 1-62.

27. Klug D, Wallet F, Kacet S, Courcol RJ (2003) Involvement of adherence and adhesion *Staphylococcus epidermidis* genes in pacemaker lead-associated infections. J Clin Microbiol 41: 3348-3350.

28. Bongiorni MG, Mariniskis G, Lip GYH, Jesper HS, Dan D, et al. (2012) How European centres diagnose, treat and prevent CIED infections: Results of an European Heart Rhythm Association survey Europace 14:1666-1669.

29. Sarrazin JF, Philippin F, Teslier M, Guimond J, Molin F, et al. (2012) Usefulness of Fluorine-18 Positron Emission Tomography/ Computed...
30. Polewczuk A., Janion M., Podlaski R, et al Clinical manifestations of lead dependent infective 339 endocarditis: analysis of 414 cases. Eur. J. Clin. Microbiol. Infec. Dis. 2014; 33:1601-8.

31. Lee DH, Gracey EJ, Aleem SY, Sarah YA, Steven P, et al. (2015) Differences of mortality rates between pocket and nonpocket cardiovascular implantable electronic device infections. Circulation 132:1435-1486.

32. Sandoe JA, Barlow G, Chambers JR, Gammage M, Guleri A, et al. (2014) Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE) J Antimicrob Chemother 383.

33. LE KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, et al. (2012) Clinical Features and Outcome of Cardiovascular Implantable Electronic Device Infections Due to Staphylococcal species. Am J Cardiol 15:1143-1149.

34. Mazurek M, Grzegorzewski B, Kargul W (2009) Infections associated with permanent pacemakers and implantable cardioverters-defibrillators. Kardiol Pol 67: 365-309.

35. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, et al. (2007) Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. J Am Coll Cardiol 49: 1851-1859.

36. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, et al. (2008) Infective endocarditis complicating permanent pacemaker and implantable cardioverter-defibrillator infection. Mayo Clin. Proc., 2008; 83:46-53.

37. Uslan DZ, Dowsley TF, Sohail MR, Hayes DL, Friedman PA, et al. (2010) Cardiovascular implantable electronic device infection in patients with Staphylococcus aureus bacteremia. Pacing Clin Electrophysiol 4: 407-13.

38. Uslan DZ, Muhammad R, Sohail MR, Sauver JL, Friedman PA, et al. (2007) Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. Arch Intern Med 167: 669-675.