Oregon Heart & Vascular INSTITUTE

Atherosclerosis – A Spectrum of Disease: February 4, 2020

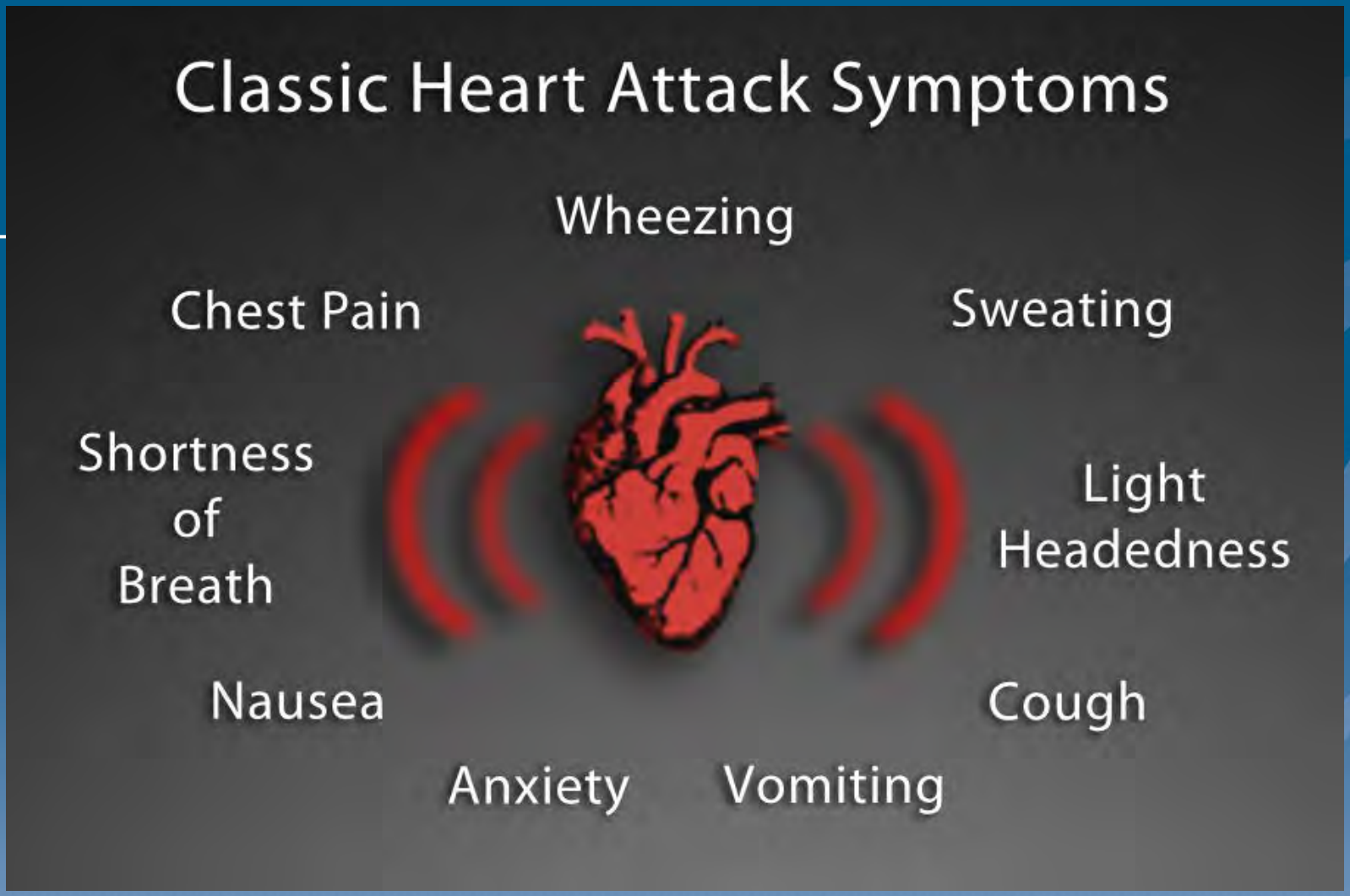
Richard Cameron Padgett, MD

Executive Medical Director Oregon Heart & Vacular Institute

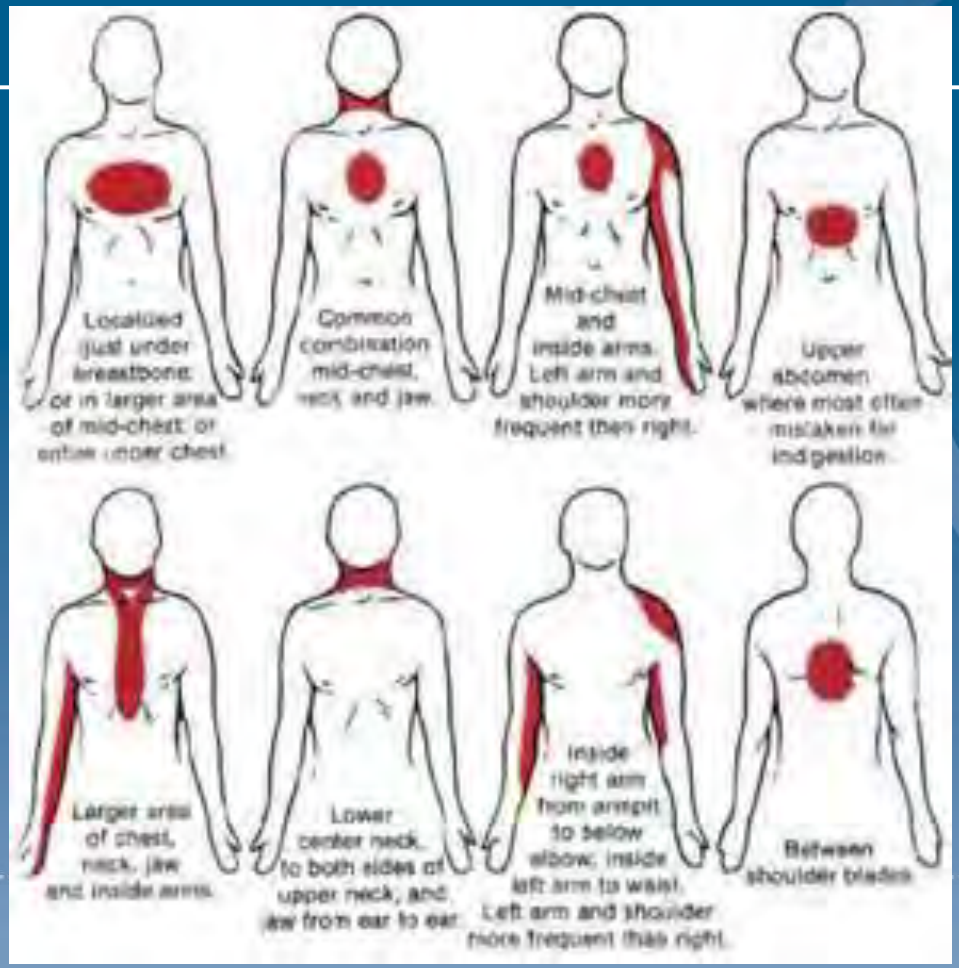
Angina or “Heart Pain”
Well described 600 BCE

