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THE TENDENCIES OF SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS DURING THE PERIOD OF 2007-2009 YEARS IN VILNIUS UNIVERSITY HOSPITAL SANTARIŠKIŲ KLINIKOS

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Key words: infective endocarditis, heart failure, heart valve prosthesis implantation.

Summary

This article describes the tendencies of surgical treatment of the patients, admitted to Vilnius University Hospital Santariškių Klinikos due to infectious endocarditis, during the period of 2007-2009 years.

Objective. To assess the factors influencing the timing of surgery. To determine if timing of surgery impacts an outcome of infective endocarditis.

Design and methods: Demographic, clinical, transthoracic/transesophagal echocardiographic, microbiological, operation protocol data were analyzed. During the research patients were defined into two different groups by timing of surgical treatment. Surgery performed during the first 7 days after an admission to hospital was named as an emergent/urgent (n=50), later surgery – as an elective (n=50). Finally, 100 patients with *Duke* Criteria based diagnosis entered the research.

Results. There was a relation between the timing of surgery and etiologic factors of infective endocarditis evaluated, p = 0,034. Patients with diagnosis of prosthetic infective endocarditis received an elective surgical treatment usually - 9 (90%), p = 0,008. Refracteric lung edema required an urgent surgical treatment - 9 (82%), p = 0,050. If intracardiac complications were present, surgical treatment was usually delayed - 20 (70%) cases, p=0,008. The length of vegetations (more than 15 mm) did not influence on timing of surgery. The timing of surgical treatment due to infective endocarditis had no influence on the mortality rates, which were the same - 14% - in both groups.

Conclusions. The surgery due to infective endocarditis in Vilnius University Hospital Santariškių Klinikos during the period of 2007-2009 years was urgent if congestive heart failure and refracteric lung edema presented. In most of other cases (presence of intracardiac complications, prosthetic infective endocarditis) it was delayed.

Introduction

IE is a microbal *invasion* into the endocardial surface, prosthetic or natural heart valves and other structures of the heart. [1] It is a changing disease, which, despite advances in diagnosis and treatment, remains very dangerous and challenging. [2] An outcome of endocarditis may be associated with a number of clinical variables, e.g. age or underlying diseases of the patient, delayed diagnosis of IE, development of complications, echocardiographic findings, laboratory parameters of inflammation, the virulence of the causative microorganisms, and delayed surgical treatment. [1, 3] IE requires a collaborative approach, involving primary care physicians, cardiologists, surgeons, microbiologists, infectious disease specialists, and frequently others, including neurologists, neurosurgeons, radiologists, and pathologists. [4] Mortality rates due to IE were very high until 1961 year when Kay and colleagues excised fungal vegetations from the tricuspid valve of a patient with IE. [5] In the last 50 years, widespread use of antibiotics and advancements in cardiac surgery have contributed to major changes. First, there has been a significant decrease in mortality, provided that an early diagnosis is established and appropriate treatment is administered as soon as possible. [2, 4, 6] Besides all the changes mortality rates still remains high, accordingly to many studies and researches it varies between 12 - 41%. [1, 3, 5, 7 - 10] There is an evidence that an outcome for patients receiving medical only treatment

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comparing with those who receive combined medical-surgical is worse. [11, 12] Accordingly to this fact, it is highly recommended to use both medical-surgical treatment in all IE cases, especially for those patients who additionally suffer from NYHA IV functional class congestive heart failure, prosthetic IE, IE caused by *Staphylococcus aureus*, if paravalvular extension presents. [2, 4, 8, 11, 13] Furthermore, it is said that early use of surgery has been associated with better outcome. [4, 11, 12]

Objective: To analyze the tendencies of surgical treatment of infective endocarditis during the period of 2007-2009 years in Vilnius University Hospital Santariškių Klinikos. To assess the factors influencing the timing of surgery. To determine if timing of surgery impacts an outcome of IE.

