Milano 10-12 marzo 2010

L'indicazione: quanto l'insorgenza di complicazioni modifica l'outcome, quando decidere per l'intervento precoce

Come scegliere il timing ideale in una patologia multiforme che sfugge a classificazioni schematiche

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Premesse:

- La terapia chirurgica è impiegata in circa la metà dei pazienti con endocardite batterica.
- L'età non rappresenta una controindicazione alla chirurgia " per se".
- Il concetto di "endocardite batterica attiva" non è fattore limitante nel "decision-making process" quando è presente scompenso.
- Le condizioni emodinamiche sono la variabile più importante per decidere quando operare.
- La persistenza di infezione non controllata è motivo di indicazione chirurgica.

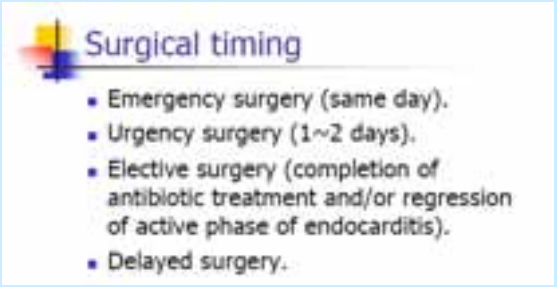
Surgical Management of Endocarditis

THE SOCIETY OF THORACIC SURGEONS CLINICAL PRACTICE GUIDELINE

Indicazioni alla terapia chirurgica generalmente accettate :

- Malfunzionamento valvolare con scompenso
- Microorganismi non sensibili a terapia antibiotica (micosi)
- Presenza di tramiti fistolosi, ascessi, embolia ricorrente
- Persistenza di vegetazioni o febbre/batteriemia nonostante una terapia antibiotica ottimale
- Vegetazioni mobili maggiori di 10 mm sulla valvola mitrale e 15 mm sulla valvola aortica
- Vegetazioni con misure in aumento nonostante terapia antibiotica
- Estensione di sede delle vegetazioni (mitral kissing)

- Indicazione emergente
  - Insufficienza aortica acuta con precoce chiusura mitrale
  - Rottura seno di valsalva a dx
  - Rottura in pericardio



- Indicazione Urgente
  - Ostruzione valvolare
  - Insufficienza Aortica o Mitralica con scompenso
  - Difetto interventricolare o tramite fistoloso
  - Comparsa di evidenza di estensione anulare o circostante
  - Non efficacia clinica terapia antibiotica
  - Embolia maggiore con vegetazioni mobili
  - Vegetazioni >15 mm mobili

➢ Le tre principali motivazioni per intervento precoce sono:

- Scompenso cardiaco,
- Infezione non controllata
- Prevenzione degli eventi embolici.

Table 19 Indications and timing of surgery in left-sided native valve infective endocarditis

Recommendations: Indications for surgery	Timing[a]	Class[b]	Level[b]
A - HEART FAILURE			
Aortic or mitral IE with severe acute regurgitation or valve obstruction causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B
Aortic or mitral IE with fistula into a cardiac chamber or pericardium causing refractory pulmonary oedema or shock	Emergency	I	B
Aortic or mitral IE with severe acute regurgitation or valve obstruction and persisting heart failure or echocardiographic signs of poor haemodynamic tolerance (early mitral closure or pulmonary hypertension)	Urgent	I	B
Aortic or mitral IE with severe regurgitation and no HF	Elective	IIa	B
B - UNCONTROLLED INFECTION			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B
Persisting fever and positive blood cultures > 7–10 days	Urgent	I	B
Infection caused by fungi or multiresistant organisms	Urgent/elective	I	B
C - PREVENTION OF EMBOLISM			
Aortic or mitral IE with large vegetations (> 10 mm) following one or more embolic episodes despite appropriate antibiotic therapy	Urgent	I	B
Aortic or mitral IE with large vegetations (> 10 mm) and other predictors of complicated course (heart failure, persistent infection, abscess)	Urgent	I	C
Isolated very large vegetations (> 15 mm)[c]	Urgent	IIb	C

[a] Class of recommendation.
[b] Level of evidence.
[c] Emergency surgery: surgery performed within 24 h; urgent surgery: within a few days; elective surgery: after at least 1 or 2 weeks of antibiotic therapy.
[d] Surgery may be preferred if procedure preserving the native valve is feasible.