- From a cemetery in Cambridge

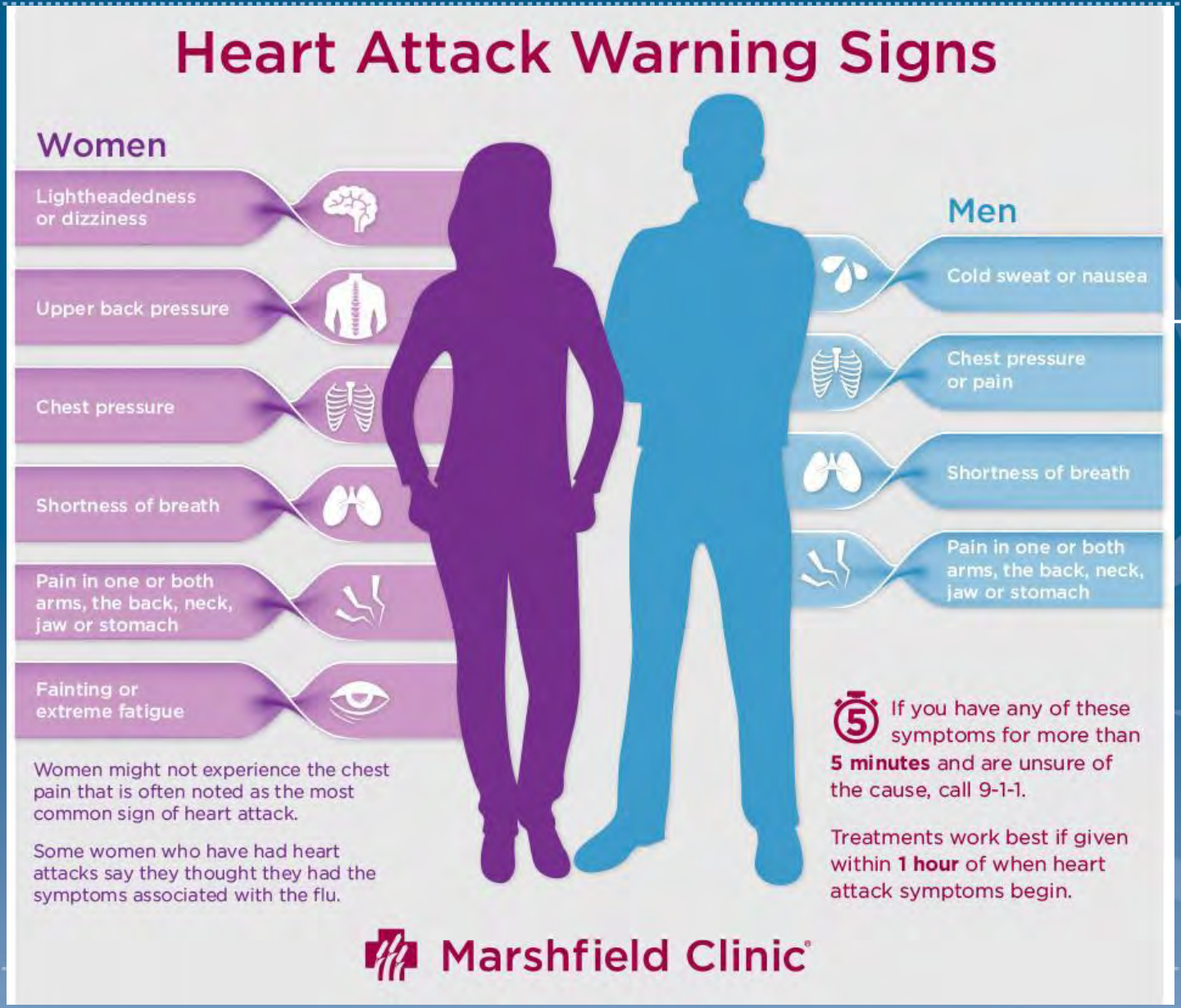
Classic Heart Attack Symptoms



Chest Pain Variants




Do you know your
HEART ATTACK
symptoms?


Heart Attack Warning Signs
Women
Lightheadedness or dizziness
Upper back pressure
Chest pressure
Shortness of breath
Pain in one or both arms, the back, neck, jaw or stomach
Fainting or extreme fatigue
Men
Cold sweat or nausea
Chest pressure or pain
Shortness of breath
Pain in one or both arms, the back, neck, jaw or stomach
Women might not experience the chest pain that is often noted as the most common sign of heart attack.
Some women who have had heart attacks say they thought they had the symptoms associated with the flu.
If you have any of these symptoms for more than 5 minutes and are unsure of the cause, call 9-1-1.
Treatments work best if given within 1 hour of when heart attack symptoms begin.
Marshfield Clinic

