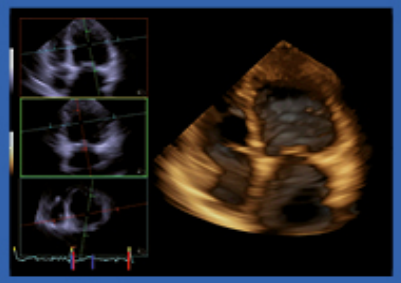


# EuroValve

March 27 - 28, 2015

## How to Manage Anticoagulant Therapy in Valve Disease

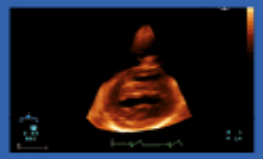
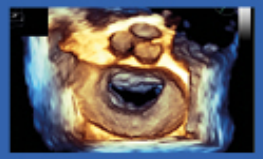
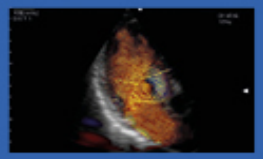
## Infective Endocarditis


**Dr Bernard Prendergast DM FRCP FESC**

**St Thomas' Hospital**

**London UK**



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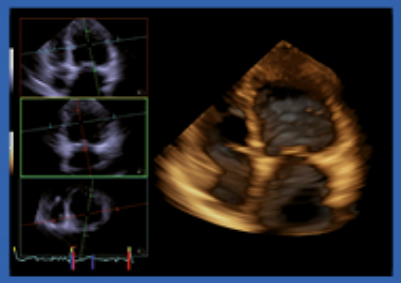

# EuroValve

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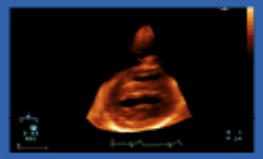
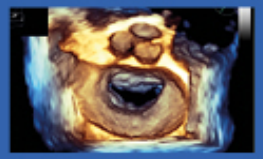
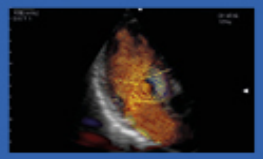
## Faculty disclosure

***Bernard Prendergast***

*I disclose the following financial relationships:*

**No conflict of interest to declare**

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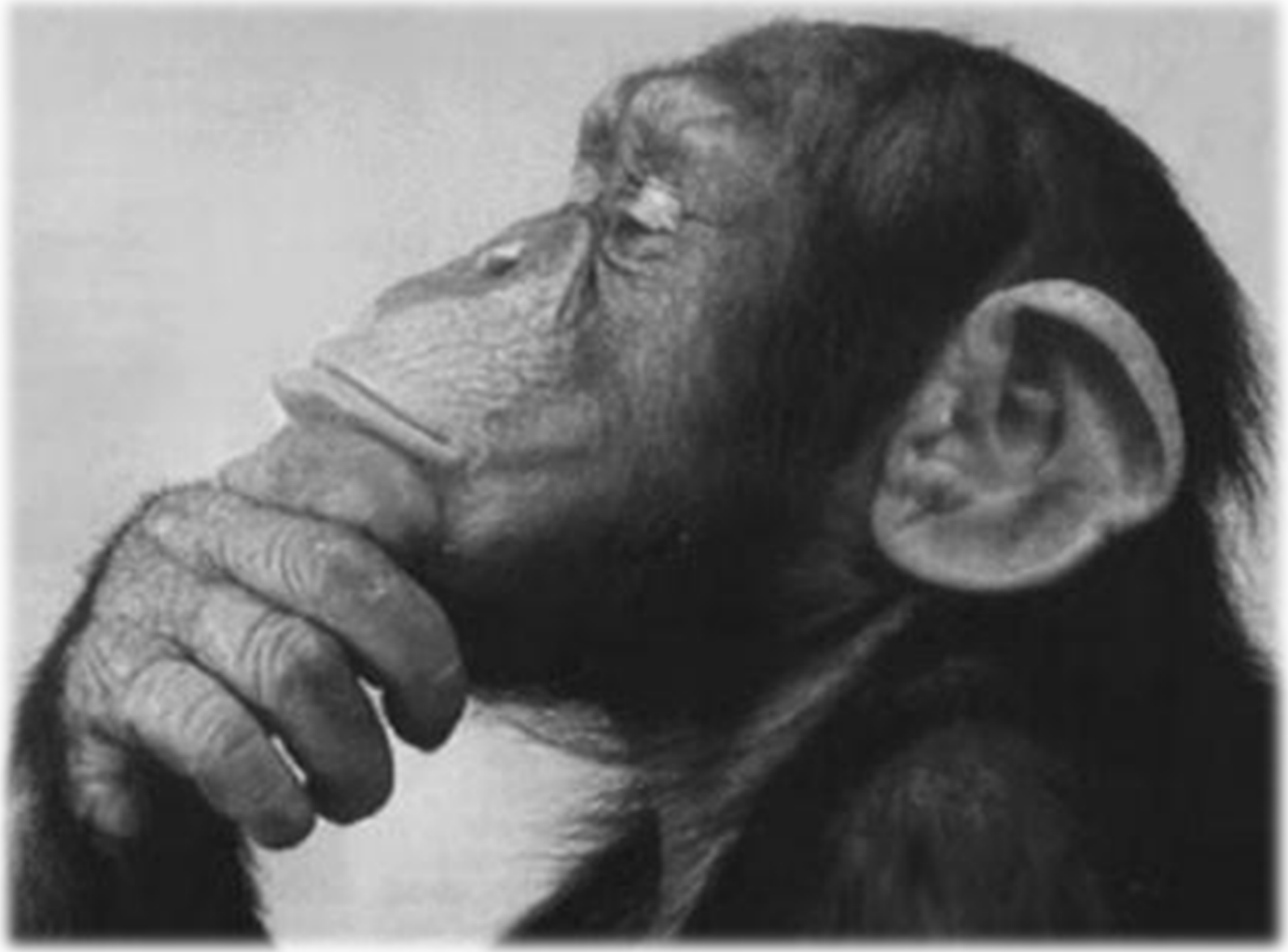
# Anticoagulation in Infective Endocarditis

