State of the art in endocarditis treatment

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Declaration of interest

I have nothing to declare!
Early clinical descriptions

French renaissance physician

Jean Fernel (1497-1558)

- Described unusual “outgrowths” from autopsy.
- Detected murmurs by placing hand on patient’s chest

Lazare Riviere (1589-1655)

- 1881 - Synthesized work of others

William Osler (1849-1919)

Earliest report
Bactericidal antibiotic regimens are usually required in combination.

Before the discovery of penicillin, IE was an untreatable disease!

Mortality has not improved in over 2 decades (30%)

A rare and devastating disease with heterogeneous clinical manifestations

Hospital charges $120,000 per patient

Demographic changes: in pre-antibiotic era it affected young people, now it affects older and frailer with comorbidities

Health care–acquired in >25%.

S. aureus (1/3 cases - The microbe makes the difference: independent risk factor for in-H death!) overtook oral Streptococci

Antibiotic prophylaxis is a controversy, today limited to high-risk groups

Only 7 RCT due to: lack of funding, logistics problems and ethical debate

Management is both a clinical and logistical challenge: Team Work

The current priorities challenges are: Stroke, CDREI, TAVI …

Surgery is performed in 50-60% (higher in left-sided prosthetic valve), but the right timing is uncertain.

Guidelines don’t help!
Guidelines are of great importance since IE is specifically challenging due to a marked disease heterogeneity.

Over three cycles of Guidelines (2004 → 2015 ESC and AHA) the advice for IE has become more extensive but less evidence-based (the increase is only in LOE C recommendations).

IE Guidelines: The More the Merrier? … Maybe Not
They categorized and combined IE guidelines published by AHA and ESC in three time periods:
1) 2004 (AHA) and 2005 (ESC)
2) 2007 (AHA) and 2009 (ESC)
3) 2015 (AHA) and 2015 (ESC)

From period 1 to period 3 they found a statistical significant increase in total number of IE recommendations from 37 to 253 (p<0.01) (Managing treatments)

- There was a significant decrease in LOE A
- A non-significant decrease in LOE B
- A significant increase in LOE C recommendations

Conclusions:
- The number of IE guideline recommendations has increased 6-7 fold during the last decade without a corresponding increase in evidence.
- These results highlight the strong need for multiple RCT to improve the level of evidence.

Østergaard Lauge et al., American Heart Journal, 2017
Main reasons of IE treatment

1. **Drug choice** due to pathogen and **bactericidal regimen** should be used

2. **Surgery** is used mainly for treating structural cardiac complications, removing abscesses and sources of embolism

3. Success relies on **eradication of pathogen**, clearing and debriding paravalvular infection, removing of infected tissue, foreign material and hardware

Other reasons for in H treatment in IE

• To treat associated infections

• To treat co-morbidities: dialysis, strokes, COPD, DM

• To reduce and treat frequent other complications:
  • Heart failure
  • Splenic abscess
  • Neurological
  • Acute renal failure
  • Conduction defects
  • Miocarditis
  • Pericarditis
  • Drug fever
First to report **surgical cure** with open-heart surgery (**TV vegetectomy**) of pts with medically resistant IE (**Candida albicans**)
They described a 45 year old man with Klebsiella endocarditis affecting the aortic valve in whom severe aortic regurgitation and congestive heart failure developed which failed to respond to medical therapy. Excision of the valve and replacement with a Starr-Edwards prosthesis was curative.

The advent of a wide spectrum of bactericidal antibiotic agents has enabled physicians to treat many cases of bacterial endocarditis with a high likelihood of success. There remain, however, a significant number of patients with endocarditis in whom the infection is more resistant to antimicrobial therapy, valve destruction more rapid, and a satisfactory response to medical therapy sufficiently infrequent to warrant consideration of a new therapeutic approach.
Early Surgical Treatment of Valvular Endocarditis

Benson R. Wilcox, MD; Herbert J. Proctor, MD; Charles E. Rackley, MD; et al

Three patients with valvular destruction secondary to bacterial endocarditis were treated by early valvular replacement. Operative intervention prior to completion of the conventional prolonged course of antibiotic therapy was necessitated by hemodynamic collapse in two patients and by drug resistance in a third patient. Six weeks after valve replacement in the patient in case 1, he successfully underwent left pneumonectomy for carcinoma of the lung. Following surgery, the three patients are doing well, with no evidence of infection or congestive heart failure.
The dilemma as to “when” is the right time to perform surgery

- Should we operate early to reduce the risk of progressive deterioration of cardiac function?

  or

- Should we perform the surgery after the effective control of infection to reduce the surgical risks and complications?

  This was the dogma!
A “paradigm shift” in the management of IE

- Historically, the dogma was to avoid surgery during the acute phase, since the tissues are inflamed and infected, making surgery very difficult, and leading to high postoperative mortality and high risk of valve dysfunction.