ESC Guidelines 2009

Surgical Management of Infective Endocarditis: Early Predictors of Short-Term Morbidity and Mortality

(Ann Thorac Surg 2006;82:524–9)

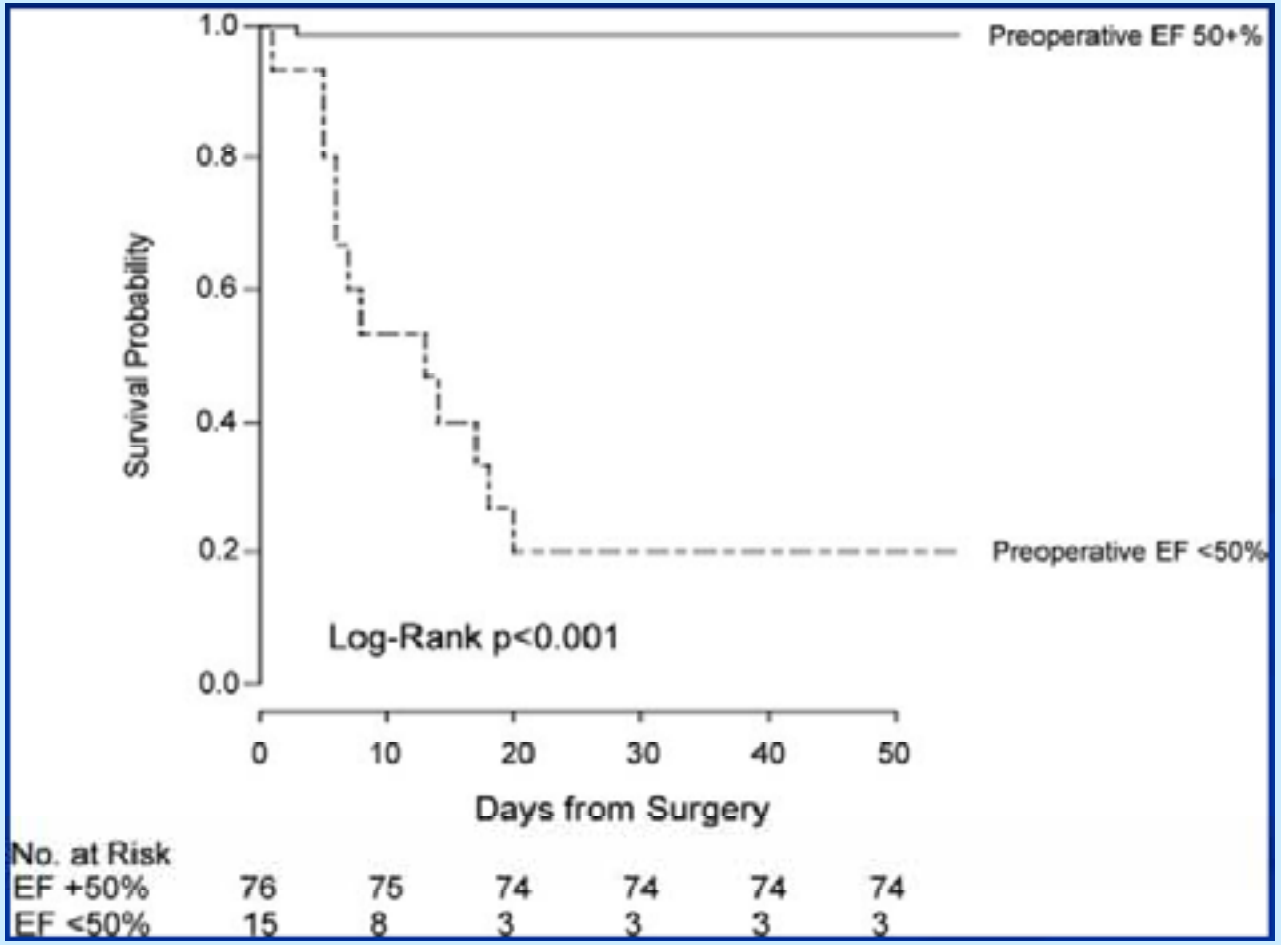
Davinder S. Jassal, MD, Tomas G. Neilan, MD, Aruna D. Pradhan, MD, Karen E. Lynch, RN, Gus Vlahakes, MD, Arvind K. Agnihotri, MD, and Michael H. Picard, MD

