Congestive Heart Failure I

- Congestive heart failure (CHF) is a major contributor to morbidity and mortality worldwide. There are approximately 5 million established cases of heart failure in the United States alone; a similar number of patients have asymptomatic left ventricular dysfunction and are therefore at risk to develop CHF.
- Heart failure accounts for more than half a million deaths annually in the United States; mortality in patients with advanced heart failure exceeds 50% at 1 year. The most common cause of heart failure in the USA is coronary artery disease.
Congestive Heart Failure II

• Fortunately, substantive advances in the understanding of CHF at the organ systems and cellular-molecular levels have driven important advances in the pharmacotherapy of heart failure that have revolutionized clinical practice.

• While palliation of symptoms and improvement in the quality of life remain important goals, it now is possible to approach therapy with the expectation that disease progression can be attenuated, and, in many instances, survival prolonged.

Pathophysiology of Cardiac Performance

• Cardiac performance is a function of four primary factors:
  1. Preload
  2. Afterload
  3. Contractility
  4. Heart rate
Preload

- When some measure of left ventricular performance such as stroke volume or stroke work is plotted as a function of left ventricular filling pressure or end-diastolic fiber length, the resulting curve is termed the left ventricular function curve.
- The ascending limb (< 15 mm Hg filling pressure) represents the classic Frank-Starling relation.
- Beyond approximately 15 mm Hg, there is a plateau of performance. Preloads greater than 20–25 mm Hg result in pulmonary congestion.
- Preload is usually increased in heart failure because of increased blood volume and venous tone.
- Because the curve of the failing heart is lower, the plateau is reached at much lower values of stroke work or output.
- Increased fiber length or filling pressure increases oxygen demand in the myocardium. Reduction of high filling pressure is the goal of salt restriction and diuretic therapy in heart failure. Venodilator drugs (eg, nitroglycerin) also reduce preload by redistributing blood away from the chest into peripheral veins.
Afterload

- Afterload is the resistance against which the heart must pump blood and is represented by aortic impedance and systemic vascular resistance.
- As cardiac output falls in chronic failure, there is a reflex increase in systemic vascular resistance, mediated in part by increased sympathetic outflow and circulating catecholamines and in part by activation of the renin-angiotensin system.
- Endothelin, a potent vasoconstrictor peptide, may also be involved. This sets the stage for the use of drugs that reduce arteriolar tone in heart failure.

Contractility

- Heart muscle obtained by biopsy from patients with chronic low-output failure demonstrates a reduction in intrinsic contractility.
- As contractility decreases in the patient, there is a reduction in the velocity of muscle shortening, the rate of intraventricular pressure development (dP/dt), and the stroke output achieved.
- However, the heart is still capable of some increase in all of these measures of contractility in response to inotropic drugs.
Heart Rate

- The heart rate is a major determinant of cardiac output.
- As the intrinsic function of the heart decreases in failure and stroke volume diminishes, an increase in heart rate—through sympathetic activation of adrenoceptors—is the first compensatory mechanism that comes into play to maintain cardiac output.
Systolic and Diastolic Failure

- Heart failure occurs when cardiac output is inadequate to provide the oxygen needed by the body. Two major types of failure may be distinguished:
  - In **systolic failure**, the mechanical pumping action (contractility) and the ejection fraction of the heart are reduced (< 45%).
  - In **diastolic failure**, stiffening and loss of adequate relaxation plays a major role in reducing cardiac output and ejection fraction may be normal. Heart failure due to diastolic dysfunction does not usually respond optimally to positive inotropic drugs.
- Because other cardiovascular conditions are now being treated more effectively (especially myocardial infarction), more patients are surviving long enough for heart failure to develop, making this one of the cardiovascular conditions that is actually increasing in prevalence.
Severity of CHF

- The severity of heart failure is usually described according to a scale devised by the New York Heart Association.
- **Class I** failure is associated with no limitations on ordinary activities and symptoms that occur only with greater than ordinary exercise.
- **Class II** is characterized by slight limitation of ordinary activities, which result in fatigue and palpitations with ordinary physical activity.
- **Class III** failure results in no symptoms at rest, but fatigue, etc, with less than ordinary physical activity.
- **Class IV** is associated with symptoms even when the patient is at rest.

