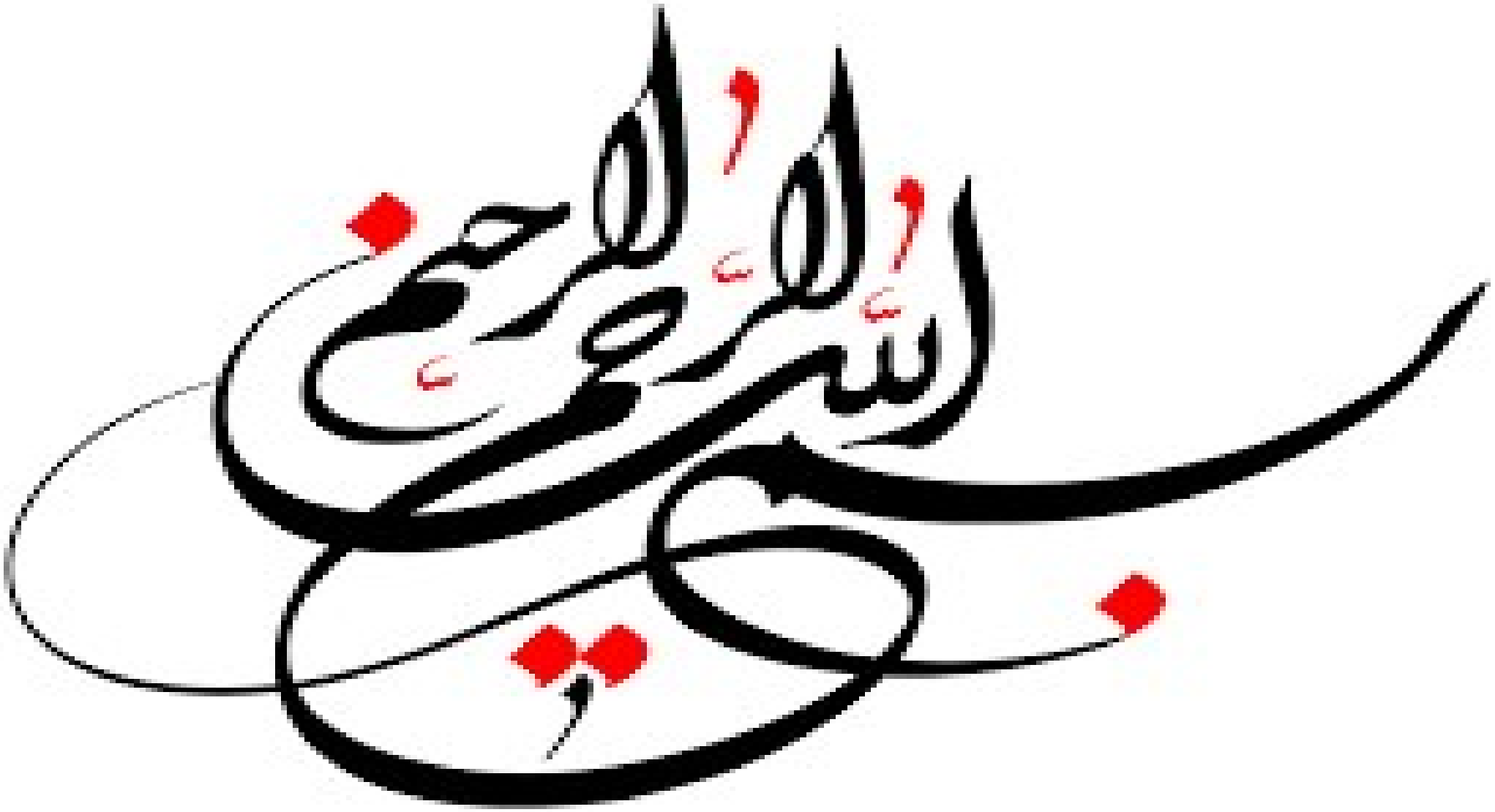

Cardiovascular Effects of Cardiotoxins

Davood Shafie,MD