Disfunzione ventricolare

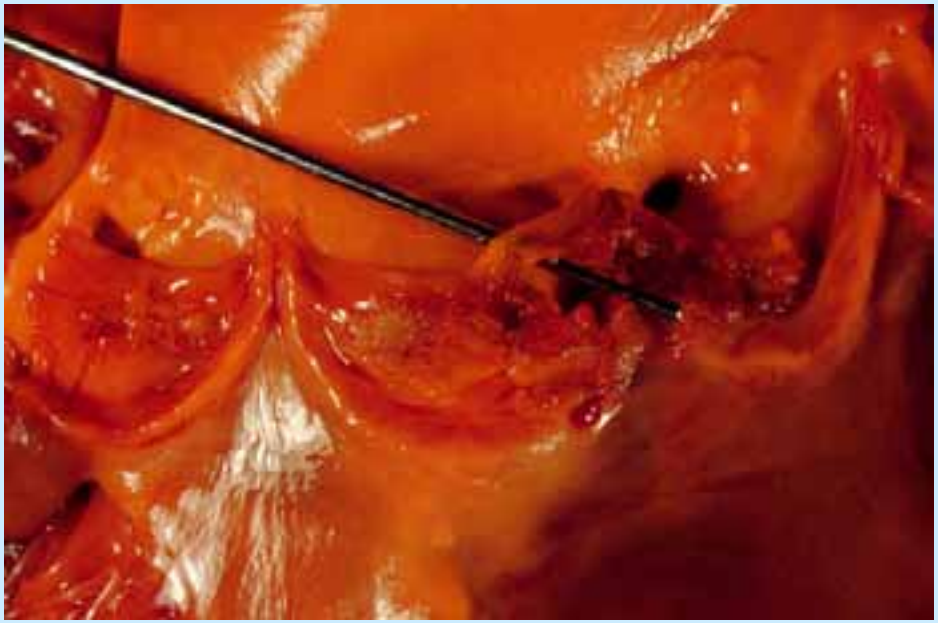
fattore prognostico dopo chirurgia

primitivo o secondario

stato settico?



Diffusione locale dell’infezione



Acute *S. aureus* IE with perforation of the aortic valve and aortic valve vegetations.

Acute *S. aureus* IE with mitral valve ring abscess extending into myocardium.

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Indication e “timing” della chirurgia per evitare embolie

- La maggior parte dei fenomeni embolici avviene **prima del ricovero** o della diagnosi
- Il miglior mezzo per ridurre il rischio di embolia è rappresentato dal **precoce inizio di terapia antibiotica efficace**.
- Nell’ “Euro Heart Survey” le dimensioni delle vegetazioni sono state motivo di indicazione chirurgica nel 54% dei pazienti con forme su valvola nativa ma raramente qiesta è stata l’unica ragione.
- Il ruolo della chirurgia nella prevenzione rimane controverso
- La chirurgia fatta con finalità preventive sul rischio embolico deve essere effettuata **molto presto**, nei primi giorni dopo la diagnosi,.con criteri di urgenza

Complicazioni dell’ endocardite batterica che possono interferire con il “timing” chirurgico

- Presenza di aneurismi “micotici”
- Complicanze Neurologiche
- Insufficienza renale acuta
- Complicanze osteoarticolari
- Ascessi splenici
- Miocardite, Pericardite

ANEURISMI “MICOTICI”: bassa inferenza

- Sono il risultato di embolie settiche nello spazio endoluminale o nei vasa vasorum.
- La sede intracranica è molto frequente, la prevalenza del f 2–4% riportata è probabilmente sottostimata. La angiografia rimane il test di “imaging” fondamentale e deve essere impiegato in caso di negatività di altre tecniche con sospetto clinico.
- Non esistono studi randomizzati e la terapia deve essere individualizzata.
- La rottura dell’aneurisma “micotico” ha una cattiva prognosi. Non ci sono indicatori predittivi. Molti aneurismi non rotti guariscono con la terapia antibiotica. E’ richiesta una valutazione con “imaging” seriale.
- In casi con ampi, progressivi aneurismi cerebrali può essere indicato un intervento neurochirurgico o endovascolare

COMPLICAZIONI NEUROLOGICHE: alta inferenza

- Tra I pazienti con endocardite batterica il 20 - 40% hanno complicanze neurologiche: quasi sempre per embolia di materiale settico o trombotico dalle valvole cardiache
- Sono *rare* le embolia asintomatiche
- 35% dei pazienti con endocardite hanno un' evidenza RNM di embolia cerebrale, 90% dei quali con sintomi neurologici.
- Circa il 75% degli "strokes" sono forme primitivamente ischemiche, circa la metà di questi diviene successivamente emorragico
- Un quarto degli "strokes" sono emorragici (subaracnoidei o intraparenchimali o entrambi)

Surgical Management of Endocarditis

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Subclinical Brain Embolization in Left-Sided Infective Endocarditis

Results From the Evaluation by MRI of the Brains of Patients With Left-Sided Intracardiac Solid Masses (EMBOLISM) Pilot Study

Howard A. Cooper, MD; Elissa C. Thompson, MD; Robert Laureno, MD; Anthon Fuisz, MD; Alexander S. Mark, MD; Mark Lin, MD; Steven A. Goldstein, MD

(*Circulation*. 2009;120:585-591.)

