Nosocomial Endocarditis: the changing face of high-risk outcome

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No conflicts of interest to declare

ce of infective endocarditis

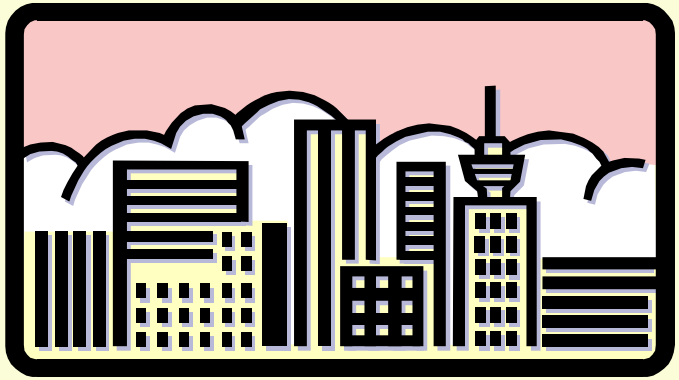
chero

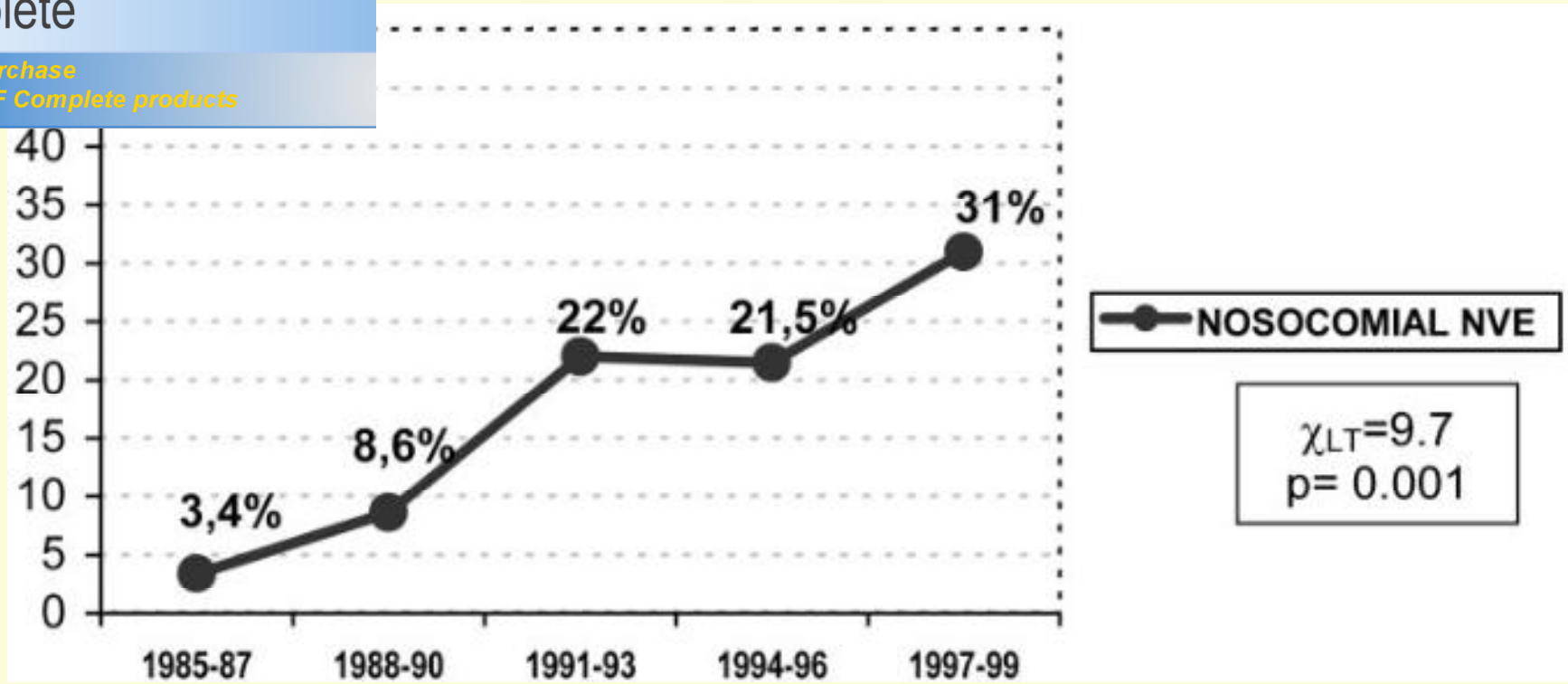
Heart 2006;92:1365–1366. doi: 10.1136/hrt.2006.092635

Infective endocarditis is a disease that continues to evolve in response to changing host conditions and other factors

the development of the disease.[2 8 11 12] Limited data are available on other subgroups at risk of IE, such as those with congenital heart disease, where the frequency of endocarditis could be

- **Population ageing**
- **Medical care**
- **Also without predisposing heart disease**
- **Often with prosthetic material (valves or devices)**
- **Different infectious sources**
- **Common acute forms**



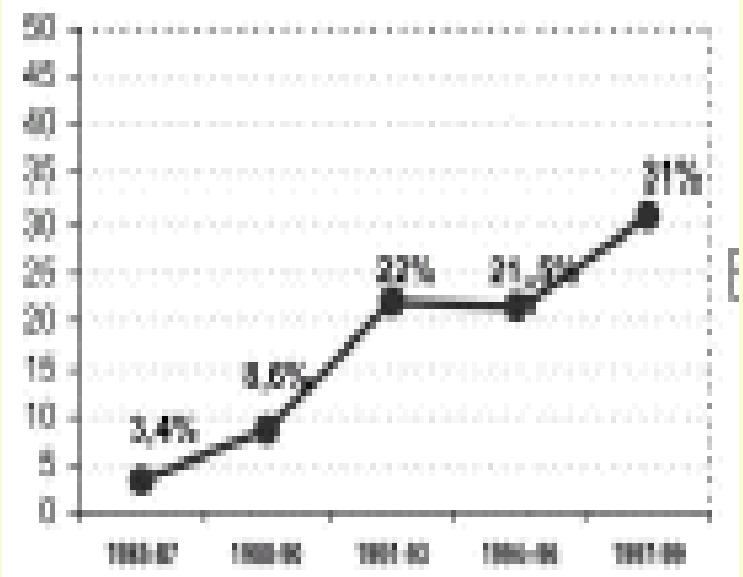


Martin-Davila P. Chest 2005; 128:772-779

	Health care	Nosoco-miale	Nosous-siale
ICE. 1620 cases	34%	19%	15%
RIEI. 682 cases	24%	13%	11%