## *What are the issues?*



# Anticoagulation in Infective Endocarditis
## *What are the issues?*

- Are there scenarios where introduction of antithrombotic or anticoagulant medication could reduce the risk of systemic embolism in IE?
- How do we manage patients with IE who are already taking antithrombotic or anticoagulant medication?
- Are there specific scenarios where special caution is required?

European Heart Journal
doi:10.1093/eurheartj/ehp285

ESC GUIDELINES

# Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)

## The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC)

### Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and by the International Society of Chemotherapy (ISC) for Infection and Cancer

Authors/Task Force Members: Gilbert Habib (Chairperson) (France)*, Bruno Hoen (France), Pilar Tornos (Spain), Franck Thuny (France), Bernard Prendergast (UK), Isidre Vilacosta (Spain), Philippe Moreillon (Switzerland), Manuel de Jesus Antunes (Portugal), Ulf Thilen (Sweden), John Lekakis (Greece), Maria Lengyel (Hungary), Ludwig Müller (Austria), Christoph K. Naber (Germany), Petros Nihoyannopoulos (UK), Anton Moritz (Germany), Jose Luis Zamorano (Spain)

# Summary of the ESC 2009 Guidelines

- There is no indication for the introduction of antithrombotic drugs during the active phase of IE

- Recommendations for the management of anticoagulant therapy are based on low levels of evidence

# Thromboembolism and Bleeding

## *Between the Devil and the Deep Blue Sea*

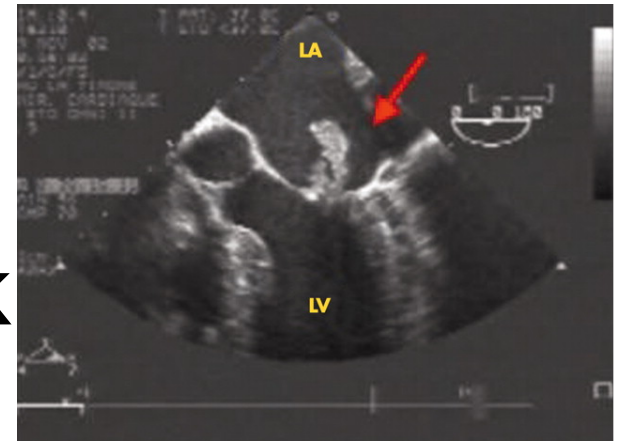
*The Travels of Odysseus: Scylla and Charybdis*