- **Acute brain embolization (ABE)** in left-sided infective endocarditis has significant implications for clinical decision making.
- The incidence rates of subclinical brain embolization and any ABE were 48% and 80%, respectively. ABE was present in 18 of 19 patients (95%) with Staphylococcus aureus infection.
- In line with previous studies, the incidence of clinical stroke in our patient population was 25%.Brain MRI confirmed the presence of ABE in each of these patients in whom it was performed.
- In addition, however, brain MRI **detected ABE in 70% of patients in whom the clinical neurological evaluation did not reveal evidence of acute stroke.**

Subclinical Brain Embolization in Left-Sided Infective Endocarditis

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(*Circulation*. 2009;120:585-591.)

- What are the **implications for surgical treatment** when ABE, whether acute stroke or SCBE, complicates left-sided IE?
- Current ACC/AHA treatment guidelines provide a **Class IIa recommendation for surgery of the native valve in patients with IE who present with recurrent emboli and persistent vegetations** despite appropriate antibiotic therapy.
- According to the present study, however, the clinical examination appears to be insensitive to the presence of ABE.
- Therefore, **the use of brain MRI** at baseline in patients with left-sided IE should be considered to more accurately determine whether an embolic event has occurred and **may play a role in the complex decision about surgical intervention in infective endocarditis.**

Subclinical Brain Embolization in Left-Sided Infective Endocarditis

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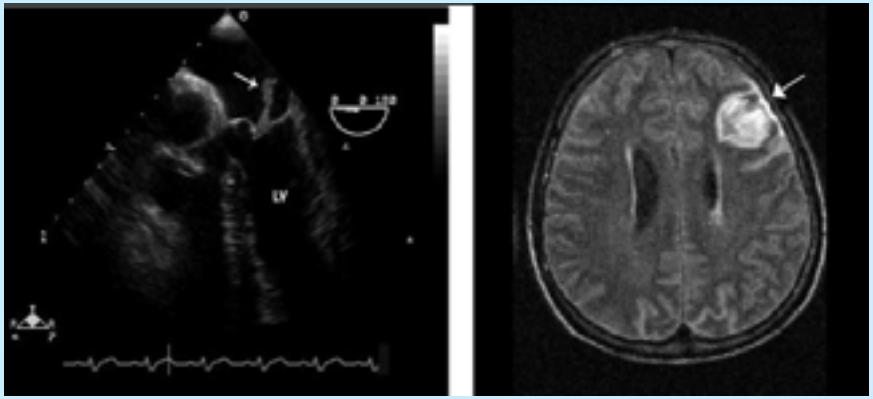
(*Circulation*. 2009;120:585-591.)

- Conclusions—Magnetic resonance imaging detected subclinical brain embolization in a substantial number of patients with left-sided infective endocarditis, suggesting that the incidence of ABE may be significantly higher than reports based on clinical and computed tomography findings have indicated.
- **Brain magnetic resonance imaging may play a role in the complex decision about surgical intervention in infective endocarditis.**



Cerebral Microbleeds Are Frequent in Infective Endocarditis

A Case–Control Study

(*Stroke*. 2009;40:3461-3465.)

Isabelle Klein, MD, PhD; Bernard Iung, MD; Julien Labreuche, BST; Agathe Hess, MD; Michel Wolff, MD; David Messika-Zeitoun, MD; Philippe Lavallée, MD; Jean-Pierre Laissy, MD, PhD; Catherine Lepert, MD, PhD; Xavier Duval, MD, PhD; the IMAGE Study Group

- The first 60 patients with community-acquired IE included in the single-center prospective **IMAGE Study**. For all patients,echocardiography and brain MRI were performed within the first week after patient admission.
- We randomly selected for each case 2 age-gender-matched control subjects, one under active anticoagulation therapy and the other not
- In our study, cerebral microbleeds were not associated with ischemic lesions. In patients with IE, cerebral microbleeds were mostly homogeneous, <5 mm, and predominantly located in cortical areas rather than subcortical areas.
- Other case characteristics, including imaging data such as acute ischemic stroke, were not significantly related to cerebral microbleeds presence (data not shown).

Cerebral Microbleeds Are Frequent in Infective Endocarditis

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- In IE cases, cerebral microbleeds prevalence was 57% (95% CI, 44.1% to 69.2%), significantly higher than the control group (matched OR, 10.06; 95% CI, 3.88 to 26.07; P<0.001).
- Although we cannot be sure that the presence of cerebral microbleeds indicates early stages of infective endocarditis, the high frequency of cerebral microbleeds suggests that they should be evaluated as new diagnostic markers of IE.