Historical and Modern Approaches to Therapy

- Historically, drug therapies have focused on the endpoint components of this syndrome, volume overload (congestion) and myocardial dysfunction (heart failure).
- Treatment strategies have typically emphasized the use of diuretics and cardiac glycosides, with investigative efforts directed at the development of new agents that improved contractile performance.
- While effective in providing relief of symptoms and in stabilizing patients with hemodynamic decompensation, such therapies have not been proven to improve survival.
- More recent work has provided greater insight into the induction and propagation of CHF, providing a conceptual framework in which heart failure is viewed as a consequence of disordered circulatory dynamics and pathologic cardiac remodeling.
- These developments have had a major positive impact on the treatment of CHF.
Pharmacotherapy of CHF
Table 13–3. Steps in the Treatment of Chronic Heart Failure.

1. Reduce workload of the heart
   a. Limit activity, put on bed rest
   b. Reduce weight
   c. Control hypertension
2. Restrict sodium intake
3. Restrict water (rarely required)
4. Give diuretics
5. Give ACE inhibitor or angiotensin receptor blocker
6. Give digitalis if systolic dysfunction with 3rd heart sound or atrial fibrillation is present
7. Give β-blockers to patients with stable class II–IV heart failure
8. Give vasodilators
9. Cardiac resynchronization if wide QRS interval is present in normal sinus rhythm

---

**Figure 33–12. Stages of heart failure.** (Reproduced with permission from Isserow and Braeza [2003].)
### Vazodilators

**ACE inhibitors**
1. Enalapril (Renitec)
2. Fosinopril (Monopril)
3. Captopril (Kapril)
4. Quinapril (Acuitel)
5. Lisinopril (Rilace)

**Direct vasodilators**
1. Hidralazine (*Apresoline*)
2. Isosorbid dinitrate (Tsordil)
3. Minoxidil (*Loniten*)
4. Sodium nitroprusside (Nipruss)

### Diuretics
1. Bumetanide (Bumid)
2. Furosemide (Lasix)
3. Hydrochlorothiazide (Aldactazide)
4. Metolazon (*Mykrox*)
5. Spironolactone (Aldactone)

### Inotropic drugs

**Cardiac glycosides**
1. Digitoxin (*Digimerck*)
2. Digoxin (Digoxin)

**β-adrenergic agonists**
1. Dobutamine (Dobutrex)
2. Dopamine (generic)

**Calcium sensitzers**
1. Levosimendan (Simdax)

**Phosphodiesterase inhibitors**
1. Amrinone (*Inocor*)
2. Enoksimone (*Perfan*)
3. Milrinone (*Primacor*)

### β-blockers
1. Bisoprolol (Concor)
2. Carvedilol (Dilatrend)
3. Metoprolol (Beloc)
**Digitalis**

- Digitalis is the genus name for the family of plants that provide most of the medically useful cardiac glycosides, eg, digoxin. Such plants have been known for thousands of years but were used erratically and with variable success until 1785, when William Withering, an English physician and botanist, published a monograph describing the clinical effects of an extract of the purple foxglove plant (*Digitalis purpurea*, a major source of these agents).

- All of the cardiac glycosides, or cardenolides—of which digoxin is the prototype—combine a steroid nucleus linked to a lactone ring at the 17 position and a series of sugars at carbon 3 of the nucleus. Because they lack an easily ionizable group, their solubility is not pH-dependent. Digoxin is obtained from *Digitalis lanata*, the white foxglove, but many common plants contain cardiac glycosides.

---

**Figure 33-7. Structure of digoxin.**

*Goodman & Gilman’s Pharmacological Basis of Therapeutics 11th Edition 2006*
Pharmacokinetics

Absorption and distribution

- Digoxin, the only cardiac glycoside used in the USA, and Turkey is 65–80% absorbed after oral administration. Absorption of other glycosides varies from zero to nearly 100%. Once present in the blood, all cardiac glycosides are widely distributed to tissues, including the central nervous system.

Metabolism and excretion

- Digoxin is not extensively metabolized in humans; almost two thirds is excreted unchanged by the kidneys. Its renal clearance is proportionate to creatinine clearance. Equations and nomograms are available for adjusting digoxin dosage in patients with renal impairment.

