

## Clinical, Echocardiographic and Microbiological Evaluation Of Infective Endocarditis In Cardiac Patients

Research Article

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### Abstract

**Background:** We planned to study cases of Infective endocarditis (IE) to define diagnostic criteria and to arrange treatment protocol.

**Methods:** The study included 1121 patients, divided in to two groups. Group 1 included 57 patients with IE. Those were collected over a period of 37 months. Group 2 included 1064 patients who under went cardiac surgery or intervention. Patients were examined clinically, had ECG, X-ray, Echocardiography, and blood culture. Then they were followed up for six months.

**Results:** The incidence of IE was 15 patients/ 1000 cardiac admissions. The incidence of Prosthetic Valve Endocarditis (PVE) was found to be 1.7% of PV replacement. Group I (57 IE patients). Preexisting heart disease was present in 55 patients (96.5%). The underlying heart diseases were rheumatic in 39 (68.4%). Echocardiography detected vegetations in 86% of patients with NVE, while only 28.6% of PVE. Positive blood culture was found in 72%. 58% lived the follow-up period (33/57). The causes of death were heart failure, pulmonary embolism, and cerebral hemorrhage. There was no correlation between the change in vegetation size and success of therapy.

**Conclusions:** We defined diagnostic criteria of IE and set the antimicrobial protocol of management.

**Keywords:** Infective Endocarditis; Vegetations; Blood Culture; Rheumatic Heart Disease; Duke Criteria.

**Abbreviation:** IE: Infective Endocarditis; NVE: Native Valve Endocarditis; PVE: Prosthetic Valve Endocarditis; P.Acc.t: Pulmonary Acceleration Time.

### Introduction

The incidence of IE caused by *Staphylococcus aureus* has increased, Characteristics of IE patients have also shifted toward a higher proportion of prosthetic valves and other cardiac devices, and a decreasing proportion of rheumatic heart disease [1-6].

### Endocarditis Diagnostic Criteria - Modified Duke Criteria

**Diagnostic:** 2 Major Criteria and 0 Minor Criteria.

**Diagnostic:** 1 Major Criteria and 3 Minor Criteria.

**Diagnostic:** 0 Major Criteria and 5 Minor Criteria

### Major Diagnostic Criteria

Positive blood culture for typical infective endocarditis organisms (*S. viridans* or *S. bovis*, HACEK organisms, *S. aureus* without other primary site, Enterococcus), from 2 separate blood cultures or 2 positive cultures from samples drawn >12 hours apart.

Echocardiogram with oscillating intracardiac mass on valve or supporting structures or new partial dehiscence of prosthetic valve or new valvular regurgitation.

### Minor Diagnostic Criteria

Predisposing heart condition or intravenous drug use.

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Temp >38 degrees C (100.4 degrees F).

**Vascular Phenomena:** Arterial emboli, pulmonary infarcts, mycotic aneurysms, intracranial bleed, conjunctival hemorrhages, Janeway lesions.

**Immunologic Phenomena:** Glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor.

**Microbiological Evidence:** Positive blood culture but does not meet a major criterion as noted above.

We planned to study cases of IE to define diagnostic criteria, echocardiographic features, to arrange treatment protocol, and to set criteria for prevention and control of infection.

## Methods

The study included 1121 patients, divided in to two groups. Group 1 included 57 patients with IE. Those were collected through a period of 37 months. Group 2 included 1064 patients who underwent cardiac surgery or intervention. Group 1 patients were submitted to:

### 1) Detailed history.

### 2) Clinical examination .

### 3) Investigations:

a. Routine laboratory investigations including complete blood picture.

b. Electrocardiography:

c. Chest x-ray:

d. ECHO-Doppler study: Philips system. The study was done on admission and repeated during hospital stay, two months later, and six months when feasible.

All images were recorded on video tape for review. For assessment of vegetation size, 2-D planimetry was adopted. Other evidence of endocarditis as ruptured chordae, ring abscess, aneurysm of the sinus of Valsalva was searched for [7].

e. Blood culture: Three sets of venous samples were drawn on admission. This was done before antimicrobial treatment was started. The samples were taken one hour apart, through separate venipuncture using iodine / alcohol as skin antiseptic. Each sample was inoculated on Oxoid Signal bottle [8]. In case of a negative result, an arterial sample and another venous one were taken and treated as above.

