Cardiovascular Drugs in the Top 200: Clinical Implications

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Continuing Education Units: 3 hours


Disclaimer: Participants must always be aware of the hazards of using limited knowledge in integrating new techniques or procedures into their practice. Only sound evidence-based dentistry should be used in patient therapy.

The risk of perioperative cardiac complications associated with dental treatment depends on procedure-specific and patient-specific factors. Important co-determinants of patient-specific risk factors include disease-related factors, the patient's functional capacity, and pharmacotherapeutic variables. This course presents information essential for risk stratification of patients with cardiac dysfunction based on cardiovascular pharmacotherapy predicated on the top 200 drugs dispensed by U.S. community pharmacies.

Conflict of Interest Disclosure Statement

• Drs. Banasik, Al-saadi and Faddoul report no conflicts of interest associated with this course.
• Dr. Terézhalmy has done consulting work for Procter & Gamble and is a member of the dentalcare.com Advisory Board.

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Introduction

During the past 25 years clinicians have seen an exponential increase in the number of medically compromised patients who seek dental care and because of advances in dental research and education oral healthcare providers perform increasingly more complex procedures on these patients. As a result, clinicians can expect to face situations during the perioperative period that may threaten the physical well-being of patients. The risk of perioperative medical complications depends on procedure-specific and patient-specific factors.

Procedure-specific Risk Factors

Every procedure elicits a physiological stress-response. This response is initiated by tissue injury and mediated primarily by the sympathoadrenal system. Sympathoadrenal activity can induce tachycardia and hypertension and increase myocardial oxygen demand. The magnitude of procedure-related stress is predicated on the extent of procedure-related tissue trauma, duration of the procedure, volume of blood loss, fluid shifts, and changes in core body temperature.¹

The rates of catecholamine release are the primary determinants of the biologic expression of sympathoadrenal activity. The basal range steady-state plasma concentration for epinephrine is 10-70 pg/ml.² Specific effects, e.g., changes in heart rate
and blood pressure, are produced at particular threshold plasma concentrations. In two studies in dental settings, the resting supine steady-state plasma concentration of epinephrine was reported to be 27±4 and 28±8 pg/ml, respectively.\textsuperscript{3,4}

The first study evaluated the sympathoadrenal and hemodynamic effect of local dental anesthesia (administered as a mandibular nerve block).\textsuperscript{3} The administration of 1.8 cc of lidocaine 2\% without epinephrine did not significantly alter the resting supine steady-state plasma epinephrine concentrations of 27±4 pg/ml over the 60 minute study period. Similarly, heart rate (HR) and mean arterial pressure (MAP = systolic blood pressure + 2(diastolic blood pressure)/3) were also unaltered following injection.

The administration of 1.8 cc of lidocaine 2\% with epinephrine 1:100,000 (administered as a mandibular nerve block) resulted in a transient elevation of epinephrine from the resting supine steady-state plasma concentration of 27±4 pg/ml to a maximum of 94 pg/ml at 8 minutes after injection.\textsuperscript{3} MAP was unaffected. Threshold concentrations required to affect diastolic blood pressure (BP) range from 150-200 pg/ml.\textsuperscript{2} HR increased by only a few beats per minute for the initial 2 minutes after injection. Threshold concentrations required to affect heat rate range from 50-100 pg/ml.\textsuperscript{2}

The second study evaluated the sympathoadrenal and hemodynamic effect of routine restorative dental care (two or three surface amalgams) under local dental anesthesia.\textsuperscript{4} Following the administration of 1.8 cc of lidocaine 2\% with epinephrine 1:100,000 (administered as a mandibular nerve block) plasma epinephrine levels increased from the resting supine steady-state plasma epinephrine concentrations of 28±8 pg/ml to 105±28 pg/ml and 73±14 pg/ml at 5 and 10 minutes after injection, respectively.

After rubber dam application (13 to 18 minutes after injection) the plasma epinephrine level had further decreased to 51±7 pg/ml and within minutes returned to resting supine steady-state levels. One procedure was done on each patient and the total chair-time per procedure was 60±4 minutes. Corresponding to increased plasma epinephrine concentrations at 5 and 10 minutes after injection, HR increased by only a few beats per minute (threshold concentrations required to affect heat rate range from 50-100 pg/ml. No significant alterations were noted in MAP.

Surgical stress can also cause alterations in the balance between prothrombotic and fibrinolytic factors, resulting in hypercoagulability and possible coronary thrombosis (elevation of fibrinogen and other coagulation factors, increased platelet activation and aggregation, and reduced fibrinolysis).\textsuperscript{1} The extent of such changes is proportional to the degree and duration of surgical stress. These factors can contribute to myocardial ischemia and heart failure.

Perioperative cardiac risk, defined as myocardial infarction and cardiac death within 30 days of noncardiac procedures, has been assessed.\textsuperscript{5} It was concluded that non-cardiac procedures can be divided into high-, intermediate-, and low-stress groups with estimated rates of cardiac events of >5\%, 1-5\%, and <1\%, respectively (Box 1). With low-stress non-cardiac procedures the risk of a cardiac event is negligible unless strong patient-specific risk factors are present.\textsuperscript{5}

There are no adequately controlled or randomized clinical trials that help define perioperative cardiac risk for various dental procedures. However, according to a retrospective analysis of EMS data in Seattle and King Counties, WA, with a combined population 1.5 million, over a seven-year period six major cardiac events were documented in community based dental practices for an annual incidence of <0.002 per dental practice.\textsuperscript{6}

Two independent prospective surveys over a 10-year period, involving 4,309 dentists, documented a total of 30,602 medical emergencies.\textsuperscript{7} Based on these data, the number of medical emergencies per dental practice per year was 0.5. Cardiovascular emergencies included postural hypotension (17.8\%), angina pectoris (4.6\%), myocardial infarction (1.4\%), and cardiac arrest (1.1\%) at an annual rate of 0.08, 0.02, 0.007, and 0.005 per dental practice per year, respectively.

It can be concluded that the risk of perioperative cardiac events in association with dental procedures is low-to-very low. In a low-risk situation the likelihood of a major cardiac event (MACE) of death or myocardial infarction (MI) is
Functional capacity relates to a person’s functional reserve and correlates well with maximum oxygen uptake by treadmill testing. Functional capacity is expressed in metabolic equivalents (METs). One MET equals the resting or basal oxygen requirement (i.e., 3.5 ml of O2 per kg per minute) of a 40–year-old, 70-kg man.

Functional capacity is reflected in a person’s ability to perform a spectrum of common daily activities (Box 2).

It is classified as excellent (>10 METs), good (7 METs to 10 METs), moderate (6 METs to 4 METs), or poor (<4 METs). The inability to climb two flights of stairs or run a short distance indicates poor functional capacity (<4 METs). A functional capacity of 4 METs is predictive of increased incidence of perioperative and long-term cardiac events.

When functional capacity is high, the risk of MACE is low. For example, a patient classified as having

<1%. Elevated-risk defines a situation in which the risk of MACE is ≥1%. Consequently, dental procedure-specific variable are less important than patient-specific variables in predicting a MACE in oral healthcare settings.

**Patient-specific Risk Factors**

Patient-specific problems, which may interfere with the clinical process and/or patients’ quality of life, must be identified. The ability of a patient to undergo dental procedures is predicated on his/her medical history. Past and present illnesses, major hospitalizations, review of organ systems, drug allergies, other adverse drug effects, medications, vitamins, dietary supplements, or special diets must be considered in determining perioperative risk.