<table>
<thead>
<tr>
<th>Table 9.1: Cardiac glycosides' characteristics and clinical usages. The values refer to renal and hepatic functions that are normal or average among the patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Age category</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Oral bioavailability (%)</td>
</tr>
<tr>
<td>Plasma protein binding (%)</td>
</tr>
<tr>
<td>Elimination half-life (h)</td>
</tr>
<tr>
<td>Metabolic clearance (ml/min)</td>
</tr>
<tr>
<td>Clearance at 0.5 mg/L</td>
</tr>
<tr>
<td>Toxic plasma concentration (μg/mL)</td>
</tr>
<tr>
<td>Toxic plasma concentration (mg/L)</td>
</tr>
<tr>
<td>Standard dose (mg/kg)</td>
</tr>
<tr>
<td>Initial digitalization rate (mg/m)</td>
</tr>
<tr>
<td>6-hour interval rate</td>
</tr>
<tr>
<td>Top and total dose</td>
</tr>
</tbody>
</table>

Süzer Farmakoloji 3. Baskı 2005

Pharmacodynamics

- Digoxin has multiple direct and indirect cardiovascular effects, with both therapeutic and toxic consequences. In addition, it has undesirable effects on the central nervous system and gut.
- At the molecular level, all therapeutically useful cardiac glycosides inhibit \( \text{Na}^+/\text{K}^+ \text{ATPase} \), the membrane-bound transporter often called the sodium pump.
- It is probable that this inhibitory action is largely responsible for the therapeutic effect (positive inotropy) as well as a major portion of the toxicity of digitalis.
- The fact that a receptor for cardiac glycosides exists on the sodium pump has prompted some investigators to propose that an endogenous "digitalis-like" steroid, possibly ouabain, must exist.

Cardiac Effects:  
A. Mechanical Effects I

- Cardiac glycosides increase contraction of the cardiac sarcomere by increasing the free calcium concentration in the vicinity of the contractile proteins during systole.
- The increase in calcium concentration is the result of a two-step process:  
  first, an increase of intracellular sodium concentration because of \( \text{Na}^+/\text{K}^+ \text{ATPase} \) inhibition;  
  second, a relative reduction of calcium expulsion from the cell by the sodium-calcium exchanger caused by the increase in intracellular sodium.
Cardiac Effects: A. Mechanical Effects II

- The increased cytoplasmic calcium is sequestered by the SERCA in the SR for later release.
- The net result of the action of therapeutic concentrations of a cardiac glycoside is a distinctive increase in cardiac contractility.
- This effect occurs in both normal and failing myocardium, but in the intact animal or patient the responses are modified by cardiovascular reflexes and the pathophysiology of heart failure.
**Cardiac Effects:**

**B. Electrical Effects**

- The effects of digitalis on the electrical properties of the heart are a mixture of direct and autonomic (i.e. parasympathomimetic) actions.
- Direct actions on the membranes of cardiac cells follow a well-defined progression: an early, brief prolongation of the action potential, followed by shortening (especially the plateau phase).
- The decrease in action potential duration is probably the result of increased potassium conductance that is caused by increased intracellular calcium.
- All of these effects can be observed at therapeutic concentrations in the absence of overt toxicity.

---

**Table 13-2. Effects of digoxin on electrical properties of cardiac tissues.**

<table>
<thead>
<tr>
<th>Tissue or Variable</th>
<th>Effects at Therapeutic Dosage</th>
<th>Effects at Toxic Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus node</td>
<td>↓ Rate</td>
<td>↓ Rate</td>
</tr>
<tr>
<td>Atrial muscle</td>
<td>↓ Refractory period</td>
<td>↑ Refractory period, arrhythmias</td>
</tr>
<tr>
<td>Atrioventricular node</td>
<td>↓ Conduction velocity, ↑ refractory period</td>
<td>↑ Refractory period, arrhythmias</td>
</tr>
<tr>
<td>Purkinje system, ventricular muscle</td>
<td>Slight ↓ refractory period</td>
<td>Extrasystoles, tachycardia, fibrillation</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>↑ PR interval, ↓ QT interval</td>
<td>Tachycardia, fibrillation, arrest at extremely high dosage</td>
</tr>
</tbody>
</table>
Electrocardiographic record showing digitalis-induced bigeminy. The complexes marked NSR are normal sinus rhythm beats; an inverted T wave and depressed ST segment are present. The complexes marked PVB are premature ventricular beats and are the electrocardiographic manifestations of depolarizations evoked by delayed oscillatory afterpotentials as shown in Figure 13–4. (Modified and reproduced, with permission, from Goldman MJ: Principles of Clinical Electrocardiography, 12th ed. Lange, 1986.)