**4) Antimicrobial Therapy:** According to the Sensitivity tests. In case of a negative result, empirical therapy was given. In case of acute IE, antibiotics were started after taking the first 3 samples.

**5) Follow Up:** All patients were followed up for six months. Microbiological cure (a negative culture result) was a necessity.

Group 2 patients were submitted to.

1) Pre-interventional clinical assessment.

2) They were followed for two months post-intervention or surgery for any feature suggestive of IE. Any one of them who proved to have the disease was included in group 1.

3) Culture and sensitivity tests from any local source of infection were done.

Diagnosis of IE was based on Duke Criteria.

**Statistical Methods:** Data were analyzed using the IBM SPSS software package. The tests used were: 1- Chi-square test. 2- Fisher's Exact or Monte Carlo correction. 3- Student t-test. 4- Paired t-test.

## Results

Group 1 included 57 patients with IE. Group 2 included 1064 patients who underwent cardiac surgery or intervention (e.g. catheterization). Those were collected through the same period.

Group 1 patients were 41 males (72%) and 16 females (28%) with a ratio of 2.6: 1. Their ages ranged from 10 to 76 years with a mean of 30 years. Pre-existing heart disease was present in 55 patients (96.5%). The remaining two patients (3.5%) caught the infection via repeated IV injections.

The underlying heart diseases were rheumatic in 39 patients (68.4%). Congenital heart disease was in 3 patients (5.3%); one of them had Down's syndrome, ASD, Ostium primum defect, the second had tetralogy of Fallot and the third had Marfan's syndrome. Senile fibrotic and calcific valves were in 4 patients (7%). PVE occurred in 7 patients (12.3%). Post-surgical with no implanted prostheses were two (3.5%).

The main symptoms encountered in patients with IE were fever in 53 (93%). Arthralgia was complained of in 37 patients (64.9%). Dyspnoea was present in 47 patients (82.4%). Symptoms denoting focal neurological injury due to emboli were in 7 patients (12.3%). Painful cold extremities due to major arterial embolization were in 3 patients (5.3%), two of them had femoropopliteal artery occlusion and one had right axillary artery occlusion. Sudden loss of vision in one eye occurred in one patient.

The route of entry was known in 29 out of 41 culture positive patients (70.7%). Oro-dental procedures were in 16 (39%), Otorhino-pharyngeal cause was in 3 (7.3%), lower respiratory infection was in one patient, skin infection in 4 patients (9.8%), IV drug abuse in one patient (2.4%), genito-urinary instrumentation in one patient (2.4%), gastrointestinal in one patient (2.4%) and peri-operative causes were in two patients (4.9%).

**Clinical Signs:** Fever in 53 patients (93%). It was absent in four patients. Clubbing was found in 9 patients (15.8%). The patient with tetralogy of Fallot was excluded. Skin petechiae in 16 patients (28.1%). Splinter hemorrhages in 3 patients (5.3%). Janeway lesions were present in 2 patients (3.5%). Osler's nodes were found in 3 patients (5.3%). Conjunctival petechiae in 18 patients

(31.6%). Retinal haemorrhages in 10 patients (17.5%). Roth spots in 2 patients (3.5%). Splenomegaly in 22 patients (38.6%). During the period of follow up, four patients developed new murmur (7%) and six patients (10.5%) showed change of the intensity of an already present murmur.

Routine laboratory investigations showed that patients with hemoglobin not more than 11 g/dl were 48 patients (84.2%). Anaemia was hemolytic in 11 patients (23%). Haemolysis was found in 5 patients with PVE and 6 of those with acute IE.

Leukocytosis (WBC's > 11000/ cu m) was found in 19 patients (33.3%). Haematuria (Erythrocyturia) was found in 34 patients (59.6%). Serum creatinine above 1.5 mg /dl was found in 9 patients (15.8%). Only one patient required dialysis.