Surgical Management of Endocarditis

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- Follow-up MRI or CT imaging after completion of a routine course of antibiotics should be undertaken to rule out the development of an abscess within the infarct cavity; the latter may require more prolonged antibiotic therapy or surgical intervention.
- Patients with **infected mechanical valves pose a challenging clinical dilemma about anticoagulation regimen**
- While definitive studies are lacking, “general advice” from the ACC/AHA guidelines suggest **discontinuation of anticoagulation for 2 weeks** in the presence of recent stroke due to infection with high-risk organisms such as S. aureus.
- Anticoagulation should also be withheld in the presence of large brain infarction, hemorrhagic transformation, uncontrolled infection, or in the presence of a mycotic aneurysm.
- Vascular imaging prior to anticoagulation should be performed.

Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study

European Heart Journal (2007) 28, 1155–1161

Franck Thuny[1], Jean-François Avierinos[1], Christophe Tribouilloy[2], Roch Giorgi[3], Jean-Paul Casalta[4], Loïc Milandre[5], Amel Brahim[2], Georges Nadji[2], Alberto Riberi[5], Frédéric Collart[6], Sebastien Renard[1], Didier Raoult[4], and Gilbert Habib[1]*

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Received 29 October 2006; revised 27 January 2006; accepted 7 February 2007; online publish-ahead-of-print 15 March 2007

Conclusion

- Patients with silent cerebrovascular complications or TIA have a relatively good prognosis, whereas those with stroke have significant excess mortality particularly in case of mechanical prosthetic valve IE or impaired consciousness.
- Valvular surgery can be safely performed after silent cerebrovascular complications or TIA and may improve survival in selected patients with stroke.

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COMPLICAZIONI NEUROLOGICHE

- Dopo un evento neurologico molti pazienti possono conservare indicazione a terapia chirurgica cardiaca.
- Il rischio di ulteriore deterioramento cerebrale post-operatorio è basso dopo TIA o evento embolico asintomatico. Non c'è motivo di ritardare la chirurgia.
- Dopo un ictus cerebrale la chirurgia cardiaca non è controindicata se la prognosi neurologica lo consente.
- Ci sono dati non uniformi sull'intervallo di tempo che è idoneo interporre tra l'ictus cerebrale e la chirurgia cardica

Surgical Management of Endocarditis

THE SOCIETY OF THORACIC SURGEONS CLINICAL PRACTICE GUIDELINE

Timing of surgery in patients with neurologic complications

- In patients who have had a major ischemic stroke or any intracranial hemorrhage, it is reasonable to delay valve replacement for at least 4 weeks from the stroke, if possible.
  (Class IIa, Level of Evidence C)
- If there is a decline in cardiac function, recurrent stroke or systemic embolism or uncontrolled infection despite adequate antibiotic therapy, a delay of less than 4 weeks may be reasonable, particularly in patients with small areas of brain infarction (Class IIb, Level of Evidence C)

INSUFFICIENZA RENALE ACUTA: bassa inferenza

- Complicanza comune in corso di endocardite: presente in circa il ~30% dei casi, indicatore di cattiva prognosi.
- Può essere necessaria terapia dialitica ma spesso il deficit è reversibile
- Cause multifattoriali:
  - Glomerulonefrite da immunocomplessi e vasculite
  - Infarto renale embolico
  - Bassa portata cardiaca primitiva o secondaria
  - Tossicità da terapia antibiotica (nefrite acuta interstiziale) collegata ad aminoglicosidi, vancomicina e persino alte dosi penicillina
  - Nefrotossicità da mezzo di contrasto usato a scopo diagnostico

COMPLICANZE OSTEOARTICOLARI: ritardo chirurgia

- I sintomi osteo-mio-articolari sono frequenti e possono essere I sintomi di esordio (artralgia, mialgia, lombalgia).
- Artrite periferica è presente in ~14%, spondilodiscite è descritta con prevalenza variabile tra 3–15% dei casi (anche oltre con infezioni streptococciche)
- RNM e TC sono indicati nei pazienti con dolori alla schiena
- Una terapia antibiotica prolungata è indicata e richiesta se si documenta spondilodiscite settica.