Heart With Muscle Damage and a Blocked Artery

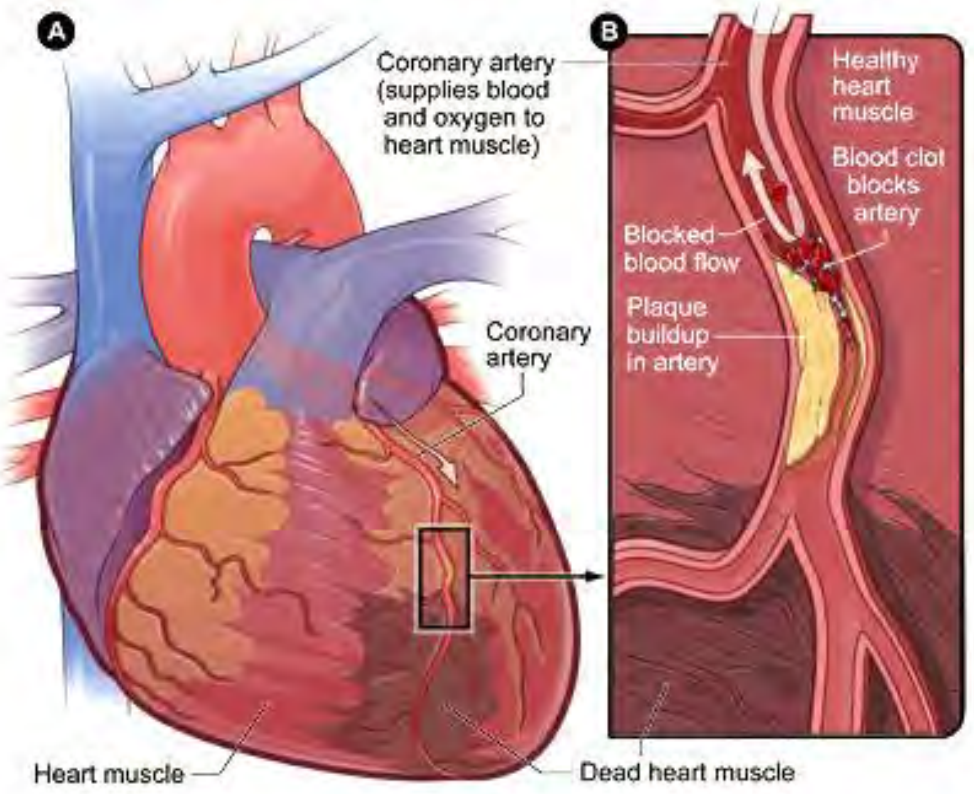
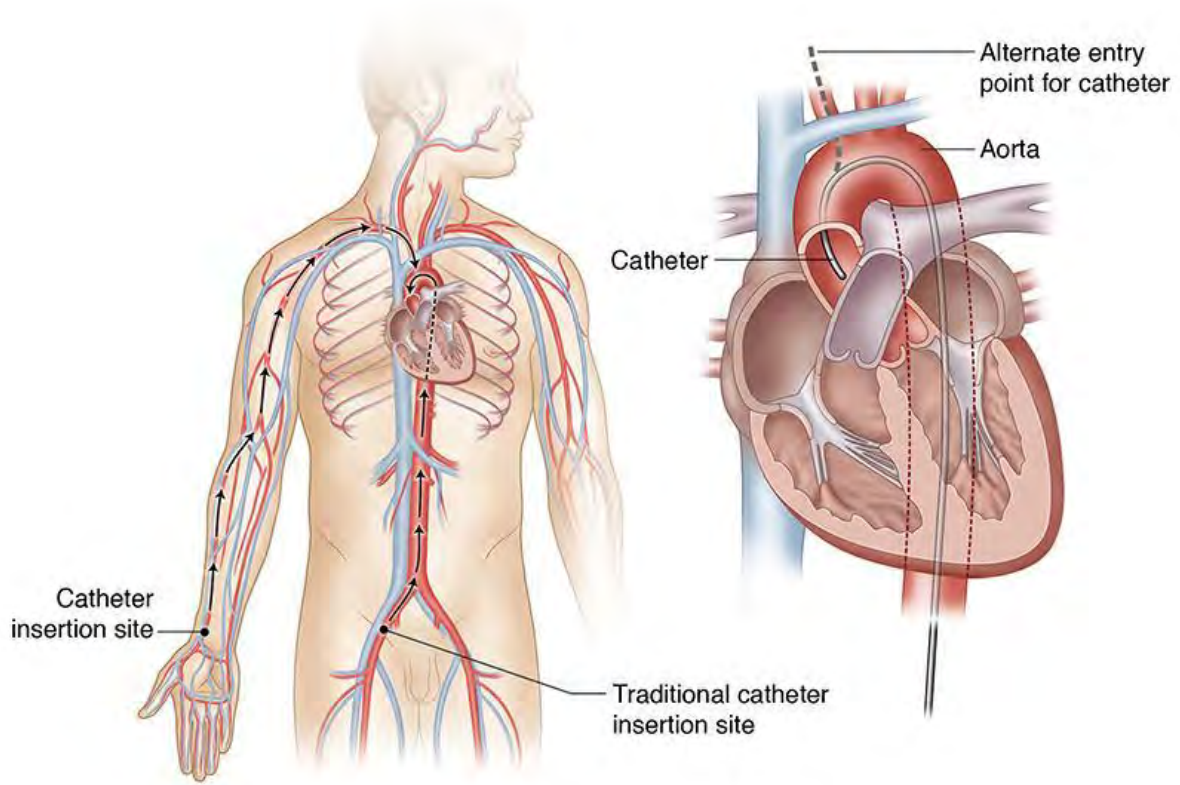


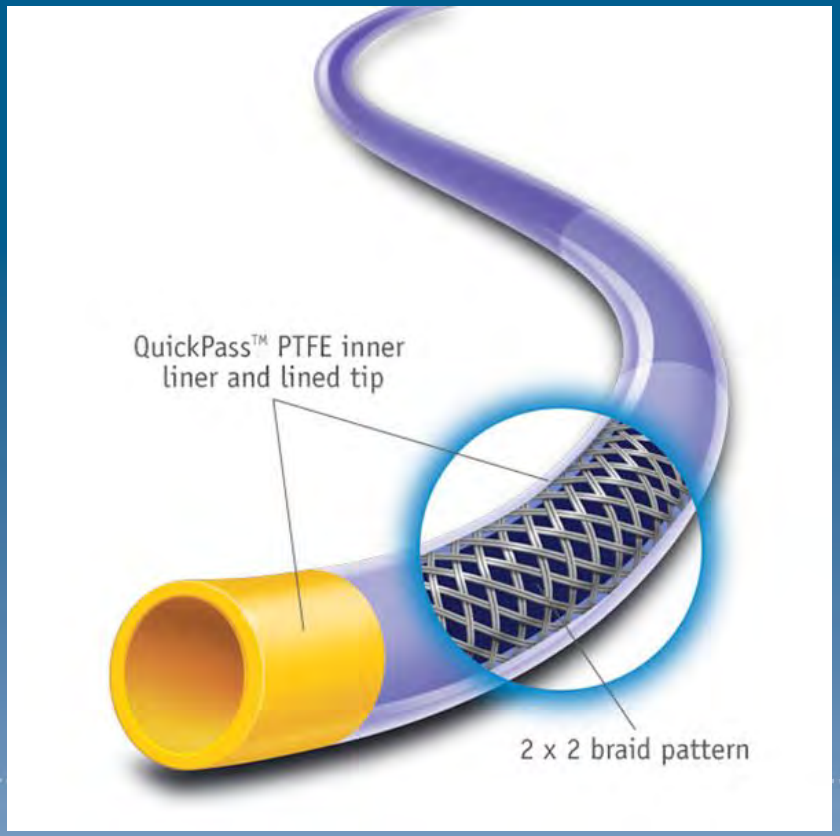
Figure A is an overview of a heart and coronary artery showing damage (dead heart muscle) caused by a heart attack. **Figure B** is a cross-section of the coronary artery with plaque buildup and a blood clot.