### Complications:

Heart failure in 23 patients (40.4%); Pulmonary embolism in 7 patients (12.3%). Peripheral embolization occurred in three patients (5.3%). Central nervous system embolization occurred in 7 patients (12.3%). Central retinal artery embolism occurred in one patient (1.8%). Splenic embolisation occurred in one patient (1.8%); Renal artery embolization in one patient (1.8%). Renal failure occurred in 9 patients (15.8%), only one of them required dialysis. Hepatocellular failure occurred in two patients (3.6%).

### Echocardiography

Out of the 57 patients with NVE, vegetations could be visualized in 43 patients (86%), four of them had also ruptured chordae tendineae. The total number of patients with ruptured chordae tendineae was 7 (14%). Endocardial mass not involving the valve leaflets was in two patients (4%). Ruptured sinus of Valsalva aneurysm occurred in one patient (2%). Aortic valve ring abscess was in one patient (2%).

In PVE, vegetations could be seen in two patients (28.6%). Paravalvular leakage was in 4 patients (57.1%). Rocking or instability of prosthesis was in two patients (28.6%).

### Characteristics Of Vegetations:

As regards the site of vegetations, they were visualized on the mitral valve leaflets in 24 patients (55.8%); those were on the anterior leaflet in 11 cases, on the posterior leaflet in 9 patients and on both leaflets in 4 patients. Aortic valve vegetations were seen in 10 patients (23.3%). Both mitral and aortic valves in 7 patients; one of them had mitral kissing vegetations. Vegetations seen on the mitral, aortic and tricuspid valves were in one patient (2.3%). Vegetations seen on the tricuspid valve were in one patient (2.3%). Masses equivalent to vegetations were seen in two patients.

The size of the vegetations ranged from 53 mm<sup>2</sup> to 487 mm<sup>2</sup>. The sessile vegetations were 37 while the pedunculated were 28 vegetations.

It was found that the vegetation size was affected by the duration of IE. With duration less than two months, the vegetation size was: size < 100 mm<sup>2</sup>: 7 patients; 100- to less than 200:9; 200- to less than 300: 2 patients. With duration of more than 2 months,

the sizes were < 100: 12; 100- to less than 200:14; 200 to less than 300: 11; >300:10. The results were statistically significant.

The average vegetation Size on the mitral valve leaflets was 291 mm<sup>2</sup>, on the aortic valve leaflets was 103 mm<sup>2</sup>, on the tricuspid valve leaflets were 307 mm<sup>2</sup>.

The vegetations size was related to the micro-organism; with *Str viridans*, the average size was 221 mm<sup>2</sup>, with *Str pyogenes*, it was 189, with *Staph aureus*, 309, which is the largest size, with *Staph epidermidis*, it was 159, with *Pseudomonas cepacia*, it was 162 mm<sup>2</sup>.

Follow up of vegetation size: ECHO for NVE demonstrated no change in 11 patients (25.6%), decrease in 14 patients (32.6%), and increase in 12 patients (27.9%).

The decrease in size correlated with embolization in 9 patients. No correlation was found between change in size and success of treatment.

Pericardial effusion was demonstrated echocardiographically in eight patients (14%).

### Blood Culture

Repeated blood cultures detected positive results in 41 patients out of 57 (71.9 %). Negative cultures were in 16 patients (28.1%). Gram-positive bacteria in 39 patients (95.1%); Gram - negative bacteria were in 2 cases (4.9 %).

The Gram-positive bacteria were *Streptococcus viridans* in 23 cases (56.1%). *Streptococcus pyogenes* was in six cases (14.6%). *Streptococcus pneumoniae* was in one patient (2.4%). *Streptococcus bovis* was in one patient (2.4%). *Enterococcus* was in one patient (2.4%). *Staphylococcus aureus* was in five cases (12.2%). *Staphylococcus epidermidis* was in two cases (4.9%). The Gram-negative bacteria were *Pasteurella multocida* in one patient (2.4%) and *Pseudomonas cepacia* in one patient (2.4%).

*Str. pneumoniae* was isolated from a patient with a late PVE. *Enterococcus faecalis* was isolated from a patient with a late PVE. *Str. bovis* was isolated from a patient with senile fibrocalcific aortic valve. *Pseudomonas cepacia* was isolated from a patient with early double valve replacement.