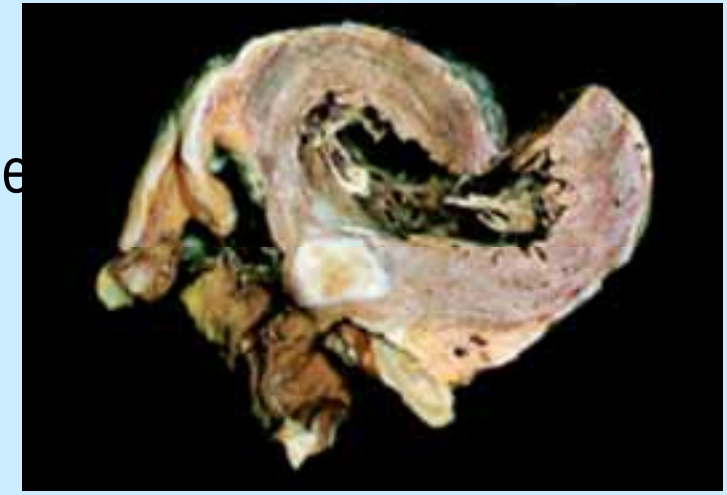
ASCESSI SPLENICI: bassa inferenza

- Benchè le embolie spleniche siano frequenti gli **ascessi splenici sono rari..**
- La diagnosi è suggerita dalla presenza di febbre persistente con battreiemia. La diagnosi è fatta con eco, RNM o TC.
- Il trattamento , oltre l'antibiotico, può comprendere la **splenectomia in casi selezionati** con rottura splenica per grandi ascessie deve essere effettuata prima della chirurgia cardiaca se questa non è urgente.
- In pazienti ad alto rischio può essere indiocato il drenaggio percutaneo

MIOCARDITE, PERICARDITE

- **L'insufficienza cardiaca** può essere causata anche dalla miocardite che spesso si associa all'endocardite batterica. Questa può associarsi alla formazione di **ascessi cardiaci**.
- **Necrosi** locali possono essere causate da embolie coronariche o compressione estrinseche. La comparsa di **aritmie ventricolari** può indicare un coinvolgimento miocardico e segnala una cattiva prognosi.

- La pericardite purulenta è rara e può richiedere drenaggio chirurgico
- **La rottura nel cavo** di ascessi o fistole spesso causa drammatiche e fatali conseguenze



“PRE AND PERI - OPERATIVE MANAGEMENT”

- Coronarografia è raccomandata:
  - Negli uomini >40 anni,
  - Nelle donne dopo la menopausa
  - Nei pazienti con almeno un fattore di rischio per malattia cardiovascolare o con storia di malattia coronarica.

- Eccezioni:
  - Presenza di ampie vegetazioni valvolari aortiche
  - Quando è necessario un intervento chirurgico urgente
  - In queste situazioni è giustificato l’impiego di TC ad alta risoluzione per escludere malattia coronarica

“PRE AND PERI - OPERATIVE MANAGEMENT”

- Infezioni extracardiache:
  - Se il verosimile focolaio primario di infezione è identificato deve essere eradicato prima dell’intervento chirurgico, se questo non è urgente.

- ETE intraoperatorio:
  - molto utile per determinare la sede e l’estensione dell’infezione, oltre che per la normale gestione peri-operatoria

Dramatic Reduction in Infective Endocarditis–Related Mortality With a Management-Based Approach

Arch Intern Med. 2009;169(14):1290-1298

Elisabeth Botelho-Nevers, MD; Franck Thuny, MD; Jean Paul Casalta, MD; Hervé Richet, MD, PhD; Frédérique Gouriet, MD, PhD; Frédéric Collart, MD; Alberto Riberi, MD; Gilbert Habib, MD; Didier Raoult, MD, PhD

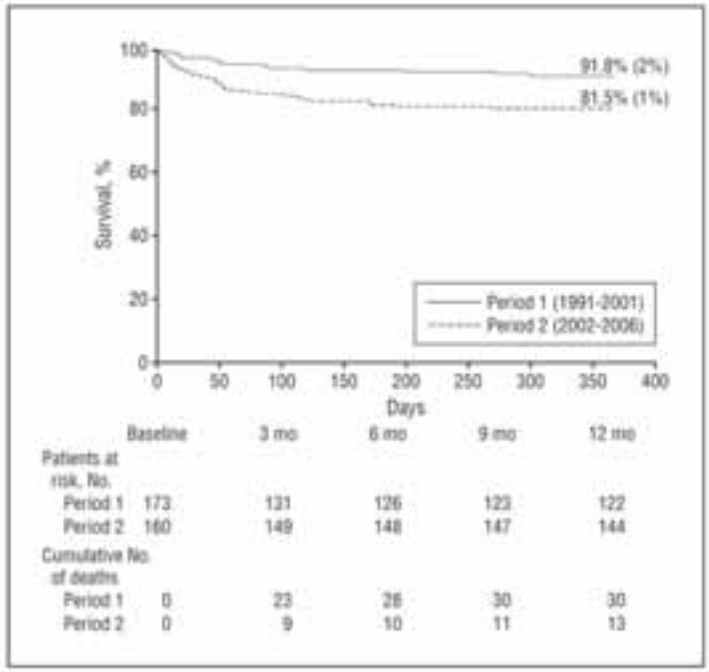


Figure. Kaplan-Meier curve relating survival (percentage [SE]) according to the period of infective endocarditis management (hazard ratio, 0.41; 95% confidence interval, 0.21-0.79 [*P*=.008]).