# Embolic risk

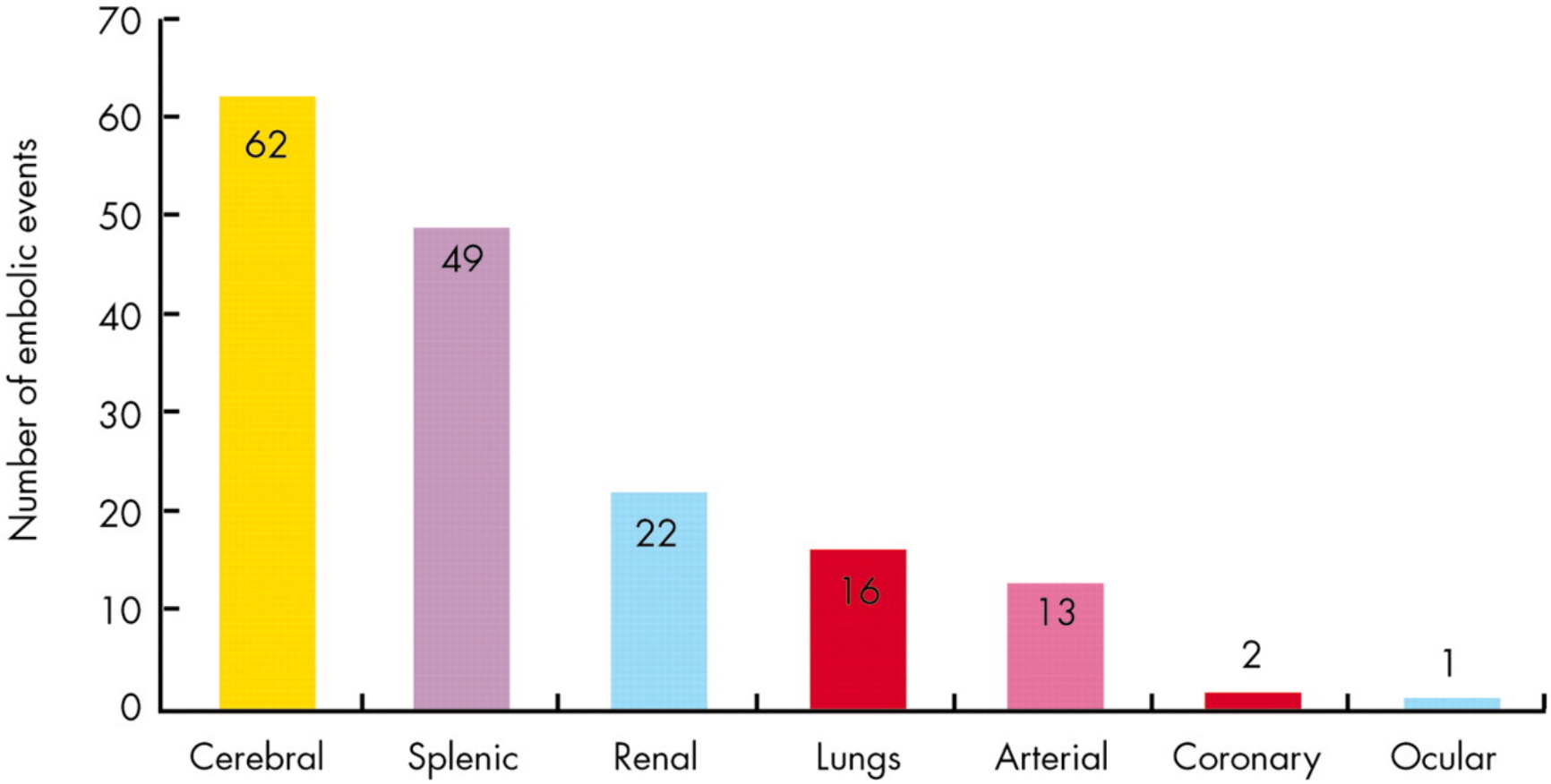
- **Embolic complications are common (22-50%), most frequently affecting the brain**
- **Potential devastating consequences**
- **Risk highest in first 2 weeks and falls rapidly with successful antibiotic therapy**

Dickerman SA. Am Heart J 2007;154:1086-1094.

