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TEE Guided Surgical Treatment in Active Infective Endocarditis: Results of a Single Centre Four Year Experience

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Abstract

Background: Recently developed strategies (valve repair, homograft implantation) may improve clinical outcome in surgical treatment of infective endocarditis. Careful TEE examination may allow to choice the proper surgical treatment in relation to observed anatomic abnormalities. Aim of present investigation was to analyse survival and recurrent endocarditis in patients in whom surgical strategy was planned by TEE examination.

Methods: 80 consecutive patients with active infective endocarditis (52 males, 28 females, mean age 59.2 years) were investigated. All patients underwent TEE examination within 24 hours from hospital admission. 78 patients underwent surgery, 2 patients died before intervention.

Results: Aortic was involved more frequently than mitral valve (38 vs. 28 patients). In 10 both valves were involved. Four had tricuspid endocarditis. 24 underwent aortic valve replacement, 12 aortic homograft implant, 2 aortic valve repair, 18 mitral valve replacement and 13 mitral valve repair. Five underwent mitral and aortic replacement. In tricuspid endocarditis valve was repaired in 2 and replaced in 2. Only in one patient surgical exploration induced to change planned strategy. Hospital mortality was 10.2%. 3 discharged patients died at 18 months follow-up. Endocarditis recurred in 4, 2 being S. Aureus prosthetic tricuspid endocarditis in drug addicts. All patients who underwent valve repair or homograft implant were alive and free of recurrence.

Conclusion: Our results suggest that TEE guided surgical treatment of active infective endocarditis is associated with a low mortality and recurrence rate.

Keywords: Endocarditis; Surgery; Valve Repair; Transoesophageal Echocardiography

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Introduction

Surgery is the treatment of choice in complicated prosthetic valves endocarditis [1, 2]. Medical treatment alone is rarely effective in active Infective Endocarditis (IE) on native valves [3]. In patients microbiologically "cured" residual valve damage may be associated with significant hemodynamic changes leading to a decreased life expectancy. Surgical treatment has been demonstrated to be the only independent predictor of long-term survival in a large study conducted in France on patients admitted to hospital for IE [4]. Recently a large multicentre study showed that surgery was associated with a decreased risk of both in-hospital and late mortality [5].

In the active phase of the disease guidelines suggest an early surgical approach, associated with and followed by antibiotic therapy for 6-8 weeks after surgery [6]. In most previous reported series IE surgery was aimed to the replacement of affected valve eventually associated with aggressive debridement of infected tissue and reconstruction of inflow and outflow tracts in the case of perivalvular extension. The use of homograft in patients with complicated aortic endocarditis [7] and valve repair instead of valve replacement when anatomically possible [8] may decrease the risk of infective recurrences, decrease long-term morbidity and mortality including complications related to anticoagulant treatment. A careful anatomic evaluation by transoesophageal echocardiography may allow planning the proper surgical strategy in these patients.

The purpose of our study was to assess in patients period of 4 years, the effectiveness on hospital mortality, recurrent endocarditis and survival of surgical treatment planned in relation to anatomic abnormalities detected at TEE examination, with the aim, when possible, to repair the valve in native valve endocarditis and to substitute aortic root with homograft in complicated aortic prosthetic valve endocarditis.

Materials and Methods

All consecutive patients admitted with diagnosis of active endocarditis in the period of examination entered in the study. At admission in our department patients underwent: accurate history collection, physical examination with particular attention to heart, neurological findings, skin or ocular manifestations, clinical evidence of systemic embolism, Assessment of vital signs, measurement of body temperature, ECG, and laboratory examinations (haemoglobin concentration, leukocyte count, serum creatinine) were performed within 2 hours . Within the first 12 hours from admission at least 3 samples for blood cultures were collected. Finally transthoracic and transesophageal echocardiography were performed.

Diagnosis of endocarditis was made in the presence of major echocardiographic criteria and confirmed by anatomical observation at surgery [10]. In patients with positive blood cultures, antibiotic treatment was administered according to results of antibiotic susceptibility testing. Large spectrum empiric antibiotic treatment was prescribed in patients with culture negative endocarditis [6, 11]. Eight patients with Methicillin Resistant Staphylococcus Aureus (MRSA) were treated with linezolid, vancomycin or teicoplanin in association with an aminoglycoside.