HCARE ASSOCIATED IE IS CORRELATED TO

- Healthcare-associated bloodstream infections
- Patients admitted to ICUs
- Invasive interventions
- Degenerative valve diseases in the elderly
- Prosthetic valves and devices



Martin-Davila P. Chest 2005;128;772.
Fowler VG. JAMA 2005; 293:3012

Health care associated endocarditis

1620 PAZIENTI

Benito N. Ann Intern Med. 2009;150:586-594.

	Nosocomial	Non nosocomial	P
Mean age	66	58	<0.001
Hemodialysis	28 (9%)	138(54%)	<0.001
Diabetes mellitus	60(20%)	77(31%)	0.003
Immunosoppressive therapy	33(11%)	48(19%)	0.007
Predisposing valvular disease	144(38%)	73(29%)	0.023
Non dental proc.	136(48%)	78(35%)	0.002
Intravasc cath.	134(44%)	137(54%)	0.022

aphic Findings in Patients With NVE*

Characteristic	All Patients With NVE, *n/n* (%)		*P* Value	Patients With Health Care–Associated NVE, *n/n* (%)		*P* Value
	Community-Associated	Health Care–Associated		Nosocomial	Non-nosocomial	
Clinical findings at presentation						
Fever	913/945 (96)	461/489 (94)	0.23	257/273 (94)	204/216 (94)	0.89
New murmur or worsening of old murmur	609/881 (69)	272/456 (60)	0.001	137/250 (55)	135/206 (66)	0.020
Vascular or immunologic evidence of endocarditis†	275/1028 (27)	117/538 (22)	0.030	62/289 (21)	55/249 (22)	0.86
Splenomegaly	131/1027 (13)	44/537 (8)	0.007	27/288 (9)	17/249 (7)	0.28
Echocardiographic findings						
Vegetations	952/1058 (90)	510/554 (92)	0.173	276/301 (92)	324/253 (92)	0.73
Mitral valve	503/1049 (48)	277/547 (51)	0.31	149/297 (50)	128/250 (51)	0.81
Aortic valve	474/1049 (45)	193/547 (35)	<0.001	102/297 (34)	91/250 (36)	0.62
Tricuspid valve	76/1048 (7)	85/547 (16)	<0.001	53/297 (18)	32/250 (13)	0.105
Pulmonary valve	15/1048 (1)	4/547 (1)	0.22	3/297 (1)	1/250 (0.4)	0.40
Paravalvular complications‡	245/1044 (23)	107/545 (20)	0.081	63/293 (22)	44/252 (17)	0.23

***Benito N. Ann Intern Med.* 2009;150:586-594.**

Health care associated endocarditis

1620 patients

	Comunità	Health care -associated	P
St. aureus	20%	45%	<0.001
MRSA	12%	47%	<0.001
Enterococci	9%	15%	<0.001
St. Coagulasi -	6%	13%	<0.001
Str. Viridans	28%	8%	<0.001
Blood culture -	11%	5%	<0.001

Benito N. Ann Intern Med. 2009;150:586-594.

Health care associated endocarditis. Outcome. 1620 PAZIENTI

	Comunity	Health care -associated	P
Surgery	51%	41%	<0.001
Heart failure	34%	37%	NS
Stroke	17%	20%	NS
Syst. embolizat	24%	21%	NS
Persistent bacteremia	4%	18%	<0.001
Abscess	13%	12%	NS
In-hospital death	13%	25%	<0.001

Benito N. Ann Intern Med. 2009;150:586-594.

Multivariate risk factor for death

Acquisition of Infection		
Community	1.00 (reference)	
Health care–associated	1.28 (1.02–1.59)	0.030
Age (≥60 y)	1.52 (1.27–1.82)	<0.001
Male sex	1.03 (0.80–1.32)	0.82
Diabetes	1.55 (1.11–2.17)	0.011
Cancer	0.97 (0.69–1.36)	0.86
Immunosuppressive therapy	1.25 (0.98–1.61)	0.075
Staphylococcus aureus	1.59 (1.27–2.00)	<0.001
Paravalvular abscess	1.47 (1.09–1.98)	0.012
Surgery	0.68 (0.55–0.85)	0.001
Stroke	2.00 (1.57–2.55)	<0.001
Heart failure	2.46 (1.97–3.07)	<0.001
New conduction abnormality	1.52 (1.02–2.25)	0.040

***Benito N. Ann Intern Med.* 2009;150:586-594**

rditis in the real world: the Italian Registry ocarditis (Registro Italiano Endocardite Infettiva – RIEI)

Enrico Cecchi[a], Massimo Imazio[a], Francesco Giuseppe De Rosa[b], Fabio Chirillo[c], Francesco Enia[d], Daniela Pavan[e], Moreno Cecconi[f], Angelo Squeri[g] and Rita Trinchero[a]

In the last 30 years, major improvements have been recorded on the pathogenesis, diagnosis and treatment of infective endocarditis. Nevertheless, mortality still remains high, close to 30–40% at 1 year, and its reduction remains the main challenge over the next years. Moreover, important epidemiological changes have been recorded. Social changes of Western countries have determined an increase of the mean length of life, and thus of degenerative valvular diseases, whereas rheumatic heart disease is almost disappeared. Increasing medicalization has determined a rise of complications and diseases related to longer hospital stay, surgical therapies and other invasive interventions. At the same time, there is an increase of immunosuppressive therapies, diseases such as cancer, endocarditis (RIEI) will overcome these limitations and provide a wide picture of the national presentation of the disease. The aim of the registry is to improve the management of infective endocarditis, through a better comprehension of demographic, clinical, therapeutic and prognostic features of the disease in the real world. The background, rationale, aims and expected results of the registry are reviewed. *J Cardiovasc Med* 9:000–000 © 2008 Italian Federation of Cardiology.