- Dramatic reduction in mortality between the 2 periods analyzed, suggesting a beneficial impact of our multidisciplinary management strategy of IE.
- Related to the **creation of a local task force**, leading to the implementation in 2002 of a therapeutic protocol including both medical and surgical management
- This spectacular improvement in the outcome of IE occurred **while the population was significantly older and had more comorbidities** in period 2.

Dramatic Reduction in Infective Endocarditis–Related Mortality With a Management-Based Approach

Elisabeth Botelho-Nevers, MD; Franck Thuny, MD; Jean Paul Casalta, MD; Hervé Richet, MD, PhD; Frédérique Gouriet, MD, PhD; Frédéric Collart, MD; Alberto Riberi, MD; Gilbert Habib, MD; Didier Raoult, MD, PhD

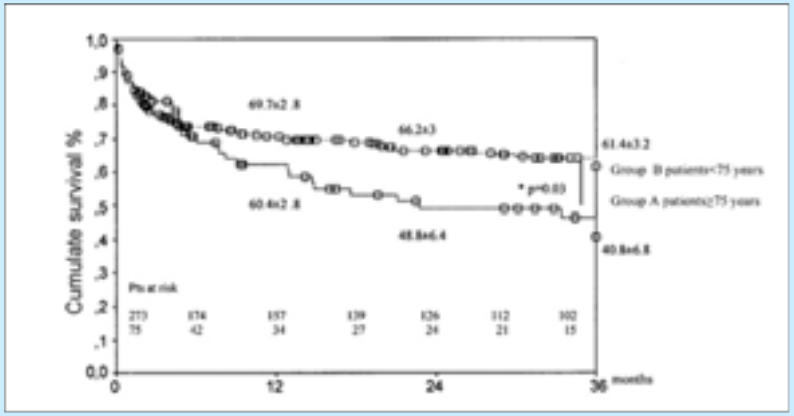
Arch Intern Med. 2009;169(14):1290-1298

- The overall surgery rate (valvular surgery-ablation of pacemaker) was not significantly different between period 1 and period 2 .
- Surgery was performed at a **median time (range) of 14 (0-150) days and 11 (0-76) days after the beginning of antibiotic therapy in the 2 periods, respectively (P=.35)**
- This standardized management is similar to oncological protocols, with drastic monitoring of compliance and codified and standardized therapeutic indications.
- The risk of dying from IE is important, and we believe that it is necessary to have a global standardized management to treat this disease;
- Our management based protocol led to a **2.43-fold decrease in mortality in a 15-year period.**

Infective endocarditis in elderly patients: clinical characteristics and outcome

Jean Paul Remadi[b,*], Georges Nadji[a], Thomas Goissen[a,b], N. Alphonse Zomvuama[b], Claire Sorel[a], Christophe Tribouilloy[a]

European Journal of Cardio-thoracic Surgery 35 (2009) 123–129



Principali osservazioni:

- La presentazione clinica dell'endocardite infettiva acuta dei pazienti anziani è differente da quella dei giovani ed è caratterizzata da un peggior stato clinico e dall'interessamento più frequente del cuore destro;
- La prognosi a lungo termine è peggiore negli anziani
- La chirurgia talvolta non viene considerata per il rischio operatorio proibitivo correlato allo stato clinico dovuto alla sepsi
- Nonostante questo la chirurgia negli anziani è associata ad una miglior sopravvivenza a breve/lungo termine del trattamento medico.

Preoperative risk stratification in infective endocarditis. Does the EuroSCORE model work? Preliminary results☆,☆☆

Carlos A. Mestres*, Miguel A. Castro, Eduardo Bernabeu, Miguel Josa, Ramón Cartañá, José L. Pomar, José M. Miró, Jaime Mulet and the Hospital Clínico Endocarditis Study Group