Since the main physiologic stimulus to epinephrine secretion is exercise, the history should also seek to determine the patient’s functional capacity.

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**Box 1. Procedure-related Stress Estimates**

<table>
<thead>
<tr>
<th>High-stress procedures</th>
<th>Intermediate-stress procedures</th>
<th>Low-stress procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic and other major vascular surgery</td>
<td>Neurological</td>
<td>Breast surgery</td>
</tr>
<tr>
<td>Peripheral vascular surgery</td>
<td>Pulmonary</td>
<td>Dental procedures</td>
</tr>
<tr>
<td></td>
<td>Major orthopaedic (hip, spine)</td>
<td>Eye surgery</td>
</tr>
<tr>
<td></td>
<td>Renal transplantation</td>
<td>Gynecological procedures</td>
</tr>
<tr>
<td></td>
<td>Head and neck surgery</td>
<td>Minor orthopaedic (knee)</td>
</tr>
</tbody>
</table>

**Box 2. Estimated Energy Requirement for a Spectrum of Common Daily Activities**

<table>
<thead>
<tr>
<th>1 MET Can you...</th>
<th>2 METs Can you...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take care of yourself?</td>
<td>Climb two flights of stairs or walk uphill, or run a short distance?</td>
</tr>
<tr>
<td>Eat, get dressed, or use the toilet?</td>
<td>Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?</td>
</tr>
<tr>
<td>Walk indoor around the house?</td>
<td>Participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?</td>
</tr>
<tr>
<td>Walk 100 m on level ground at 3 to 5 km per hour</td>
<td></td>
</tr>
</tbody>
</table>

<4 METs

>10 METs
elevated-risk because of age or known coronary artery disease (CAD), but who is asymptomatic and runs 30 minute daily may need no further cardiovascular testing before proceeding with planned non-cardiac procedures. In contrast, a sedentary patient without a history of CAD, but with poor functional capacity may benefit from a preoperative evaluation.

The cardiovascular effects of infiltration anesthesia compared with those produced by ergometric exercising have been evaluated. The hemodynamic effects of infiltration anesthesia with 0.045 mg of epinephrine (4.5 cc of a local anesthetic agent with epinephrine 1:100,000) were found to be less than those produced by ergometric-stress testing at 25 watts in young patients and at 15 watts in older subjects. The workload of ergometric-stress testing at these levels is >4 METs.

Consequently, patients whose functional capacity is ≥4 METs can safely be administered at least 4.5 cc of a local anesthetic agent with epinephrine 1:100,000. In this study, there were no differences in hemodynamic responses (evaluated by echocardiography) between normotensive and hypertensive patients. This is of note because hypertension and structural coronary arterial abnormalities are the cause of 90-95% of the arrhythmias, which lead to sudden cardiac death.

Physical examination is also part of risk assessment. The general appearance of the patient provides invaluable clues regarding his/her overall cardiac status. Cyanosis, pallor, diaphoresis, shortness of breath, tightness and/or pain in the chest with minimal activity, tremor, anxiety, and peripheral edema are signs and symptoms of underlying CVD. Critically, the physical examination must also include a determination of the patient’s vital signs.

Predicated on patient-specific risk factors the American Society of Anesthesiology (ASA) Physical Status (PS) Classification system provides a practical method to determine perioperative risk for patients undergoing surgical (and by extension dental) procedures. The rate of perioperative medical complications correlates closely to the ASA PS classification of patients and ranges from 0.4/1000 for ASA PS I to 9.6/1000 for ASA PS IV.

Cardiovascular Drugs in the Top 200
In identifying patient-specific risk factors, the major role played by drugs in modern healthcare cannot be over-emphasized. The per capita utilization of prescription medications, predicated on the top 200 drugs dispensed by U.S. community pharmacies is about 12 prescriptions per person per year. Adults over 50 years of age consume the largest volume of prescription medications and account for 64% of the total number of prescriptions dispensed.

To test the hypothesis that the top 200 drugs reliably reflect disease trends in oral healthcare settings, data were collected (age, gender, medical diagnoses, and pharmacological status), tabulated, and evaluated on 1,000 consecutive

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**Box 3. Vital Signs: Normal Values.**

- Pulse pressure, rate and rhythm
  - Normal: 60 to 100 beats per minute
- Blood pressure
  - Normal: <120/80 mmHg
- Respiration
  - Normal: 16 to 20 breaths per minute
- Temperature
  - Normal: 37°C (98.6°F)

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**Box 4. Modified ASA Physical Status Classification.**

| I. | Normal healthy patient – no limitation of physical activity |
| II. | Patient with mild systemic disease – no or minimal limitation on physical activity |
| III. | Patient with severe systemic disease – moderate to marked limitation on physical activity |
| IV. | Patient with incapacitating systemic disease – no residual functional reserve |
| V. | Moribund patients not expected to survive 24 hours |
patients in a large general dental practice. Cardiovascular drugs identified by the current and a previous survey closely mirror those in the top 200 and fall into 10 sub-classes (Tables 1-10).19-22

Prevalent Cardiovascular Diagnoses
Cardiovascular drugs represent the highest volume of prescription medications in the top 200 and those commonly taken by patients in a general dental practice (Box 5). Based on the mechanisms of action of these drugs, the most common cardiovascular diseases (CVDs) encountered in oral healthcare settings include hypertension, coronary artery disease, cardiac arrhythmias, heart failure, and thromboembolic complications.

Hypertension
Blood pressure (BP), the lateral pressure exerted by blood in a unit area of blood vessel wall, is a function of cardiac output and peripheral vascular resistance. When blood volume becomes greater than the limited volume capacity of the vascular compartment, the patient develops hypertension (HTN). BP is classified as normal (<120/80 mmHg), pre-HTN (120–129/80–89 mmHg), stage 1 HTN (140–159/90–99 mmHg), or stage 2 HTN (160/100 mmHg).24

HTN is a useful marker for CAD. The blood pressure also correlates well with obesity and sedentary lifestyle; significant use of tobacco, coffee, and alcohol; and a number of systemic diseases, e.g., dyslipidemia, diabetes mellitus (DM), thyroid dysfunction, adrenal disease, and renal insufficiency.25 Hypertension is known as the "silent killer." High blood pressure is often asymptomatic (Box 6) until target organ damage develops (Box 7).

Drug therapy for HTN may include diuretics to reduce volume overload; electrolyte modifiers

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Box 5. Top 200 Prescription Drugs Dispensed by U.S. Community Pharmacies.19-21

<table>
<thead>
<tr>
<th>Major drug classes</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>1</td>
</tr>
<tr>
<td>Analgesics</td>
<td>2</td>
</tr>
<tr>
<td>CNS</td>
<td>3</td>
</tr>
<tr>
<td>Antimicrobial</td>
<td>4</td>
</tr>
<tr>
<td>Endocrine/metabolic</td>
<td>5</td>
</tr>
<tr>
<td>Respiratory</td>
<td>6</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>7</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>8</td>
</tr>
</tbody>
</table>

Box 6. Signs and Symptoms of Severely Elevated Blood Pressure.
- Flushed face
- Restlessness
- Headache
- Dizziness
- Tinnitus
- Visual disturbances
- Dyspnea
  - Pulmonary edema
  - Congestive heart failure
- Systolic BP ≥180 mmHg OR diastolic BP ≥110 mmHg
- A “hammering” pulse

Box 7. Complications of Hypertension.
- Kidneys
  - Renal insufficiency
  - End-stage renal disease
- Cardiovascular system
  - Coronary artery disease
  - Left ventricular hypertrophy
  - Heart failure
- Cerebrovascular system
  - Ischemic and hemorrhagic stroke
- Peripheral vascular system
  - Absence of one or more major pulses in the extremities
- Eyes
  - Hypertensive retinopathy
to prevent hypokalemia; and ACE inhibitors, AT II-receptor antagonists, and calcium-channel blocking agents to dilate blood vessels. 