Journal of Cardiovascular Medicine 2008, 9:000–000

Keywords: endocarditis, management, prognosis, prophylaxis, registry, therapy

682 Episodes. **16 Centres.**

RIEI

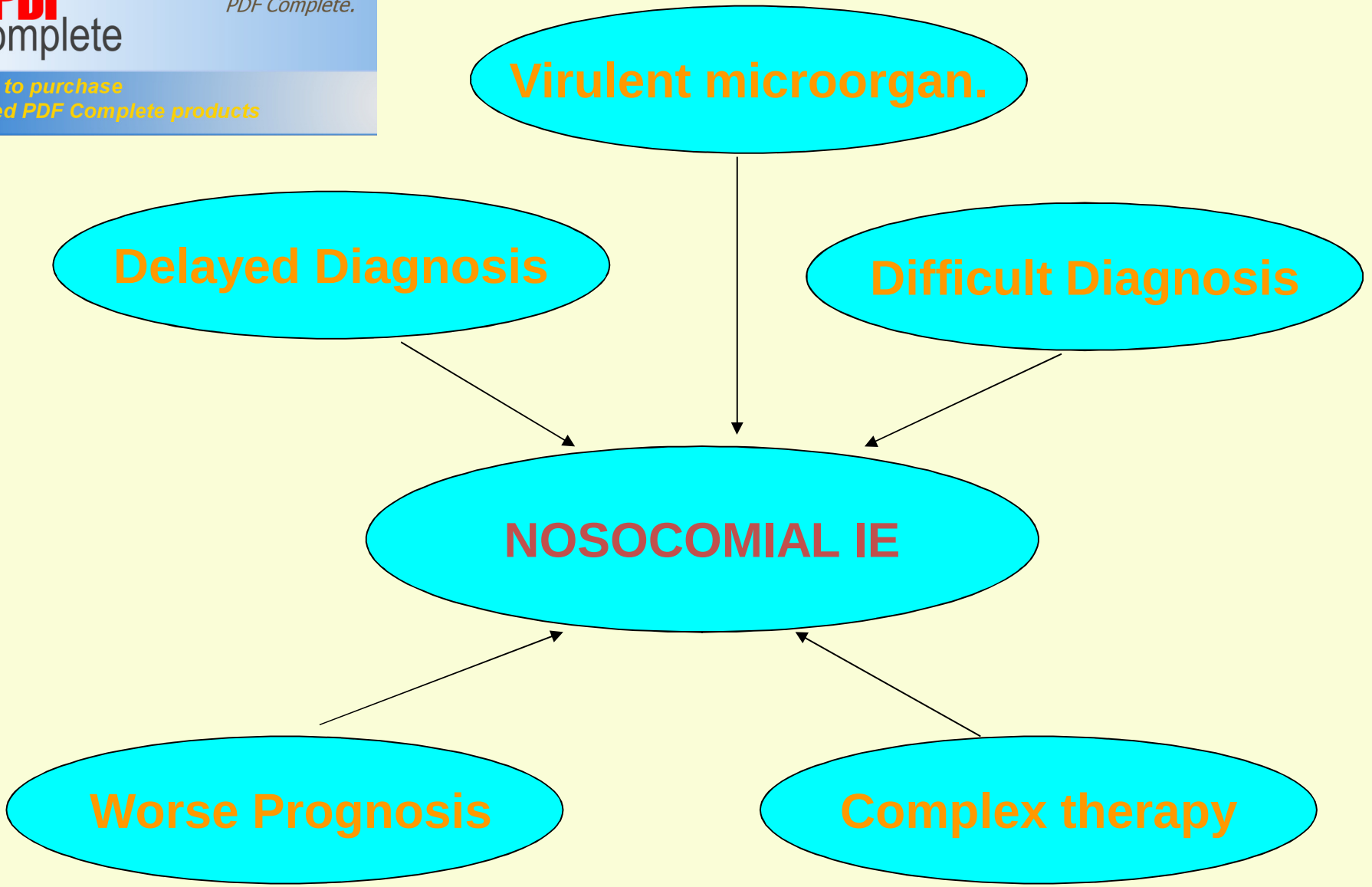
682 Cases (90 excluded)

	Community IE	Health care IE	P	Non Nosocomial IE	Nosocomial IE	P
Age						
Hemodialysis	0	17(11%)		11(14%)	6(7%)	NS
Immunosuppressive Th.	11(3%)	10(6%)	NS	3(4%)	7(8%)	NS
Predisposing Cardiop.	255(60%)	99(62)	NS	50(66%)	49(59%)	NS
Non dental proc.	20(5%)	87(55%)	<0.001	35(46%)	52(63%)	<0.05
Intravasc Access	65(15%)	74(47%)	<0.001	31(41%)	43(52%)	NS
New murmur	154(36%)	52(33%)	NS	27(36%)	25(30%)	NS
Inflammation	378(89%)	122(77%)	<0.001	48(63%)	74(89%)	<0.001
Embolic event	90(21%)	30(19%)	NS	12(16%)	18(22%)	NS
Splenomegaly	79(19%)	18(11%)	<0.03	12(16%)	6(7%)	NS

RIEI

682 Cases (90 excluded)

	Community IE	Health care IE	P	Non Nosocomial IE	Nosocomial IE	P
St. aureus	83(19%)	38(24%)	NS	15(20%)	23(28%)	NS
MRSA	10(2%)	16(10%)	<0.001	5(7%)	11(13%)	NS
St. Coagulasi neg	60(14%)	28(18%)	NS	12(16%)	16(19%)	NS
Enterococci	44(10%)	20(13%)	NS	11(15%)	9(11%)	NS
Str. viridans	53(12%)	9(6%)	<0.05	4(5%)	5(6%)	NS
Surgery	234(55%)	86(54%)	NS	42(55%)	44(53%)	NS
Heart failure	110(26%)	42(26%)	NS	25(33%)	17(20%)	NS
Stroke	48(11%)	15(9%)	NS	5(7%)	10(12%)	NS
Abscess	51(12%)	21(13%)	NS	11(15%)	10(12%)	NS
In-hospital death	49(12%)	31(19%)	<0.05	20(26%)	11(13%)	NS (0.06)



What to do?

