The future: cardiovascular medicine in 10 years

Karl Swedberg

In the last 10 years important developments have taken place in cardiovascular medicine, and it is necessary to consider these in order to understand fully what can be expected in the coming decade.

Speaking to the Royal College of Physicians in London during 1944, Winston Churchill said "the more you can look back, the further you can look forward". In the 1970s Julius Comroe, a physiologist at the Cardiovascular Research Institute in San Francisco, coined the term "retrospectoscope" to describe a useful tool for looking at the past with the benefit of hindsight. He discovered that in over 40% of the key discoveries in cardiovascular medicine, the clinical potential of the finding was not realised at the time. It is clearly very difficult to predict the future. Comroe also appreciated the importance of pioneers having ‘the courage to fail’ and a willingness to take risks.

**Hypertension**

**PAST 10 YEARS**

Looking back over 10 years in the management of hypertension, there have been some major breakthroughs: recognition of the importance of systolic hypertension and the treatment of elderly patients; definition of blood pressure targets; and the individualising of treatment based on patient risk factors.

In terms of treatment, many of the drugs used today were available 10 years ago: diuretics, β blockers, angiotensin converting enzyme (ACE) inhibitors, and calcium channel blockers (table 1). One important new class of drugs that has since become available is the angiotensin receptor antagonists.

**THE FUTURE**

It is probable that the most important treatments in the future will be those that are already available today. However, blood pressure targets will change and treatment will become more individualised. There are some new drugs on the horizon that may be important in the future. Endothelin antagonists are now in clinical trials and vasopetidases are currently at phase III of development. Insulin sensitisers or metabolic modifiers will also probably be of importance.

**Myocardial infarction**

**PAST 10 YEARS**

In 1988 there was a major breakthrough in the treatment of myocardial infarction (MI) with the introduction of thrombolytic treatment. ISIS-II clearly documented the importance of streptokinase and aspirin in the acute phase of MI. This has had a huge impact on the management of acute MI.

The aim of treatment today is the same as it was 10 years ago: infarct limitation and reperfusion. This goal can now be achieved using several different approaches (table 2). Ten years ago, ACE inhibitors, antiplatelet blockers, primary percutaneous transluminal coronary angioplasty, and IIb/IIIa blockers were not generally used. These agents and techniques are now in various stages of documentation and introduction.

**THE FUTURE**

In the next 10 years these treatments will become more justified (table 2). Cardiac repair will become a new target and myocardial damage will be treated with therapeutic agents. Interestingly, as in hypertension, most of the treatments that will be used in the future management of MI are already available today.

**Heart failure**

**PAST 10 YEARS**

In 1987 the CONSENSUS trial documented the importance of enalapril in severe heart failure. These findings had a significant impact on clinical management and since then there have been no further placebo controlled trials in heart failure. However, it is now realised that the treatment effect is transient; after 10 years all the patients in the CONSENSUS trial had died.

The SOLVD trial was published in the early 1990s and supported a role for ACE inhibition in the management of heart failure. There was overwhelming evidence for the use of ACE inhibitors in terms of both mortality and morbidity.
Table 3: Previous, current, and future drug treatment strategies for heart failure with accepted treatment targets

<table>
<thead>
<tr>
<th>Treatment targets</th>
<th>Then</th>
<th>Now</th>
<th>Future</th>
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</thead>
<tbody>
<tr>
<td>Improve symptoms</td>
<td>Improve symptoms</td>
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<td>and morbidity</td>
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<tr>
<td>Prolong life</td>
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<td>Prolong life</td>
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<table>
<thead>
<tr>
<th>Tools</th>
<th>Then</th>
<th>Now</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Digitalis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ACE inhibitors</td>
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<tr>
<td>ARB</td>
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<td></td>
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<tr>
<td>Beta blockers</td>
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<tr>
<td>Spironolactone</td>
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<td>Anticoagulants</td>
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<tr>
<td>Aspirin</td>
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<td>Anticoagulants</td>
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<td>CCB</td>
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<td>Nitrate</td>
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<td>Blockers</td>
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</table>

Table 4: Primary outcome events in the HOPE trial

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Ramipril (%)</th>
<th>Placebo (%)</th>
<th>Relative risk</th>
<th>95% confidence intervals</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction, stroke, cardiovascular death</td>
<td>13.9</td>
<td>17.5</td>
<td>0.78</td>
<td>0.70 to 0.86</td>
<td>0.000002</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>6.0</td>
<td>8.0</td>
<td>0.75</td>
<td>0.64 to 0.87</td>
<td>0.0002</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>9.8</td>
<td>12.0</td>
<td>0.80</td>
<td>0.71 to 0.91</td>
<td>0.0005</td>
</tr>
<tr>
<td>Stroke</td>
<td>3.3</td>
<td>4.8</td>
<td>0.68</td>
<td>0.56 to 0.85</td>
<td>0.0002</td>
</tr>
<tr>
<td>Non-cardiovascular death</td>
<td>4.3</td>
<td>4.2</td>
<td>1.00</td>
<td>0.82 to 1.22</td>
<td>0.98</td>
</tr>
<tr>
<td>Mortality</td>
<td>10.3</td>
<td>12.2</td>
<td>0.83</td>
<td>0.74 to 0.94</td>
<td>0.0035</td>
</tr>
</tbody>
</table>

Beta blockers have been another important therapeutic tool. Trials such as CIBIS-2 and MERIT have demonstrated that beta blockers can have an enormous impact on the prognosis of heart failure.

Spironolactone was available 10 years ago, although its real importance has only recently been appreciated.

THE FUTURE

The renin-angiotensin system will continue to be targeted more closely in heart failure (table 3). The results of ELITE-II have shown how difficult it is to predict the future. There will be additional drugs that will replace some of the agents currently used. Nurse directed clinics to care for cardiac patients will become better established. Management of patients with cardiac transplants will also be improved. In addition, the use of mechanical assist devices will be increased and gene therapy will be seen as an alternative in some patients.

The results of the recent HOPE trial will have a major impact on future clinical practice (table 4). This study confirms that ACE inhibitors are extremely important in vascular disease and provides overwhelming evidence that ramipril prevents vascular diseases and heart failure, in particular among diabetics. In the future there will be new uses of ACE inhibitors and also statins. The treatment goal of attenuating disease progression will be added.

The use of more selective antithrombotic treatments, to avoid vascular occlusion and attenuate progression, will be documented in the next 10 years.

Gene therapy

Gene therapy continues to create a great deal of hope in many aspects of cardiovascular medicine. However, experts in this area believe that the development of gene therapy products, including delivery systems, is so complex that it will require 10 or more years before these products reach the market place.

Information technology

The major impact on cardiovascular medicine will not come from new treatments and clinical practice but from information technology. There will be major developments in information systems used in all areas of medicine. The enormous amount of information available to physicians as well as patients will require new approaches to clinical management. In disease management, for example, home care monitoring will develop enormously. In addition, quality assurance and surgical techniques will benefit from the introduction of more advanced technology.

Conclusion

In the past decade there have been major therapeutic developments. There is, of course, a long time from the first detection to the documentation of a new treatment. Major, rapid changes will therefore not be seen in the management of cardiovascular diseases.

The major treatments today are treatments that were available 10 years ago. It is therefore probable that the new treatments in the next 10 years are currently in phase I to IV trials. Importantly, the renin-angiotensin system will remain an important target for treatment.

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