### Treatment

The patients under study were treated medically alone in 41 Patients, and with both medical and surgical treatment in 16 patients.

### Antimicrobial Therapy

**Culture-positive cases:** *Streptococcus viridans*: 17 out of 23 isolates were sensitive to Penicillin (73.9%); these were treated with penicillin G 3 Million IV 6 hourly for 4 weeks. Six isolates (26.1%) showed intermediate sensitivity and were treated with penicillin G 3 Mi 4 hourly for 4 weeks along with gentamicin 80 mg IV 12 hourly for the first two weeks. The dosage of gentamicin was modified according to the age of the patient and in renal failure according to the creatinine clearance.

All *Streptococcus pyogenes*, *bovis* and *pneumoniae* were sensitive to penicillin and so were treated as in the sensitive *Streptococcus viridans*.

The enterococcus case was treated with ampicillin-sulbactam 1500 mg IV 8 hourly, along with gentamicin 80 mg IV 12 hourly and her aortic valve prosthesis was replaced after 4 weeks.

**Staph aureus cases:**

Three patients were treated with piperacillin 2 g IV 8 hourly and the other patient was treated with cephapirin 1 g IV 8 hourly along with gentamicin 80 mg IV 12 hourly and rifampicin 300 orally 12 hourly.

The patient with *Pasteurella multocida* IE was treated with sulfamethoxazole-trimethoprim 800 mg-160 mg orally 12 hourly and tetracycline 500 mg orally 6 hourly for 4 weeks.

The patient with *Pseudomonas cepacia* 113 was treated with piperacillin 2 g N 8 hourly and amikacin 0.5 g IV 12 hourly.

**Culture negative IE:**

For NVE with subacute course, penicillin G 3 Mi IV 4 hourly for 4 weeks and gentamicin 80 mg IV 8 hourly for the first 2 weeks.

For NVE with acute course, ampicillin-sulbactam 1500 IV 8 hourly along with gentamicin 80 mg IV 8 hourly for 4 weeks.

In case there is no adequate response in 1 week and in PVE rifampicin 300 mg orally 12 hourly is added.

**Prognostic Determinants:**

After six months follow up, 24 patients were dead (42%). The remaining 33 (58%) were alive with cure rate of 100% (survival 58%). Out of the 33 patients who survived, 16 underwent prosthetic valve replacement with good prognosis.

The factors implicated in prognosis were:

**1. Predisposing Disease:**

All patients with congenital heart disease lived the follow up period (3/3 = 100%).

Patients with PV had 57% survival (4/7). IV drug IE had 50% survival (1/2).

Patients with senile fibrotic and calcific valves had the poorest Prognosis (25% survival 8 1/4).

**2. Type Of Organism:**

The most favorable outcome was encountered in Streptococcal IE (75% survival 24/32). Gram-negative IE resulted in 50% survival (1/2).

Staphylococcal IE gave the lowest survival rate (14% = 1/7).

In culture positive cases the relation between survival and type of organism was statistically significant.

**3. Vegetations:**

It was demonstrated that absence of vegetations had better prognosis than when present (survival 67% = 8/12 versus 56% = 25/45 respectively). However, the results were statistically insignificant. Also, no relation was found between change between vegetation size and success of therapy.

Tables 1,2

**4. Heart Failure:**

The survival of those without heart failure was 25 out of 34 (73.5%) where as in those with heart failure only 8 out of 23 survived (34.8%). The results were statistically significant.

**5. Heart Size:**

Patients with normal heart size had 80% survival (12/15) while

**Table 1. Prognosis in relation to type of organism.**

Organism	Alive (number/%)	Dead (number/%)
Streptococci (n=32)	24 (75%)	8 (25%)
Staphylococci (n=7)	1 (14%)	6 (86%)
Gram negative bacilli (n=2)	1 (50%)	1 (50%)
Culture negative	26 (63%)	15 (37%)

X<sup>2</sup> = 9.289 , P<0.05 between Strept. and Staph.

