Technologies for Treatment of Heart Disease
Lectures 17-19
3.18.08
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Four Questions
• What are the major health problems worldwide?
• Who pays to solve problems in health care?
• How can technology solve health care problems?
• How are health care technologies managed?

Outline: Treatment of Heart Disease
• Burden of cardiovascular disease (CVD)
• Cardiovascular system
• Measuring cardiovascular health
• Valve diseases
• Atherosclerosis and treatments
  – Stroke
  – Heart attack
• Heart failure and treatments

Muddiest point/Clearest point

From Last Tuesday 3/11
• Cost-effectiveness of new technologies
• Advantages and disadvantages
  – Balancing effectiveness with cost-effectiveness
  • What's a good sell?
  • What's ethical?
  • Variations between developed and developing countries

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Muddiest point/Clearest point
What is Cardiovascular Disease (CVD)

• Generally: all diseases that involve the heart and blood vessels
  – Valve diseases
• Typically: those diseases related to atherosclerosis
  – Cerebrovascular disease
    • Stroke
  – Ischemic heart disease
    • Coronary artery disease (CAD)

Global Burden of CVD

• In 1999: CVD contributed to a third of global deaths
  – 80% are in low and middle income countries
• By 2010: CVD is estimated to be the leading cause of death in developing countries
  – General improvements in health make CVD a factor in overall mortality rates
• In 2003: 16.7 million deaths due to CVD
  – Cost of care for these conditions is high

2002 Worldwide Mortality

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>Deaths (1991)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Cerebrovascular disease</td>
<td>272,000</td>
</tr>
<tr>
<td>2</td>
<td>Ischemic heart disease</td>
<td>202,000</td>
</tr>
<tr>
<td>3</td>
<td>Hypertension</td>
<td>152,000</td>
</tr>
<tr>
<td>4</td>
<td>Diabetes</td>
<td>135,000</td>
</tr>
<tr>
<td>5</td>
<td>COPD</td>
<td>117,000</td>
</tr>
<tr>
<td>6</td>
<td>Tuberculosis</td>
<td>47,000</td>
</tr>
<tr>
<td>7</td>
<td>Diarrheal disease</td>
<td>41,000</td>
</tr>
<tr>
<td>8</td>
<td>Acute respiratory infections</td>
<td>24,000</td>
</tr>
<tr>
<td>9</td>
<td>Lower respiratory infections</td>
<td>20,000</td>
</tr>
<tr>
<td>10</td>
<td>Chagas disease</td>
<td>18,000</td>
</tr>
</tbody>
</table>

Mortality in Developing Countries

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mortality (1991)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory infections</td>
<td>21,000</td>
</tr>
<tr>
<td>Diarrheal disease</td>
<td>19,000</td>
</tr>
<tr>
<td>Acute respiratory infections</td>
<td>17,000</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>15,000</td>
</tr>
<tr>
<td>Chagas disease</td>
<td>12,000</td>
</tr>
</tbody>
</table>

US Burden of CVD

• CVD:
  – 61 million Americans (~25% of population)
    – Accounts for > 40% of all deaths – 950,000/year
• Cost of CVD disease:
  – $351 billion
    • $209 billion for health care expenditures
    • $142 billion for lost productivity from death and disability
• Stroke
  – Third leading cause of death in the US
• Ischemic Heart/CAD
  – Leading cause of death in US
  – Coronary heart disease is a leading cause of premature, permanent disability among working adults

US Burden of CVD: Heart Attack

• Consequences of ischemic heart disease
  – Narrowing of the coronary arteries that supply blood to the heart
• Each year:
  – 1.3 million Americans suffer a heart attack
  – 460,000 (~40%) are fatal
  – Half of those deaths occur within 1 hour of symptom onset, before person reaches hospital
• Onset is often sudden
  – Importance of prevention
Risk Factors of CVD

- Risk Factors:
  - Tobacco use
  - Low levels of physical activity
  - Inappropriate diet and obesity
  - High blood pressure
  - High cholesterol

For almost all individuals these are modifiable!!!