Design and methods

Retrospective analysis of 101, older than 22 years old, patients, with *Duke* Criteria based diagnosis of definite or possible infective endocarditis (IE), surgically treated during the period of 2007 - 2009 years in Vilnius University Hospital Santariškių Klinikos, was made. During the operation mechanical or biological St. Jude, Medtronic, Carbomedics, or Hancock prostheses were used to implant. In some cases valve reconstruction, annuloplasty, aortocoronary bypass performed. Demographic, clinical, transthoracic/transesophagal echocardiographic, microbiological, operation protocol data analyzed. 1 case was excluded because both right and left heart valves were affected. After all, final analysis was made using health histories and electronic health histories of 100 patients. The indications for surgery were: severe heart failure with or without a refractory pulmonary edema; development of intracardiac complications: paravalvular extension, abscess, aneurism or fistula of a valve cuspid; IE caused by fungi; vegetations longer than 10 mm following an embolic episode; vegetations of the heart valves longer than 15 mm. [2, 4, 7] The presence of one or more of these indications requires an urgent surgery to be performed.

During the research patients were defined into two different groups by timing of surgical treatment. Surgery performed during the first 7 days after an admission to hospital was named as an emergent/urgent (n = 50), later surgery – as an elective (n = 50).

Data analysis performed using statistical package SPSS 17.0. Mean and standard deviation were counted. Chi-square test was used for categorical variables. Fisher`s exact test (two - tailed) was used if the expected count in any cell was less than five. $p < 0,05$ was considered as statistically significant.

Table1. Clinical and biological characteristics of the respondents

Characteristic	Data
Age (years ± standart deviation)	55,61 ± 14,69
Prosthetic IE	10 (10%)
Native valve endocarditis	90 (90%)
– **Aortic valve**	43 (43%)
– **Mitral valve**	31 (31%)
– **Aortic and mitral valves**	15 (15%)
– **Tricuspid valve**	11 (11%)
Length of the vegetations (mm ± standart deviation)	12,62 ± 8,06
Delay since an admission to surgery (days ± standart deviation)	10,10 ± 9,66
NYHA functional class	
– **II**	8 (8%)
– **III**	53 (55%)
– **IV**	34 (35%)

Results

100 patients, 72 (72%) men and 28 (28%) women, constituted the group of participants. Mean age was 55, 61 ± 14, 79 (range 22 - 80). IE usually occurred on aortic valve – 43 (43%) cases, less commonly on mitral valve – 31 (31%), both left heart side valves – 15 (15%) or tricuspid valve – 11 (11%) cases (Table 1). Statistically significant relation was established between the etiological factors of IE which were assessed in 72 (72%) cases, and timing of surgery (Table 2).

All the patients were treated surgically: in 97 (97%) cases heart valve prosthesis implanted, 1 (1%) – affected valve was reconstructed, 1 (1%) – fistula of the valve was sutured. Additionally, during the heart valve prosthesis implantation in 24 (24%) cases tricuspid valve anulloplasty was made, in 4 (4%) cases – aortocoronary bypass, in 1 (1%) case – ventricular septal defect was fixed. A mean delay since the first symptoms occurred till the diagnosis of IE was 139, 03 ± 210, 70: minimally – 7 days, maximally – more than 4 years. A mean delay since an admission till surgery was 10,30 ± 9,65 days (ranged between 0 and 49 days).

Native heart valve IE was dominant – diagnosed in 90 (90%) cases, while only 10 (10%) respondents had prosthetic IE. Elective surgery had been usually chosen for the patients with prosthetic IE, in 9 (90%) cases, $p = 0,008$.

Severe congestive heart failure was the most common indication for cardiac surgery due to IE, diagnosed in 33 (35%) cases. More frequent it was diagnosed for those with

left sided IE – 31 (94%) of all, but this difference was not statistically significant – p > 0,05. Refracteric lung edema developed in 11 (11%) cases, 9 (82%) of them received emergent/urgent surgery, p = 0,05.

In 85 (85%) cases blood samples were taken once or more. In 42 (49%) of them infective agent was identified. *Staphylococcus aureus* was the most frequent causative microorganism – 15 (36%) - followed by *Staphylococcus coagulase negative,* identified in 11 (26%) positive blood cultures. *(Graph. 1)* There was 1 case with IE caused by *Candida parapsilosis*. Surgery was performed in 2 days since an admission to hospital as recommended.

