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Clinically overt infections and markers of inflammation in patients admitted to Emergency Department due to high-energy discharges of implantable cardioverter-defibrillator**

Występowanie klinicznie jawnych infekcji i poziom markerów stanu zapalnego u pacjentów przyjętych do Szpitalnego Oddziału Ratunkowego z powodu terapii wysokoenergetycznej kardiowertera-defibrylatora

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Keywords

Hospital Emergency Department, implanted cardioverter-defibrillator, C-reactive protein, infection

Słowa kluczowe

Szpitalny Oddział Ratunkowy, implantowany kardiowerter-defibrylator, białko C-reaktywne, infekcja

Summary

Introduction. Overt infection is a reversible factor that may contribute to the occurrence of high-energy interventions of implanted cardioverter-defibrillators (ICD).

Aim. To assess the incidence of clinically overt infections and the analysis of C-reactive protein (CRP) concentration in patients admitted to Emergency Department (ED) after ICD shock.

Material and methods. A total of 167 patients aged 63.2 ± 12.1 admitted to ED due to high-energy therapy from ICD in whom CRP level was measured. A retrospective analysis of the correlation of CRP concentration on admission and the next morning from gender, age, the adequate or inadequate character of the shocks, the number of shocks and clinical overt infections was performed.

Results. Infection was recognized in 16 (9.6%) patients. CRP level on admission (CRP-1) was 11.0 ± 34.7 mg/dL and was elevated in 46 patients (27.5%). In the subgroup of 53 patients with the second measurement, CRP significantly increased. In multivariate analysis an increase in CRP was related with 1 electroshock in patients without overt infection or at least 5 electroshocks in patients with ≥ 2 shock.

Conclusions. 1. The increased CRP concentration on admission to ED after ICD high-energy intervention is significantly more common than clinically recognized overt infection. 2. The increased level of CRP in patients admitted to ED due to ICD shocks may be related to infection or may be secondary to the multiple shocks.

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

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Streszczenie

Wstęp. Klinicznie jawne infekcje są czynnikiem odwracalnym, który może mieć znaczenie w występowaniu terapii wysokoenergetycznych kardiowertera-defibrylatora (ICD).

Cel pracy. Ocena częstości występowania klinicznie jawnych infekcji oraz ocena stężenia białka C-reaktywnego (CRP) i jego dynamiki u pacjentów przyjętych do Szpitalnego Oddziału Ratunkowego (SOR) po terapii wysokoenergetycznej ICD.

Materiał i metody. Grupa badana składa się ze 167 pacjentów w wieku 63,2 ± 12,1 roku przyjętych do SOR-u z powodu terapii wysokoenergetycznej ICD, u których zmierzono poziom CRP. Przeprowadzono retrospektywną analizę zależności pomiędzy poziomem CRP a płcią, wiekiem, liczbą i charakterem elektrowstrząsów oraz występowaniem klinicznie jawnych infekcji.

Wyniki. Infekcję rozpoznano u 16 (9,6%) pacjentów. Średni poziom CRP-1 przy przyjęciu wynosił 11,0 ± 34,7 mg/dL i był podwyższony u 46 pacjentów (27,5%). W grupie pacjentów, gdzie wykonano kolejny pomiar CRP, uległ on istotnemu wzrostowi. W analizie

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wieloczynnikowej wzrost CRP był powiązany z jednym wstrząsem elektrycznym u pacjentów bez jawnej infekcji i z przynajmniej 5 elektrowstrząsami u pacjentów z ≥ 2 elektrowstrząsami.

Wnioski. 1. Podwyższone stężenie CRP przy przyjęciu do SOR-u po terapii wysokoenergetycznej jest znacznie częstsze niż klinicznie rozpoznane jawne infekcje. 2. Podwyższony poziom CRP przy przyjęciu do SOR-u może być związany z infekcją lub licznymi elektrowstrząsami.

INTRODUCTION

Implanted cardioverter-defibrillators (ICD) play an important role in prolonging life in patients at risk of sudden cardiac death (SCD) (1). Electrical shocks can terminate ventricular arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF). This is referred as an adequate therapy (1). Shocks may also be inadequate e.g. in a person without ventricular arrhythmia due to: incorrect T waves double counting, electromagnetic interference, the occurrence of supraventricular arrhythmia with rapid ventricular rate or ICD electrode damage (2). The occurrence of adequate ICD discharges may be precipitated by: electrolyte disturbances, diarrhea, mental and physical stress, infection, drug withdrawal, cardiac decompensation, myocardial ischemia, depression and alcohol abuse (3). Clinical significance of plasma markers of inflammation such as CRP in patients with ICD implanted in prevention of sudden cardiac death is unclear. Biasucci et al. (4) showed that elevated CRP level was a risk factor for death but not for high-energy therapy. However, Theuns et al. (5) documented that the elevated level of CRP before ICD implantation was associated with an increased risk of adequate discharges in long-term follow-up. Streitner et al. (6) observed differences in CRP serum concentrations between patients without ICD intervention (lowest level), patients with a single discharge (intermediate level) and in patients hospitalized with electric storm (ES), highest level. In 45% of patients with ES, the CRP test result was available in basic conditions before the ES took place and it was significantly lower (6). Electric current can be a tissue damaging factor and can lead to an increase in CRP level (7). In patients who underwent external cardioversion (CV) of atrial fibrillation, CRP levels significantly increased on the second day after CV compared to baseline values. This increase did not depend on the energy released during the electrical CV treatment (8).