Early Detection of CVD

- Screening for CVD:
  - Measure blood pressure (BP) annually
    - 12-13 point reduction in blood pressure can reduce heart attacks by 21%
  - Check cholesterol every 5 years
    - 10% drop in cholesterol can reduce heart attacks by 30%

- Patient compliance
  - High BP: not under control in 70% of patients
  - High cholesterol: not under control in 80% of patients

The Cardiovascular System

- Anatomy and Physiology
  - Vessels
  - Heart
  - Valves

- How to we assess our risk factors?
  - Measure BP and cholesterol levels

- How to we measure the health and functionality of our cardiovascular system?
  - Listen to heart sounds
  - Quantitative parameters for heart function
The Heart as a Pump

• The right atria fills with blood returning to heart from the vena cava
  – Tricuspid valve separates right ventricle
• Right ventricle pumps blood to lungs to be oxygenated
  – Pulmonary valve separates pulmonary artery
• Left atria fills with oxygen rich blood from pulmonary vein
  – Mitral (bicuspid) valve separates the left ventricle
• Left ventricle pumps blood to body
  – Aortic valve separates the aorta
• Filling is the “resting” state -- diastole
• Pumping/contraction is the “active” state -- systole

Four Heart Valves

• Two types
  – AV
  • Atria/ventricle
  • 2 or 3 flaps
  • Right: tricuspid
  • Left: mitral/bicuspid
  – Semilunar
  • Blood leaves the heart
  • 3 cusps
  • Right: pulmonary
  • Left: aortic

Measuring CV Health

• Heart sounds
• Blood Pressure (BP)
• Serum cholesterol levels/lipid panel
• Echocardiogram
• Electrocardiogram

Measuring CV Health: Heart Sounds

• Heart sounds are produced by valve closure
• Normal heart sound is “lub-dup”
  – Lub: AV valves close
  – Dup: Semilunar valves close
• Abnormalities can produce heart murmurs
  – Not always though
  – Echocardiography

Measuring CV Health: Blood Pressure

• Normal blood pressure:
  – Varies from minute to minute
  – Varies with changes in posture
  – Should be < 120/80 mm Hg for an adult
    • The higher/top number + systolic
    • The lower/bottom number = diastolic
• Pre-hypertension:
  – Blood pressure that stays between 120-139/80-89
• Hypertension:
  – Blood pressure above 140/90 mm Hg
• My blood pressure = 108/64

http://www.medicaldiscoverynews.com/shows/bloodpressure.html
**How Do We Measure Blood Pressure?**

Sphygmomanometer

- Increase cuff pressure > systolic
  - No blood flow in arm
- Gradually release pressure
- Cuff pressure = systolic
  - Turbulent rush of blood gives Korotkoff sounds
- Cuff pressure = diastolic
  - No compression of

**Blood Pressure Activity**

- Groups of 6
  - Even numbers since you’ll need a partner
- Measure each person’s blood pressure twice
- Write down the results each time
- Get an average BP for each person
- Get an average for your entire group
- We’ll make a class average and compare

**Measuring CV Health: Serum Cholesterol**

- LDL (low-density)
  - “bad” cholesterol
  - Cholesterol builds up inside blood vessels
- HDL (high-density)
  - “good” cholesterol
  - Removes cholesterol from vessels to liver for

**Interpretation of Serum Lipid Levels**

<table>
<thead>
<tr>
<th>Total Cholesterol</th>
<th>LDL</th>
<th>HDL</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Optimal</strong></td>
<td>Under 100</td>
<td>Above 60</td>
<td></td>
</tr>
<tr>
<td><strong>Desirable</strong></td>
<td>Under 200</td>
<td>Under 130</td>
<td>Below 150</td>
</tr>
<tr>
<td><strong>Borderline</strong></td>
<td>Over 200</td>
<td>Over 150</td>
<td>Below 200</td>
</tr>
<tr>
<td><strong>Abnormal</strong></td>
<td>Above 200</td>
<td>Above 160</td>
<td>Above 40</td>
</tr>
</tbody>
</table>

**Serum Cholesterol Levels: Case Study**

<table>
<thead>
<tr>
<th>Patient A</th>
<th>Total Cholesterol</th>
<th>LDL</th>
<th>HDL</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient C</td>
<td>Total cholesterol</td>
<td>LDL</td>
<td>HDL</td>
<td>Triglycerides</td>
</tr>
<tr>
<td>A</td>
<td>192</td>
<td>135</td>
<td>67</td>
<td>44</td>
</tr>
<tr>
<td>B</td>
<td>235</td>
<td>136</td>
<td>63</td>
<td>182</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient D</th>
<th>Total cholesterol</th>
<th>LDL</th>
<th>HDL</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
<td>Total cholesterol</td>
<td>LDL</td>
<td>HDL</td>
<td>Triglycerides</td>
</tr>
<tr>
<td>B</td>
<td>197</td>
<td>97</td>
<td>77</td>
<td>116</td>
</tr>
<tr>
<td>D</td>
<td>195</td>
<td>109</td>
<td>66</td>
<td>99</td>
</tr>
</tbody>
</table>