-effects on other organs

- Cardiac glycosides affect all excitable tissues, including smooth muscle and the central nervous system. The gastrointestinal tract is the most common site of digitalis toxicity outside the heart. The effects include anorexia, nausea, vomiting, and diarrhea. This toxicity may be partially caused by direct effects on the gastrointestinal tract but is also the result of central nervous system actions.
- Central nervous system effects include vagal and chemoreceptor trigger zone stimulation. Less often, disorientation and hallucinations—especially in the elderly—and visual disturbances are noted. The latter effect may include aberrations of color perception. Gynecomastia is a rare effect reported in men taking digitalis.
Interactions with potassium, calcium, and magnesium

- **Potassium** and digitalis interact in two ways. First, they inhibit each other’s binding to Na⁺/K⁺ ATPase; therefore, hyperkalemia reduces the enzyme-inhibiting actions of cardiac glycosides, whereas hypokalemia facilitates these actions. Second, abnormal cardiac automaticity is inhibited by hyperkalemia. Moderately increased extracellular K⁺ therefore reduces the effects of digitalis, especially the toxic effects.

- **Calcium** ion facilitates the toxic actions of cardiac glycosides by accelerating the overloading of intracellular calcium stores that appears to be responsible for digitalis-induced abnormal automaticity. Hypercalcemia therefore increases the risk of a digitalis-induced arrhythmia.

- The effects of **magnesium** ion appear to be opposite to those of calcium. These interactions mandate careful evaluation of serum electrolytes in patients with digitalis-induced arrhythmias.

---

Other Positive Inotropic Drugs Used in Heart Failure: Amrinone, Milrinone, Levosimendan

- Drugs that inhibit **phosphodiesterases**, the family of enzymes that inactivate cAMP and cGMP, have long been used in therapy of heart failure. Although they have positive inotropic effects, most of their benefits appear to derive from vasodilation.

- The bipyridines **amrinone** and **milrinone** are the most successful of these agents found to date, but their usefulness is quite limited.

- **Levosimendan**, sensitizes the troponin system to calcium, also appears to inhibit phosphodiesterase and cause some vasodilation in addition to its inotropic effects.
**Beta-adrenoceptor stimulants**

- The selective β₁ agonist that has been most widely used in patients with heart failure is dobutamine. This parenteral drug produces an increase in cardiac output together with a decrease in ventricular filling pressure. Some tachycardia and an increase in myocardial oxygen consumption have been reported.
- Therefore, the potential for producing angina or arrhythmias in patients with coronary artery disease must be considered, as well as the tachyphylaxis that accompanies the use of any stimulant. Intermittent dobutamine infusion may benefit some patients with chronic heart failure.
- Dopamine has also been used in acute heart failure and may be particularly helpful if there is a need to raise blood pressure.
Drugs Without Positive Inotropic Effects Used in Heart Failure

- Paradoxically, these agents—not positive inotropic drugs—are the first-line therapies for chronic heart failure.
- The drugs most commonly used are diuretics, ACE inhibitors, angiotensin receptor antagonists, and β-blockers.
- In acute failure, diuretics and vasodilators play important roles.
Diuretics

- Their major mechanism of action in heart failure is to reduce venous pressure and ventricular preload. This results in reduction of edema and its symptoms, and reduction of cardiac size, which leads to improved pump efficiency.
- Spironolactone and eplerenone, the aldosterone antagonist diuretics, have the additional benefit of decreasing morbidity and mortality in patients with severe heart failure who are also receiving ACE inhibitors and other standard therapy.
- One possible mechanism for this benefit lies in accumulating evidence that aldosterone may also cause myocardial and vascular fibrosis and baroreceptor dysfunction in addition to its renal effects.
Angiotensin-Converting Enzyme Inhibitors, Angiotensin Receptor Blockers, & Related Agents

- The ACE inhibitors such as captopril reduce peripheral resistance and thereby reduce afterload; they also reduce salt and water retention (by reducing aldosterone secretion) and in that way reduce preload. The reduction in tissue angiotensin levels also reduces sympathetic activity, probably through diminution of angiotensin's presynaptic effects on norepinephrine release. Finally, these drugs reduce the long-term remodeling of the heart and vessels, an effect that may be responsible for the observed reduction in mortality and morbidity.

- Angiotensin AT1 receptor-blockers such as losartan appear to have similar but more limited beneficial effects. Angiotensin receptor blockers should be considered in patients intolerant of ACE inhibitors. In some trials, candesartan was beneficial when added to an ACE inhibitor.
**Vasodilators I**

- The vasodilators are effective in acute heart failure because they provide a reduction in preload (through venodilation), or reduction in afterload (through arteriolar dilation), or both.
- Some evidence suggests that long-term use of hydralazine and isosorbide dinitrate can also reduce damaging remodeling of the heart.