- **Most common in**
  - **left-sided IE**
  - **staphylococcal, fungal, HACEK**



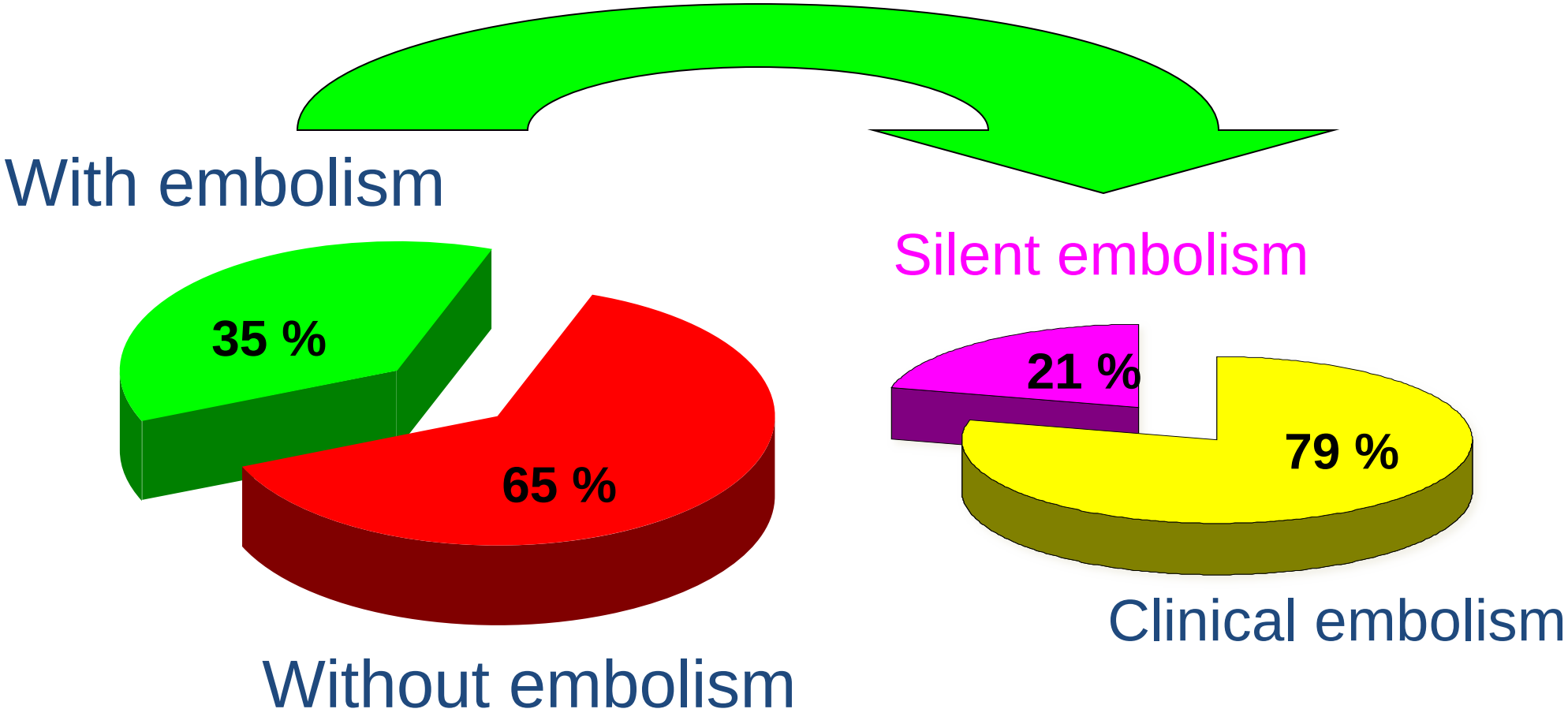
# Distribution of embolic events (n=365)




Overall rate of embolism: 34% (>1 event in some patients)

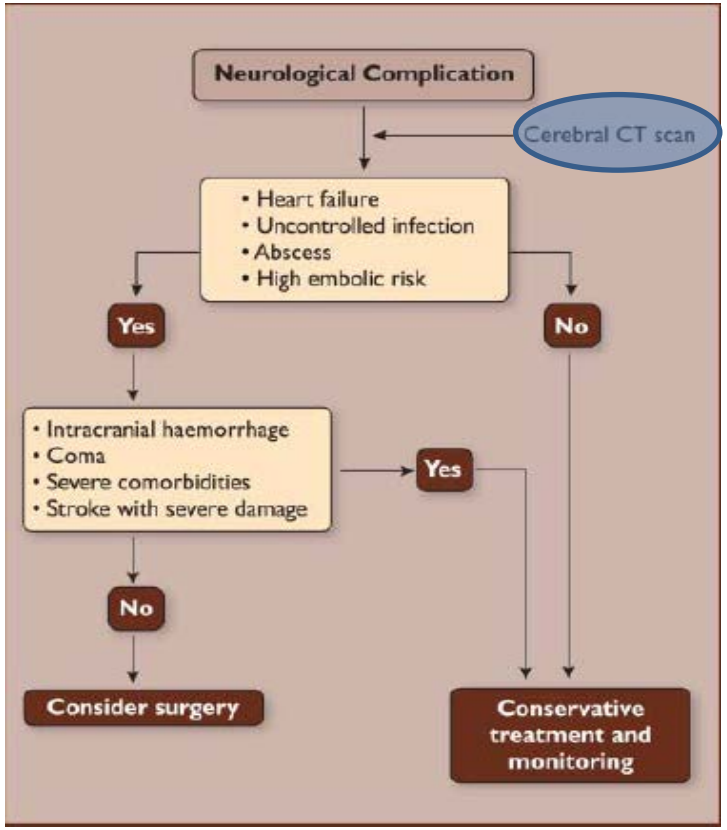
Habib G. Heart 2006;92:124-130.