- **Prophylaxis**
- **Improvement of early diagnosis and start of appropriate therapies**
- **Multidisciplinar Team**
- **Risk stratification of patients at high risk for surgery**

Staphylococcus aureus bacteremia

+

Prosthetic valves

Pacemakers

Worse outcome

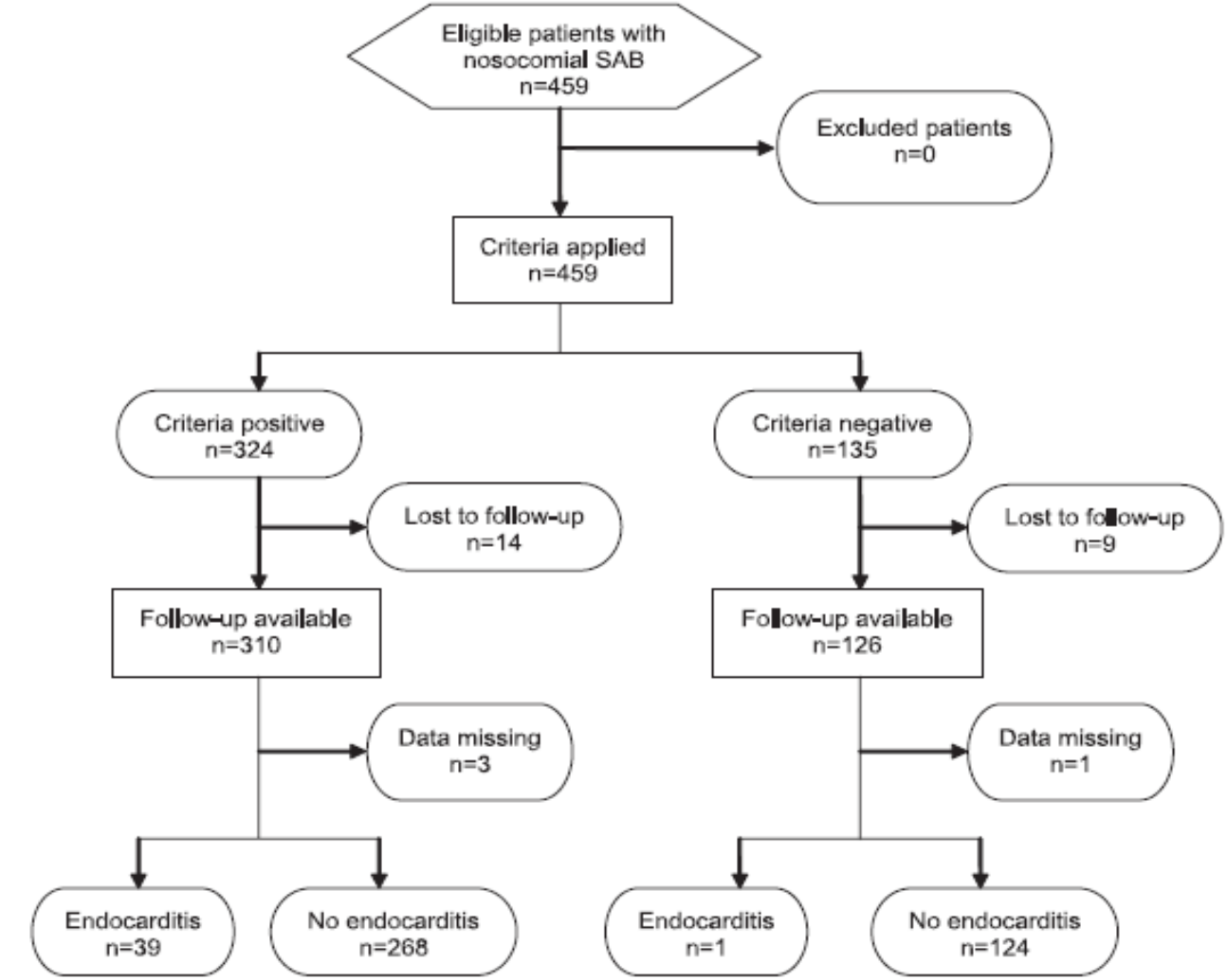
Dialysis

High risk of IE

Siegman-Igra Y. J Clin MIcrobiol 1997;35:928.

Simple Criteria Set for Guiding iography in Nosocomial *Staphylococcus aureus* Bacteremia

- **Persistent bacteremia**
- **Intracardiac device**
- **Hemodialysis**
- **Spinal infection**
- **Nonvertebral osteomyelitis**