As long as diagnosis of IE was suspected transthoracic echocardiography was performed – 100 (100%) cases, contrary to transesophagal echocardiography, which had been performed in 38 (38%) cases only. The vegetations of the heart valves were visible in 89 (89%), measured in 42 (56%) of cases. The length of the vegetations measured just in 46 (46%) cases. 22 (48%) respondents had vegetations longer than 10 mm. 3 of them underwent an embolic episode during the period of 14 days before hospitalization. Only 1 of these 3 received an urgent surgery, other 2 – elective, p > 0,05. Intracardiac complications such as paravalvular extension, abscess, aneurism or fistula of a valve cuspid developed in 30 (30%) cases. 20 (70%) of them received elective surgery, p = 0,008. 4 (13%) of them had vegetations on the valves of the heart longer than 10 mm. Just one respondent among these 4 received an urgent surgery, p > 0,05. All the patients were diagnosed with congestive heart failure. In 21 (21%) cases, additionally, vegetations of aortic or mitral valves longer than 10 mm were measured. An urgent surgery performed for 9 (43%) of them, p > 0,05. Vegetations of the heart valve longer than 15 mm were measured in 11 (24%) cases. Urgently operated 5 (46%) of them, p > 0,05.

Timing of surgery did not influence the mortality rates. In each of the group there were 7 (14%) cases of the death set, totally – 14 (14%) deaths among all the respondents.

The variety of factors make an influence in choosing the type of heart valve (biologic (n = 78) or mechanic (n = 19) to implant. Biologic prosthesis usually was used to implant into young (22 - 39 years) – 9 (47%), p = 0,011; intravenous drugs users – 6 (38%), p = 0,026, hearts. They mostly suffered from tricuspid valve IE – 10 (53%), p < 0,001. The inotropic function of the heart was usually sufficient (EF > 50%) – 17 (90%), p = 0,007. The most common leading disease was hepatitis C, diagnosed in 6 (32%) cases. IE usually complicated with septic pneumonia in this group of patients – 5 (26%), p < 0,001.

Discussion

The population of the respondents meets the other groups, described by different authors. This fact allows to think that etiologic factors of IE are similar in different countries. [8, 9, 11, 14] Our research found trauma or/and injury to be the most frequent. Ratio of native heart valve and prosthetic IE determined to be 9 : 1 unlike to the rates introduced by other authors, where they mention about an increasing number of prosthetic IE cases, accordingly to different researchs during the last years it ranges between 13, 4 and 31%. [1, 9, 14, 15]

There are the recommendations of performing reconstruction of infected heart valve instead of replacement [7],

Table 2. The dependence of timing of surgery on etiological factors of IE

Etiologic factor of IE	Emergent/ urgent surgery	Elective surgery	*Total:*	Frequency among all the etiological factors
Trauma/injury	8 (50%)	8 (50%)	16	22%
Congenital heart disease	8 (80%)	2 (20%)	10	14%
Intravenous narcotics use	5 (56%)	4 (44%)	9	13%
Severe pneumonia	4 (44%)	5 (56%)	9	13%
Anamnesis of operation	6 (67%)	3 (33%)	9	13%
Anamnesis of cardiac operation	2 (29%)	5 (71%)	7	10%
Dental infection	0 (0%)	6 (100%)	6	8%
Hemodialysis	0 (0%)	4 (100%)	4	6%
Pielonefritis	0 (0%)	1 (100%)	1	1%
Intramuscular injection, complicated with an abscess	1 (100%)	0 (0%)	1	1%
Total:	34 (48%)	37 (52%)	72	100%