**Vasodilators II**

- A synthetic form of the endogenous peptide brain natriuretic peptide (BNP) is approved for use in acute cardiac failure as nesiritide. This recombinant product increases cGMP in smooth muscle cells and reduces venous and arteriolar tone in experimental preparations. It also causes diuresis. The peptide has a short half-life of about 18 minutes and is administered as a bolus intravenous dose followed by continuous infusion. Excessive hypotension is the most common adverse effect. Reports of significant renal damage and deaths have resulted in application of extra warnings regarding this agent and it should be used with great caution.
- Measurement of endogenous BNP has been proposed as a diagnostic test because plasma concentrations rise in most patients with heart failure.
Vasodilators III

- **Bosentan**, an orally active competitive inhibitor of endothelin, has been shown to have some benefits in experimental animal models of heart failure, but results in human trials have been disappointing.
- This drug is approved for use in pulmonary hypertension. It has significant teratogenic and hepatotoxic effects.

Beta-Adrenoceptor Blockers

- Most patients with chronic heart failure respond favorably to certain blockers in spite of the fact that these drugs can precipitate acute decompensation of cardiac function.
- Studies with bisoprolol, carvedilol, and metoprolol showed a reduction in mortality in patients with stable severe heart failure but this effect was not observed with another blocker, bucindolol.
- A full understanding of the beneficial action of blockade is lacking, but suggested mechanisms include attenuation of the adverse effects of high concentrations of catecholamines (including apoptosis), up-regulation of receptors, decreased heart rate, and reduced remodeling through inhibition of the mitogenic activity of catecholamines.
Figure 33-4. Time-dependent effects of metoprolol on left ventricular ejection fraction in patients with heart failure. In patients with severe left ventricular dysfunction, the initial increase in left ventricular ejection fraction observed with metoprolol was not significantly different from that observed with standard therapy (day 1). However, over time and despite optimization of metoprolol to full therapeutic levels, ejection-fraction returned to baseline (3 months), and by 3 months was significantly higher than at baseline. In the group given standard therapy, ejection fraction did not change significantly. An increase in left ventricular ejection fraction between 1 and 4 months after initiation of therapy is seen commonly with β-receptor antagonists used in patients with heart failure. This observation suggests that the direct hemodynamic effect of a β-adrenergic antagonist in patients with heart failure is in addition to the hemodynamic effects of further interventions. (Adapted with permission from Bristow et al., 1994.)

Figure 33-5. Dose-dependent effect of carvedilol on left ventricular ejection fraction. In the U.S. Carvedilol Trials Program, a subgroup of patients were randomized to placebo or carvedilol (in the standard dose (25 mg twice daily) or in a reduced dose of 12.5 or 6.25 mg twice per day). After 6 months of treatment, left ventricular ejection fraction (ΔLVEF) increased with all three doses of carvedilol, but not with placebo. The increase in ejection fraction was strongly related to the dose of carvedilol. These data emphasize the importance of titrating doses of β-receptor antagonists to the target or the highest tolerated dose. (Adapted with permission from Bristow et al., 1996.)
Management of Acute Heart Failure I

• Acute heart failure occurs frequently in patients with chronic failure. Such episodes are usually associated with increased exertion, emotion, salt in the diet, noncompliance with medical therapy, or increased metabolic demand occasioned by fever, anemia, etc.

• A particularly common and important cause of acute failure—with or without chronic failure—is acute myocardial infarction.

Management of Acute Heart Failure II

• Patients with acute myocardial infarction are best treated with emergency revascularization using either coronary angioplasty and a stent or a thrombolytic agent. Even with revascularization, acute failure may develop in such patients.