AIM

The aim of the study was to assess the incidence of infection and increased plasma CRP on admission (CRP-1) to the Hospital Emergency Department (ED) of patients after ICD electrical discharges and to identify factors associated with elevated CRP-1 and increase in CRP (CRP-2) on the next day.

MATERIAL AND METHODS

To conduct the study the permission of the bioethical commission was obtained. Documentation of patients who were admitted to ED due to high-energy therapies from ICD was analyzed. The patients in whom the CRP measurement test was carried out on admission were qualified for the study. On the basis of data in the medical documentation, gender, age, and adequacy of ICD discharges were analysed. Additionally the number of discharges and the level of CRP-1 were established. The infection was recognized based on medical records. In case of a re-evaluation of CRP level within 24 hours from the admission to hospital, this level was also recorded and marked as CRP-2.

Statistical analysis

Continuous variables were presented as means and standard deviations or medians and interquartile range (IQR) and were compared using the Student's t test or Mann-Whitney U test depending on the distribution of variables and the type of comparisons. Categorical variables were presented as counts and percentages and assessed using chi-square test. P value < 0.05 was considered statistically significant. Logistic regression analysis of the relationship between increased levels of CRP-1 and the occurrence of infections, adequate discharges, the number of discharges, gender and age of patients was performed. An analysis using the classification and regression trees method was carried out exploring the CRP plasma growth.

RESULTS

The study group consisted of 167 patients aged 63.2 ± 12.1 years, including 134 (80.2%) men and 33 (19.8%) women. In 135 (81.3%) of them adequate shocks and in 32 (18.7%) inadequate shocks were found. In 16 (9.6%) of the patients a diagnosis of infection was made. The mean value of the CRP-1 level was 11.0 ± 34.7 mg/dL. In the group of 53 patients in whom the measurements were performed at least twice, the mean CRP-1 level was 14.0 ± 27.6 mg/dL, and the mean CRP-2 was 21.3 ± 34.1 mg/dL ($p = 0.003$). Table 1 presents the characteristics of patients admitted to ED after ICD shocks with normal and elevated levels of CRP-1. Among 16 patients diagnosed with the infection, in 8 patients (50%), CRP-1 was elevated. Among patients with elevated CRP-1, 17.4% were diagnosed with the infection.

Tab. 1. Comparison of patients admitted to ED after ICD discharges with normal and elevated levels of C-reactive protein on admission (CRP-1)

Parameters	CRP-1 elevated N = 46	CRP-1 normal values N = 121	p value
Age (years)	64.0 ± 11.9	62.8 ± 13.6	0.60
Gender: men, N (%)	40 (87.0)	94 (77.6)	0.18
Adequate therapy, N (%)	38 (82.6)	97 (80.2)	0.72
Number of ICD discharges, N	2 (1-4)	2 (1-5)	0.80
Infection, N (%)	8 (17.4)	8 (6.6)	0.034

A stepwise backward logistic regression analysis showed that increased CRP-1 level is associated with over infection (HR = 2.98, 95% Confidence Interval [CI] 1.04-8.53; p = 0.04). A regression and classification trees(CART) analysis demonstrated that the increase in CRP-2 compared to CRP-1 was associated with the occurrence of 1 ICD shock in patients without infection or with multiple ICD shocks in patients with at least 2 shocks (fig. 1).

