

SURGICAL OUTCOMES IN NATIVE VALVE INFECTIOUS ENDOCARDITIS: THE EXPERIENCE OF THE CARDIOVASCULAR SURGERY DEPARTMENT – CLUJ-NAPOCA HEART INSTITUTE

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Abstract

Background and aims. The introduction of Duke's criteria and the improvement of imaging methods has led to an earlier and a more accurate diagnosis of infectious endocarditis (IE). The options for the best therapeutic approach and the timing of surgery are still a matter of debate and require a close collaboration between the cardiologist, the infectionist and the cardiac surgeon.

Methods. We undertook a retrospective, descriptive study, spanning over a period of five years (from January 1st, 2007 to December 31st, 2012), on 100 patients who underwent surgery for native valve infectious endocarditis in our unit.

Results. The patients' age varied between 13 and 77 years (with a mean of 54 years), of which 85 were males (85%). The main microorganisms responsible for IE were: *Streptococcus Spp.* (21 cases – 21%), *Staphylococcus Spp.* (15 cases – 15%), and *Enterococcus Spp.* (9 cases – 9%). The potential source of infection was identified in 26 patients (26%), with most cases being in the dental area (16 cases – 16%). The lesions caused by IE were situated in the left heart in 96 patients (96%), mostly on the aortic valve (50 cases – 50%). In most cases (82%) we found preexisting endocardial lesions which predisposed to the development of IE, most of them being degenerative valvular lesions (38 cases – 38%). We performed the following surgical procedures: surgery on a single valve - aortic valve replacement (40 cases), mitral valve replacement (19 cases), mitral valve repair (1 case), surgery on more than one valve – mitral and aortic valve replacement (20 cases), aortic and tricuspid valve replacement (1 case), aortic valve replacement with a mechanical valve associated with mitral valve repair (5 cases), aortic valve replacement with a biological valve associated with mitral valve repair (2 cases), and mitral valve replacement with a mechanical valve combined with De Vega procedure on the tricuspid valve (1 case). In 5 patients (5%) the bacteriological examination of valve pieces excised during surgery was positive. In 3 cases it matched the germ identified in the hemocultures, and in 2 cases it evidenced another bacterium.

Conclusion. The overall mortality of 5% is well between the limits presented in literature, being higher (30%) in patients who required emergency surgery. For the patients who return into our clinic with prosthetic valve endocarditis, the mortality after surgery was even higher (50%).

Keywords: infectious endocarditis, antibiotic therapy, emergency surgery, mortality

Background and aims

The introduction of Duke's criteria and the improvement of imaging methods has led to diagnosing infectious endocarditis (IE) earlier and more accurately. Choosing the exact therapeutic approach and the timing of surgery are still a matter of debate and require a close collaboration between the cardiologist, the infectionist and the cardiac surgeon.

The surgical treatment of active infectious endocarditis still presents a high mortality and morbidity. Consequently there are still controversies regarding the timing of surgery, either in the active phase of IE or after the completion of the antibiotic therapy and the full regression of the infectious process [1,2].

The main issue concerns surgical sanction before the onset of haemodynamic degradation: patients who meet the criteria for emergency will be operated in full acute process, patients who do not meet the emergency criteria will receive antibiotic therapy under constant clinical and ultrasound monitoring [1,3].

This paper presents our clinical experience in the treatment of acute IE on native valves.

Patients and methods

We undertook a retrospective, descriptive study, spanning over a period of five years (January 1st 2007, to December 31st, 2012). Of the patients operated for IE during this period, we took into consideration only those with native valve IE – 100 patients.

For data collection we used the observation sheets, operative protocols, the electronic data-base of the institution, and the outpatient consultation registry. For statistical analysis we used the resources of the Microsoft Office Suite.

Results

The patients' age varied between 13 and 77 years (with a mean of 54 years), of which 85 were males (85%); 37 patients (37%) came from a rural environment. In 56 cases (56%) we succeeded in identifying the microorganism responsible for the IE (positive hemocultures). The main microorganisms responsible were: Streptococcus Spp. (21 cases – 21%), Staphylococcus Spp. (15 cases – 15%), Enterococcus Spp. (9 cases – 9%) (Table I).