European Journal of Cardio-thoracic Surgery 32 (2007) 281–285

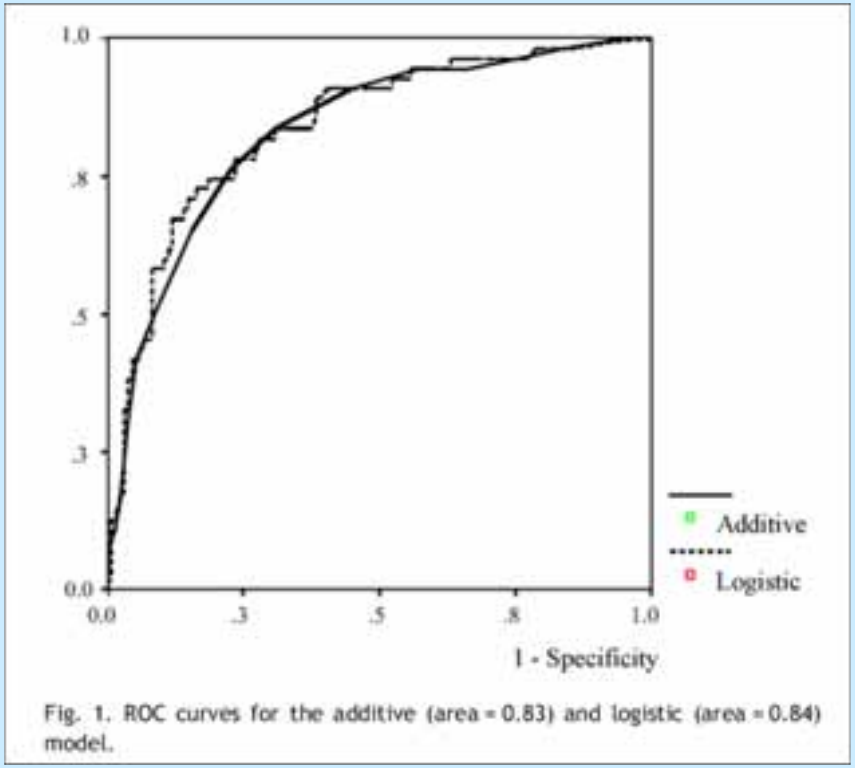


Fig. 1. ROC curves for the additive (area = 0.83) and logistic (area = 0.84) model.

- L'EUROSCORE è in grado di predire in maniera soddisfacente la mortalità perioperatoria nella chirurgia dell'endocardite infettiva.
- L'EUROSCORE, logistico e additivo, ha dimostrato una calibrazione e discriminazione adeguate

Surgical Management of Endocarditis

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Intracranial hemorrhage and mycotic aneurysms

1. Heparin is the major modifiable risk factor for brain hemorrhage in IE. It should be used cautiously in all patients, and should be withheld for 4 weeks after brain hemorrhage in the context of IE. (Class I, B)
2. For patients with IE and intracranial hemorrhage, catheter angiography should be performed to rule out MA with consideration of surgical or endovascular therapy. (Class 1, B)
3. Once patients with IE but without neurological symptoms have been screened to identify MA, it may be reasonable to follow mycotic aneuysms non-invasively to rule out aneurysmal expansion during antibiotic therapy. (Class IIb, C).
4. Aneurysms that expand during antibiotic therapy may be considered for surgical therapy. It may be reasonable to follow conservatively aneurysms that remain stable or decrease in size during antibiotic treatment. (Class IIb, C)

Surgical Management of Endocarditis

THE SOCIETY OF THORACIC SURGEONS CLINICAL PRACTICE GUIDELINE

Radiographic evaluation of patients with endocarditis and stroke

1. Brain imaging is required if there is suspicion of stroke in the setting of endocarditis. Either MRI or CT is an acceptable initial study. (Class 1,B)
2. If MRI is chosen, Diffusion Weighted Imaging, FLAIR imaging, Gradient Echo Imaging, and a post-contrast study, should be performed. (Class 1,B)
3. If MRI is not feasible, CT should be performed. (Class 1, B)
4. Vascular imaging should be performed contemporaneously with brain imaging. MRA and CTA are both acceptable vascular imaging modalities to screen for mycotic aneurysm in patients without evidence of intracranial hemorrhage. (Class 1,C)
5. It is reasonable to reserve Catheter Angiography for patients with evidence of intracranial bleeding, or non-invasive vascular imaging suggestive of mycotic aneurysm. (Class IIa, C)

Surgical Management of Endocarditis

THE SOCIETY OF THORACIC SURGEONS CLINICAL PRACTICE GUIDELINE

Timing of surgery in patients with neurologic complications

- In general, patients with ischemic stroke should be treated with antibiotics and followed with serial brain imaging and serial TEE.
- Valve replacement surgery should be delayed for four weeks unless a second embolic event occurs despite adequate antibiotic therapy.
- Surgery may be considered sooner if vegetations enlarge during therapy or if infection, monitored by blood cultures, persists despite antibiotic therapy.
- Delaying surgery by 3-4 weeks, if the patient is hemodynamically stable, lowers the risk of neurological complications to that seen in patients without a history of ischemic stroke.
- Decisions about the timing of surgery are complex and should be made by a multidisciplinary team.