Endovascular Infections

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Disclosure: Dr. Lynch has no significant financial interest in any of the products or manufacturers mentioned.
Endovascular Infections

- Endocarditis
- Vascular infections
- Device-associated infections
Case 1

- 45 yo woman s/p MVA with ARDS in the ICU
- IJ central line + 2 peripheral lines
- New fever

Does she have a central venous catheter infection?
Central Venous Catheter Infections

- Draw 2 sets of blood cultures (1 percutaneously)
- Check paired quantitative or qualitative with time to positivity monitoring
- If catheter is removed, send tip for culture

Criteria for positivity:
- >15 CFU by semi-quantitative method (roll plate)
- >100 CFU by quantitative method (sonication)
Criteria for positivity

- Paired quantitative: catheter:vein CFU ratio >3
- Unpaired quantitative: catheter cx >100 cfu/mL
- Differential time: >120 minutes

<table>
<thead>
<tr>
<th></th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paired quantitative</td>
<td>79</td>
<td>94</td>
</tr>
<tr>
<td>Unpaired quantitative</td>
<td>78</td>
<td>96</td>
</tr>
<tr>
<td>Differential time to positivity</td>
<td>100</td>
<td>94</td>
</tr>
</tbody>
</table>

Siegman-Igra, meta-analysis (cath:vein ratio>3-10:1)
Siegman-Igra, meta-analysis (CFU/ml>15-100)
Gaur et al, n=33 (time>120 minutes)
Blot et al (1998), n=64, (time > 120 minutes)
Blot et al (1999), n=28, (time > 120 minutes)
# Types of Catheters

<table>
<thead>
<tr>
<th>Type of intravascular device</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral venous catheter</td>
<td>Usually inserted into the veins of the forearm or the hand; the most commonly used short-term intravascular device</td>
</tr>
<tr>
<td>Peripheral arterial catheter</td>
<td>For short-term use; commonly used to monitor hemodynamic status and to determine blood gas levels of critically ill patients; risk of bloodstream infection may approach that of CVCs</td>
</tr>
<tr>
<td>Midline catheter</td>
<td>Peripheral catheter (size, 7.6–20.3 cm) is inserted via the antecubital fossa into the proximal basilic or cephalic veins, but it does not enter central veins; it is associated with lower rates of infection, compared with CVCs</td>
</tr>
<tr>
<td>Short-term CVC</td>
<td>Most commonly used CVC; accounts for the majority of all catheter-related bloodstream infections</td>
</tr>
<tr>
<td>Pulmonary artery catheter</td>
<td>Inserted through a teflon introducer and typically remains in place for an average duration of only 3 days</td>
</tr>
<tr>
<td>Pressure-monitoring system</td>
<td>Used in conjunction with arterial catheter; associated with both epidemic and endemic nosocomial bloodstream infections</td>
</tr>
<tr>
<td>Peripherally inserted central catheter</td>
<td>Provides an alternative to subclavian or jugular vein catheterization; is inserted via the peripheral vein into the superior vena cava, usually by way of cephalic and basilic veins; similar risk of infection as CVCs in patients hospitalized in intensive care units</td>
</tr>
<tr>
<td>Long-term CVC</td>
<td>Surgically implanted CVC (e.g., Hickman, Broviac, or Groshong catheter) with the tunneled portion exiting the skin and a dacron cuff just inside the exit site; used to provide vascular access to patients who require prolonged chemotherapy, home-infusion therapy, or hemodialysis</td>
</tr>
<tr>
<td>Totally implantable device</td>
<td>A subcutaneous port or reservoir with self-sealing septum is tunneled beneath the skin and is accessed by a needle through intact skin; associated with low rates of infection</td>
</tr>
</tbody>
</table>

**NOTE.** CVC, central venous catheter
Short Term CVC Management

Short-term central venous catheter (CVC) or arterial catheter (AC) infection – related bloodstream infection

Complicated

Uncomplicated (bloodstream infection and fever resolves within 72 hours in a patient who has no intravascular hardware and no evidence of endocarditis or suppurative thrombophlebitis and for S. aureus is also without active malignancy or immunosuppression)

Suppurative thrombophlebitis, endocarditis or osteomyelitis, etc

Remove catheter & treat with systemic antibiotic for 4-6 weeks; 6-8 weeks for osteomyelitis in adults

Coagulase-negative staphylococci

Staphylococcus aureus

Enterococcus

Gram-negative bacilli

Candida spp.