- Over the past two decades, this dogma has changed dramatically, owing to the improvements in surgical techniques and earlier diagnosis. Although various surgical techniques have been used (e.g., mitral valve repair, aortic homograft implantation), a clear long-term advantage of one technique has yet to be proven. Regardless of approach, the long-term results are inferior to elective valve surgery: 10-year survival ranges from 40% to 60%.

Infected endocarditis: Is it primarily a surgical disease?

September 11, 2008 by drs venkatesan

Infected endocarditis is a serious clinical cardiac problem. The disease has evolved over many decades and now we are witnessing the most virulent forms of the disease. Infection of heart, can occur in a native healthy valve, native diseased valve, or a prosthetic valve. Further, IE can occur either as an acute (usually non diseased valve), or sub acute form (usually in diseased valve). The changing microbial pattern has made this entity very complex. The vigorous treatment protocols are available for IE. Still the prognosis and outcome with medical management is dismal even in best centers. So the role of surgery in IE has increased over the years. We propose here, a radically different approach to the problem.

Final remarks

• The 50% mortality in medical management is very high!
• Patients should be triaged early and the dominant theme should be surgery (cancer surgery): commonly valve replacement or valve repair.
METHODS
76 pts with left-sided IE (NO HF, abscess, fungal cause), severe valve disease and large vegetations (>10mm) randomized to early surgery (37 pts) or conventional treatment (27/39).

CONCLUSIONS
As compared with conventional treatment, early surgery in patients with infective endocarditis and large vegetations significantly reduced the composite end point of death from any cause and embolic events by effectively decreasing the risk of systemic embolism.
One major role of the “endocarditis team” is to define:

- Optimal medical and antibiotic therapy
- The optimal timing of cardiac surgery

The 2015 ESC guidelines provide an accurate staging of early surgery, according to hemodynamic status, that is graded as:

- “emergency” for surgery performed within 24 hours
- “urgent” for surgery performed in < 7 days (few days)
- “elective” when surgery is to be performed after at least 1-2 weeks of antibiotic therapy

The main indications for “early surgery” in AHA 2015 and ESC Guidelines 2015

<table>
<thead>
<tr>
<th>Heart failure</th>
<th>Uncontrolled infection</th>
<th>Prevention of embolism</th>
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<tbody>
<tr>
<td>Early surgery is indicated in patients with IE who present with valve dysfunction resulting in symptoms or signs of HF.</td>
<td>Early surgery is indicated in patients with PVE with symptoms or signs of HF resulting from valve dehiscence, intracardiac fistula, or severe prosthetic valve dysfunction.</td>
<td>Early surgery is indicated in patients who present with recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy.</td>
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<tr>
<td>Early surgery is indicated in patients with IE who present with PVE with symptoms or signs of HF resulting from valve dehiscence, intracardiac fistula, or severe prosthetic valve dysfunction.</td>
<td>Early surgery is indicated in patients when IE is complicated by heart block, annular or aortic abscess, or destructive penetrating lesions.</td>
<td>Early surgery is indicated in patients with severe valve regurgitation and mobile vegetations &gt;10 mm.</td>
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<td>Early surgery should be considered, particularly in patients with IE caused by fungi or highly resistant organisms (e.g., VRE, multidiagnostic-resistant gram-negative bacilli).</td>
<td>Early surgery is reasonable for patients with relapsing PVE.</td>
<td>Early surgery may be considered in patients with mobile vegetations &gt;10 mm, particularly when involving the anterior leaflet of the mitral valve and associated with other relative indications for surgery.</td>
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</table>

<table>
<thead>
<tr>
<th>AHA Guidelines 2015 (89)</th>
<th>Class, Level of Evidence</th>
<th>ESC Guidelines 2015 (68)</th>
<th>Class, Level of Evidence</th>
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<tbody>
<tr>
<td>Aortic or mitral NVE, or PVE with persistent vegetations &gt;10 mm after ≥1 embolic episode despite appropriate antibiotic therapy.</td>
<td>Ia, B</td>
<td>Aortic or mitral NVE, or PVE with vegetation &gt;10 mm, associated with severe valve stenosis or regurgitation, and low operative risk.</td>
<td>Ia, B</td>
</tr>
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<td>Aortic or mitral NVE, or PVE with isolated very large vegetations (&gt;30 mm).</td>
<td>Ia, B</td>
<td>Aortic or mitral NVE, or PVE with isolated large vegetations (&gt;15 mm) and no other indication for surgery.</td>
<td>Iib, C</td>
</tr>
<tr>
<td>Aortic or mitral NVE, or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary edema or cardiogenic shock.</td>
<td>I, B</td>
<td>Early surgery is reasonable in patients with valvular regurgitation or obstruction causing symptoms of HF, or echocardiographic signs of poor hemodynamic tolerance.</td>
<td>I, B</td>
</tr>
<tr>
<td>Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation).</td>
<td>I, B</td>
<td>Infection caused by fungi or multiresistant organisms.</td>
<td>I, C</td>
</tr>
<tr>
<td>Early surgery is reasonable for patients with relapsing PVE.</td>
<td>I, B</td>
<td>Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci.</td>
<td>Iib, B</td>
</tr>
<tr>
<td>Early surgery is indicated in patients who present with recurvent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy.</td>
<td>Ia, B</td>
<td>PVE caused by staphylococci or non-HACEK gram-negative bacteria.</td>
<td>Ia, C</td>
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*Defined as “during initial hospitalization and before completion of a full course of antibiotics.” ♂Defined as: emergency surgery — performed within 24 h; urgent surgery — within a few days; elective surgery — after at least 1 to 2 weeks of antibiotic therapy.