• Many of the signs and symptoms of acute and chronic failure are identical, but their therapies diverge because of the need for more rapid response and the relatively greater frequency and severity of pulmonary vascular congestion in the acute form.
Management of Acute Heart Failure III

- Measurements of arterial pressure, cardiac output, stroke work index, and pulmonary capillary wedge pressure are particularly useful in patients with acute myocardial infarction and acute heart failure.
- Such patients can be usefully characterized on the basis of three hemodynamic measurements: arterial pressure, left ventricular filling pressure, and cardiac index.
- One such classification and therapies that have proved most effective are set after this slide. When filling pressure is greater than 15 mm Hg and stroke work index is less than 20 gm/m², the mortality rate is high. Intermediate levels of these two variables imply a much better prognosis.
### Hiperlipoproteineminin Frederickson/WHO sınıflaması

<table>
<thead>
<tr>
<th>Tip</th>
<th>Artan lipoproteinler</th>
<th>Kolesterol</th>
<th>Trigliserit</th>
<th>Ateroskleroz riski</th>
<th>İlaç tedavisi</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Silomikronlar</td>
<td>+</td>
<td>+++</td>
<td>Artmış</td>
<td>Yok</td>
</tr>
<tr>
<td>IIa</td>
<td>LDL</td>
<td>++</td>
<td>Artmış</td>
<td>Yüksek</td>
<td>HMG-CoA redüktaz inhibitörleri ve/veya reçine ler</td>
</tr>
<tr>
<td>IIb</td>
<td>LDL + VLDL</td>
<td>++</td>
<td>++</td>
<td>Yüksek</td>
<td>Fibratlar, HMG-CoA redüktaz inhibitörleri, nikotinik asit</td>
</tr>
<tr>
<td>III</td>
<td>β-VLDL</td>
<td>++</td>
<td>++</td>
<td>Orta</td>
<td>Fibratlar</td>
</tr>
<tr>
<td>IV</td>
<td>VLDL</td>
<td>+</td>
<td>++</td>
<td>Orta</td>
<td>Fibratlar (ve/veya balık yağı)</td>
</tr>
<tr>
<td>V</td>
<td>Silomikronlar + VLDL</td>
<td>+</td>
<td>++</td>
<td>Artmış</td>
<td>Yok (ve/veya balık yağı)</td>
</tr>
</tbody>
</table>


---

### Tablo 13.1 HMG-CoA redüktaz inhibitörlerin özellikleri

Ator, atorvastatin; flu, fluvastatin; lo, lovastatin; pra, pravastatin; rosu, rosuvastatin; sim, simvastatin.

<table>
<thead>
<tr>
<th>Özellik</th>
<th>Ator</th>
<th>Flu</th>
<th>Lo</th>
<th>Pra</th>
<th>Rosu</th>
<th>Sim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum LDL kolesterol düşmesi (%)</td>
<td>50</td>
<td>24</td>
<td>34</td>
<td>34</td>
<td>50</td>
<td>41</td>
</tr>
<tr>
<td>Serum trigliserit düşmesi (%)</td>
<td>28</td>
<td>10</td>
<td>16</td>
<td>24</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Serum HDL kolesterol yüksemesi (%)</td>
<td>6</td>
<td>8</td>
<td>9</td>
<td>12</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Plazma yanılması ömrü (saat)</td>
<td>14</td>
<td>1-2</td>
<td>2</td>
<td>1-2</td>
<td>19</td>
<td>1-2</td>
</tr>
<tr>
<td>Santral sinir sistemine geçiş</td>
<td>Yok</td>
<td>Yok</td>
<td>Var</td>
<td>Yok</td>
<td>Yok</td>
<td>Var</td>
</tr>
<tr>
<td>Emilin ilacın böbreklerde atılan oranı (%)</td>
<td>2</td>
<td>&lt;6</td>
<td>10</td>
<td>20</td>
<td>10</td>
<td>13</td>
</tr>
</tbody>
</table>

Kaynak: 2, Şekil 21.7 temel alınmıştır.
Tablo 13.2 Antihiperlipidemik ilaçların LDL, HDL ve trigliseritler üzerine etkile-ринin özetı.

<table>
<thead>
<tr>
<th>İlaç sınıfı</th>
<th>LDL</th>
<th>HDL</th>
<th>Trigliseritler</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG-CoA redüktaz inhibitoryleri</td>
<td>↓↓↓↓</td>
<td>↑</td>
<td>↓↓</td>
</tr>
<tr>
<td>Fibratlar</td>
<td>↓</td>
<td>↑↑↑</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>Niasin</td>
<td>↓↓</td>
<td>↑↑↑↑</td>
<td>↓↑↓↓</td>
</tr>
<tr>
<td>Safra asidi bağlayıcı reçineler</td>
<td>↓↓↓↓</td>
<td>↑</td>
<td>Çok az</td>
</tr>
<tr>
<td>Kolesterol emiliminini düşürenler</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
</tr>
</tbody>
</table>

Kaynak 2, Şekil 21.14 temel alınmıştır.

Thank you...