We administered antibiotic therapy to all patients according to the indications of the infectious disease specialist (adapted to renal and liver function) as follows: in patients with positive hemocultures, according to the antibiogram, in patients with negative antibiogram – empiric treatment with a broad spectrum to cover both Gram negative and Gram positive bacteria (quinolones or aminoglycosides combined with cephalosporine or vancomycin), chosen considering the clinical aspect and the potential entrance point.

The duration of antibiotic therapy ranged from 0

Table I. The results for pre-operative hemocultures.

Microorganism	Number of Patients (%)
Positive hemoculture	56 (56%)
Streptococcus spp.	21 (21%)
Staphylococcus spp.	15 (15%)
S. aureus	8 (8%)
(of which 4 were MRSA)	
S. epidermidis	2 (2%)
(of which 1 was MRSE)	
Other Staphylococcus	5 (5%)
Enterococcus spp.	9 (9%)
Other microorganisms	10 (10%)
Enterobacter	4 (4%)
Klebsiella pneumoniae	4 (4%)
Serratia marescens	1 (1%)
Chorynebacterium	1 (1%)
Negative hemoculture	44 (44%)

to over 43 days. Most patients (66 cases – 66%) received between 3 and 6 weeks of antibiotic treatment, 10 patients (10%) received between 0 and 7 days of treatment (they met the criteria for emergency surgical treatment). The potential source of infection was identified in 26 patients (26%), with most cases being in the dental area (16 cases – 16%) (Table II).

Table II. The entrance point for IE.

Entrance point	Number of Patients (%)
Identified	26 (26%)
Dental	16 (16%)
Pulmonary	3 (3%)
Urinary	2 (2%)
Dialysis catheter	1 (1%)
Other	4 (4%)
Unidentified	74 (74%)

The lesions caused by IE were situated in the left heart in 96 patients (96%), mostly on the aortic valve (50 cases – 50%), localized in both the left and the right heart in 3 cases (3%), and 1 case localized only on the tricuspid valve (Table III).

Table III. Location of IE lesions.

Location	Number of Patients
Left heart	96
Mitral valve	28
Aortic valve	50
Mitral + aortic valve	18
Left heart + right heart	3
Mitral + tricuspid valve	1
Aortic + tricuspid valve	2
Right heart	1
Tricuspid valve	1

In most cases (82%) we found preexisting endocardial lesions which predisposed to the development of IE, most of them being degenerative valvular lesions (38 cases – 38%) (Table IV).

Table IV. Pre-existing cardiac lesions.

Cardiac lesions	Number of Patients
Known	82
Degenerative	38
- aortic	28
- mitral	10
Mitral valve prolapse	12
Rheumatic disease	10
Congenital	14
- aortic bicuspidy	8
- VSD	2
- ASD	4
Prior cardiac surgery	2
Unknown	18

In association with the IE lesions, 10 patients (10%) presented acute cardio-embolic events (6 cases of ischemic stroke, 1 case of spleen infarction, 3 cases of peripheral artery embolisms), and 5 cases (5%) presented secondary septic determinations (cerebral abscess – 2 cases, spleen abscess - 1 case, peripheral mycotic aneurysms – 2 cases).

All patients benefited from trans-thoracic or trans-esophageal echocardiogram, in 44 patients (44%) we performed a pre-operative coronary angiography and in 11 patients we performed head or abdomen CT. Regarding the timing of surgery, 10 patients (10%) underwent emergency surgery (less than a week from the diagnosis) and 90 patients (90%) were operated after at least 10 days of antibiotic therapy.

We performed the following surgical procedures: surgery on a single valve - aortic valve replacement (37 cases mechanical, 3 cases biological), mitral valve replacement (19 cases, all mechanical), mitral valve repair in 1 case, surgery on more than one valve – mitral and aortic valve replacement (17 mechanical and 3 biological), aortic and tricuspid valve replacement (mechanical respectively biological) in 1 case, 5 cases of aortic valve replacement with a mechanical valve associated with mitral valve repair, 2 case of aortic valve replacement with a biological valve associated with mitral valve repair, and one case of mitral valve replacement with a mechanical valve combined with De Vega procedure on the tricuspid valve. We also performed combined procedures: coronary by-pass surgery combined with valve replacement 8 cases (4 mitral and 4 aortic, all with mechanical valves), and 3 cases of valve replacement combined with congenital heart defect surgery (2 procedures of ventricular septum defect closure and 1 procedure of atrial septum defect closure) and one procedure of tricuspid valve replacement with a biological valve and VSD and ASD closure.