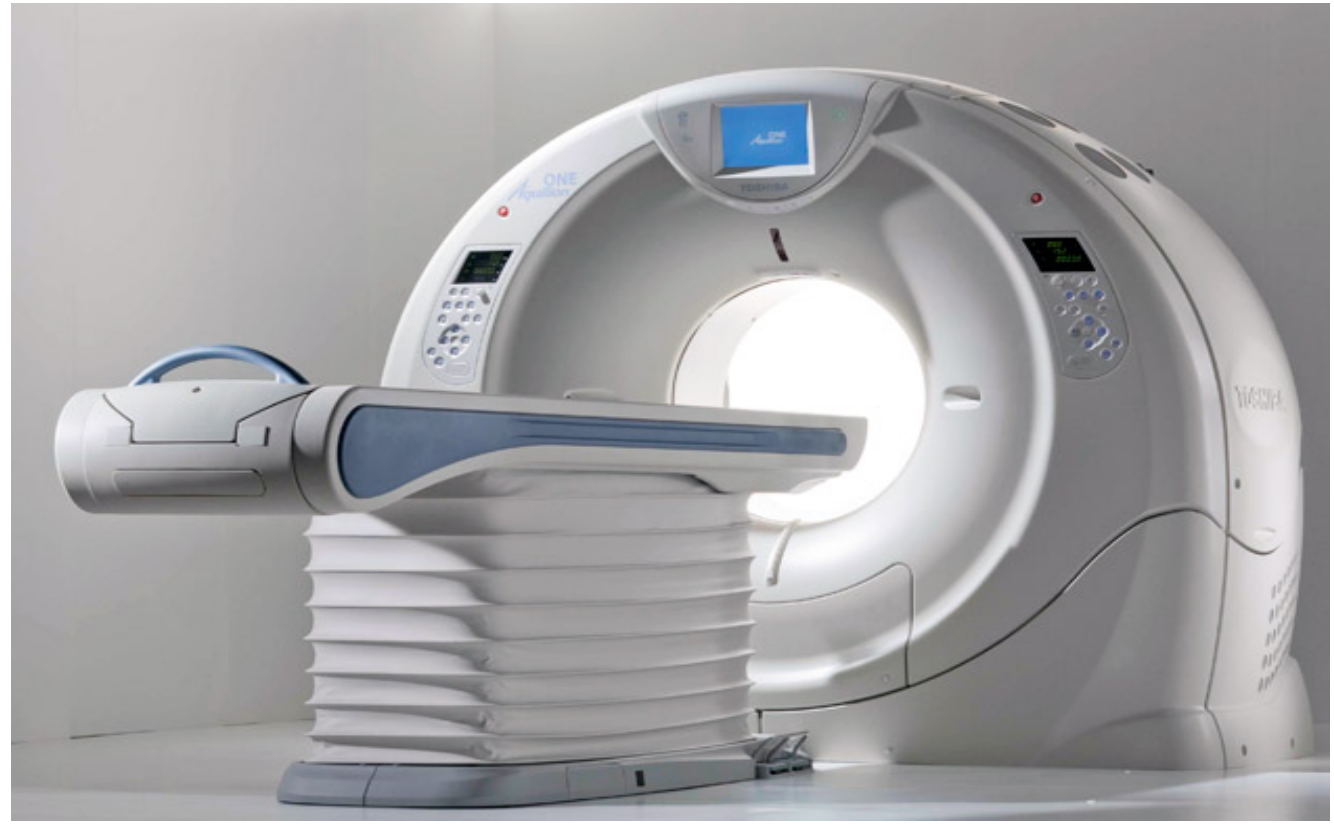
# Overall incidence of embolism



# Neurological complications

- Common: 20-40% of cases (often silent)
- Ischaemic/haemorrhagic stroke or TIA
- Aneurysm/abscess/meningitis/encephalopathy
- Other indications for surgery are frequent
- NO REASON TO DELAY
- Ischaemic stroke: SURGERY
  - Small stroke/TIA: < 3 days
  - Large stroke: surgery after 2-4 weeks
- Hemorrhagic stroke: surgery after 4 weeks