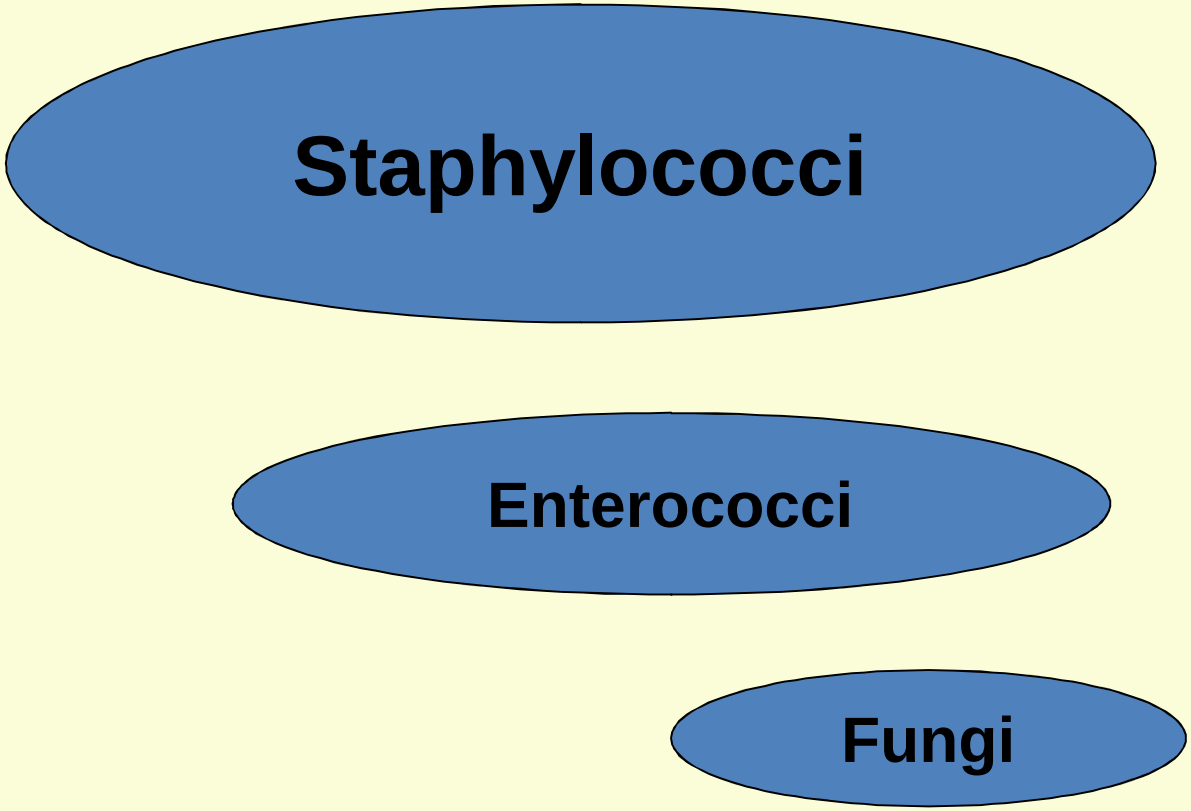


Kaarsh AJ et al. Clinical Infectious Diseases 2011; 53:1-9

Sources of bacteremia

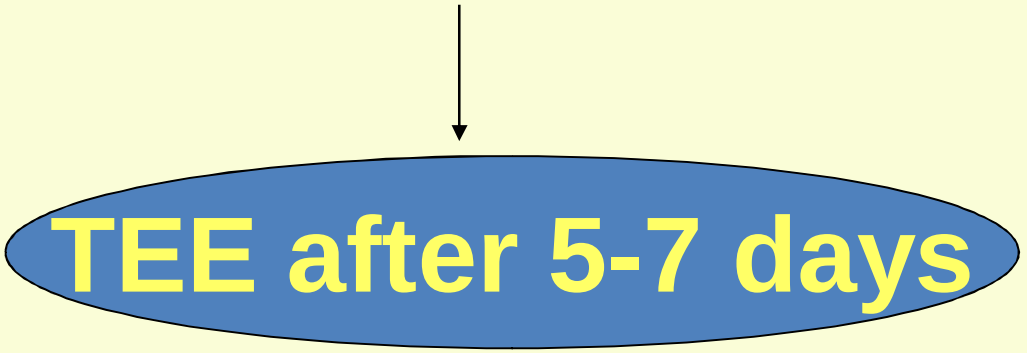
Endovascular devices	Central iv lines
	Peripheral iv lines
	Pacemakers
	Swan Ganz cat
	Angiography
AV FISTULA- HEMODIALYSIS	
Genitourinary surgery/interv.	
Gastrointestinal surgery/interv.	
Cardiac surgery	
Wounds and skin infections	

Infected catheters ---> 2/3 of Nosocomial IE



Fernandez-Guerrero ML. Clin Infect Dis 1995;20: 16-23

FUNGEMIA, PERSISTENT BACTEREMIA



Unless

Recovery after 72 h from catheter removal without predisposing heart diseases and without clinical features of IE

Non-cardiac surgery

- General preventive issues
- Prompt treatment of concomitant infections
- Antibiotic prophylaxis for infected wounds
- In high risk patients antibiotic prophylaxis for Staphylococci-Enterococci
- Treatment of nasal mucosa with mupirocin and use of clorexidin for skin washing *

*Bode LGM. Preventing surgical-site infections in nasal carriers of Staphilococcus aureus . N Engl J Med 2010; 362:9-17

Early diagnosis

- Early suspicion for high risk patients
- Prolonged infections of catheters with microorganisms responsible for IE
- Bacteremia from Staphylococcus aureus, Enterococci, other Staphylococci, and fungi
- Early blood cultures and serology
- PCR
- Early access to echocardiography

eduction in Infective s–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

Background: Despite improvements in medical and surgical therapy, infective endocarditis (IE) is still associated with a severe prognosis and remains a therapeutic challenge. We aimed to evaluate the impact of a standardized diagnostic and therapeutic protocol on mortality and to correlate the outcome with compliance with our management-based protocol.

Methods: We conducted an observational before-after study that included 333 consecutive patients treated for IE at a referral center from 1991 to 2006, which was divided into 2 periods: period 1 (1991-2001), before implementation of our therapeutic protocol (n=173), and period 2 (2002-2006), after implementation of our protocol (n=160). Our protocol was created by a multidisciplinary task force including a sampling of biological specimens, the use of only 4 antimicrobial agents, a standardized duration of treatment, standardized surgical indications, and 1 year of close follow-up. Because our protocol was based on a local consensus by physicians and surgeons, it was not possible to randomize the study.

Results: The 1-year mortality significantly decreased from 18.5% during period 1 to 8.2% during period 2 (hazard ratio, 0.41; 95% confidence interval, 0.21-0.79 [*P*=.008]). After multivariable analysis, the management during period 2 remained a strong protective factor (adjusted hazard ratio, 0.26; 95% confidence interval, 0.09-0.76 [*P*=.01]). During period 2, we observed a statistically significantly better compliance in antimicrobial therapy and fewer cases of renal failure. Deaths by embolic events and multiple organ failure syndrome also significantly decreased during period 2.

