Question 13
The major cause of death in patients more than 6 months following cardiac transplantation is:

A. Graft versus host disease  
B. Opportunistic infection  
C. Rejection  
D. Malignancy  
E. Coronary artery disease

Answer:

The provided answer (E) might have changed in light of the 2005 report from the Registry of the International Society for Heart and Lung Transplantation (ISHLT) data from 1984 to 2004

- Major limitations to survival in 1st 6 months: graft failure, rejection and infection
- “Graft failure” possibly represents deaths not specified (thus statistics of early rejection and late vasculopathy likely underestimated)
- Beyond 1st year, malignancy then coronary disease as the main cause of death

(Previously: beyond 6-12 months, coronary disease (25%) then malignancy (18%) were the leading causes of death because newer and heavier immunosuppressive regimes used)

Cardiac transplantation
- indicated in end-stage cardiac failure with symptoms despite optimal medical therapy (Stage 4)
- donor and recipient hearts excised in identical operations
- mortality highest in 1st year post transplant (mostly in 1st 6 months)
- half-life of transplant is 9-10%
- heavy immunosuppression (even worse than renal transplant)
- surgically denervated heart thus:
  - does not respond to any direct autonomic stimuli but responds to circulating catecholamines
  - no angina even with advanced coronary disease

5 major causes of death post cardiac transplant
1) Graft failure (primary and non-specific)  
2) Acute allograft rejection  
3) Infections other than CMV  
4) Allograft vasculopathy (ie coronary disease)  
5) Malignancy (notably lymphomas)

<table>
<thead>
<tr>
<th></th>
<th>30 days</th>
<th>31 days to 1 year</th>
<th>1-3 years</th>
<th>&gt; 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft failure</td>
<td>14%</td>
<td>18%</td>
<td>17%</td>
<td>14%</td>
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<tr>
<td>Acute rejection</td>
<td>7%</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Infection</td>
<td>13%</td>
<td>33%</td>
<td>13%</td>
<td>10%</td>
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<tr>
<td>Allograft</td>
<td></td>
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<tr>
<td>vasculopathy</td>
<td>5%</td>
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<td>14%</td>
<td>15%</td>
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<tr>
<td>Malignancy</td>
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<tr>
<td></td>
<td>4%</td>
<td></td>
<td>14%</td>
<td>23%</td>
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* CMV related death contributed to <1% of infective deaths
Determinants of prognosis

1) Recipient factors
   - underlying congenital heart disease and use of mechanical support are most closely related to poor outcome (but only present in low numbers of recipients)
   - others: hospitalization at time of transplant, female donor to male recipient, donor death from CVA, donor coronary heart disease

2) Donor factors
   - worse prognosis if advanced age (> 50 years old) and female donor to female recipient

3) Late mortality
   - Most important risk factors (but in <5% patients) at > 5 years: stroke, repeat transplant and coronary disease within the 1st year
   - Commoner risk factors: older recipient and donor age, diabetes, having had treatment for rejection, infection

A. Graft vs host disease (GVH)
   - only applicable in haematopoietic stem cell transplants
   - result of donor T cells either transferred with donor stem cell inoculum or developing from it -> recognizing recipient organs as “foreign” antigen
   - Acute GVH: within 3 months (need skin, liver or endoscopic Bx for Dx)
   - Chronic GVH: beyond 3 months (usually in older patients/ mismatched or unrelated stem cell donors/ previous acute GVH)

C. Rejection
   - Symptoms of LV failure +/- GIT symptoms (hepatic congestion)
   - Arrhythmias uncommon
   - In pre-cyclosporin era: fever and reduced QRS voltages were “diagnostic”
   - Dx: endomyocardial biopsy histopathology
   - 2 types: cellular (T cell infiltrate) and less commonly, non-cellular (antibody mediated)

D. Malignancy
   - 2-4x more common in heart transplant vs renal transplant
   - Commonest (5-20x): lymphoma, skin cancers, Kaposi sarcomas, renal cell carcinomas
   - In contrast, solid organ cancers common in normal population (eg prostate, breast, colon) only modestly increased (2x)
   - Screening (pre and post transplant), decrease immunosuppression and exposure to carcinogens eg sunlight