Surgery was scheduled within seven days from admission. Surgical strategy, in individual patient, was made on the basis of anatomical abnormalities found at TEE evaluation and careful consideration of the balance between pro and cons of every surgical option. All patients were treated under cardiopulmonary bypass. Wide resection of infected valvular and paravalvular tissue was followed in the case by annular reconstruction and valve replacement. In patients with severe tissue destruction autologous pericardium, glutaraldehyde-fixed bovine pericardium, or Dacron patch were used to allow complete reconstruction. 32 patients with NVE underwent valve replacement while in 18 (36 %) had been possible valve repair (Table II a) (Figure 1). Valve repair was more consecutively admitted to Florence Heart Surgery Department in a frequently performed in mitral valve endocarditis (13/20 patients) than in aortic (2/10) or associated mitral and aortic valve disease. Aortic valve and aortic root were replaced with a homograft in 12/13 patients with aortic PVE and perivalvular spreading.

Additional operative procedures included the closure of infection related ventricular septal defects in 2 patients, and closure of a congenital atrial septal defect in 1 patient.

After discharge, all patients were admitted to a rehabilitation centre and thereafter followed by their general practitioner. Clinical examinations were scheduled (at 3, 9, 18, 24 months). Average follow-up period after hospital discharge has been 18 months (range 3 to 48 months). In 26 patients living far from Florence information on clinical conditions was obtained through a telephonic questionnaire in which data about survival, hospital readmissions, recurrences of endocarditis and exercise capacity at the time of interview were collected. All patients gave informed consent to the study at hospital admission and the ethical committee of the hospital approved the study.

Figure 1: TEE in mitral valve endocarditis. A severe regurgitant eccentric jet directed towards lateral wall of left atrium due to perforation of posterior leaflet is appreciable. Mitral valve repair with partial posterior leaflet resection and pericardial reconstruction allowed optimal functional result.

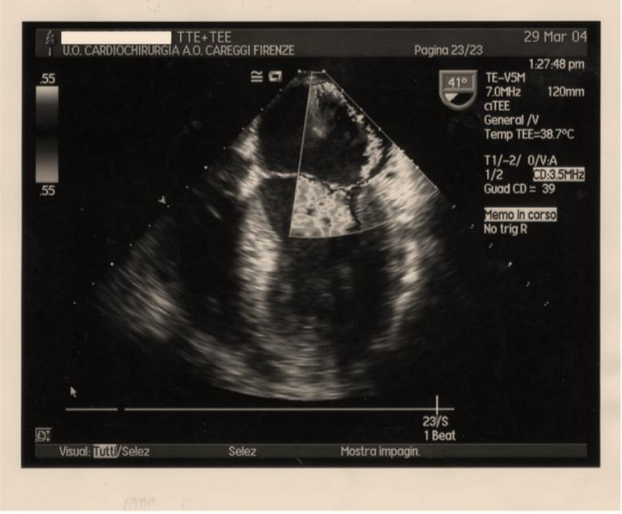


Table IIa: Surgical procedures performed in patients with native (NVE) and prosthetic valve endocarditis (PVE).

Surgical Procedures	NVE (tOT: 50, Ao: 20, Mt: 20, Tc: 4, Mt+Ao: 6)	PVE (Tot: 30, Ao: 18, Mt: 12)
Aortic valve replacement	18	7
Mitral valve replacement	7	10
Mitral and aortic valve replacement	5	1
Tricuspid valve replacement	2	0
Mechanical prosthesis	24	10
Biologic prosthesis	8	8
Homograft	1	12
Valve repair	18	0

Statistical Analysis

The quantitative variables are reported as means and standard deviations. In case of not continuous parameters the frequency of distribution has been reported.

The statistical analysis of clinical data was carried out by the student t test for continuous data, while for not continuous variables χ^2 test or Fisher exact test when appropriated were used.