| Recommendations: neurological complications | Class[a] | Level[b] |
|---|---|---|
| After a silent cerebral embolism or transient ischaemic attack, surgery is recommended without delay if an indication remains | I | B |
| Following intracranial haemorrhage, surgery must be postponed for at least one month | I | C |
| Neurosurgery or endovascular therapy are indicated for very large, enlarging, or ruptured intracranial aneurysm | I | C |
| After a stroke, surgery indicated for heart failure, uncontrolled infection, abscess, or persistent high embolic risk should not be delayed.<br>Surgery should be considered as long as coma is absent and cerebral haemorrhage has been excluded by cranial CT | IIa | B |

Habib G et al. Eur Heart J 2009 ;30:2369-2413.

# Can antithrombotic therapy reduce the risk of embolic complications?

- In IE animal models, aspirin
  - reduces vegetation size
  - prevents septic emboli
- In clinical RCTs, aspirin
  - has no net benefit
  - may cause increased bleeding


Chen K-L et al. J Am Coll Cardiol 2003;42:775-780.
Nicolau DP et al. Infect Immun 1993, 61:1593–1595.
Nicolau DP et al. Antimicrob Agents Chemother 1995, 39:1748–1751.

# Can antithrombotic therapy reduce the risk of embolic complications?

**Table 3.** Outcome of Patients With Left-Sided Infective Endocard

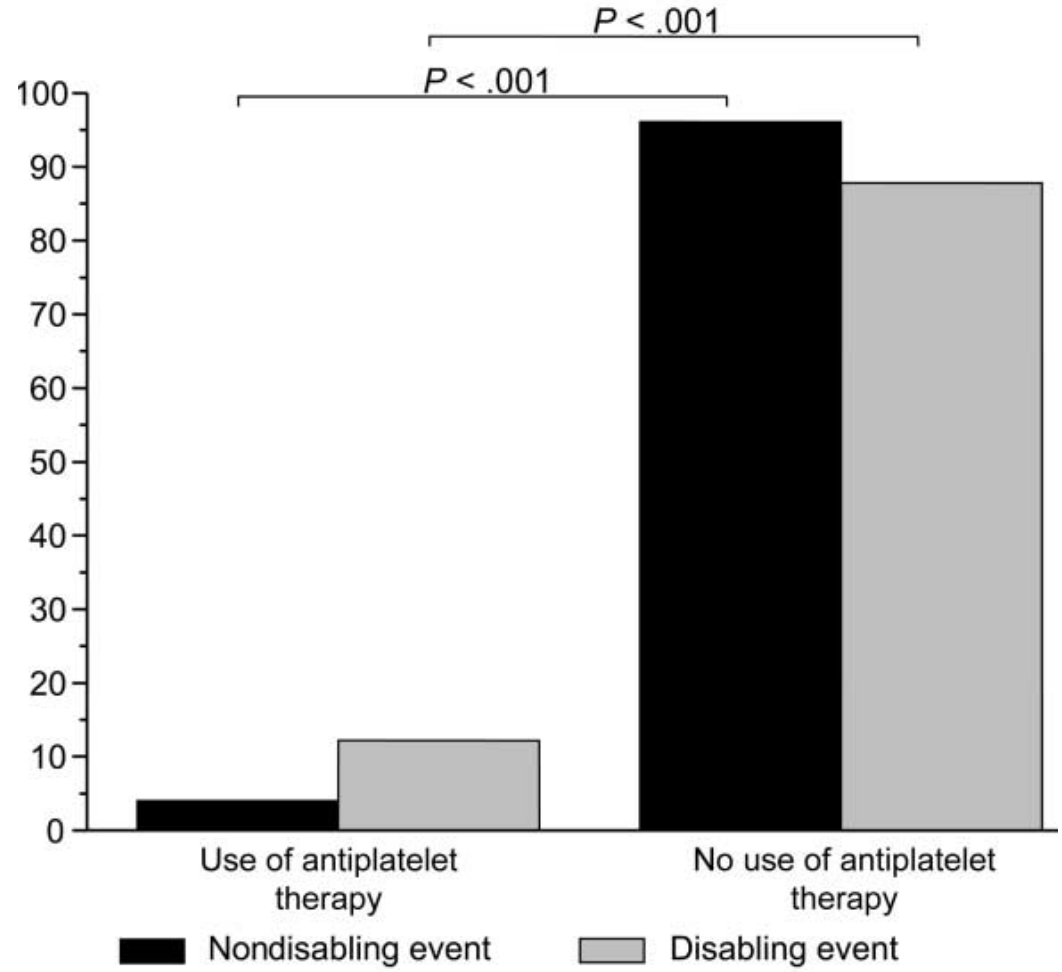
| | Aspirin (n | | CI) | p Value |
|---|---|---|---|---|
| Embolism or intracranial hemorrhage | | | 0 (0.67–3.38) | 0.413 |
| Embolism | | | 1.62 (0.68–3.86) | 0.287 |
| Heart failure | | (30.9) | 1.47 (0.68–3.20) | 0.431 |
| Renal dysfunction | | 16 (29.1) | 0.69 (0.30–1.61) | 0.400 |
| Perivalvular abscess | .1) | 2 (3.6) | 1.42 (0.23–8.83) | 1.000 |
| Valve surgery | 18 (30.5) | 13 (23.6) | 1.42 (0.62–3.26) | 0.528 |
| In-hospital death | 4 (6.7)† | 6 (10.9) | 0.58 (0.16–2.19) | 0.516 |
| Duration of | 5.9 ± 0.9‡ | 5.3 ± 1.0 | — | 0.689 |
| Major | | | | |
| | 7 (11.9) | 3 (5.5) | 2.33 (0.57–9.52) | 0.324 |
| bin or into confined space | 9 (15) | 5 (10.9) | 1.76 (0.55–5.63) | 0.400 |
| Mino | 8 (13.6) | 2 (3.6) | 4.16 (0.84–20.52) | 0.096 |
| Major bleeding | 17 (28.8) | 8 (14.5) | 1.92 (0.76–4.86) | 0.075 |