Coronary Angio Suite

All roads lead to Rome



Coronary Catheters



Pt RB

Age 38

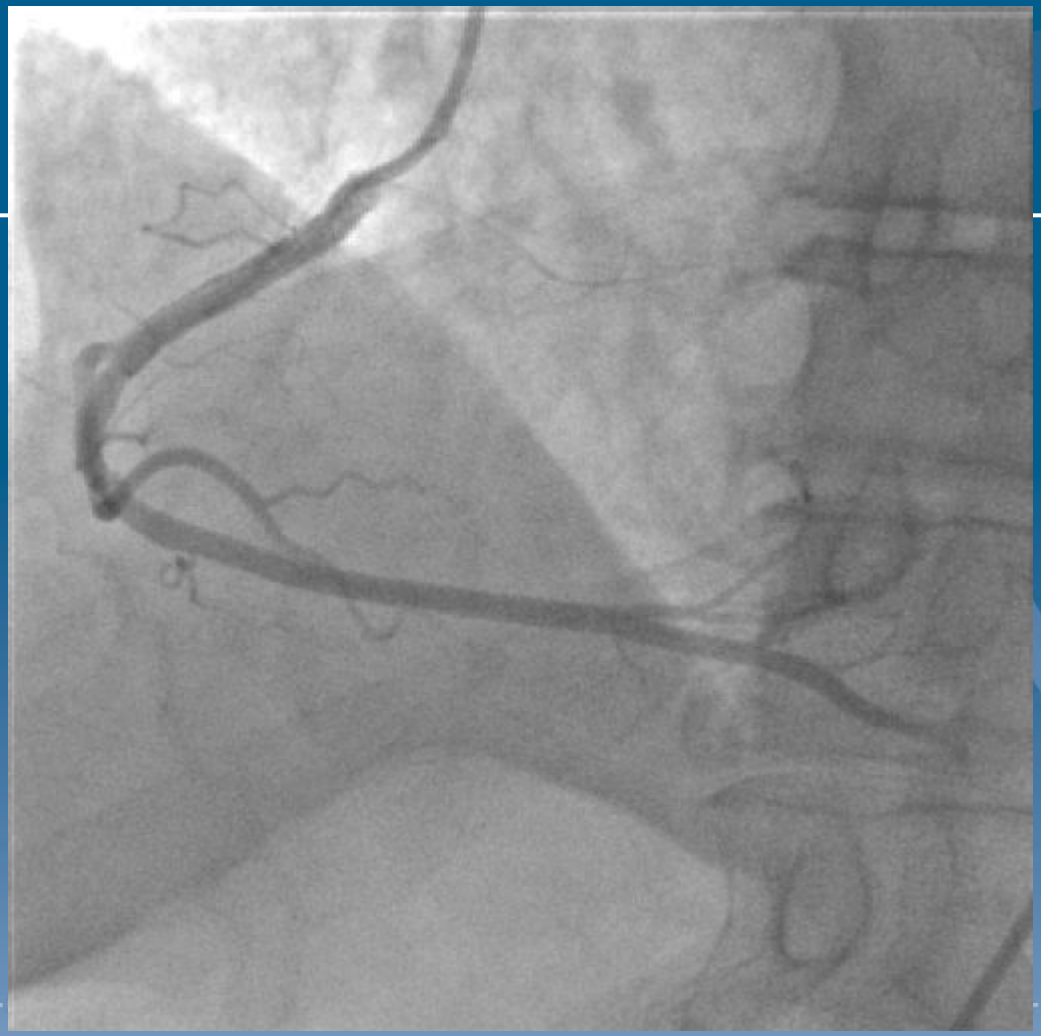
1ppd Smoker

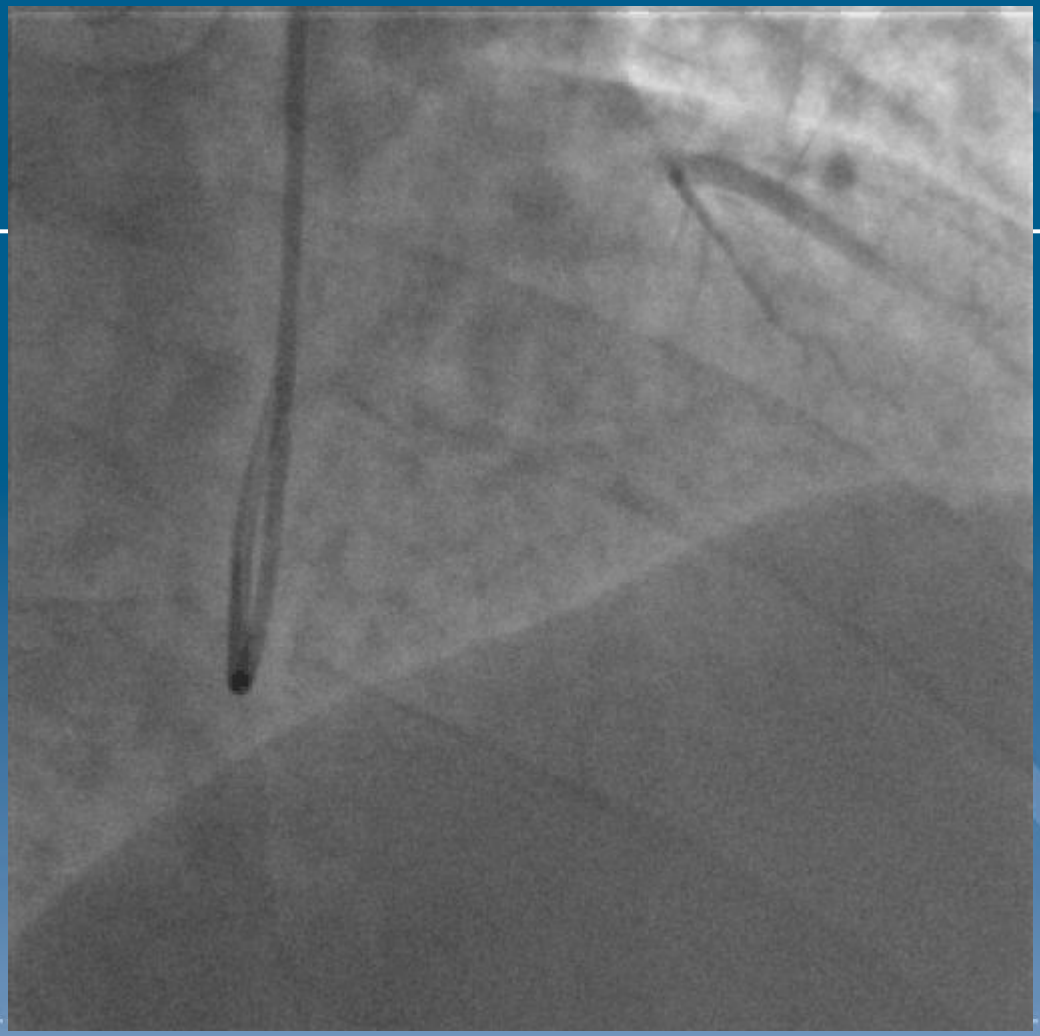