Remove catheter & treat with systemic antibiotic for 5-7 days

If catheter is retained, treat with systemic antibiotic + antibiotic lock therapy for 10-14 days

Remove catheter & treat with systemic antibiotic for ≥14 days

Remove catheter & treat with systemic antibiotic for 7-14 days

Remove catheter & treat with systemic antibiotic for 7-14 days

Remove catheter & treat with antifungal therapy for 14 days after the first negative blood culture
Uncomplicated CVC Bacteremia

- No septic emboli
- Neg surveillance cultures 1-3 days after starting therapy
- Removable focus of infection
- Not immunocompromised
- Rapid clinical resolution of sxs w/in 72 hours of starting abx and removing focus of infection
- No indwelling prosthetic devices or underlying heart disease
Long Term CVC Management

Long-term central venous catheter (CVC) – or port (P) – related bacteremia or fungemia

Complicated
- Tunnel infection, port abscess
  - Remove CVC/P & treat with antibiotics for 7-10 days
- Septic thrombosis, endocarditis, osteomyelitis
  - Remove CVC/P & treat with antibiotics for 4-6 weeks; 6-8 weeks for osteomyelitis in adults
- Coagulase-negative staphylococcus
  - May retain CVC/P & use systemic antibiotic for 10-14 days + antibiotic lock therapy for 10-14 days
  - Remove CVC/P if there is clinical deterioration persisting or relapsing bacteremia, work-up for complicated infection and treat accordingly

Uncomplicated (Fig. 2)
- Staphylococcus aureus
  - Remove the infected catheter and treat with 4-6 weeks of antimicrobial therapy unless the patient has exceptions listed in Recommendation 80
- Enterococcus
- Gram-negative bacilli
- Candida spp.
  - May retain CVC/P & use systemic antibiotic for 7-14 days + antibiotic lock therapy for 7-14 days
  - Remove CVC/P if there is clinical deterioration persisting or relapsing bacteremia, work-up for complicated infection and treat accordingly

Defines uncomplicated bacteremia
Case 2

- 65 yo woman with ICD x 5 years presents with swelling over device site
- Erythema and tenderness over right pectoralis with palpable ICD
- How to diagnose an IECD infection?
- How do you treat?
- Should the device be removed?
CIED Infections

AHA Class I Recommendations for Diagnosis:

1. 2 sets of blood Cxs before Abx
2. If device removed:
   - Pocket tissue gram stain & cx
   - Lead tip gram stain & cx
3. If + Bld Cx or – Bld Cx on Abx: Obtain a TEE

AHA Class III Recommendations
Percutaneous aspiration of pocket not recommended
CIED Management Recs

1. If superficial or incisional level,
   leave device in, oral abx x 7-10d

2. If CIED infection established:
   **REMOVE ENTIRE DEVICE** (including leads)

3. Pocket infection (no bacteremia)
   7-10 d abx, oral OK
Should device be removed? YES

- ICE-PCS, prospective observational study
- 2769 with definite endocarditis
- 177 with CIED endocarditis
- 37.3% with co-existing valve & lead infection
- Device removal associated with lower 1 year removal (19.9% vs 38.2%)

Athan, JAMA, 2012
TTE has low sensitivity

Rarely concluded

Maintain high suspicion that infection is beyond pocket
Cases 3 and 4

- 14 yo M with 2 m of fever, HA, myalgias. RLQ pain led to appy with necrotizing lymphadenitis
- Left calf pain resolved with abx. Fever returned after abx, then R wrist swollen/tender, R thigh pain
- T 39.3, P 108, II/IV SM, splinter hemorrhages in 3 nails, petechial rash on legs
- 6/6 bottles growing Viridans strep