Aspirin is not indicated as a de novo preventative therapy in IE

Chen K-L et al. J Am Coll Cardiol 2003;42:775-780.

# What about patients already taking antiplatelet therapy?

- Retrospective IE cohort (n=600) at Mayo Clinic sub-divided according to :
  - >6/12 continuous use of antiplatelet therapy
  - Incidence of symptomatic embolism (n=147)




Anavekar NS et al. Clin Infect Dis 2007;44:1180-1186.

# What about patients already taking antiplatelet therapy?

- Retrospective IE cohort (n=600) at Mayo Clinic sub-divided according to :
  - >6/12 continuous use of antiplatelet therapy
  - Incidence of symptomatic embolism (n=147)

- Prospective IE cohort (n=684) Sweden/Denmark
- Logistic regression analysis
- No impact of established anti-platelet therapy on:
  - Incidence of CVC
  - Haemorrhagic complications
  - Mortality

Anavekar NS et al. Clin Infect Dis 2007;44:1180-1186.
Snygg-Martin U et al. Scand J Infect Dis 2011;43:899-904.

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  - Incidence of CVC
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  - Mortality

**It is safe (and may even be beneficial) to continue antiplatelet therapy in IE**

Anavekar NS et al. Clin Infect Dis 2007;44:1180-1186.
Snygg-Martin U et al. Scand J Infect Dis 2011;43:899-904.

# Why is anticoagulation difficult in IE?

- Complex haemodynamics
- Multiple drug interactions (including antibiotics)
- Anticoagulant prescribing by junior medical staff
- Occult cerebral pathology (including aneurysms)
- Risk of bleeding (especially intracranial) highest in:
  - Staphylococcus aureus prosthetic valve IE
  - Previous neurological event

Tornos P et al. Arch Int Med 1999;159:473-475.