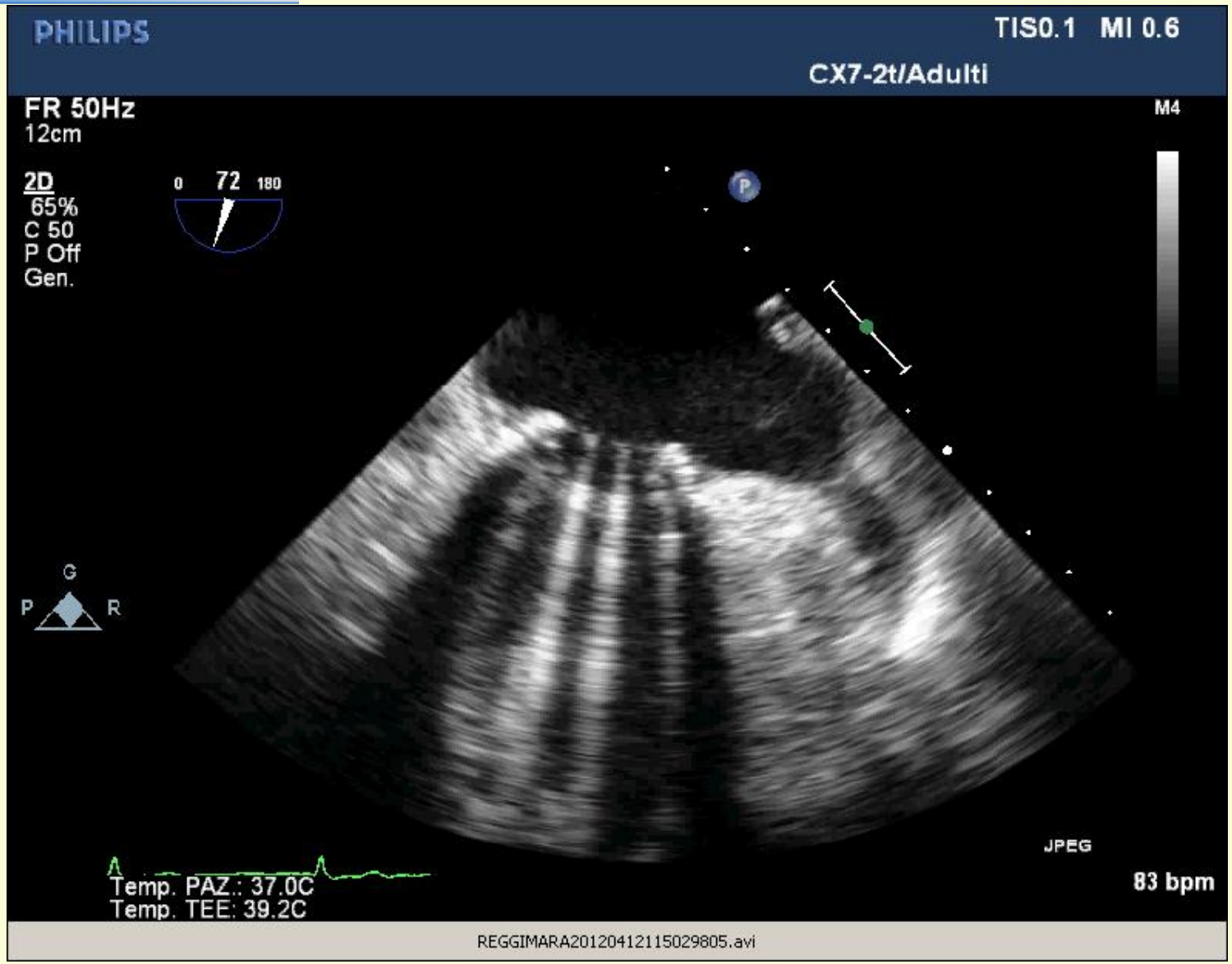
Conclusion: A dramatic reduction in mortality was observed during this study, suggesting that a management-based approach has a significant impact on IE outcome.