- 45 yo M with ESLD, HCV, ETOH with 3 d of fever, SOB, abd pain.
- T 38.5, gingivitis, III/VI SM LUSB, maybe splinter hemorrhages in 2 nails
- 1/6 bottles growing Viridans strep
Questions

- What is your DDx?
- How many modified Duke criteria does this patient have?
- How useful are the modified Duke criteria?
- What work-up is needed?
Endocarditis as a Syndrome

- Infective endocarditis
- Acute versus subacute
- Definite/suspected/possible
- Right-sided versus left-sided
DDx of Endocarditis

- Associated with neoplasms: atrial myxoma, marantic (adenocarcinoma), carcinoid
- Associated with autoimmune: rheumatic heart disease, SLE (Libman-Sacks endocarditis), anti-phospholipid syndrome, polyarteritis nodosa, Behcet's disease
- Postvalvular operation: thrombus, sutures
- Other: eosinophilic heart disease, ruptured mitral chordae, myxomatous degeneration

Staphylococcus aureus Bacteremia

- Source determined in 60-80% of cases with extensive evaluations
- IE in 5-17% of SAB
  - Less likely with negative f/u cultures
  - Less likely with removable focus of infection
  - Less likely with rapid clinical response (<72 hours)
  - More likely: prolonged SAB, permanent intracardiac devices, ESRD/HD, osteomyelitis, long-term access devices
- TTE versus TEE?

Kaasch, CID, 2011
Fowler, CID, 1998
<table>
<thead>
<tr>
<th>Clinical Prediction Criteria</th>
<th>INSTINCT</th>
<th>SABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged bacteremia</td>
<td>0.78</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Documented prolonged bacteremia</td>
<td>0.46</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Possible prolonged bacteremia</td>
<td>0.99</td>
<td>0.12</td>
</tr>
<tr>
<td>Permanent Intracardiac device</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prosthetic heart valve</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pacemaker/cardioverter-defibrillator</td>
<td>0.08</td>
<td>0.33</td>
</tr>
<tr>
<td>Hemodialysis dependency</td>
<td>0.99</td>
<td>0.05</td>
</tr>
<tr>
<td>Spinal infection or nonvertebral osteomyelitis</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No criteria filled</td>
<td>0%</td>
<td>2.50%</td>
</tr>
<tr>
<td>≥ criterion filled</td>
<td>100%</td>
<td>97.50%</td>
</tr>
</tbody>
</table>

Kaasch, CID, 2011
Definite IE

Pathological criteria:
Microorganisms: demonstrated by culture or histology in a vegetation, in a vegetation that has embolized, or in an intracardiac abscess, or
Pathologic lesions: vegetation or intracardiac abscess present, confirmed by histology showing active endocarditis.

Clinical criteria
2 major criteria, or
1 major and 3 minor criteria
5 minor criteria
Modified Duke Clinical Criteria

Possible IE
1 major and 1 minor
3 minor

Rejected
Firm alternate diagnosis for manifestations of endocarditis
Resolution of manifestations of endocarditis with antibiotic therapy for ≤ 4 days, or
No pathological evidence of IE at surgery or autopsy, after antibiotic therapy for ≤ 4 days.
Major Criteria

1. Positive blood culture for IE

A. Typical microorganism consistent with IE from 2 separate blood cultures as noted below:
   Viridans streptococci, *Streptococcus gallolyticus* (=*S. bovis*), HACEK group, *Staphylococcus aureus*, or community-acquired enterococci, in the absence of a primary focus

B. Microorganisms consistent with IE from persistently positive blood cultures as defined as
   (i) ≥2 positive cultures of blood samples drawn >12 hours apart
   (ii) all of 3 or a majority of ≥4 separate cultures of blood (with the first and last samples drawn ≥1 hour apart)
   iii. *Coxiella*: + Bld cx or anti-phase I Ab titer>1:800
## Bacteremia and IE Likelihood