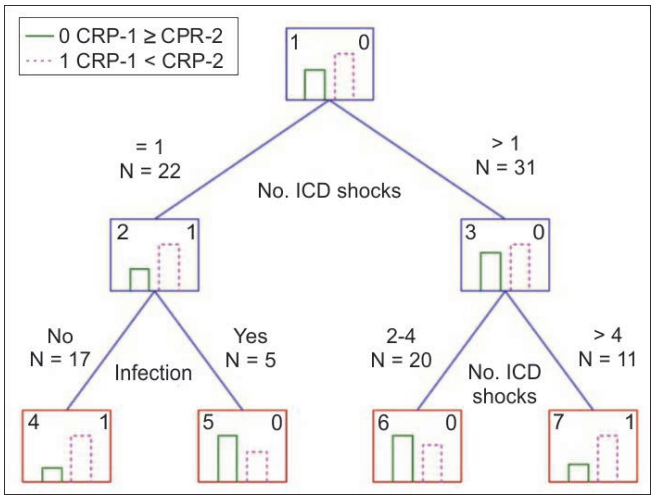

Fig. 1. Analysis by classification and regression trees (CART). In relation to the prevalence of CRP level increase in the baseline population, CRP level increase is associated with 1 shock and no infection (1 in upper right panel of rectangle 4) and shock number at least 5 when there are at least 2 shocks (1 in the right upper rectangle 7). The rectangle's number is in the upper left corner of the rectangle

DISCUSSION

The results of the study indicate that clinically overt infections occur in approximately 10% of patients admitted to ED due to the high-energy ICD interventions. This result is consistent with the observations of other authors who showed that the frequency of infection in this group of patients is relatively low (9-11). In the case of ICD interventions, the search for causes and causative treatment is necessary in order to prevent further arrhythmia recurrences and subsequent high-energy ICD therapies. We know from other studies that ICD shocks are not harmless to the human body and may increase the risk of death in long-term observations (12). Patients admitted to ED due to high-energy ICD therapy are evaluated clinically for overt infection. CRP testing to detect or confirm infection is often carried out. However, the obtained test result cannot be assessed unambiguously as confirmation of the occurrence of infection.

The CRP level may increase as a result of infections or electrical shocks and may also be raised chronically as a marker of chronic proinflammatory activity associated with atherosclerotic plaques inflammation in patients with cardiovascular disease (8, 13, 14). Therefore, in patients admitted to ED after ICD shock the assessment of the underlying causative factor for CRP level elevation is difficult.

Elevated levels of CRP are more common than the incidence of clinically overt infections. The increase in plasma CRP concentration 8 hours after internal electrical cardioversion of atrial fibrillation in patients with heart failure using ICD was demonstrated by Stieger et al. (7) who did not find changes in CRP concentration 8 hours after external electrical cardioversion in this group of patients. These observations confirm the existence of the influence of ICD shocks on the increase CRP concentration in the blood plasma. The finding of an elevated level of CRP in a patient is a sign of a possible infection, which is why it is not surprising that patients with elevated levels of CRP were assessed on the next day more often than in the entire study population. The study showed that the CRP levels performed on the second day after admission significantly increased. This may be a consequence of ongoing infection or response to damage to the body's tissues by electrical shocks. The relationship between electrical shocks and CRP level may depend on the number of the shocks and on the time which elapsed from their occurrence. In the case when a patient is admitted to ED due to one ICD shock, the first blood collection may take place in different time after ICD discharge comparing to the patients with multiple shocks. In the latter situation the patients may be referred to hospital after a longer duration from the first shock, which may cause them to be admitted to ED already during the period of CRP increase. Elevated CRP levels on admission due to a large number of the ICD shocks may not increase furthermore. On the contrary, reporting the patient directly after ICD shock may not result in an increased CRP level, which may occur only on the next day. These assumptions require further research to assess their accuracy. However, they might explain the associations found in the presented work.

The provided hypothesis explains the results of multivariate analysis, in which patients with single ICD shock without evidence of clinically overt infection had increased CRP on the second day after admission. This increase is also observed in patients with multiple shocks. Patients with a single ICD shock and infection rarely have a further increase in CRP level the next day because the main cause of CRP increase may be infection.

Limitations

The main limitation of the study is its retrospective character and related problems like the possible lack of complete clinical data. However, patients with ICD shocks are perceived as being in a life-threatening condition, and the inclusion of an antibiotic in course of treatment is one of the standard procedures when infection is suspected, therefore the chances for full clinical data in this case are high. Another limitation is the inability to perform precise analysis concerning the time between ICD shocks and the level of CRP. This limitation warrants a prospective study in which

additionally recorded intervention times as well as the occurrence and number of VT-s treated with anti-tachycardia pacing and VT-s below the detection window will be collected.

CONCLUSIONS

1. Clinically overt infections in patients with ICD admitted to ED due to high-energy discharges are less frequent than CRP elevated levels. It indicates the possible association between elevated CRP level also and other factors including potentially damaging effects of electrical current from ICD shock on the body's tissues.
2. Based on only a moderately elevated CRP level, the patient after ICD shock cannot be diagnosed with an infection.
3. The assessment of the time relationships between ICD shock, their number and time of CRP level may be useful for differentiating the reasons for the elevated CRP level.

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