# What to do?

**Anticoagulation in Patients With Stroke With Infective Endocarditis Is Safe**

Rasmus Vedby Rasmussen, MD

**Anticoagulation Should Not Be Used in Most Patients With Stroke With Infective Endocarditis**

Cathy Sila, MD

**Anticoagulation in Patients With Stroke With Infective Endocarditis**

**The Sword of Damocles**

Carlos A. Molina, MD, PhD; Magdy H. Selim, MD, PhD

**REMEMBER: *Cerebral haemorrhage is a game changer in IE***

***High mortality and low likelihood of cardiac surgery***

| Strong indication for anticoagulation? | No cerebrovascular complication | Cerebral infarction | Cerebral haemorrhage |
|---|---|---|---|
| Yes (eg. Metallic MVR) | Continue warfarin* | Continue warfarin* | Stop warfarin |
| No (eg. AF) | Stop warfarin | Stop warfarin | Stop warfarin |

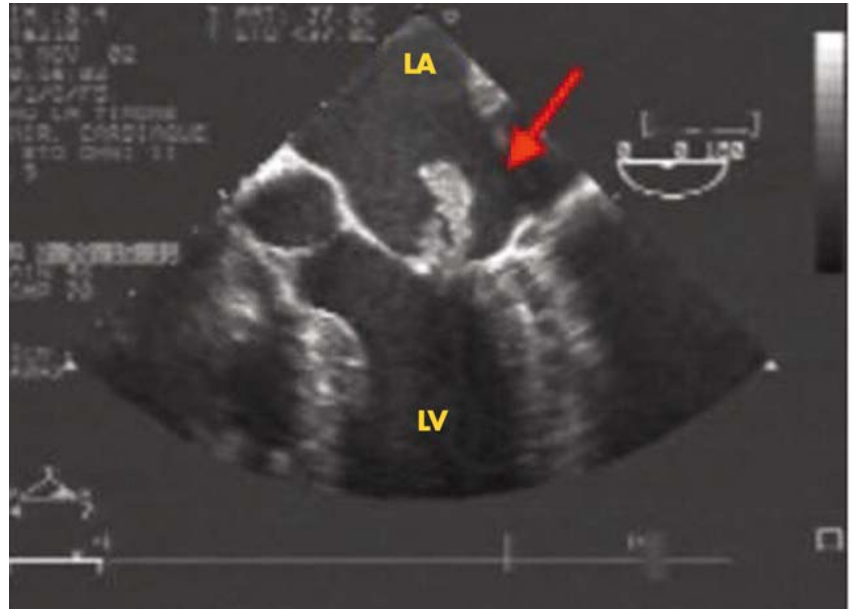
*NB: Switch to unfractionated heparin if early cardiac surgery likely

Stroke 2011:42:1795-6, 1997-8, 1799-800.

# The Fundamental Role of Imaging

- Cerebral
  - Diffusion weighted MRI
  - MR angiography
  - T2 weighted scanning

- Cardiac
  - Location (mitral vs.aortic)
  - Length
  - Mobility
  - Valve lesion
  - Other thromboembolic risks



# ESC Guidelines – the Detail (2015 update awaited)

| Recommendations: antithrombotic therapy | Class[a] | Level[b] |
|---|---|---|
| Interruption of antiplatelet therapy is only recommended in the presence of major bleeding | I | B |
| In ischaemic stroke without cerebral haemorrhage, replacement of oral anticoagulant therapy by unfractionned heparin for 2 weeks is indicated with a close monitoring of activated partial thromboplastin or the activated cephalin clotting time | I | C |
| In intracranial haemorrhage, interruption of all anticoagulation is recommended | I | C |
| In patients with intracranial haemorrhage and a mechanical valve, unfractionated heparin should be reinitiated as soon as possible (with close monitoring of activated partial thromboplastin or activated cephalin clotting time) following multidisciplinary discussion | IIa | C |
| In the absence of stroke, replacement of oral anticoagulant therapy by unfractionned heparin during 2 weeks may be considered in case of *S.aureus* IE with a close monitoring of activated partial thromboplastin or the activated cephalin clotting time | IIb | C |

# Conclusions

- Pre-emptive strategies to prevent embolic complications with *de novo* anti-platelet or anticoagulant therapy are not justified
- Continuation of established antiplatelet therapy is safe (and possibly beneficial)
- *De novo* and continued oral anticoagulation is risky (especially in staphylococcal and prosthetic valve IE) – a tailored approach and judicious use of unfractionated heparin are preferred
- Management of the patient with current or threatened IE-associated cerebral complications should focus on:
  - Accurate neurological diagnosis and state of the art cerebral imaging
  - Prompt antibiotic therapy and consideration of surgery
  - Low threshold for cerebral angiography
  - Consideration of neurovascular interventional options