HACEK = Haemophilus species, Aggregatibacter species, Cardobacterium hominis, Eikenella corrodens, and Kingella species; HF = heart failure; NVE = native valve infective endocarditis; PVE = prosthesis valve infective endocarditis; VRE = vancomycin-resistant Enterococcus; other abbreviations as in Tables 1 and 2.
Conclusions: The results of our meta-analysis suggest that early surgical intervention is associated with significantly lower risk of mortality in IE.
Risk stratification plays an important role in the decision-making for surgery in IE. A prognostic scoring system, if accurate, could be of help in this scenario. Predicted risk of postoperative mortality associated with individual RISK-E scores.

Scoring systems extensively used in heart surgery (EuroSCORE) and (STS) score, are neither specific nor accurate for IE.

Conclusions: IE-specific factors (*Staphylococcus aureus* or fungi, periannular complications and sepsis) beside classical variables in heart surgery (age, haemodynamic condition and renal failure) independently predicted perioperative mortality.
Contemporary management challenges in the treatments of IE

- Stroke
- Cardiac Device Infection (CIEDs)
- TAVR
Symptomatic neurological events develop in 15–30% and are associated with excess mortality.

If cerebral haemorrhage has been excluded by cranial CT and if neurological damage is not severe (i.e. coma), surgery should not be delayed in:

- HF
- Uncontrolled infection
- Abscess
- Persistent high embolic risk

Can be performed with a low neurological risk (3–6%) and good probability of complete neurological recovery.

In cases with intracranial haemorrhage neurological prognosis is worse and surgery should generally be postponed for at least 1 month.

An alien in the heart.
Agrawal Y¹, Kalavakunta JK², Gupta V².

Abstract
We report a case of a 38-year-old man who presented with altered mental status. The patient was diagnosed with infective endocarditis (IE) originating from the GORE HELEX septal occluder device, which was placed 15 months earlier for symptomatic atrial septal defect. Brain imaging revealed shower emboli phenomena from the known IE. The patient developed hydrocephalus for which external ventriculostomy was performed. Improved neurological status warranted open heart surgery. The patient was later confirmed to be an intravenous drugs abuse prejudicing IE. This case highlights the importance of meticulously monitoring patients with suspected high-risk behavior with an implanted intracardiac prosthetic device.

Keywords: Atrial septal defect; Gore HELEX septal occluder device; Infective endocarditis; Interatrial septum; Ventriculostomy
When treating infective endocarditis should involve treating opioid use disorders (hint hint: always)
El post-TAVI

- L’El rappresenta un’inattesa condizione sfidante anche perché abbiamo poche informazioni e raccomandazioni (0,5-3% ma nel Partner Trial a due anni 1,5% vs CCH 1%)
- Il tasso di mortalità ospedaliera è del 36%, a 2 anni del 67%
- La diagnosi è più difficile e probabilmente richiede tecniche multi-imaging da affiancare all’eco, come la CT o la PET/CT
- Il frequente rigurgito paravalvolare aortico dopo TAVI potrebbe giocare un ruolo determinante nel predisporre alla El, così come uno stato di immunosenescenza

Cahill TJ., et al. JACC 2017
Early hospital discharge is frequently facilitated by the use of outpatient parenteral antibiotic therapy (OPAT).


**Conclusioni**

- L’endocardite infettiva è ancora un vecchio problema clinico, con una veste nuova

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<tr>
<th>Preventive strategies</th>
<th>Improving diagnosis</th>
<th>Optimal management</th>
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<tr>
<td>Reduce hospital acquired bacteremia</td>
<td>High index of clinical suspicion in at-risk groups</td>
<td>Evaluation by an endocarditis team</td>
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<td>Good oral hygiene for at-risk groups</td>
<td>Patient education</td>
<td>Early risk stratification</td>
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<td>Antibiotic prophylaxis for high risk groups</td>
<td>Early echocardiography</td>
<td>Early transfer to center of expertise</td>
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<td>In future, antibacterial coatings/materials</td>
<td>Adjunctive imaging if echocardiography non-diagnostic</td>
<td>Tailored antibiotic therapy</td>
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<td>Rapid microbiology results with antibacterial sensitivity</td>
<td>Early surgery for selected patients</td>
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<td></td>
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<td>No “cookbook” approach!</td>
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</tbody>
</table>

- E’ ora di trasformare le sfide sul trattamento in risposte, magari con uno shift da studi osservazionali ai RCT

Looking for and treating the POE is important