Heart Failure Specialist
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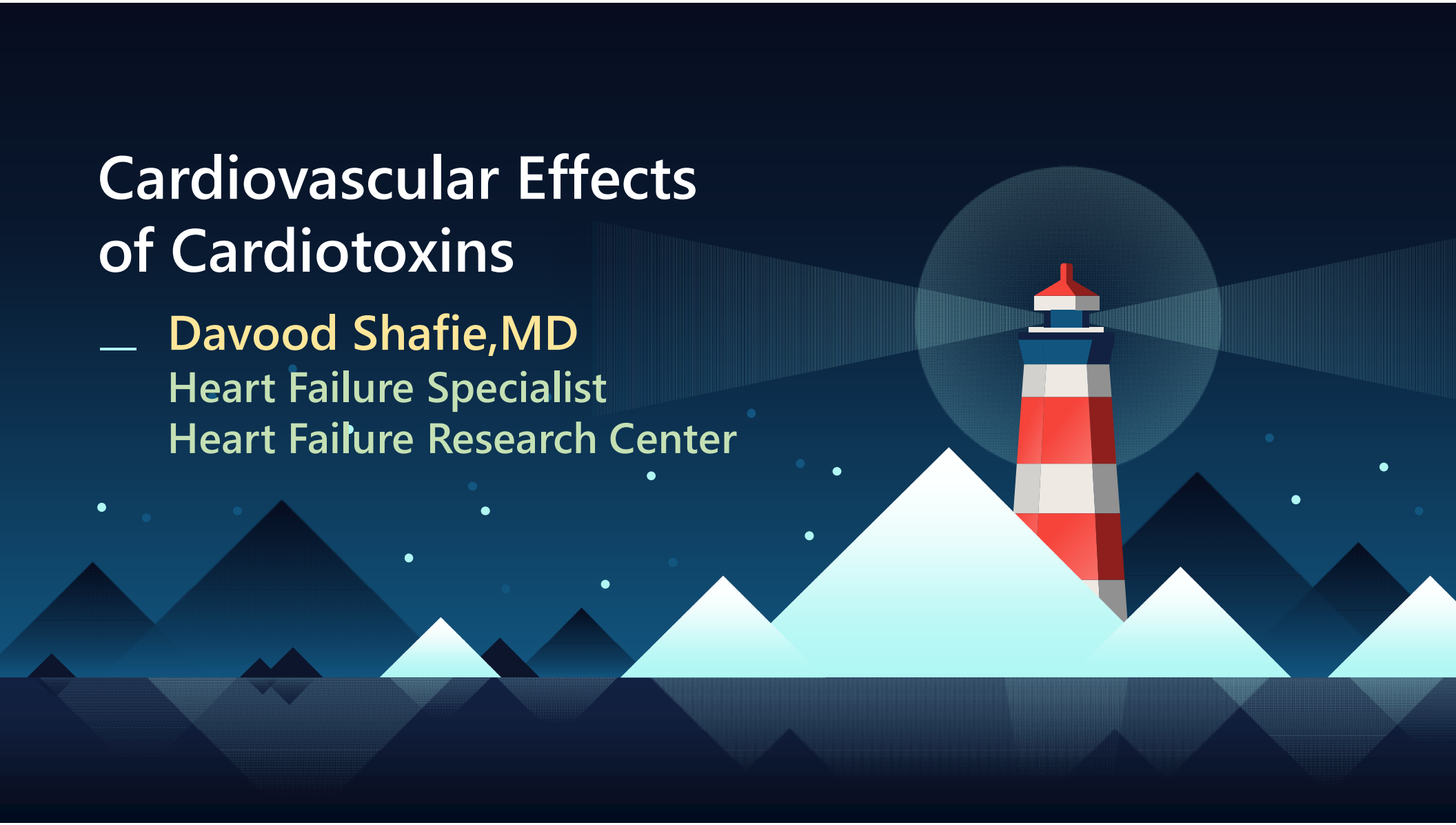