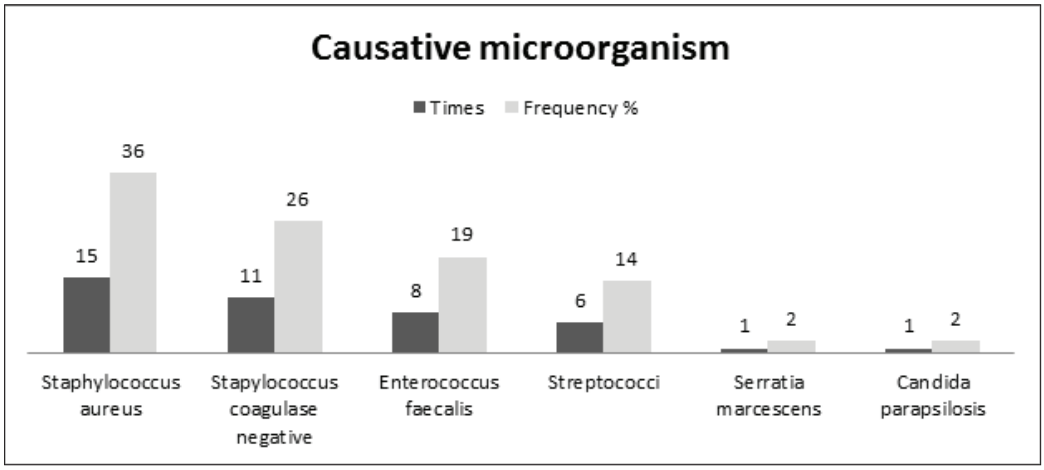

Figure 1. The distribution of causative microorganisms among the respondents

but, during the period of our research, replacement performed in 97 (97%) cases. Probably, infected heart valves were usually destroyed or infectious process spread into paravalvular structures. Reconstruction should be strongly aspired in those cases of intravenous drugs users, because usually no compliance is reachable. That is why an implantation of the mechanical prostheses is contraindicated, on the other hand biological heart valve prostheses looses their function in some years.

If the diagnosis of IE is suspected, echocardiography must be performed, as it was during our research. It helps to evaluate a function of the heart valves, to set the grade of valve insufficiency or obstruction, to find out the appearance of vegetations on the heart valves, to measure them etc. If long heart valves vegetations measured, urgent surgery is recommended because there is a highest risk of embolisation during the first week. [2, 4, 12, 16]

It is known that two - dimensional transthoracic echocardiography is cheaper and more frequently used among doctors though transesophagal is more sensible, invoked in 38% of cases during this research, comparing to 55 - 39% according to other researches [3, 7, 8]. Using transesophagal echocardiography you can earlier notice a development of intracardiac complications and measure smaller vegetations of the valves. That explains a recommendation to invoke it more frequent. [17] Alternative non invasive techniques such as multislice CT or MRI may be used if available too. [4]

Severe congestive heart failure (NYHA IV functional class) is the most important and frequent indication for surgery due to IE, because many authors determined it`s negative impact on survival rates. [2, 4] Congestive heart failure is usually the result of valvular regurgitation, which may develop acutely as a result of perforation of a native valve or bioprosthetic valve leaflet or rupture of infected mitral chordae. [4]

Paravalvular complications (paravalvular abscess, aneurism or fistula of a valve cuspid) are the most frequent reason of extension of the infection, which increases the mortality rates. [4, 7] Paravalvular abscess develops in 10 - 40% of native valve IE and even in 56 - 100% of prosthetic IE cases. [4] Pseudoaneurism or fistula usually appears when the valves of the heart are destroyed and destructed, that is why this complication is named among the indications for an urgent surgery. Just in few rare cases, while the fever is successfully controlled by antibacterial treatment and there are no more indications to operate, small abscess or aneurism of the heart valves can be treated conservative. [7] Controversially, our group of patients with intracardiac complications usually received delayed surgery.

One more indication for an urgent surgical treatment is IE caused by fungal microorganisms, [4, 12] which was faced in one case. A patient with IE caused by *Candida parapsilosis* was operated since 2 days after an admission and survived, even though it is said that mortality due to fungal IE reaches 50%.

An opinion about the timing of surgery due to IE is controversial. In one of the researches it is said that early operative treatment (if less than 7 days passed since an admission) increases the mortality rates twice [1], while in another study there was an information that early performed heart valve replacement operation decreases the mortality 5, 9%. [11] In Prendergast and Tornos study were reviewed several clinical trials where findings were controversial too. In one of them poor clinical outcome due

to persistent infection and renal failure after urgent surgery. However, in another one there was strong correlation between propensity score and timing of surgery. [4] Half of our respondents received an early and the rest – delayed surgical treatment. Timing of surgery didn`t influence the mortality. The mode of surgery (replacement versus repair) or type of prosthesis used (mechanical versus biological) has no influence on operative mortality. [4] However, a surgeon performing an operation due to IE should carefully remove all the infected, necrotized tissues from the heart valves and other cardiac structures, so that maximally decrease the possibility of the relapse of IE. Repair techniques offer long-term advantages, including a reduced risk of late complications (notably, recurrent IE) and obviation of the need for lifelong anticoagulation. [4]