Father had MI @ Age 46

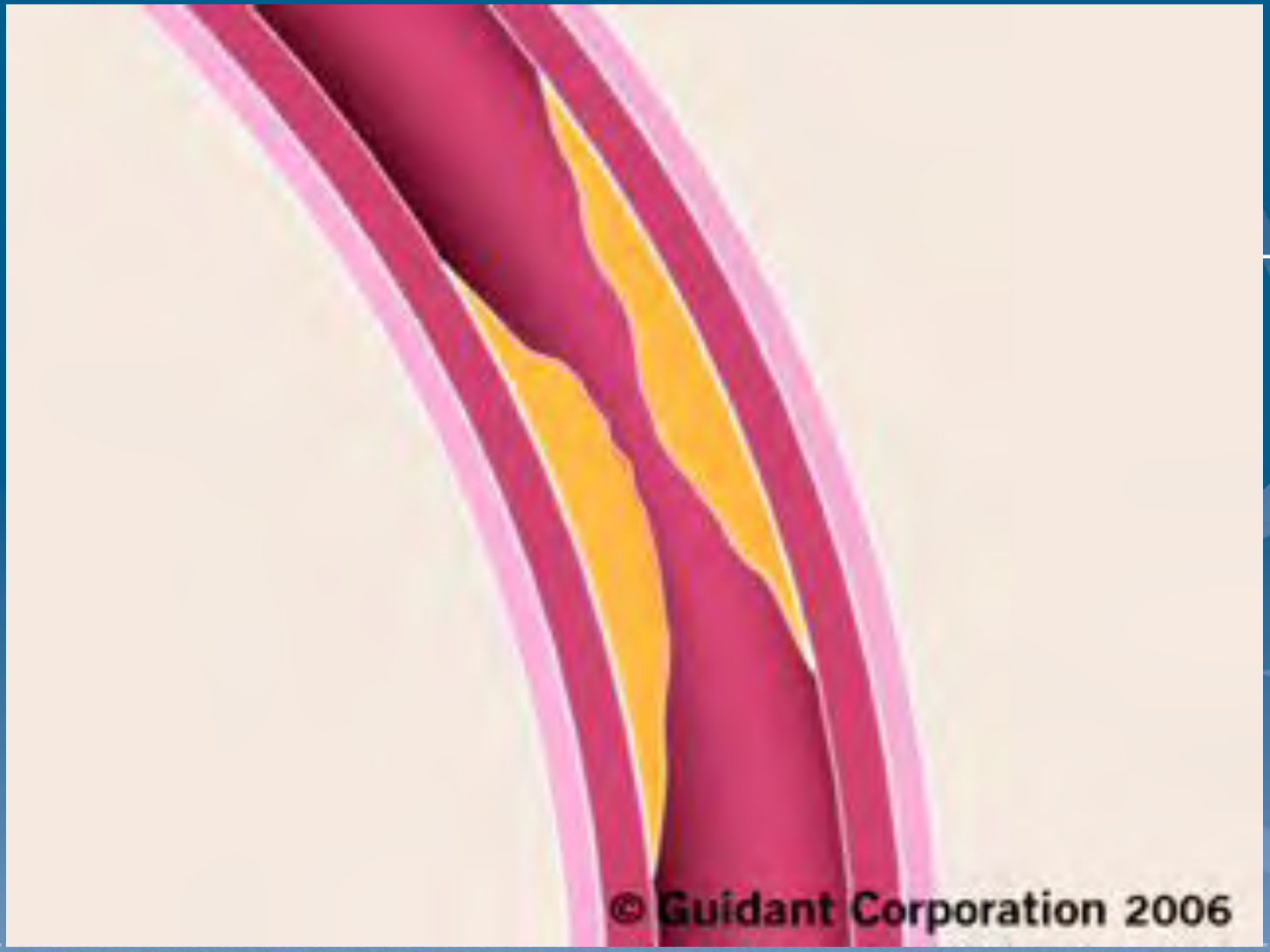
Total Chol 189