Agenda

01 Cardiotoxic Effects of Cancer Therapies

02 Ethanol

03 Cocaine

04 Amphetamines

05 Questions

Cardiotoxic Effects of Cancer Therapies

Anthracyclines

Doxorubicin, daunorubicin, epirubicin, idarubicin, mitoxantrone

1- Cardiac Arrhythmias

2- Heart Failure

Acute Onset

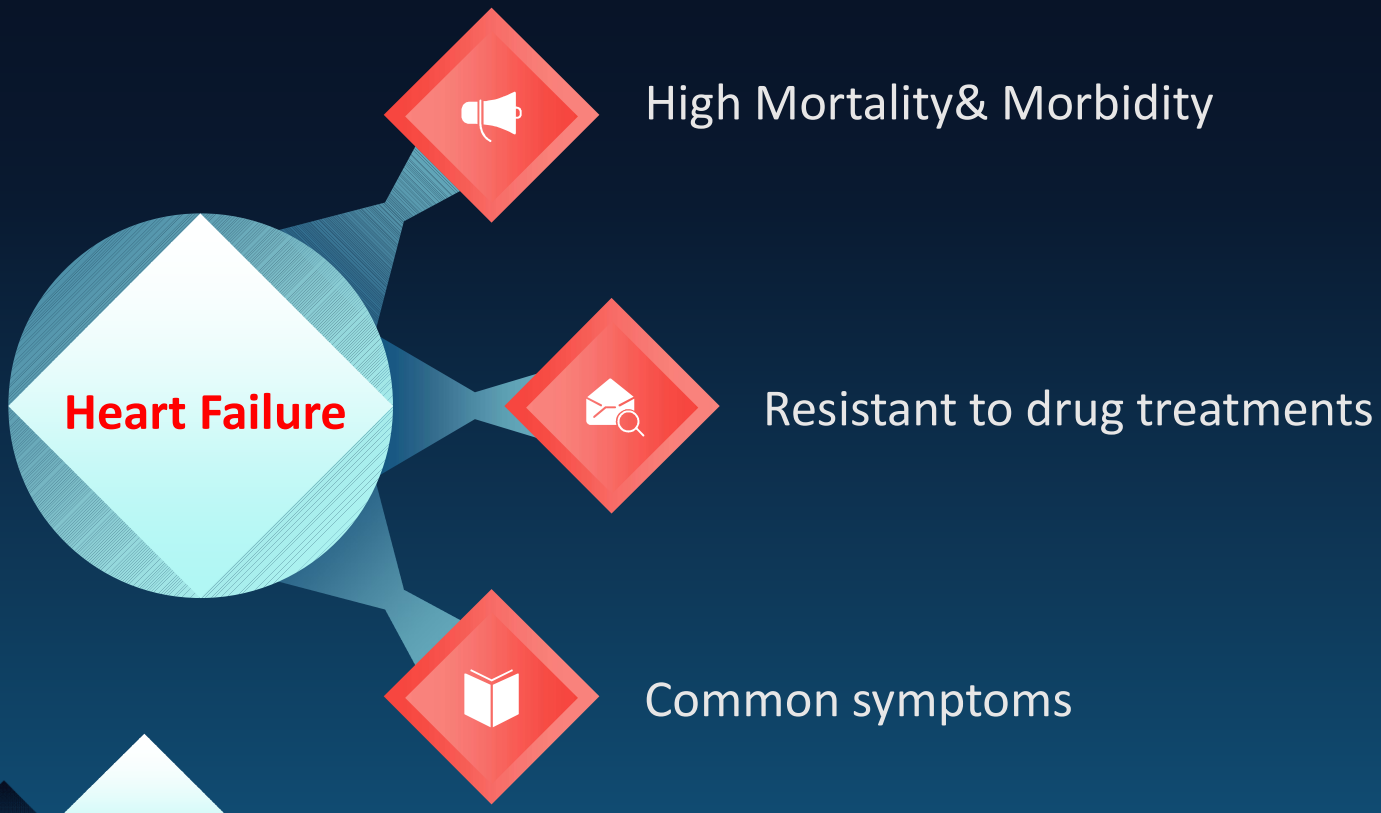
rare (≈1%), manifesting as arrhythmias, electrocardiogram changes, pericarditis,

Subacute Onset

HF, typically occurs within 1 year of therapy

Late Onset

HF, more frequent occurrence, from 1.6% to 23%


Heart Failure
High Mortality& Morbidity
Resistant to drug treatments
Common symptoms

Cardiotoxic Drug Usage = Stage A

of Heart Failure

Risk factors

1- Cumulative dose
2- Conventional CV risk factors (Age>60) and disease (DM)
3- Additional cardiotoxic therapies
4- RT

AGENT	REPORTED CARDIOTOXIC EFFECTS	COMMENTS
Anthracyclines		
Doxorubicin, daunorubicin, epirubicin, idarubicin, mitoxantrone	Cardiac arrhythmias, CM, HF	Risk factors include cumulative dose, although genetic variation may confer increased risk at lower dosages; conventional CV risk factors and disease; additional cardiotoxic therapies, including RT or trastuzumab
Taxanes		
Paclitaxel	Arrhythmia, myocardial ischemia	May exacerbate risk of anthracycline cardiotoxicity secondary to pharmacokinetic effects
Alkylating and Alkylating-Like Agents		
Cyclophosphamide	Myopericarditis, arrhythmias	Rare; CV complications reported only at high dosages
Cisplatin, carboplatin, oxaliplatin	Endothelial dysfunction, arterial vasospasm, HTN	
Antimetabolites		
5-Fluorouracil, capecitabine	Coronary vasospasm, myocardial ischemia, infarction, arrhythmias, ECG changes, sudden death	May be related to endothelial injury, vasoconstriction, and vasospasm; typically managed with nitrates and calcium channel blockers
Monoclonal Antibody Tyrosine Kinase Inhibitors		
Bevacizumab	HTN, CM, HF, thrombosis	Low risk of CM or HF
Trastuzumab	CM, HF	Increased risk of CM and HF with anthracyclines; HTN, obesity, and borderline normal baseline LVEF are also established risk factors; many LVEF declines are reversible, but in approximately 20% of patients, reversibility is not seen
Pertuzumab	CM, HF	Risk of CM and HF remains incompletely defined, but thus far, it has been modest
Proteasome Inhibitors		
Bortezomib	CM, HF, edema	Reversible proteasome inhibitor
Carfilzomib	CM, HF, edema	Irreversible proteasome inhibitor; cardiotoxicity rates greater
Small-Molecule Tyrosine Kinase Inhibitors		
Sunitinib	HTN, CM, HF, thrombosis	Risk of HTN that tends to occur early; relationship between afterload and CM risk remains to be determined
Sorafenib	HTN, CM, ischemia, thrombosis	Risk of HTN; also associated with ischemia
Imatinib	CM, edema, pericardial effusion	Risk of CM very low
Nilotinib	Peripheral vascular disease, ischemic heart disease	
Ponatinib	Peripheral vascular disease, ischemic heart disease	
Dasatinib	Pulmonary HTN, pericardial effusion	
Immune-Modulating Agents		
Thalidomide	Edema, thrombosis, arrhythmia	
Lenalidomide	Edema, thrombosis, arrhythmia	
Immune check-point inhibitors	Myocarditis	
Androgen-Deprivation Therapy		
Leuprolide, goserelin, triptorelin, flutamide, bicalutamide	Metabolic syndrome, ischemia, coronary artery disease	