In 5 patients (5%) the bacteriological examination of valve pieces excised during surgery was positive. In 3 cases it matched the germ identified in the hemocultures, and in 2 cases it revealed another bacterium.

Early post-operative complications (less than 30 days from surgery) are presented in Table V.

Table V. Early complications after cardiac surgery for IE.

Complication	Number of Patients
Early hemorrhage after surgery	13
Aortic para-prosthetic leak which determined minor valvular insufficiency	10
Mitral para-prosthetic leak which determined minor valvular insufficiency	6
Presternal wound dehiscence	5
Sternal dehiscence	2
Mediastinitis	1
Pericardial effusion	4
Pleural effusion	6
Pneumothorax	2
Arrhythmia	22
- atrial fibrillation	17
- III rd degree atrio-ventricular block	4
- bradycardic junctional rhythm	1
Acute myocardial infarction	1
Post-operative stroke	4
Acute renal failure	6
Acute respiratory failure	3
Multiple system organ failure	1

Early post-operative mortality was 5 % (5 cases out of 100). In what concerns the 10 cases who benefited from emergency surgery the mortality was 30 % (3 cases out of 10). In Table VI we present particular details concerning the 5 patients who died.

Out of the 100 cases studied 5 cases (5%) returned in our clinic with a second IE process on a prosthetic valve. Of the 5 cases one patient died before surgery, we operated 4 cases. Out of these four, two died (50% mortality). The interval between the first surgical intervention of valvular replacement for IE and the second episode of IE on prosthetic valve was between 5 and 156 weeks. In none of these cases the microorganism responsible for prosthetic valve IE matched the one found in the first episode of native valve IE.

Discussion

Identifying the microorganism responsible for IE is often difficult. In our study we identified the germ in only 56% of the cases. We can attribute this fact to the fact that most of the patients already received antibiotic treatment for other diseases (dental, urinary, pulmonary), before the hemoculture harvest. As described in literature [1,2], the most frequent microorganisms responsible for native valve IE were gram positive cocci, belonging the Streptococcus group (21%) and to the Staphylococcus group (15%).

We administered antibiotic therapy to all patients according to the indications of the infectious disease specialist (changed and adjusted based on the renal and liver functions) as follows: in patients with positive hemocultures, according to the antibiogram, in patients with negative antibiogram – empiric treatment with a broad

Table VI. Particular details concerning the 5 cases of death.

Affected valve	Surgery	Emergency/Elective	Post-operative complications	Death cause
Ao+Mi	Mi+Ao valve replacement with mechanical valves	Emergency (large vegetations, peripheral embolism)	Atrial fibrillation, fever, GI bleeding, MSOF	MSOF
Ao	Ao valve replacement with mechanical valve	Emergency (large vegetations, peripheral embolism)	Early post-op haemorrhage, left atrial thrombosis, stroke, masive cerebral edema	Massive cerebral edema
Mi	Mi valve replacement with mechanical valve and CABG	Emergency (Severe Mi regurgitation, pulmonary edema, acute myocardial infarction)	Atrial fibrillation, fever severe heart failure	Acute mtocardial infarction, cerebral abscess
Ao	Ao valve replacement with mechanical valve	Elective	-	Cardiac arrest (possibly rhythm abnormality)
Ao	Ao valve replacement with mechanical valve and foramen ovalis closure	Elective	Atrial fibrillation, acute renal failure, severe heart failure	Acute intestinal infarction

Deaths = 5/100 cases = 5%; Deaths in emergency cases = 3/10 cases = 30%

spectrum to cover both Gram negative and Gram positive bacteria (a quinolone or an aminoglycoside combined with cephalosporine or vancomycine), chosen considering the clinical aspect and the potential entrance point.

Once the surgical indication has been made (evidence class I and II), there comes the matter of timing of the surgical intervention. As such we divide patients with IE into 3 groups: emergency, urgency and elective [4,5]. Emergency implies undertaking the surgical intervention in less than 24 hours from the diagnosis and is applied in patients with: severe acute valve regurgitation or valvular obstruction with pulmonary edema or cardiogenic shock, or IE with cavity fistula or pericardial fistula with pulmonary edema or cardiogenic shock [6].