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>IE:non IE Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. mutans</td>
<td>14.2 : 1</td>
</tr>
<tr>
<td>S. bovis</td>
<td>5.9 : 1</td>
</tr>
<tr>
<td>S. sanguis</td>
<td>3.0 : 1</td>
</tr>
<tr>
<td>S. mitior</td>
<td>1.8 : 1</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>1.0 : 1.2</td>
</tr>
<tr>
<td>S. anginosus</td>
<td>1.0 : 2.6</td>
</tr>
<tr>
<td>Grp G Streptococcus</td>
<td>1.0 : 2.9</td>
</tr>
<tr>
<td>Grp B Streptococcus</td>
<td>1.0 : 7.4</td>
</tr>
<tr>
<td>Grp A Streptococcus</td>
<td>1.0 : 32.0</td>
</tr>
</tbody>
</table>
2. Evidence of endocardial involvement

A. Positive echocardiogram for IE defined as

(i) oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation, or
(ii) abscess, or
(iii) new partial dehiscence of prosthetic valve, or

B. **New** valvular regurgitation (worsening or changing or pre-existing murmur not sufficient)
Minor Criteria

1. **Predisposition:** predisposing heart condition or intravenous drug use
2. **Fever:** temperature ≥ 38.0 C
3. **Vascular phenomena:** major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, and Janeway lesions
4. **Immunologic phenomena:** glomerulonephritis, Osler’s nodes, Roth spots, and rheumatoid factor
5. **Microbiological evidence:** positive blood culture but does not meet a major criteria as noted above or serologic evidence of active infection with organism consistent with IE (excludes single positive cultures for coagulase-negative *Staphylococci* and organisms that do not cause endocarditis).
Clinical Manifestations

- Splinter hemorrhages
- Osler's nodes
- Conjunctival hemorrhages
- Janeway’s lesions

Mylonakis, NEJM, 2001
Clinical Manifestations

Septic pulmonary emboli
Assessment of Duke Criteria

- Sensitivity: 80% for definite IE, 100% for definite + possible IE
- Negative predictive value: >98% for rejected category

Adopted modifications from Li et al (2000)

1. *S. aureus* bacteremia should be a major criteria regardless of the source (community or nosocomial)
2. Eliminate the ECHO minor criteria since TEE’s are more widely used now
3. Add *Coxiella* to list of major criteria (a single positive blood culture or antiphase I IgG antibody titer > 1:800).
4. To increase specificity, change the category “possible IE” to cases with 1 major and 1 minor criteria or 3 minor criteria
Case 5

- Patient with endocarditis w/u has 1 major and 1 minor Duke’s Criteria
- How hard do you search for more criteria?
- When do you recommend a brain MRI?
- When do you recommend a TEE?
- Should all patients with CVC-associated S. aureus bacteremia get a TEE?
Echocardiography in SAB

- SAB is increasing in all settings
- Endocarditis in 10-30% of SAB cases
- Clinical presentation is non-specific
- TTE sensitivity is ~50% (mitral > aortic valves)

Reynolds, J Am Soc Echo, 2003
Mugge, J Am Coll Cardiol, 1989
Erbel, Eur Hear J, 1988
TEE and IE diagnosis

- Prosthetic valves
- Suspected complication (ex. perivalvular abscess)
- IECD
- “Possible endocarditis” category
- ? Negative TTE and S. aureus bacteremia
SAB and TEE?

Arguing in favor:
1) Increased sensitivity leads to more diagnoses & better Rx
   TTE sensitivity=32%
   TEE sensitivity=100%
2) ? Cost effective (save costs of lengthy treatment)

Arguing against:
3) TEE more labor intensive
4) Small vegetations may be adequately treated with short course treatment.
Clinical Manifestations

Mycotic aneurysm
Effect of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis
A Prospective Study

Table 2. Cerebral Lesions Observed on Early Systematic Cerebral Magnetic Resonance Imaging in Patients With Infective Endocarditis