β₁-adrenergic receptor antagonists to reduce cardiac output are no longer recommended for initial therapy. Many patients will require two or more agents from different drug classes to reach target BP. Key recommendations for practice are presented in Table 11.

**Coronary Artery Disease**

Aerobic metabolism, the conversion of pyruvic acid to CO₂ and H₂O, accounts for the majority of the energy produced in cardiac muscles. When coronary arteries are unable to deliver enough oxygenated blood to myocytes, the patient develops acute coronary syndromes. Hypoxia and at times anoxia result from diseases and conditions which lead to atherosclerosis that limits or impairs coronary blood flow. Risk factors include dyslipidemia, HTN, DM, hypothyroidism, diets high in fat and calories or low in fruits, vegetables, and vitamins E and C, stress, and sedentary life-style.

In at-risk patients, pharmacological strategies include the administration of antihyperlipidemic agents. To prevent acute coronary syndromes, calcium-channel blocking agents are administered to increase circulation in coronary arteries and β₁-adrenergic receptor antagonists are prescribed to reduce the workload. Non-pharmacological strategies include coronary artery bypass grafts or percutaneous coronary intervention (PCI), i.e., balloon angioplasty or stent implantation. Key recommendations for practice are presented in Table 12.

**Cardiac Arrhythmias**

The primary pacemaker of the heart is the sinoatrial (SA) node. The SA node generates electrical impulses at regular intervals and with a frequency of 60 to 100 beats per minute. The impulses spread rapidly through the atria and enter the atroioventricular (AV) node. After a brief delay at the AV node, the impulses propagate over the His-Purkinje system as depolarization progresses over the ventricles in an anatomically synchronous and hemodynamically effective fashion. When the conduction system malfunctions, the patient develops cardiac arrhythmias.

To prevent cardiac arrhythmias β₁-adrenergic receptor antagonists are prescribed to slow depolarization, lengthen AV conduction, reduce cardiac contractility, and slow the heart rate. Calcium-channel blocking agents are prescribed to slow depolarization, repolarization, and AV conduction; cardiac glycoside are prescribed to prolong the refractory period and decrease conduction velocity at the AV node. Non-pharmacological strategies include the implantation of pacemakers or ICDs. Key recommendations for practice are presented in Table 13.

**Heart Failure**

Cardiac muscle contraction is under the regulatory control of the ANS. The interaction of a catecholamine with its membrane-bound β₁-adrenergic receptor activates the enzyme adenylate cyclase. The resultant increase in intracellular cyclic adenosine monophosphate (c-AMP) facilitates transmembrane calcium flux. In cardiac muscle, the β₁-adrenergic pathway can therefore be characterized as a series of events that begins with the interaction of a β₁-adrenergic receptor agonist with its receptor and concludes with an increase in muscle contraction.

Heart failure (HF) is a chronic contractile dysfunction characterized by myocyte loss and increased interstitial collagen deposits associated with organic cardiac diseases. Cardiac output is decreased resulting in reduced renal perfusion leading to increased renin-angiotensin-aldosterone synthesis. Decreased hepatic perfusion leads to decreased aldosterone clearance. Increased aldosterone concentrations lead to coronary and renovascular fibrosis, endothelial cell and baroreceptor dysfunction, and decreased myocardial norepinephrine uptake.

The most common cause of HF is left ventricular (LV) systolic dysfunction. Most cases are a result of CAD, previous MI, or a chronically underperfused myocardium. Other common causes are cardiomyopathy, valvular disease, and HTN. Right-ventricular (RV) systolic dysfunction is usually a consequence of LV systolic dysfunction. Other causes include right-ventricular infarction, pulmonary hypertension, chronic severe tricuspid regurgitation, or arrhythmogenic right-ventricular dysplasia.

When the heart is no longer able to pump an adequate supply of blood to meet metabolic demand for oxygen, the patient develops heart
failure. To improve myocardial contractility, the patient is prescribed a cardiac glycoside; to reduce workload, the patient may be prescribed a diuretic, an ACE inhibitor, an AT II-receptor antagonist, or a β1-adrenergic receptor antagonist. Non-pharmacological strategies include heart transplantation. Key recommendations for practice are presented in Table 14.

**Thromboembolic complications**
When vascular damage or a state of circulatory stasis occurs, patients develop thromboembolic complications.8 The clotting of blood is the sequential initiation, interaction, and completion of several stages of hemostasis. The vascular stage, initiated by tissue injury, is followed by the platelet phase resulting in platelet plug formation. In the plasma phase, a fibrin clot is generated via interactions involving numerous clotting factors. To prevent thromboembolic complications, patients are prescribed antithrombotic agents and/or an oral anticoagulant. Key recommendations for practice are presented in Table 15.

**Summary**
Familiarity with prescription medications dispensed by U.S. community pharmacies provides an insight into prevailing disease trends in the U.S. population. The top 200 prescription drugs also closely mirror the medications taken by patients in oral healthcare settings. Based on their mechanisms of action, the most common cardiovascular problems include hypertension, coronary artery disease, cardiac arrhythmias, heart failure, and thromboembolic complications.

Before treating a patient with risk factors for or known CVD, estimate the patient’s perioperative risk for MACE. If the combined procedure- and patient-specific variables predict low- or elevated-risk for MACE, but the patient’s functional capacity is ≥4 METs the patient may not need any further preoperative evaluation. If the functional capacity is <4 METs, before initiating any elective dental care, the patient should undergo medical evaluation and risk modification.
### Table 1. Diuretics.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
</table>
| hydrochlorothiazide²³ | Inhibits sodium reabsorption at the distal convoluted tubule | • Hypertension  
• Acute pulmonary edema (furosemide)  
• Adjuant in chronic edema states (furosemide)  
  • Congestive heart failure  
  • Hepatic cirrhosis  
  • Renal dysfunction  
  • Corticosteroid and estrogen therapy | • Common  
  • Hypotension  
  • Photosensitivity  
  • Hypokalemia (hydrochlorothiazide, furosemide)  
  • Hyperglycemia (hydrochlorothiazide, furosemide)  
  • Dry mouth |
| furosemide²³    | Inhibits sodium reabsorption at the loop of Henle          | • Hypertension  
• Acute pulmonary edema (furosemide)  
• Adjuant in chronic edema states (furosemide)  
  • Congestive heart failure  
  • Hepatic cirrhosis  
  • Renal dysfunction  
  • Corticosteroid and estrogen therapy | • Serious  
  • Hypotension (furosemide)  
  • Cardiac arrhythmias (hydrochlorothiazide, furosemide)  
  • Erythema multiforme  
  • Stevens-Johnson syndrome  
  • Toxic epidermal necrolysis  
  • Systemic lupus erythematosus (hydrochlorothiazide)  
  • Thrombocytopenia (furosemide)  
  • Nephrotoxicity (triamicarbene) |
| triamterene²³  | Competitive inhibitor of the principle cell sodium channels | • Hypertension  
• Acute pulmonary edema (furosemide)  
• Adjuant in chronic edema states (furosemide)  
  • Congestive heart failure  
  • Hepatic cirrhosis  
  • Renal dysfunction  
  • Corticosteroid and estrogen therapy | • Common  
  • Hypertension  
  • Photosensitivity  
  • Hypokalemia (hydrochlorothiazide, furosemide)  
  • Hyperglycemia (hydrochlorothiazide, furosemide)  
  • Dry mouth |