**Serum Cholesterol levels: Case Study**

- Physiologic measurements vary a lot!
  - Let’s see with your BP values
- What’s important is to monitor over time
  - Start young
  - Be consistent
  - Take responsibility for your health
Quantifying Heart Performance

- **Heart Rate (HR)**
  - Number of heartbeats per minute
  - Normal value is 60-90 bpm at rest
  - Can drop as low as 20 bpm when sleeping
- **Stroke Volume (SV)**
  - Amount of blood pumped by ventricle with each heartbeat
  - Normal value is 60-80 mL
- **Cardiac output (CO)**
  - Total volume of blood pumped by ventricle per minute
  - \( CO = HR \times SV \)
  - Normal value is 4-8 L/min

Quantifying Heart Performance

- **Blood volume**
  - Total volume of blood in circulatory system
  - Normal value is \( \approx 5 \) L
  - Total volume of blood is pumped through our heart each minute!
- **Ejection Fraction (EF)**
  - Fraction of blood pumped out of ventricle relative to total volume (at end diastole)
    - End diastolic volume (EDV)
    - \( EF = SV/EDV \)
    - Normal value > 60%
    - So no one’s heart is a “perfect” pump

Advanced Measures of CV Performance: Echocardiogram

- Sound waves produce images
  - Ultrasound
- Visualize complex movements within the heart
  - Ventricles squeezing and relaxing
  - Opening and closing of valves in time with heartbeat
- Identify and confirm abnormalities in muscle and valves

Advanced Measures of CV Performance: Electrocardiogram

- Electrical activity (ECG or EKG)
  - Records the electric waves generated by heart activity
    - Electric signal measured in mV
    - Different waveform is seen based on location of the electrode
  - Normal heartbeat is initiated by a small pulse of current
  - Electrical activity starts at the top of the heart, spreads downward and then up again
    - Excites the muscles in optimal way for pumping blood
- Pacemaker Cells
  - Specialize in producing electrical signal

Valve Diseases: Etiology

- Two main types of valve dysfunction
  - Regurgitation
    - Improper valve closing allows backwards leakage
  - Stenosis
    - Narrowing of opening does not let enough blood through
- Common causes
  - Congenital birth defect
  - Infective endocarditis
  - Rheumatic fever
  - Myxomatous degeneration
Valve Diseases: Detection and Treatment

- May be detectable through heart sounds
- Diagnosis with Doppler echocardiogram
  - Doppler assesses blood flow
    - Direction and velocity
- Treatment is usually surgically repairing or replacing the affected valve(s)
- > 100,000 valve replacements and repairs in the US each year

Artificial Heart Valves

- Surgical Repair or Reconstruction
  - Common for mitral valve dysfunction
  - Use pulmonary in place of aortic
- Mechanical
  - Last for 10-12 years
  - Require anticoagulation therapy
- Bioprosthetic
  - Glutaraldehyde fixed pericardium and valves
  - Calcification
  - Some can last up to 20 years
- Xenografts
  - Porcine valves; good mimic
  - Immunogenic
- Allografts
  - Good for children
  - Scarce supply

Tissue Engineered Heart Valves

- Primarily targeted for use in pediatric patients
  - No other option works well here
- Need of successful tissue-engineered living valve, which can grow with patients and last for lifetime
- Regeneration
  - Implanted matrix remodels in vivo
- Repopulation
  - Implant acellular porcine valve which fills in with patient cells

Valve Diseases: Final Thoughts

- Early concerns have been addressed
  - Replacement valve longevity
  - Surgical mortality
- Repeated use of bioprosthetic valves is common
  - Risk of second surgery is ≈ risk of thromboembolism associated with mechanical valves
- Edwards pericardial valve may last 20 years
  - Equivalent to an allograft

Valve Diseases: Final Thoughts

- The status quo seems to be acceptable
- Does this affect the field of engineering new replacement valve products?
  - A number of new innovations have failed in clinical trials
    - Physicians don't want to try new things
  - Should we spend money and resources on tissue engineering valves?
  - Still no effective therapy for children
    - Only 10% of adult market
    - First clinical tissue engineered product tested failed

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For Thursday…

- No homework is due next class
- Muddiest point & clearest point
- And thanks again to Vishal for material and expertise on heart valves!