<table>
<thead>
<tr>
<th>Lesion Characteristic</th>
<th>All Patients (n = 130), n (%)</th>
<th>Patients With Neurologic Symptoms (n = 16), n (%)</th>
<th>Patients Without Neurologic Symptoms (n = 114), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 lesion</td>
<td>106 (82)</td>
<td>16 (100)</td>
<td>90 (79)</td>
</tr>
<tr>
<td>&gt;1 lesion</td>
<td>86 (66)</td>
<td>13 (81)</td>
<td>73 (64)</td>
</tr>
<tr>
<td>Ischemic lesion</td>
<td>68 (52)</td>
<td>14 (88)</td>
<td>54 (47)</td>
</tr>
<tr>
<td>Large systematized ischemic lesion*</td>
<td>33 (25)</td>
<td>9 (56)</td>
<td>24 (21)</td>
</tr>
<tr>
<td>Small ischemic lesion</td>
<td>60 (46)</td>
<td>14 (88)</td>
<td>46 (40)</td>
</tr>
<tr>
<td>Hemorrhagic lesion</td>
<td>79 (61)</td>
<td>10 (63)</td>
<td>69 (61)</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhagic lesion</td>
<td>10 (8)</td>
<td>3 (19)</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Microhemorrhage</td>
<td>74 (58)</td>
<td>7 (44)</td>
<td>67 (59)</td>
</tr>
<tr>
<td>Subarachnoidal hemorrhage</td>
<td>11 (8)</td>
<td>2 (13)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Unruptured aneurysm</td>
<td>10 (8)</td>
<td>1 (6)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Cerebral abscess</td>
<td>8 (6)</td>
<td>1 (6)</td>
<td>7 (6)</td>
</tr>
</tbody>
</table>

High rate of lesions in neurologically asymptomatic cases
Does it change management?

Yes, but not sure if affects outcome.
16 yo male with a 1 week history of fever to 103 F. Developed confusion, blurred vision and abdominal pain. Head CT showed hypodense lesions bilaterally in the parietal lobe, abdominal CT showed a 2 cm splenic infarct, and an ophthalmologic exam showed bilateral emboli.

4 out of 4 cultures grew MRSA. ECHO showed mild MR and a vegetation on the anterior leaflet.

Does this patient need cardiac surgery?
Indications for Cardiac Surgery

Valvular dysfunction
- Acute aortic or mitral insufficiency with signs of ventricular failure
- Heart failure unresponsive to medical therapy
- Valve perforation or rupture

Perivalvular extension
- Valvular dehiscence, rupture, or fistula
- New heart block
- Large abscess, or extension of abscess despite appropriate antimicrobial therapy.
Indications for Cardiac Surgery

Vegetation

Persistent vegetation after systemic embolization:
- Anterior mitral leaflet vegetation, particularly >1 cm
- One or more embolic events during the 1st 2 wks of therapy
- 2 or more embolic events during or after antimicrobial therapy

Increase in vegetation size after 4 weeks of antimicrobial therapy
RCT, >17 y, 37 vs 39 patients with left-sided endocarditis (mitral>aortic)

- >95% w/ pre-existing valve disease
- veg >10 mm
- S aureus in 13% and 8% (mostly strep spp).

Early Surgery? Kang, NEJM 2012
Figure 1  In-hospital mortality as a function of the rate of early surgery. This linear regression was done with the data from the 24 investigations.