### Table 2. Electrolyte Modifiers.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
</table>
| potassium chloride²³  
Klor-Con M20 (potassium chloride)²³ | Promote normal muscle contraction and nerve impulse generation  
  • Maintain normal renal function, acid-base balance, carbohydrate metabolism, and gastric acid secretion | • To prevent diuretic-induced hypokalemia | • Common  
  • GI discomfort  
  • Hyperkalemia (mild)  
  • Paresthesia of extremities  
  • Listlessness  
  • Weak or heavy limbs  
  • Serious  
  • Hyperkalemia (severe)  
    • Hypotension  
    • Arrhythmias  
    • Heart block  
    • Cardiac arrest |
### Table 3. β-adrenergic Blocking Agents.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>atenolol23</td>
<td>• Selective β&lt;sub&gt;1&lt;/sub&gt;-adrenergic receptor blocking agents</td>
<td>• Hypertension</td>
<td>• Common</td>
</tr>
<tr>
<td>metoprolol23</td>
<td></td>
<td>• Angina pectoris</td>
<td>• Sedation, depression</td>
</tr>
<tr>
<td>Bystolic (nebivolol)23</td>
<td></td>
<td>• Cardiac arrhythmias</td>
<td>• Mask symptoms of hypoglycemia</td>
</tr>
<tr>
<td>carvedilol23</td>
<td>• Blocks α&lt;sub&gt;1&lt;/sub&gt;-, β&lt;sub&gt;1&lt;/sub&gt;-, and β&lt;sub&gt;2&lt;/sub&gt;-adrenergic receptors</td>
<td>• Hypertension</td>
<td>• Dyspnea, wheezing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Angina pectoris</td>
<td>• Dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiac arrhythmias</td>
<td>• Lichenoid stomatitis</td>
</tr>
</tbody>
</table>

### Table 4. Angiotensin Converting Enzyme (ACE) Inhibitors.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>enalapril23</td>
<td>• Inhibit conversion of angiotensin I to angiotensin II</td>
<td>• Hypertension</td>
<td>• Common</td>
</tr>
<tr>
<td>lisinopril23</td>
<td>• Decrease arteriolar vasoconstriction</td>
<td>• Heart failure</td>
<td>• Cough</td>
</tr>
<tr>
<td>lisinopril w/ hydrochlorothiazide23</td>
<td>• Increase aldosterone synthesis</td>
<td>• Diabetic nephropathy</td>
<td>• Angioedema</td>
</tr>
<tr>
<td></td>
<td>• Inhibit degradation of bradykinin</td>
<td></td>
<td>• Hypotension</td>
</tr>
<tr>
<td></td>
<td>• Increase renal proximal tubule sodium chloride resorption</td>
<td></td>
<td>• Hyperkalemia</td>
</tr>
<tr>
<td></td>
<td>• Decrease ADH release</td>
<td></td>
<td>• Serious</td>
</tr>
<tr>
<td></td>
<td>• Increase vasodilation</td>
<td></td>
<td>• Angioedema</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Agranulocytosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Neutropenia</td>
</tr>
</tbody>
</table>

### Table 5. Angiotensin II-receptor Antagonists.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>losartan23</td>
<td>• Antagonize the action of angiotensin II at AT1-receptors</td>
<td>• Hypertension</td>
<td>• Common</td>
</tr>
<tr>
<td>Benicar (olmesartan)23</td>
<td>• May indirectly increase vasorelaxant AT2-receptor activit</td>
<td>• Heart failure</td>
<td>• Hypotension</td>
</tr>
<tr>
<td>Benicar HCT (olmesartan w/hydrochlorothiazide)23</td>
<td>• Increase AT2-receptor activity</td>
<td>• Diabetic nephropathy</td>
<td>• Dizziness</td>
</tr>
<tr>
<td>Diovan (vasartan)23</td>
<td></td>
<td></td>
<td>• Serious</td>
</tr>
<tr>
<td>Diovan HCT (vasartan w/ hydrochlorothiazide)23</td>
<td></td>
<td></td>
<td>• Rare thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Rhabdomyolysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Rare angioedema</td>
</tr>
</tbody>
</table>
### Table 6. Calcium-channel Blocking Agents.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
</table>
| • amlopidine<sup>23</sup> | • Blocks voltage-gated L-type calcium channels and prevents the influx of calcium  
  - Relaxes vascular smooth muscle  
  - Reduces myocardial contraction | • Exertional angina  
  • Unstable angina  
  • Coronary spasm  
  • Hypertension  
  • Hypertrophic cardiomyopathy  
  • Raynaud’s phenomenon  
  • Pre-eclampsia | • Common  
  - Palpitations  
  - Peripheral edema  
  - Flushing  
  - Dizziness  
  - Gingival overgrowth  
  • Serious  
  - Increased incidence of angina pectoris  
  - Rare myocardial infarction |

### Table 7. Antihyperlipidemic Agents.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
</table>
| • pravastatin<sup>23</sup>  
  • lovastatin<sup>23</sup>  
  • simvastatin<sup>23</sup>  
  • Crestor (rosuvastatin sodium)<sup>23</sup>  
  • Lipitor (atorvastatin)<sup>23</sup> | • Inhibit HMG-CoA reductase  
  - Reduce VLDL and LDL | • Hyperlipidemia | • Common  
  - Abdominal pain ("statins")  
  - Constipation  
  - Diarrhea  
  - Dry mouth (fenofibrate)  
  - Myalgia  
  • Serious  
  - Myopathy  
  - Rhabdomyolysis ("statins")  
  - Hepatotoxicity  
  - Dermatomyositis ("statins") |
| • Niaspan (niacin)<sup>23</sup> | • Promotes lipid metabolism  
  - Reduces total cholesterol, LDL, and triglycerides |  |  |
| • Tricor (fenofibrate)<sup>23</sup> | • Promotes the synthesis of lipoprotein lipase  
  - Increases the catabolism of triglycerides and VLDL |  |  |
| • Zetia (ezetimibe)<sup>23</sup>  
  • Vytorin (ezetimibe w/ simvastatin)<sup>23</sup> | • Inhibits the absorption of cholesterol from the small intestine  
  - Reduce LDL and triglycerides |  |  |
| • Lovaza (omega-3/fish)<sup>23</sup> | • Incompletely understood molecular mechanisms |  |  |
### Table 8. Cardiac Glycosides.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin23</td>
<td>• Inhibits sodium/potassium ATPase</td>
<td>• Heart failure</td>
<td>• Common</td>
</tr>
<tr>
<td></td>
<td>○ Promotes intracellular sodium-calcium exchange</td>
<td>• Supraventricular arrhythmias</td>
<td>○ agitation</td>
</tr>
<tr>
<td></td>
<td>○ Inhibits sympathetic outflow in the autonomic nervous system and increases</td>
<td>• Atrial flutter</td>
<td>○ Fatigue</td>
</tr>
<tr>
<td></td>
<td>parasympathetic vagal tone</td>
<td>• Atrial fibrillation</td>
<td>○ Muscle weakness</td>
</tr>
<tr>
<td></td>
<td>○ Prolongs refractory period and decreases conduction velocity at the AV node</td>
<td>• Paroxysmal atrial tachycardia</td>
<td>○ Blurred vision</td>
</tr>
</tbody>
</table>