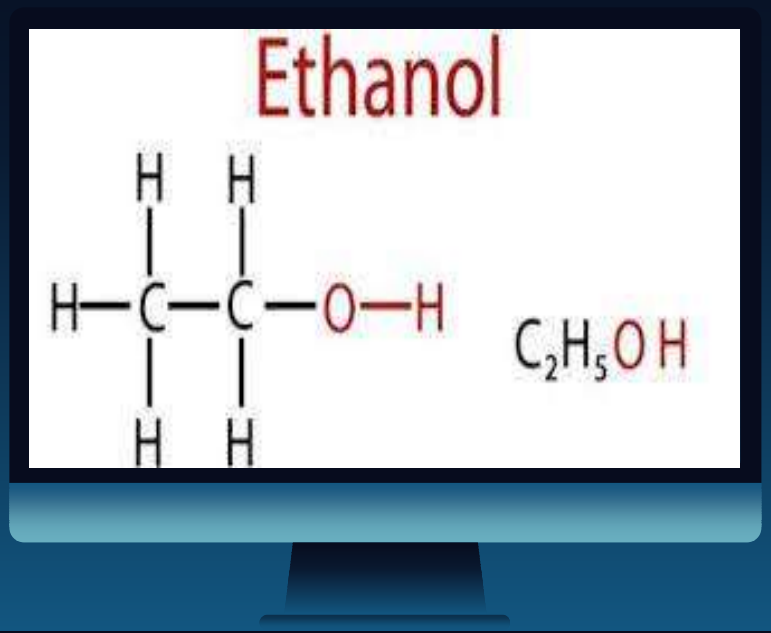
Radiation Therapy

IHD, HF, valvular disease, arrhythmia, and pericardial disease

1- Conventional CV risk factors (younger age)
2- late onset
3- Cumulative RT dose

If we think about cardiotoxicity, we can diagnose it.

Ethanol



CARDIOVASCULAR RISK FACTORS AND OUTCOMES	LIGHT TO MODERATE ALCOHOL INTAKE (<2 DRINKS PER DAY)	HEAVIER ALCOHOL INTAKE (>2 DRINKS PER DAY)
Blood pressure	↔	↑↑
HDL cholesterol	↑↑	↑↑↑
Triglycerides	↑	↑↑
LDL cholesterol	↔ or ↓	↑
Platelet aggregability/coagulability	↓	↓↓
Systemic inflammation	↓	↑
Congestive heart failure	↓	↑↑
Coronary artery disease (angina, nonfatal MI)	↓↓	↔ or ↑
Atrial fibrillation	↔	↑↑
Stroke	↓	↑↑
Sudden cardiac death	↓↓	↑

Cocaine

- Myocardial ischemia
- Angina pectoris
- Myocardial infarction
- Sudden death
- Arrhythmias
- Pulmonary edema
- Myocarditis
- Endocarditis
- Aortic dissection

Often within minutes of cocaine use
Reported as late as 5-15 hours after use

Amphetamines

1- HTN
2- Acute coronary syndromes
3- MI
4- Myocardial damage consistent with catecholamine excess (HF)
5- Aortic dissection
6- lethal arrhythmias


"اللَّهُمَّ إِنِّي أَسْأَلُكَ حُسْنَ الخَاتِمَةِ."
OH ALLAH, I ASK YOU FOR
A GOOD END.