Franck Thuny, Dominique Grisoli, Frederic Collart, Gilbert Habib, Didier Raoult

Management of infective endocarditis: challenges and perspectives

The Lancet Volume 379, Issue 9819 2012 965 - 975
<table>
<thead>
<tr>
<th>Study</th>
<th>Period of inclusion</th>
<th>Number of patients</th>
<th>Rate of surgery</th>
<th>Outcome</th>
<th>Mortality (no surgery/surgery)</th>
<th>Conclusion of the authors about the effect of surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vikram et al</td>
<td>1990-2000</td>
<td>513</td>
<td>44.80%</td>
<td>6-month mortality</td>
<td>33.0%/16%</td>
<td>Benefit</td>
</tr>
<tr>
<td>Mourvillier et al</td>
<td>1993-2000</td>
<td>146</td>
<td>49.30%</td>
<td>In-hospital mortality</td>
<td>47.3%/29.7%</td>
<td>No significant benefit</td>
</tr>
<tr>
<td>Cabell et al</td>
<td>1985-99</td>
<td>1516</td>
<td>40.20%</td>
<td>In-hospital mortality</td>
<td>16.4%/13.6%</td>
<td>Benefit in patients with high propensity score</td>
</tr>
<tr>
<td>Wang et al</td>
<td>1985-99</td>
<td>355</td>
<td>41.70%</td>
<td>In-hospital mortality</td>
<td>24.7%/23.4%</td>
<td>No significant benefit</td>
</tr>
<tr>
<td>Aksoy et al</td>
<td>1996-2002</td>
<td>333</td>
<td>23.00%</td>
<td>5-year mortality</td>
<td>21.6%/11.8%</td>
<td>Benefit</td>
</tr>
<tr>
<td>Tleyjeh et al</td>
<td>1980-98</td>
<td>546</td>
<td>23.60%</td>
<td>6-month mortality</td>
<td>23.7%/27.1%</td>
<td>No significant benefit</td>
</tr>
<tr>
<td>Sy et al</td>
<td>1996-2006</td>
<td>223</td>
<td>27.80%</td>
<td>Median: 5.2 years</td>
<td>51%/32%</td>
<td>No significant benefit</td>
</tr>
<tr>
<td>Bannay et al</td>
<td>1999</td>
<td>449</td>
<td>53.40%</td>
<td>5-year mortality</td>
<td>50%/30%</td>
<td>Benefit</td>
</tr>
<tr>
<td>Lalani et al</td>
<td>2000-05</td>
<td>1552</td>
<td>46.40%</td>
<td>In-hospital mortality</td>
<td>20.7%/12.1%</td>
<td>Benefit</td>
</tr>
</tbody>
</table>

Thuny, Lancet, 2012
1. **Embolization**: Difficult to predict who will embolize
   ↑ emboli with: AV & MV anterior leaflet,
   *S. aureus, Candida, HACEK, & Abiotrophia* organisms,
   ? Size > 1 cm

2. **CHF**: Poor prognosis with medical Rx alone
   Delaying surgery until decompensation will ↑ mortality

3. **Extracranial Mycotic Aneurysms**
   Surgical intervention advised

4. **Intracranial Mycotic Aneurysms**
   Debates @ merits of screening & surgery.
   Very little data to guide decision.
Currently recommended management

- Blood cultures and consider additional microbiological tests if negative after 48 h
- TTE and TEE

Antimicrobial treatment adapted to the microbiological results

Integration of all the clinical, microbiological, and imaging data

Refer to surgical department if complications occur

- Resection of all infected tissues
- Valve repair is preferable if possible

IE suspicion

Accelerate and improve diagnostic process

Positive and aetiological diagnosis

Reduce risk of sepsis, MODS, stroke, and sudden death

Antimicrobial treatment

Improve prognosis assessment

Risk stratification

Improve treatment compliance

Indication of early surgery for high-risk patients

Reduce postoperative complications

Choice of the type of surgery

Improve survival

Long-term outcome

Propositions and perspectives for an improved management

- IE kit (blood cultures and serology test in 2 h)
- Pathogen-specific PCR of blood
- Specific serum protein profile
- 3D-echo
- Cardiac CT scan
- PET scan, molecular imaging
- Cerebral MRI

Quick start of an empirical antimicrobial treatment and secondary adaptation

- Use of risk scores
- Use of validated biomarkers (BNP, troponin)
- Development of new biomarkers (microarrays)

- Early referral to an "IE-centre"
- Standardised treatment
- Monitoring high-risk patients in intensive care unit
- Weekly dedicated multidisciplinary staff

- Surgeons specialised in IE operations
- Minimally invasive surgery in frail patients
- Possible use of biodegradable intra-annular annuloplasty ring

- Long-term follow-up to detect late IE-related complications and antibiotic adverse events
- Nutritional programmes