### Table 9. Antithrombotic Agents.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plavix (clopidogrel)23</td>
<td>• Blocks ADP-dependent platelet aggregation</td>
<td>• Secondary prevention of thromboembolic events in patients with recent MI, stroke, or peripheral vascular disease</td>
<td>• Common</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acute coronary syndromes</td>
<td>○ Chest pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Prevention of stent thrombosis (in combination with ASA)</td>
<td>○ Edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Petechia, purpura, ecchymosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Abnormal liver function</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Serious</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Atrial fibrillation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Heart failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Erythema multiforme</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Gastrointestinal hemorrhage in combination with ASA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Rare intracranial hemorrhage</td>
</tr>
</tbody>
</table>
Table 10. Oral Anticoagulants.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanisms of Action</th>
<th>Indications</th>
<th>Adverse Drug Effects</th>
</tr>
</thead>
</table>
| • Warfarin<sup>23</sup> | • Interferes with the hepatic synthesis of vitamin K-dependent coagulation factors  
○ Factors II, VII, IX, and X | • Prophylaxis and treatment  
○ Deep vein thrombosis  
○ Pulmonary embolism  
○ Prevention and treatment of systemic embolism  
○ Myocardial infarction  
○ Atrial fibrillation  
○ Prosthetic heart valve | • Common  
○ Purpura, ecchymosis, hematoma (Figures)  
• Serious  
○ Skin and other tissue necrosis  
○ Hemorrhage  
○ Hepatitis  
○ Hypersensitivity reaction |