**Table 2. Prognosis according to management of 57 patients with infective endocarditis.**

Management	Alive (number/%)	Dead (number/%)
Medical (n=41)	17 (41.5%)	24 (58.1%)
Medical and surgical (n=16)	16 (100%)	0 (0%)

X<sup>2</sup> = 13.87, P<0.001.

those with cardiomegaly had 50% survival (21/42).  $P < 0.05$ .

## 6. Ejection Fraction:

Patients survived the follow up period had an EF of 70% on admission and 71% at two-month follow up while those who died had an E.F. of 61 (S.D. =14) and 54% respectively.  $P < 0.05$ .

## 7. Pulmonary Acceleration Time (P.Acc.t):

Patients with P.Acc.t  $>$  90 msec had 67.5% survival (27/40) whereas those with P.Acc.t  $<$  90 msec had 35.3% survival (6/17).  $P < 0.05$ .

## 8. Prognosis According To Management:

Survival in patients treated medically alone was 41.5 % (17/41), The causes of death were heart failure in 15 patients (62.5%), ventricular fibrillation in 1 patient (4.2%), pulmonary embolism in 3 patients (12.5%) and cerebral haemorrhage in two patients

(8.3%).

## Discussion

We adopted the modified Duke criteria for diagnosis of IE. We did not resort to transesophageal echo. Li et al [6] demonstrated the importance of using TEE when applying the Duke criteria to patients with suspected IE. They advocated using TEE as the initial diagnostic test of choice in patients with at least "possible IE," according to clinical criteria in patients with suspected complicated IE (i.e., paravalvular abscess) and in patients with suspected prosthetic valve IE.

Antimicrobial Treatment: The initial therapy of IE is usually empirical; exact antibiotic is given after a pathogen is identified. Published papers conform to this protocol [7-12].

## Conclusions

Rheumatic heart disease patients should be covered with antibiot-

**Figure 1. Apical 4 chamber echocardiogram of a patient with pedunculated vegetations on both anterior and posterior leaflets.**



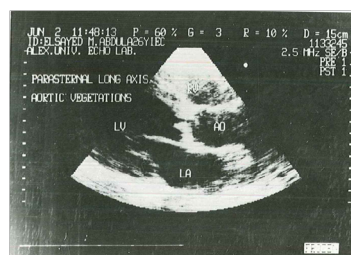
**Figure 2. Parasternal long axis echocardiogram of a patient with pedunculated vegetations on both anterior and posterior leaflets.**



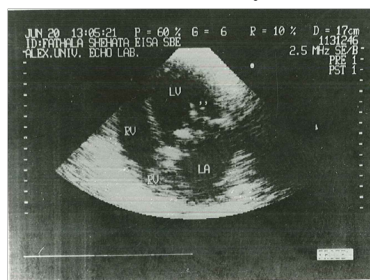
**Figure 3. Parasternal long axis echocardiogram of a patient with aortic valve vegetations.**



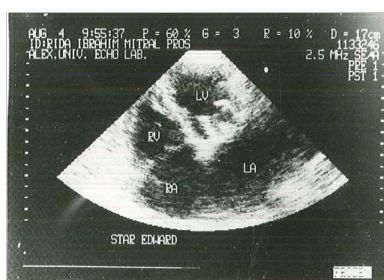
**Figure 4. Apical 5 chamber echocardiogram of a patient with aortic vegetations and anterior mitral leaflet vegetation.**



**Figure 5. Apical 4 chamber echocardiogram of a patient with Star Edwards valve endocarditis evidenced by posterior prosthetic density.**



**Figure 6. Apical 4 chamber echocardiogram of a patient with a sessile vegetation on the anterior mitral leaflet.**



ics whenever undergoing any interventional procedures.

A new regurgitant murmur is uncommon, but when it occurs it is nearly diagnostic.

There is no correlation between the change in vegetation size and success of therapy. Also, there is no correlation between the shape of vegetation and the outcome of IE.

Arterial samples are not different from venous ones. The microbiological profile differs in NVE than in early PVE. Streptococcal IE constitutes the majority of cases in NVE. The combination of penicillin-gentamicin is still successful in treating most of the patients.

Despite the success in eradicating the pathogen in all the study patients as evidenced by negative blood cultures during follow up, the mortality rate remained high. This is mainly due to haemodynamic deterioration.

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