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

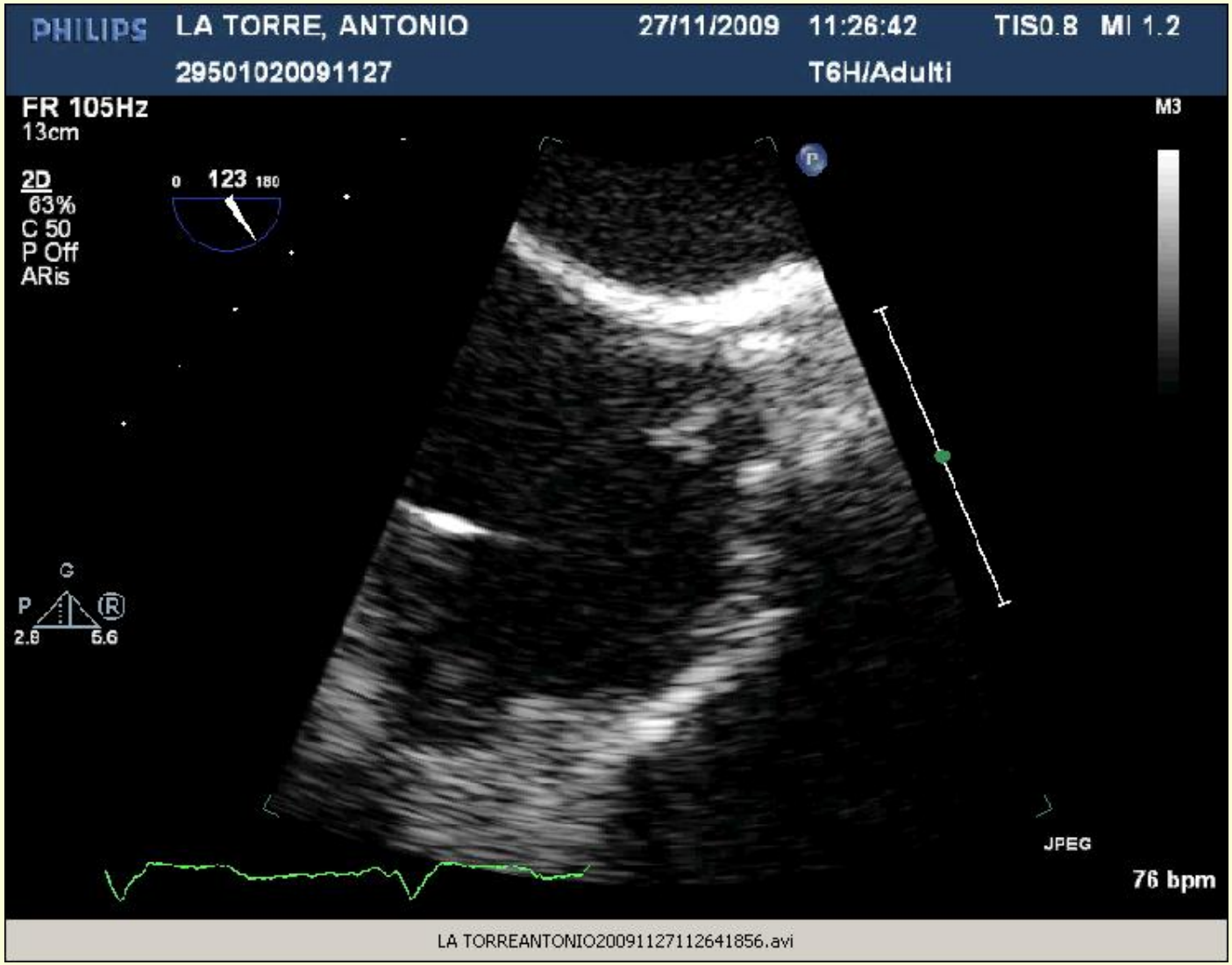
ISATION OF A SURGICAL APPROACH

- Identification of high risk patients
- Indications to surgery vs risks
- Each case discussed by a multidisciplinary team

Prosthetic valve IE



DEVICE



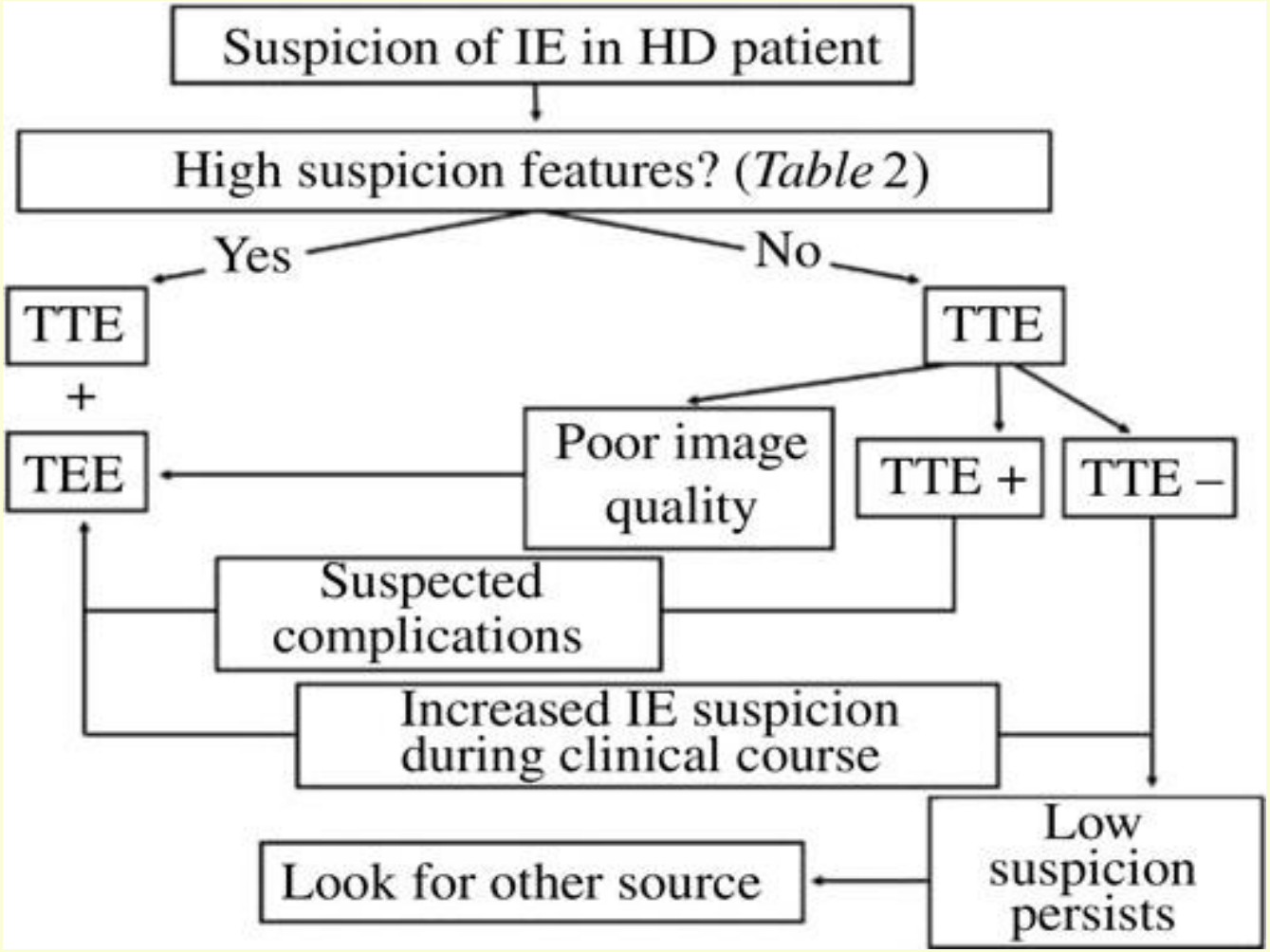
ICE. Athan E. JAMA 2012; 307: 1727-35.