### Table 11. Hypertension/Hypotension: Key Recommendations for Practice.\textsuperscript{25,27}

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
<th>Risk of MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pre-hypertension</td>
<td>• BP consistently increases with age</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o BP 120/80 to 139/89 mmHg</td>
<td>o A person with normal BP at 55 years of age has a 90% lifetime risk of progressing to pre-hypertension and then hypertension</td>
<td>o Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Uncontrolled systemic hypertension</td>
<td>• Serves as a useful marker for CAD</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o BP 140/90 to 179/109 mmHg</td>
<td>o Correlates well with clinical risk factors for CVDs</td>
<td>o Not an independent risk factor for MACE</td>
</tr>
<tr>
<td>• Severe uncontrolled hypertension</td>
<td>• No evidence of HTN-associated target organ damage (Box 7)</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>o BP &gt;180/110 mmHg</td>
<td>o Patient asymptomatic</td>
<td>o Medical evaluation and risk modification within 1 to 7 days</td>
</tr>
<tr>
<td>• Hypertensive urgency</td>
<td>• Evidence of HTN-associated target organ damage (Box 7)</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>o BP &gt;180/110 mmHg</td>
<td>o Patient asymptomatic</td>
<td>o Medical evaluation and risk modification within 24 to 48 hours</td>
</tr>
<tr>
<td>• Hypertensive emergency</td>
<td>• Evidence of HTN-associated target organ damage (Box 7)</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>o BP &gt;180/110 mmHg</td>
<td>o Patient symptomatic (Box 6)</td>
<td>o Immediate medical evaluation and risk modification</td>
</tr>
<tr>
<td>• White coat hypertension</td>
<td>• Independent of patient’s true underlying hypertensive status</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o Transient ↑ in BP by up to 20/10 mmHg</td>
<td>o Precipitated by vigorous sympathetic response to the medical or dental setting</td>
<td>o Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Hypotension</td>
<td>• Signs and symptoms</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o BP &lt;90/60 mmHg is generally</td>
<td>o Dizziness, lightheadedness, fainting (syncope)</td>
<td>o Asymptomatic patient</td>
</tr>
<tr>
<td>considered low blood pressure</td>
<td>o Rapid, shallow breathing</td>
<td>o Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>The causes range from dehydration to</td>
<td>o Fatigue, lack of concentration, depression</td>
<td>o Elevated risk</td>
</tr>
<tr>
<td>serious medical disorders.</td>
<td>o Cold, clammy, pale skin</td>
<td>o Cardiogenic shock</td>
</tr>
<tr>
<td>o Thirst</td>
<td>o Nausea</td>
<td>The condition is most often caused by a severe heart attack.</td>
</tr>
<tr>
<td>• Orthostatic (postural) hypotension</td>
<td>• Precipitated by sudden postural change usually from a supine to an upright position</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o Transient ↓ in BP by up to 20/10</td>
<td>o Impaired mechanism of BP regulation</td>
<td>o Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>mmHg and a transient ↑ in pulse rate by</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥20 beats/min.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 12. Coronary Artery Disease: Key Recommendations for Practice.\(^8\)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
<th>Risk of MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stable angina pectoris</td>
<td>• Signs and symptoms</td>
<td>• Low risk</td>
</tr>
<tr>
<td>o Transient ischemia to a portion of the myocardium</td>
<td>o Mild to moderate sub-sternal pain of sudden radiating to the shoulder, arm, neck and/or mandible</td>
<td>o If in the perioperative period a conscious patient experiences chest pain and ↑ BP from baseline consider the diagnosis of acute angina pectoris</td>
</tr>
<tr>
<td>o Precipitated by heavy exercise and stress, relieved by rest or sublingual nitroglycerin</td>
<td>o ↑ BP from baseline</td>
<td>o Emergency care appropriate for the treatment of acute angina pectoris</td>
</tr>
<tr>
<td>• Unstable angina pectoris</td>
<td>• Signs and symptoms</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>o Transient ischemia to a portion of the myocardium</td>
<td>o Same as those with stable angina pectoris, but the pain and discomfort is usually more intense, last longer, and may be progressive (crescendo) in nature</td>
<td>o Immediate medical evaluation and risk modification</td>
</tr>
<tr>
<td>o Precipitated by less exercise and stress than stable angina pectoris and may occur spontaneously at rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Myocardial infarction</td>
<td>• Signs and symptoms</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>o Abrupt anoxia to a portion of the myocardium resulting in cell death (myocardial necrosis)</td>
<td>o Severe sub-sternal pain</td>
<td>o History of cardiovascular disease, DM, and cerebrovascular disease increases overall risk of perioperative MI</td>
</tr>
<tr>
<td></td>
<td>o Nausea and vomiting</td>
<td>o If in the perioperative period a conscious patient experiences chest pain and ↓ BP from baseline consider the diagnosis of acute MI</td>
</tr>
<tr>
<td></td>
<td>o Pallor or cyanosis</td>
<td>o Emergency care appropriate for the treatment of acute MI</td>
</tr>
<tr>
<td></td>
<td>o Diaphoresis, cold clammy skin</td>
<td>o More than 60 days should elapse after a MI before elective noncardiac procedures, e.g., elective dental care</td>
</tr>
<tr>
<td></td>
<td>o Tachycardia, pulse rate &gt;100 beats/min.</td>
<td>o Recent MI, defined as having occurred within 6 months of noncardiac surgery</td>
</tr>
<tr>
<td></td>
<td>o ↓ in BP from baseline</td>
<td>o Independent risk factor for perioperative stroke</td>
</tr>
<tr>
<td></td>
<td>o Dyspnea, tachypnea, or apnea</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Comments</td>
<td>Risk of MACE</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td>• Signs and symptoms</td>
<td>• Low risk</td>
</tr>
<tr>
<td>• HR &lt; 60 beats a minute and</td>
<td>• May be asymptomatic</td>
<td>• If the resting HR is consistently below 60 beats a minute</td>
</tr>
<tr>
<td>the rhythm is regular</td>
<td>• May cause weakness, palpitation, chest discomfort, dyspnea, and syncpe</td>
<td>• Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Impulses originate from the</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA node under the influence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>of increased parasympathetic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial flutter</td>
<td>• Signs and symptoms</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>• HR is 250 to 350 beats a</td>
<td>• Ventricular rate is about 150 beats a minute</td>
<td>• Patients with symptomatic supraventricular arrhythmia with uncontrolled</td>
</tr>
<tr>
<td>minute and the rhythm is</td>
<td>• May be asymptomatic</td>
<td>ventricular rate</td>
</tr>
<tr>
<td>regular</td>
<td>• May cause weakness, palpitations, chest discomfort, dyspnea, and syncpe</td>
<td>• Immediate medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Impulses originate from a</td>
<td>• Systemic embolism may presents as a stroke-like illness</td>
<td></td>
</tr>
<tr>
<td>single abnormal focus in the</td>
<td>• Sudden confusion</td>
<td></td>
</tr>
<tr>
<td>atria</td>
<td>• Acute, painful, pulseless limbs</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>• Signs and symptoms</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>• HR is 350 to 450 beats a</td>
<td>• Ventricular rate is between 120 to 180 beats a minute</td>
<td>• Patients with symptomatic supraventricular arrhythmia with uncontrolled</td>
</tr>
<tr>
<td>minute and the rhythm is</td>
<td>• May cause weakness, palpitation, chest discomfort, dyspnea, and syncpe</td>
<td>ventricular rate</td>
</tr>
<tr>
<td>irregular</td>
<td>• Systemic embolism may presents as a stroke-like illness</td>
<td>• Immediate medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Impulses originate from</td>
<td>• Light-headedness, fatigue, syncope, and heart failure</td>
<td></td>
</tr>
<tr>
<td>multiple atrial foci, which</td>
<td>• Light-headedness, fatigue, syncope, and heart failure</td>
<td></td>
</tr>
<tr>
<td>travel in a random manner in</td>
<td>• Acute abdomen</td>
<td></td>
</tr>
<tr>
<td>the atria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atioventricular (AV) blocks</td>
<td>• Signs and symptoms</td>
<td>• Elevated risk</td>
</tr>
<tr>
<td>• Abnormal conduction at the</td>
<td>• First degree</td>
<td>• High-grade AV block</td>
</tr>
<tr>
<td>AV node</td>
<td>• Asymptomatic</td>
<td>• Immediate medical evaluation and risk modification</td>
</tr>
<tr>
<td>• First degree</td>
<td>• Second degree</td>
<td></td>
</tr>
<tr>
<td>• Delay in impulse conduction</td>
<td>• Asymptomatic or light-headedness and syncpe</td>
<td></td>
</tr>
<tr>
<td>• Second degree</td>
<td>• Third degree (high-grade AV block)</td>
<td></td>
</tr>
<tr>
<td>• Intermittent failure in</td>
<td>• Third degree (light-headedness, fatigue, syncope, and heart</td>
<td></td>
</tr>
<tr>
<td>conduction</td>
<td>failure</td>
<td></td>
</tr>
<tr>
<td>• Third degree</td>
<td>• Permanent failure in conduction</td>
<td></td>
</tr>
<tr>
<td>• Permanent failure in</td>
<td></td>
<td></td>
</tr>
<tr>
<td>conduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>• Signs and symptoms</td>
<td>• Low risk</td>
</tr>
<tr>
<td>• HR 100 to 180 beats a minute</td>
<td>• May be asymptomatic</td>
<td>• If the resting HR is consistently above 100 beats a minute</td>
</tr>
<tr>
<td>and the rhythm is regular</td>
<td>• May cause weakness, palpitation, dyspnea, chest discomfort, syncope</td>
<td>• Routine medical evaluation and risk modification</td>
</tr>
<tr>
<td>• Impulses originate at the</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>under the influence of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>increased sympathetic tone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>or vagal blockade</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 13. Ventricular Arrhythmias: Key Recommendations for Practice.\textsuperscript{8}
### Table 13. Ventricular Arrhythmias: Key Recommendations for Practice. (continued.)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
<th>Risk of MACE</th>
</tr>
</thead>
</table>
| Premature ventricular contractions (PVCs) | - Signs and symptoms  
  - May occur erratically or at predictable intervals  
  - Every second beat: bigeminy  
  - Every third beat: trigeminy | - Low risk  
  - Asymptomatic patients with frequent PVCs are not at increased risk of MACE  
  - Patients with frequent PVCs are at risk for periprocedure arrhythmias  
  - Patients who develop nonsustained or sustained VT in the perioperative period should be referred for medical evaluation and risk modification |
|   - Pronounced pause in an otherwise normal rhythm  
  - Impulses originate from an ectopic ventricular focus  
  - Occasional finding in otherwise healthy adults  
  - Incidence increases with age, fatigue, stress, and the use of tobacco and alcohol | | - Elevated risk  
  - Symptomatic patients with PVCs  
  - Immediate medical evaluation and risk modification |
| Ventricular tachycardia (VT) | - Signs and symptoms  
  - Sustained VT is almost always symptomatic causing  
  - Fatigue, palpitation, light-headedness, syncope, or sudden cardiac death | - Low risk  
  - Asymptomatic patients with nonsustained VT are not at increased risk of MACE  
  - Patients with nonsustained or sustained VT are at risk for periprocedure arrhythmias  
  - Patients who develop nonsustained or sustained VT in the perioperative period should be referred for medical evaluation and risk modification |
|   - HR 120 to 220 beats a minute  
  - Impulses usually originate from an ectopic focus in a ventricle | | - Elevated risk  
  - Patients with symptomatic VT  
  - Immediate medical evaluation and risk modification |
| Ventricular fibrillation (VF) | - Signs and symptoms  
  - The heart ceases to pump. The blood pressure drops, and the patient becomes unconscious  
  - If left untreated, death will follow in about 3 to 5 minutes | - Elevated risk  
  - If in the perioperative period a patient becomes unconscious, in the absence of a palpable pulse and ↓ in BP from baseline consider the diagnosis of cardiac arrest  
  - Emergency care appropriate for the treatment of cardiac arrest |
### Table 14. Heart Failure: Key Recommendations for Practice.\(^8,28\)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
<th>Risk of MACE</th>
</tr>
</thead>
</table>
| • Stage A | • Signs and symptoms  
  • LV failure  
  • Dyspnea  
  • Orthopnea  
  • Paroxysmal nocturnal dyspnea  
  • Fatigue  
  • RV failure  
  • Fatigue  
  • Jugular venous distention  
  • Peripheral edema  
  • Hepatosplenomegaly  
  • Ascites  
  • Dyspnea, fatigue, palpitation or angina may limit exercise tolerance | • Low risk  
  • Ordinary physical activity does not cause fatigue, dyspnea, palpitation, or angina |
| • Stage B | • Patients with structural | • Low risk (functional classification I)  
  • No symptoms at rest  
  • Ordinary physical activity does not cause fatigue, dyspnea, palpitation, or angina |
| • Stage C | • Patient with structural heart disease and with a history of prior or current symptoms of HF | • Low risk (functional classification I)  
  • No symptoms at rest  
  • Can complete any activity requiring ≤7 METs without fatigue, dyspnea, palpitation, or angina  
  • Elevated risk (functional classification II)  
  • No symptoms at rest  
  • Can complete any activity requiring ≤5 METs without fatigue, dyspnea, palpitation, or angina  
  • Elevated risk (functional classification III)  
  • No symptoms at rest  
  • Can complete any activity requiring ≤2 METs without fatigue, dyspnea, palpitation, or angina  
  • Elevated risk (functional classification IV)  
  • Symptoms at rest  
  • Cannot do or complete any activity requiring ≥2 METs |
| • Stage D | • Refractory HF requiring specialized intervention | • Elevated risk (functional classification IV)  
  • Symptoms at rest  
  • Cannot do or complete any activity requiring ≥2 METs |