The analysis of survival was made using the Kaplan-Meier method and the difference between the groups was analyzed using the log-rank test. A probability value of <0.05 was considered statistically significant.

Results

Clinical Characteristics

In the study were included 80 consecutive patients referred to our Institution between January 1, 2005 and December 31, 2008 with diagnosis of active valve endocarditis [9]. Fifty patients were males and 30 females. Mean age was 59.5 years (range 22-84 years). Men were on average 6 years younger than women (57.5 vs 63.1 years) (Table 1). Sixty eight percent were referred by first or second level hospitals of Tuscany, while the other 32% directly from the emergency department of our hospital. Fifty patients suffered from native valve endocarditis (NVE) (62%) while 30 were affected by prosthetic valve endocarditis (PVE) (38 %). Early PVE, defined as an infection occurring within 1 year after valve replacement, accounted for 40% of PVE. Late prosthetic valve endocarditis occurred in 18 patients.

At hospital admission 56% of patients were in NYHA functional class III-IV, 30% and respectively 14% in class I and in class II.

Thirty patients included in the study had prosthetic valve endocarditis (19 aortic, 11 mitral). 50 patients had native valve endocarditis (Table I).

Predisposing factors, with the exception of previous valve surgery, were rarely identified. 3 patients had history of dental procedures and Streptococcus Viridans endocarditis. Two S. Aureus tricuspid valve endocarditis were observed in intravenous drug addicts. One patient with endocarditis due to S. Bovis was affected by chronic inflammatory bowel disease. For most of late prosthetic valve endocarditis, we were not able to identify a causal event. Overall incidence of peripheral embolism confirmed by instrumental investigations was 35%.

Etiologic Infective Organisms

Blood cultures allowed identification of the etiologic agent in 58/80 patients. Staphylococci were the most common microorganisms isolated (Table III). Streptococci were identified in 26 patients while a Gram-negative was found in 5 patients. One immune depressed patient had fungal endocarditis (Candida Parapsilosis).

Blood cultures were negative in 22 subjects, 15 with native valve disease. Almost all these patients were referred from peripheral hospitals and previously treated with large spectrum empiric antibiotic therapy.

Echocardiographic Characteristics

At admission a preserved left ventricular systolic function (EF> 50%) was found in 65 % of patients. In 31% left ventricular function was moderately depressed (EF between 35 and 50%). Only 5 patients had a severe functional impairment (EF <35%).

Table I: Clinical characteristics of patients included in the study

		No	Age (Mean±SD)
Age distribution	Overall	80	59.5±16.1
	Men	50	57.3±15.8
	Women	30	63.1±16.8
Type of valve involvement	Native valve endocarditis	50	
	Prosthetic valve endocarditis	30	
Valve involved	Mitral	28	
	Aortic	38	
	Tricuspid	4	
	Mitral+Aortic	10	
ASA Physical Status	I	22	
	II	14	
	III	23	
	IV	21	

Table III: Microorganism responsible for endocarditis in relation to the type of valve affected

Aetiologic agent	***NVE (n°50)***		***PVE (n°30)***		***Total (n° 80)***	
	n°	%	n°	%	n°	%
Staph. aureus	9	18	7	23	16	20
Staph. epidermidis	3	6	5	17	8	10
Other Staph	2	4	0	0	2	2.5
Strept. faecalis	2	4	5	17	7	8.7
Strept. viridans	4	8	0	0	4	5
Other Strept.	12	24	3	10	15	18.8
Gram-negative	2	4	3	10	5	6.2
Candida	1	2	0	0	1	1.2
Negative blood colture	15	30	7	23	22	27.6

TEE showed an annular abscess (figure 2) in 12/19 patients with aortic PVE and only in 1/19 patient with aortic NVE. One or more mobile vegetations were identified in 90% of NVE. Overall moderate to severe valvular regurgitation occurred in 81% of patients with mitral valve involvement and 79% of those with aortic valve endocarditis. More than trivial tricuspidal regurgitation could be observed in 55% of patients.