Our approach concerning the moment and duration of the antibiotic therapy was as follows: in patients who were hemodynamically stable we preferred to administer at least 4 weeks of treatment, most patients (65%) received between 4 and 6 weeks of treatment; in a relatively small number of patients who underwent surgery the duration of antibiotic treatment was under 7 days (10%). A number of 25 patients received between 1 and 3 weeks of treatment. At the moment of the diagnosis they did not meet the criteria for emergency so they were on antibiotic cure. During this period of clinical and echocardiographical monitoring they showed hemodynamical deterioration or the imaging aspect changed, which lead to emergent surgery before completing the minimum of 4 weeks of antibiotic treatment.

In many cases it was difficult to establish precisely the point of entry. In our study it was identified in only 26% of the cases, most of the times (16%) in the dental area. Moreover, the surgery was delayed because they had to be sterilized. The vast majority of IE lesions were located in the left heart (96%), involving mostly the aortic valve. As expected, in 82% of the cases the IE process appeared in

the context of preexisting endocardial lesions.

Cerebrovascular complications occurred in 12–40% of patients during the active course of infective endocarditis (IE) [6,7]. The timing of cardiac surgery of IE patients with neurological complications is controversial. Cardiopulmonary bypass (CPB) may exacerbate neurological deficits. Systemic heparinization may extend brain haemorrhage and convert brain infarction to haemorrhagic infarction [8]. Hypotension during CPB may aggravate pre-existing ischaemic neurological injury, and CPB may potentiate cerebral edema in areas of blood-brain barrier disruption. Cerebral infarction, the most common of the neurological complications associated with IE, complicated the outcome of left-sided IE in 20–40% of patients [8,9]. Eishi and associates reported the mortality rate of 66.3% if the cardiac operation was performed within 24 h after the onset of cerebral infarction [9]. The risk of neurological deterioration after the valve replacement was calculated by Angstwurm et al. and they found that after brain infarction, the risk was 35% on Day 1, 15% on Days 2 and 3, 20–50% from Day 4 to Day 14, lower than 10% after 14 days and 0.4% after 4 weeks [4]. Gillinov et al. recommended a delay of 2–3 weeks in performing cardiac surgery for patients with non-haemorrhagic embolic cerebrovascular accident [5]. Piper et al. found the risk of deterioration to be low when cardiac surgery was performed within 72 h (when the blood-brain barrier was not yet altered) [10]. Our approach in patients with native valve IE associated with neurological events (6 cases of stroke and 2 cases of cerebral abscess was as follows: in patients with stroke the cardiac procedure was performed 2-3 weeks after the onset of the neurological events; in patients who presented with cerebral abscess we preferred the neurosurgical correction of the cerebral lesion as a first step. We proceeded as such in one of the 2

cases where the cardiac procedure was performed 2 weeks after the brain surgery. In the other case, the condition of the patient (marked instability, acute severe mitral regurgitation, pulmonary edema) forced an emergency cardiac intervention as a first step, without brain surgery. The patient died 13 days after surgery.

There are still controversies about performing coronary angiography in patients with IE. A series of studies in literature approached this topic: *Kung V.W.S. et al, Interactive Cardiovascular and Thoracic Surgery, 2011, Hekimian G. et al, Heart, 2010, Kilian E. et al, J Thorac Cardiovasc Surg, 2008, Shamsham F. et al, Catheter Cardiovasc Interv, 2000, etc.* The majority have shown that it can be performed safely except for patients who are unstable and require emergency surgery [11,12,13,14]. The European Society of Cardiology concluded in 2009 that coronary angiogram is recommended for: men over 40 years, post-menopause women, patients with at least one risk factor for coronary disease or with a history of cardiovascular disease, except for patients with large vegetations of the aortic valve, which might be dislodged during the procedure, and unstable patients who require emergency surgery. In our study 56% of the patients benefited from coronary angiogram: in some of these cases we had to perform emergency surgery and in others it was preferred not to be performed because of safety issues.

In only five cases (5%) the result of the bacteriological examination of endocardium fragments collected during surgery was positive. In 2 cases the result did not match that of the hemoculture obtained prior to surgery. In these cases the antibiotic was changed and continued 6 weeks. In all patients the antibiotic therapy was continued until the period of 6 weeks was finished. The fact that most of the valve cultures were negative translates to a good efficiency of the minimum of 4 weeks of antibiotic therapy.

Conclusion

The overall mortality of 5% is well between the limits presented in literature, being high (30%) in patients with emergency surgery and in patients with prosthetic valve IE (50%).

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