Table 15. Thromboembolic Complications: Key Recommendations for Practice.$^8,29,30$

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
<th>Risk of MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Arterial thrombus</td>
<td>- Develops in areas of vascular damage</td>
<td>• Low risk</td>
</tr>
<tr>
<td>- Platelets aggregate and become</td>
<td>- Platelets aggregate and become surrounded by erythrocytes</td>
<td>- Impact of antithrombotic agents on invasive dental procedures is minimal</td>
</tr>
<tr>
<td>surrounded by erythrocytes</td>
<td></td>
<td>- Risk of bleeding is increased if patient is taking both ASA and clopidogrel</td>
</tr>
<tr>
<td>• Venous thrombus</td>
<td>- Develops in areas of slow blood flow</td>
<td>- Determine platelet function</td>
</tr>
<tr>
<td>- Clot forms rapidly and lacks</td>
<td>- Clot forms rapidly and lacks organization</td>
<td></td>
</tr>
<tr>
<td>organization</td>
<td></td>
<td>• Elevated risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Clear relationship between intensity of anticoagulation with warfarin and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Determine INR on the day of an invasive procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Target INR 2.0 to 3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


1. **Which of the following statements is correct with respect to the physiological stress-response elicited by procedure-specific variables?**
   a. The physiological stress-response is initiated by tissue injury and mediated primarily by the sympathoadrenal system.
   b. The physiological stress-response can induce tachycardia and hypertension and increase myocardial oxygen demand.
   c. The magnitude of procedure-related stress is predicated on the extent of procedure-related tissue trauma, duration of the procedure, volume of blood loss, fluid shifts, and changes in core body temperature.
   d. All of the above are correct.

2. **Which of the following statements is correct with respect to the rates of catecholamine release and specific effects produced at particular threshold plasma concentrations?**
   a. The basal range steady-state plasma concentration for epinephrine is 10-70 pg/ml.
   b. Threshold concentrations required to affect heart rate range from 50-100 pg/ml.
   c. Threshold concentrations required to affect DBP range from 150-200 pg/ml.
   d. All of the above are correct.

3. **Which of the following statements related to routine restorative dental care (two or three surface amalgams) under local dental anesthesia, 1.8 cc of lidocaine 2% with epinephrine 1:100,000 (i.e., 0.018 mg of epinephrine), is correct?**
   a. Plasma epinephrine levels increased from the resting supine steady-state plasma epinephrine concentrations of 28±8 pg/ml to 105±28 pg/ml and 73±14 pg/ml at 5 and 10 minutes after injection, respectively.
   b. After rubber dam application (13 to 18 minutes after injection) the plasma epinephrine level had further decreased to 51±7 pg/ml and then returned to resting supine steady-state levels.
   c. Corresponding to increased plasma epinephrine concentrations at 5 and 10 minutes after injection, HR increased by only a few beats per minute and no significant alterations were noted in MAP.
   d. All of the above are correct.

4. **Surgical stress related alterations in the balance between prothrombotic and fibrinolytic factors can result in hypercoagulability and possible coronary thrombosis secondary to_________.**
   a. elevation of fibrinogen and other coagulation factors
   b. increased platelet activation and aggregation
   c. reduced fibrinolysis
   d. All of the above are correct.

5. **All of the following statements are correct with respect to perioperative cardiac risk in association with non-cardiac procedures EXCEPT which one?**
   a. Non-cardiac procedures can be divided into high-, intermediate-, and low-stress groups with estimated rates of cardiac events of >5%, 1-5%, and <1%, respectively.
   b. With low-stress non-cardiac procedures the risk of a cardiac event is negligible unless strong patient-specific risk factors are present.
   c. The risk of perioperative cardiac events in association with dental procedures is elevated, i.e., the likelihood of a major cardiac event is ≥1%.
   d. Dental procedure-specific variable are less important than patient-specific variables in predicting a MACE in oral healthcare settings.
6. Which of the following statements is correct with respect to a patient’s functional capacity?
   a. Functional capacity, expressed in metabolic equivalents (METs), is reflected in a person's ability to perform a spectrum of daily activities.
   b. One MET equals the resting or basal oxygen requirement of a 40–year-old, 70-kg man, which is approximately 3.5 ml of $\text{O}_2$ per kg per minute.
   c. The inability to climb two flights of stairs or run a short distance indicates poor functional capacity (<4 METs) and is predictive of increased incidence of perioperative and long-term cardiac events.
   d. All of the above are correct.

7. Which of the following statements is correct with respect to patient response to infiltration anesthesia with 0.045 mg of epinephrine?
   a. The hemodynamic effect of infiltration anesthesia with 0.045 mg of epinephrine is less than that produced by ergometric-stress testing at 4 METs.
   b. Patients whose functional capacity is ≥4 METs can safely be administered at least 4.5 cc of a local anesthetic agent with epinephrine 1:100,000.
   c. There were no hemodynamic differences between normotensive and hypertensive patients receiving infiltration anesthesia with 0.045 mg of epinephrine.
   d. All of the above are correct.

8. All of the following statements are correct with respect to the American Society of Anesthesiology (ASA) Physical Status (PS) Classification system EXCEPT which one?
   a. It provides a practical method to determine perioperative risk for patients undergoing surgical (and by extension dental) procedures.
   b. Patients with severe systemic disease (ASA PS III) have no residual functional reserve.
   c. Patient with mild systemic disease (ASA PS II) have no or minimal limitation on physical activity.
   d. The rate of perioperative medical complications correlates closely with patients’ ASA PS classification.

9. Which of the following statements is correct with respect to the top 200 drugs dispensed by U.S. community pharmacies?
   a. The per capita utilization of prescription medications, predicated on the top 200 drugs dispensed by U.S. community pharmacies is about 12 prescriptions per person per year.
   b. Adults over 50 years of age consume the largest volume of prescription medications and account for 64% of the total number of prescriptions dispensed.
   c. Cardiovascular drugs in the top 200 closely mirror those taken by patients in oral healthcare settings.
   d. All of the above are correct.