HEMODIALYSIS (HD)

- Peculiar features
- IE incidence increased in end stage renal disease, especially in HD
- > incidence of degenerative valve disease
- Staphylococcus aureus in 75% of cases with HD
- MRSA are increasing: 50% according to some AA

Nucifora G, Badano L P. Eur Heart J 2007; 28: 2307-12

HEMODIALYSIS (HD) DIAGNOSIS



Nucifora G, Badano L P. Eur Heart J 2007; 28: 2307-12

HEMODIALYSIS (HD) DIAGNOSIS

Table 2 High suspicion features for infective endocarditis mandating transoesophageal echocardiography after transthoracic echocardiography in chronic haemodialysis patients

Presence of new-onset congestive heart failure
Presence of stigmata of endocarditis
Development of HD-related hypotension, particularly in a previously hypertensive patient
Prior or repeated past episodes of IE
Prior valvular surgery
Typical organisms for IE (i.e. *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Enterococcus* species, and *Streptococcus* species) as causative pathogens
Relapsing bacteraemia after antibiotic discontinuation, regardless of the causative pathogen
Patients with HD catheters

HD, haemodialysis; IE, infective endocarditis.

Nucifora G, Badano L P. Eur Heart J 2007; 28: 2307-12

Health care associated IE

- 1/3 of all IE on native heart valves
- *Stafilococcus aureus* is the most important cause
- Clinical features are distinctive and different from those acquired in community
- Incidence is increasing and mortality is elevated

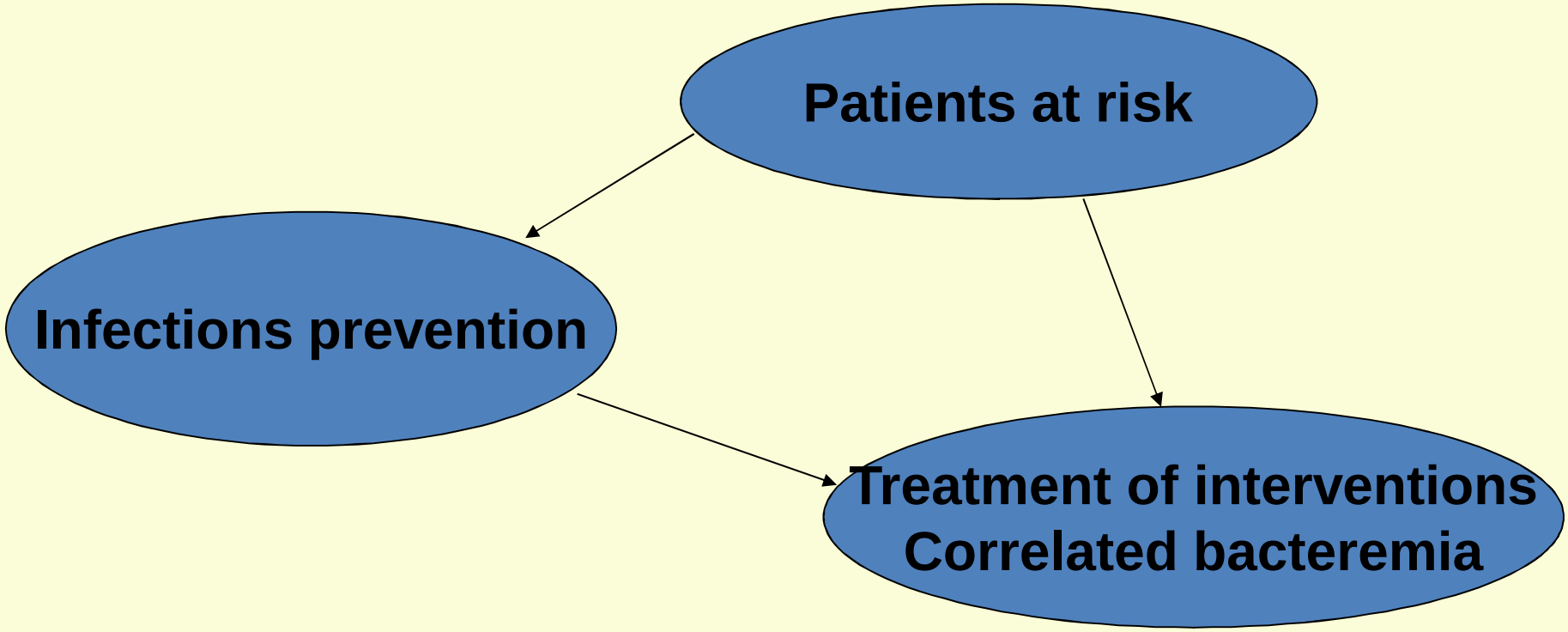
CONCLUSIONS

- **Health-care IE: a consequence of medical progress with a high risk outcome**

- **Prevention and prophylaxis**
- **Early suspicion and diagnosis**
- **Multisciplinary team**
- **Case by case discussion about therapy and surgery**

...prevention possible?

NOSOCOMIAL EI: Infectious origin often identified



HEMODIALYSIS (HD) TREATMENT

- MSSA: OXACILLIN OR CEFAZOLIN
- MRSA: VANCOMYCIN
- REMOVAL OF HD CATHETERS: ?
- SURGERY: ?
- EARLY SURGERY: ?
- TYPE OF PROSTHESIS: BIOLOGIC

- PROPHILAXIS: YES

HD IE.

POORER EARLY AND LATE PROGNOSIS

Table 3 Clinical and echocardiographic prognostic factors for early and late mortality among haemodialysis patients with infective endocarditis

Early mortality	Late mortality
Septic embolism	Age >65 years
Mitral valve involvement	Diabetes as cause of ESRD
Vegetation size >2 cm^3 at TEE	Cerebrovascular accident/transient ischaemic attack
	Mitral valve involvement (especially if mitral annular calcification or severe mitral valvular regurgitation)
	IE related to MRSA and VRE

Data from McCarthy and Steckelberg,[1] Maraj *et al.*,[4] Nori *et al.*,[24] and Shroff *et al.*[31]

ESRD, end-stage renal disease; MRSA, methicillin-resistant *Staphylococcus aureus*; TEE, transoesophageal echocardiography; VRE, vancomycin-resistant *Enterococcus* sp.

Nucifora G, Badano L P. Eur Heart J 2007; 28: 2307-12