Limitations of the study. There are few limitations to mention. Firstly, it was a retrospective analysis, so we were unable to control any selected diagnostical procedures or treatment strategy. As we mentioned before, transesophagal echocardiography was rarely performed, the length of vegetations of the heart valves was rarely measured. Also, the number of patients was low, so that some risk factors could not reach a statistical significance.

In future researches it is recommended to take a bigger number of respondents, so that you can define it into similar groups (to include only cases with left sided IE or just an active IE). That will allow to concretize the indications for surgery due to IE and optimize timing of operation.

Conclusions

The surgery due to IE in Vilnius University Hospital Santariškių Klinikos during the period of 2007 - 2009 years was urgent if congestive heart failure and refracteric lung edema presented. In most of the other cases (intracardiac complications, prosthetic infective endocarditis) it was delayed, even though there was one or more indications for an urgent intervention. On the other hand, the delay did not increase the mortality rate among the respondents.

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INFEKCINIO ENDOKARDITO CHIRURGINIO GYDYMO TENDENCIJOS VILNIAUS UNIVERSITETO LIGONINĖS SANTARIŠKIŲ KLINIKOSE 2007 - 2009 METŲ LAIKOTARPIU

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Raktažodžiai: infekcinis endokarditas, širdies nepakankamumas, širdies vožtuvo protezo implantavimas.

Santrauka

Šis straipsnis apibūdina chirurginio gydymo tendencijas ligonių, gydytų Vilniaus universiteto ligoninės Santariškių klinikose dėl infekcinio endokardito 2007-2009 metų laikotarpiu.

Tikslas. Įvertinti, kokie veiksniai turi įtakos infekcinio endokardito chirurginio gydymo atlikimo laikui. Nustatyti, ar operacijos atlikimo laikas turi įtakos pacientų, sergančių infekciniu endokarditu, išgyvenamumui.

Darbo metodika. Išanalizuoti demografiniai, klinikiniai, transtorakalinės bei transezofaginės echokardiografijų, mikrobiologiniai bei atliktų operacijų protokolų duomenys. Pacientai buvo suskirstyti į dvi grupes pagal operacijos atlikimo laiką. Pirmąją grupę sudarė 50 pacientų, kuriems operacija buvo atlikta per 7 dienas (skubi operacija), antrąją grupę sudarė 50 pacientų, kuriems operacija buvo atlikta vėliau nei per 7 dienas (atidėta operacija). Visi pacientai į tyrimą buvo įtraukti remiantis *Duke* kriterijais.

Rezultatai. Gautas statistiškai patikimas ryšys tarp operacijos atlikimo laiko ir infekcinio endokardito etiologinio veiksnio, p = 0,034. Pacientams, kuriems buvo diagnozuotas protezuoto vožtuvo infekcinis endokarditas, chirurginis gydymas dažniausiai buvo atidėtas - 9 (90%), p = 0,008. Esant refrakterinei plaučių edemai dažniausiai buvo renkamasi skubaus operacinio gydymo taktikos - 9 (82%), p = 0,050. Vegetacijų ilgis (daugiau nei 15 mm) neturėjo įtakos chirurginio gydymo laiko pasirinkimui. Operacijos atlikimo laikas neturėjo įtakos pacientų mirštamumui, abejose grupėse jis buvo vienodas - 14%.

Išvados. Pacientams, gydytiems Vilniaus universiteto ligoninės Santariškių klinikose dėl infekcinio endokardito 2007-2009 metų laikotarpiu, skubus operacinis gydymas buvo taikytas, esant staziniam širdies nepakankamumui ar refrakterinei plaučių edemai. Visais kitais atvejais operacija būdavo atidedama. Operacijos atlikimo laikas neturėjo įtakos pacientų, sergančių infekciniu endokarditu, išgyvenamumui.

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