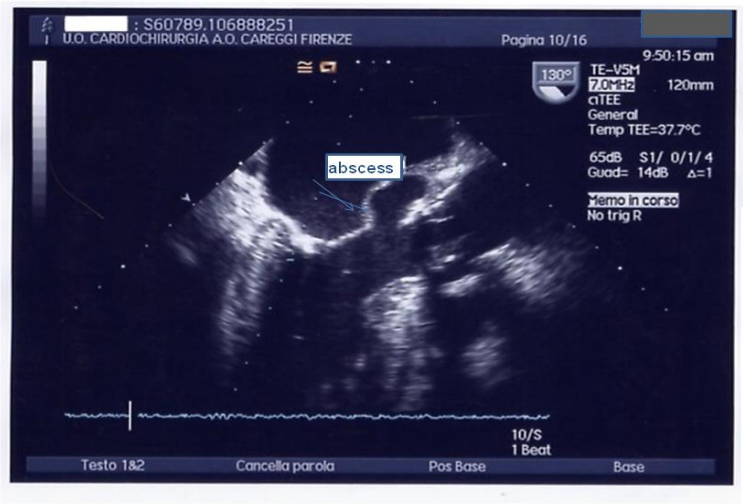
Indications for Surgery

Hemodynamic impairment associated with severe mitral or aortic valve regurgitation was the indication for surgery in 48% of patients. In 14 patients surgery was indicated for paravalvular abscesses, in one for a large aortic to right atrium fistula.

Large vegetations > 10 mm diameter (24%) and recurrent embolism were the other main indications for surgery. All patients underwent surgery within 7 days after starting maximal antibiotic treatment, unless impairment of clinical conditions suggested an earlier solution.

Figure 2: TEE in one patient with a perivalvular abscess in aortic prosthetic valve endocarditis. Aortic valve and aortic root were substituted with a homograft.

Fig. 2



Hospital Mortality and Morbidity

Of the 80 patients included in the study two died before surgery, one due to septic shock and widespread peripheral embolism, the other suddenly for the rupture of an aortic abscess. In-hospital post-surgery mortality has been 10.2 % (8 / 78). One patient died in operating room (mitral valve replacement) for rupture of the atrio-ventricular junction. The other 7 patients died within the first 30 days after surgery, 3 due to irreversible cardiogenic shock, 3 for multisystem organ failure as a result of severe septic shock and the last one for rupture of a mycotic aneurism of splenic artery.

Factors related to in-hospital mortality were advanced age, severe depression of left ventricular function and finally clinical and laboratory evidence of severe sepsis (temperature at admission over 38°C, leukocytosis with WBC>15000 mm^3, serum creatinine > 2.0 mg/dL) (table IV). We did not find any significant difference in hospital survival between NVE or PVE, between mitral or aortic valve involvement or finally between patients with or without paravalvular involvement.

In patients discharged alive from hospital survival was 95.1% (67 out of 70) at an average follow-up of 18 months (Figure 3 a). Three patients died during follow up, one for lung cancer the other two for refractory heart failure. Event free survival (death and endocarditis recurrence) is reported in figure 3b. Endocarditis recurred only in 4 patients: all needed re-intervention. Two were intravenous drug users with recurrence of staphylococci endocarditis on prosthetic tricuspid valve. Two patients with biologic aortic prosthetic valve developed a severe paravalvular leak, respectively 3 and 5 months after surgery. Blood cultures were positive for a S. Aureus in both patients. We did not find any significant difference in survival between native or prosthetic valve endocarditis (Figure 4a and 4 b).

Figure 3: Overall survival (a) and event free - death, endocarditis recurrence -survival (b) in patients discharged alive from hospital.

Fig.3

(a)

(b)

Survival was not significantly different between patients undergoing valve repair and those undergoing valve replacements. None of patients selected for valve repair strategy had recurrence of endocarditis and at follow-up echocardiography did not show more than mild residual regurgitation. Similarly none of patients treated with homograft implant had postoperative complications.

Surgical treatment was associated with a significant functional improvement. At the end of follow-up 90% of patients discharged alive from hospital were in NYHA class I-II in comparison to 58% in the preoperative period. Only 10 % had still a severe functional limitation after surgery (NYHA class III-IV).