10. Your patient relates a history of having recently been prescribed hydrochlorothiazide and potassium chloride and denies taking any other medications, the most likely medical diagnosis is _______________
    a. congestive heart failure
    b. hypertension
    c. pulmonary edema
    d. hepatic cirrhosis
11. Your patient with a history of asthma and diabetes mellitus has recently been prescribed a β1-adenrenergic receptor agonist for the prevention of angina pectoris, which potential adverse drug effects should you be concerned about?
   a. Masking symptoms of hypoglycemia
   b. Dyspnea and wheezing
   c. Bradycardia
   d. All of the above are correct.

12. All of the following statements related to angiotensin converting enzyme (ACE) inhibitors are correct EXCEPT which one?
   a. ACE inhibitors block degradation of bradykinin, which leads to increased vasodilation.
   b. Antagonize the action of angiotensin II at AT-receptors.
   c. ACE inhibitors are indicated for the treatment of hypertension, heart failure, and diabetic nephropathy.
   d. Adverse drug effects associated with ACE-inhibitors may include hypotension, angioedema, and frequent coughing.

13. Which of the following statements is correct with respect to calcium-channel blocking agents?
   a. Calcium-channel blocking agents relax vascular smooth muscles and reduce myocardial contractions.
   b. Indications for the prescription of calcium-channel blocking agents include exertional angina, unstable angina, coronary spasm, and hypertension.
   c. Adverse drug effects associated with calcium-channel blocking agents include palpitations, flushing, gingival overgrowth, acute angina pectoris, and MI (rarely).
   d. All of the above are correct.

14. Which of the following antihyperlipidemic agents inhibit HMG-CoA reductase and reduce VLDL and LDL, but may cause myalgia and rhabdomyolysis?
   a. The “statins”
   b. Niaspan (niacin)
   c. Tricor (fenofibrate)
   d. Zetia (ezetimibe)

15. Which of the following statements is correct with respect to digoxin, a cardiac glycosides?
   a. Digoxin inhibits sodium/potassium ATPase and promotes intracellular sodium-calcium exchange (positive inotropic effect).
   b. Digoxin inhibits sympathetic outflow in the ANS and increases parasympathetic vagal tone prolonging the refractory period and decreasing conduction velocity at the AV node.
   c. Digoxin is indicated for the treatment of supraventricular arrhythmias and heart failure.
   d. All of the above are correct.

16. Which of the following statements is correct with respect to Plavix (clopedigrel)? Plavix (clopedigrel) ________________.
   a. blocks ADP-dependent platelet aggregation and is used for the secondary prevention of thromboembolic events in patients with recent MI, or stroke
   b. is used for prophylaxis and treatment of deep vein thrombosis and pulmonary embolism
   c. is used for the prevention and treatment of systemic embolism with MI, atrial fibrillation, and prosthetic valves
   d. interferes with the hepatic synthesis of vitamin K-dependsnts coagulation factors
17. All of the following statements are correct with respect to initial drug therapy for hypertension EXCEPT which one? Initial drug therapy for hypertension may include _____________.
   a. diuretics to reduce volume overload
   b. electrolyte modifiers to prevent hypokalemia (with some diuretics)
   c. beta1-adrenergic receptor antagonists to reduce cardiac output
   d. ACE inhibitors, AT II-receptor antagonists, and calcium-channel blocking agents to dilate blood vessels

18. All of the following statements related to the risk of MACE in association with hypertension/hypotension are correct EXCEPT which one?
   a. Uncontrolled systemic hypertension is not an independent risk factor for MACE.
   b. The patient with hypertensive urgency is at elevated-risk, medical evaluation and risk modification within 24 to 48 hours.
   c. The patient with white-coat hypertension is at elevated-risk for MACE, immediate medical evaluation and risk modification.
   d. The patient with orthostatic (postural) hypotension is at low-risk for MACE, routine evaluation and risk modification.

19. Which of the following statements is correct with respect strategies for the prevention and treatment of coronary artery disease?
   a. In at-risk patients, pharmacological preventive strategies include the administration of antihyperlipidemic agents.
   b. To prevent acute coronary syndromes, calcium-channel blocking agents are administered to increase circulation in coronary arteries and β1-adrenergic receptor antagonists are prescribed to reduce the workload.
   c. Non-pharmacological strategies include coronary artery bypass grafts or percutaneous coronary intervention (PCI), e.g., balloon angioplasty or stent implantation.
   d. All of the above are correct.

20. All of the following statements related to the risk of MACE in association with coronary artery disease are correct EXCEPT which one?
   a. The patient with stable angina pectoris is at low-risk for MACE.
   b. The patient with unstable angina pectoris is at elevated-risk for MACE, immediate medical evaluation and risk modification.
   c. More than 6 months should elapse after MI before elective noncardiac procedures, i.e., elective dental care.
   d. Patients with a history of CVD, DM, and CV disease are at elevated overall risk of MACE.

21. Which of the following statements is correct with respect strategies for the prevention and treatment of cardiac arrhythmias? To prevent cardiac arrhythmias _____________.
   a. beta1-adrenergic receptor antagonists are prescribed to slow depolarization, lengthen AV conduction, reduce cardiac contractility, and slow the heart rate
   b. calcium channel blocking agents are prescribed to slow depolarization, repolarization, and AV conduction
   c. cardiac glycoside are prescribed to prolong the refractory period and decrease conduction velocity at the AV node
   d. All of the above are correct.
22. Which of the following statements related to the risk of MACE in association with cardiac arrhythmias is correct?
   a. The patient with symptomatic supraventricular arrhythmia with uncontrolled ventricular rate is at elevated-risk for MACE, immediate medical evaluation and risk modification.
   b. The patient with symptomatic VT is at elevated-risk for MACE, immediate medical evaluation and risk modification.
   c. When a patient becomes unconscious, in the absence of a palpable pulse and a reduction in BP from baseline consider the diagnosis of cardiac arrest.
   d. All of the above are correct.

23. Which of the following statements is correct with respect strategies for the treatment of heart failure?
   a. To improve myocardial contractility, the patient is prescribed a cardiac glycoside.
   b. To reduce workload, the patient may be prescribed a diuretic, an ACE inhibitor, an AT II-receptor antagonist, or a β₁-adrenergic receptor antagonist.
   c. Non-pharmacological strategies include heart transplantation.
   d. All of the above are correct.

24. Which of the following statements related to the risk of MACE in association with heart failure is correct?
   a. The patient at high-risk of HF but without structural heart disease or symptoms of HF is at low-risk of MACE.
   b. Patient with structural heart disease and with a history of prior or current symptoms of HF is at elevated-risk of MACE, elective care predicated on the patient’s functional capacity.
   c. Patient with refractory HF requiring specialized intervention is at elevated-risk of MACE, cannot do or complete any activity requiring a functional capacity of ≥2 METs.
   d. All of the above are correct.

25. All of the following statements related to antithrombotic and anticoagulant therapy are correct EXCEPT which one?
   a. Atrial thrombi occlude blood vessels and cause tissue ischemia.
   b. Small emboli that detach from venous thrombi travel to and wedge into pulmonary arteries and prevents deoxygenated blood from entering the lungs.
   c. Clear relationship exists between intensity of antithrombotic activity, e.g., daily clopidogrel or ASA, and problematic bleeding in association with dental procedures.
   d. When treating patients taking warfarin, determine the INR on the day of an invasive procedure – target INR is 2.0 to 3.5.
References


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