Figure 4: Comparison of overall survival (a) and survival in patients discharged alive (b) between patients with NVE and PVE.

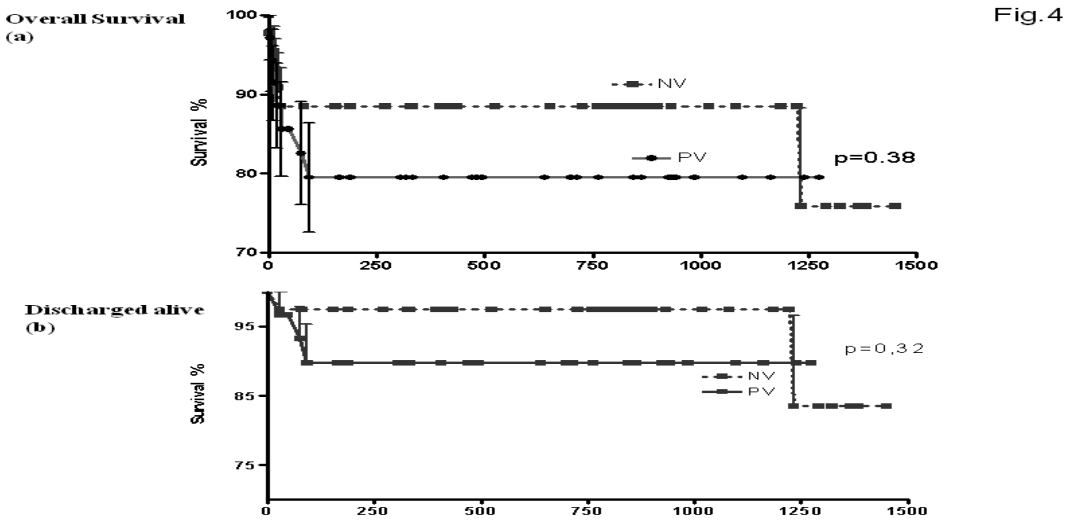


Table IV: In hospital outcome in relation to demographic, hemodynamic, echocardiographic and clinical and laboratory parameter

Parameters		Patients discharged alive (70)	Patients died after surgery (8)	t	p
Age (Years)		58.1±16.3	69.7±10	2.194	0.03
Heart rate (bpm)		87±19	105±20	2.67	0.009
SBP (mmHg)		127±22	130±23	0.384	0.710
DBP (mmHg)		67±16	71±16	0.69	0.492
LVEF (%)	>50%	57	1	26.6	<0.0001
	35-50%	12	4		
	<35%	1	3		
Aortic regurgitation	3+-4+	31	2	1.37	0.50
	<2+	22	4		
	0	17	2		
Mitral regurgitation	3+-4+	30	3	0.08	0.95
	<2+	24	3		
	0	16	2		
Temperature °C	>38	12	5	9.93	0.007
	37-38	31	3		
	<37	27	0		
Total WBC/mm^3	>15,000	6	5	21.4	<0.001
	10,000-15,000	15	3		
	<10,000	49	0		
Hemoglobin g/dL	<10	22	6	6.8	0.04
	10-12	22	2		
	>12	26	0		
Creatinine mg/dL	>2	7	1	20.33	<0.001
	1.5-2	5	5		
	<1.5	58	2		
C reactive protein (mg/L)	>10	23	3	1.0	NS
	<10	47	5		

Discussion

Previous investigations suggested a high mortality rate (>50%) in patients with active endocarditis treated with medical therapy alone [13]. Conventional surgical treatment in active infective endocarditis is associated with a better survival rate in comparison to medical therapy (range 70 - 85 %) and with a recurrence rate between 8.5 and 15% [12-15]. The availability of alternative surgical solutions to valve replacement (for example valve repair or aortic homografts), allows to choice the best technical strategy in the single patient. These solutions may improve long term clinical results and in particular decrease the risk of infectious recurrences and the need for long term anticoagulation.

In active complicated PVE spreading of infection beyond ring valve is frequent and is associated with higher incidence of congestive heart failure and mortality [16]. Early surgery should be considered the treatment of choice in patients that are not too sick to represent a prohibitive surgical challenge. Previous investigations suggested that homograft aortic root replacement might improve survival rate and in particular decrease the risk of recurrences [17]. In the study by Lopes et al. [7] 41 patients with complex PVE were treated with allograft aortic root replacement. In hospital mortality was 4.8%, two patents needed late reintervention for graft failure. No patients showed recurrence of endocarditis and overall survival at ten years was 79%. The role of homograft in treatment of aortic endocarditis has been questioned by Avierinos et al [18]. The authors did not find significant difference in survival rate between conventional treatment with valve replacement and the use of homograft. However the study suffered from several methodological limitations, mainly there was not randomization, and most of patients with complicated PVE were treated with homograft implantation (annular complications were found in 76% of the homograft group vs. 30% in conventionally treated group). The absence of differences in long-term outcome suggests that homograft may be a-safer therapeutic option in patients with more severe and advanced disease although some concerns still regard their durability. In present investigation 13/14 (92%) patients with complicated aortic endocarditis (12 PVE, 1 NVE) were treated with aortic homograft. At follow-up none of these patients died or showed recurrence.

Valve repair, in particular in patients with mitral valve endocarditis, is considered a valuable therapeutic option. Conservative surgery allows to decrease the risks related to prolonged anticoagulation and the unfavourable left ventricular geometric changes associated with valve replacement [8]. In our study in 65% (13/20) patients with isolated mitral NVE has been possible to preserve the valve. Moreover in 2 patients with tricuspid, 2 with aortic and 1 with combined aortic and mitral valve involvement valve repair was preferred to valve replacement. NVE reparative surgery was never associated with postoperative complications. Only one patient undergoing mitral valve repair had mild regurgitation at 64 weeks follow up.

Overall mortality in patients discharged alive from hospital has been less than 5 %, at an average follow-up of 18 months, a figure significantly lower than previously reported with conventional surgical approach [12-16, 19]. Wallace et al. [20] evaluated overall mortality in 200 patients admitted for endocarditis: in hospital mortality was 18%, while mortality at six months was 27%. Independent prognostic factors of mortality were significant functional impairment (III-IV NYHA Class), leucocytosis, renal failure, atrial fibrillation or severe valve regurgitation. In complicated native left sided endocarditis 6 months mortality after surgery was 15% vs. 28% in patients treated with medical therapy [21].

In conclusion results of present study suggest that early surgical treatment of active infective endocarditis allows a higher event free survival at 18 months. In particular patients undergoing valve repair and homograft implant were all alive and had no recurrent endocarditis.

The severity of the septic state at hospital admission is an important prognostic factor for perioperative mortality with a more relevant clinical impact than the degree of hemodynamic impairment.

Study Limitations

Present investigation is a relatively small single centre observational study. The length of follow-up is limited (average 18 months) and we are aware that homograft degeneration, often leading to the need of re intervention, may be observed during longer follow-up periods. However homograft treated patients is a group at high risk of early death and we must underline that at follow up these patients were all alive and free from infective recurrences.

Seventy-five per cent of patients included in present investigation were referred to our Centre from peripheral hospitals. This may have contributed to the selection for surgery of patients with more severe disease but on average younger, with a lower number of comorbidities and at overall lower surgical risk. This hypothesis is in agreement with the observations of the International Collaboration in endocarditis prospective cohort database [5].

The availability of several surgical solutions (for example valve repair or aortic homografts) other than valve replacement, allowing the choice of the proper technical strategy in the single patient is associated with an acceptable operative risk and with significant improvement in mid-term survival and decreased risk of recurrences.

Individual Contribution: Study concept and design: Carlo Rostagno , Pier Luigi Stefàno. Analysis and interpretation of the data: Carlo Rostagno , Sandro Gelsomino, Echocardiography and surgery : Carlo Rostagno , Enrico Carone , Alessandra Rossi, Pier Luigi Stefàno

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