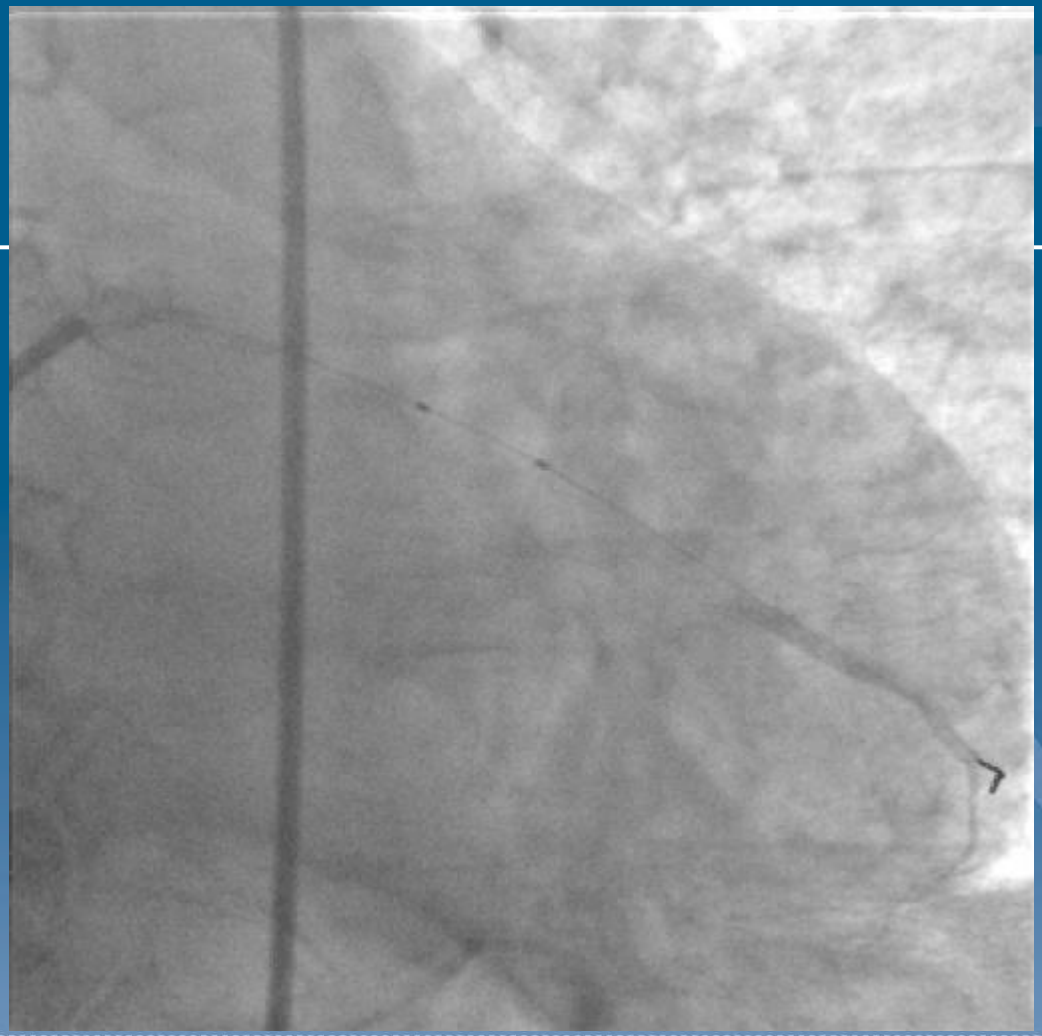
LDL 138

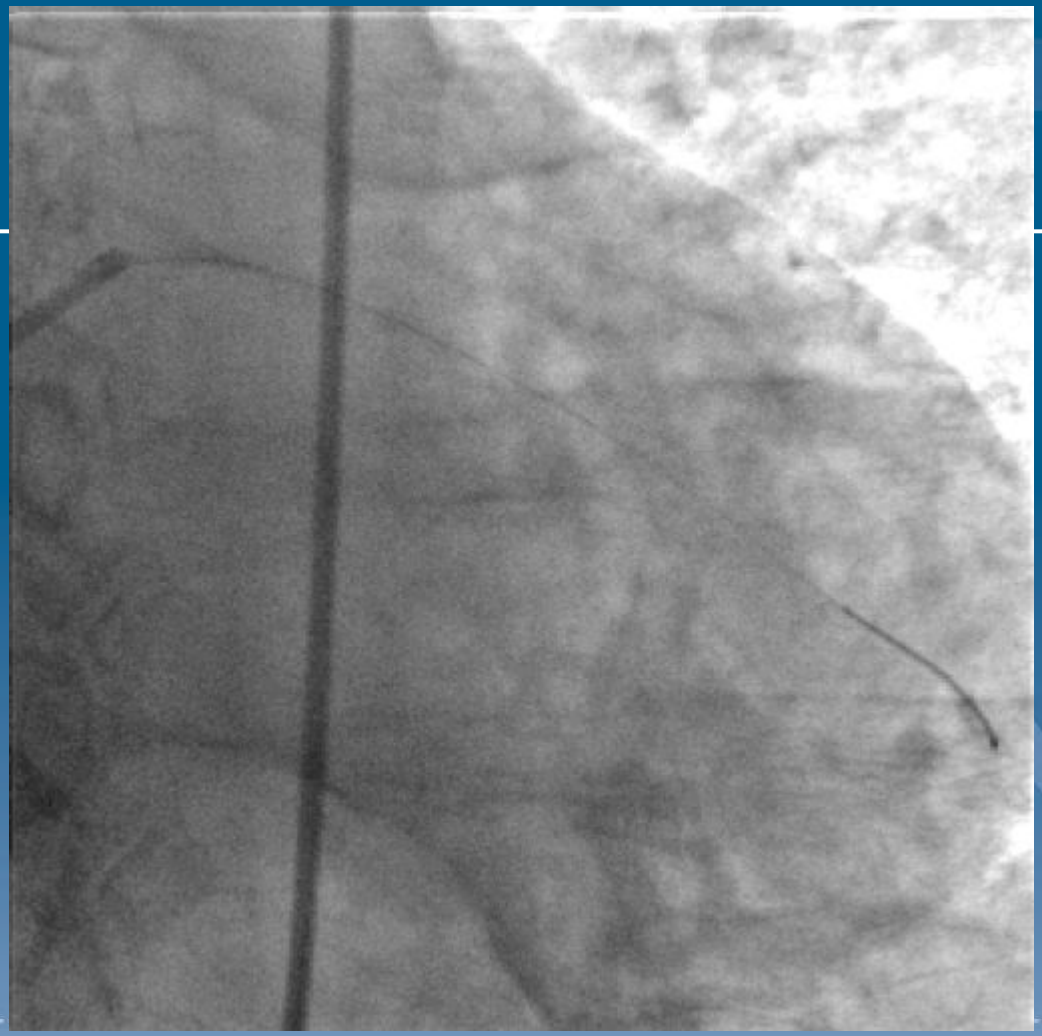
HDL 25

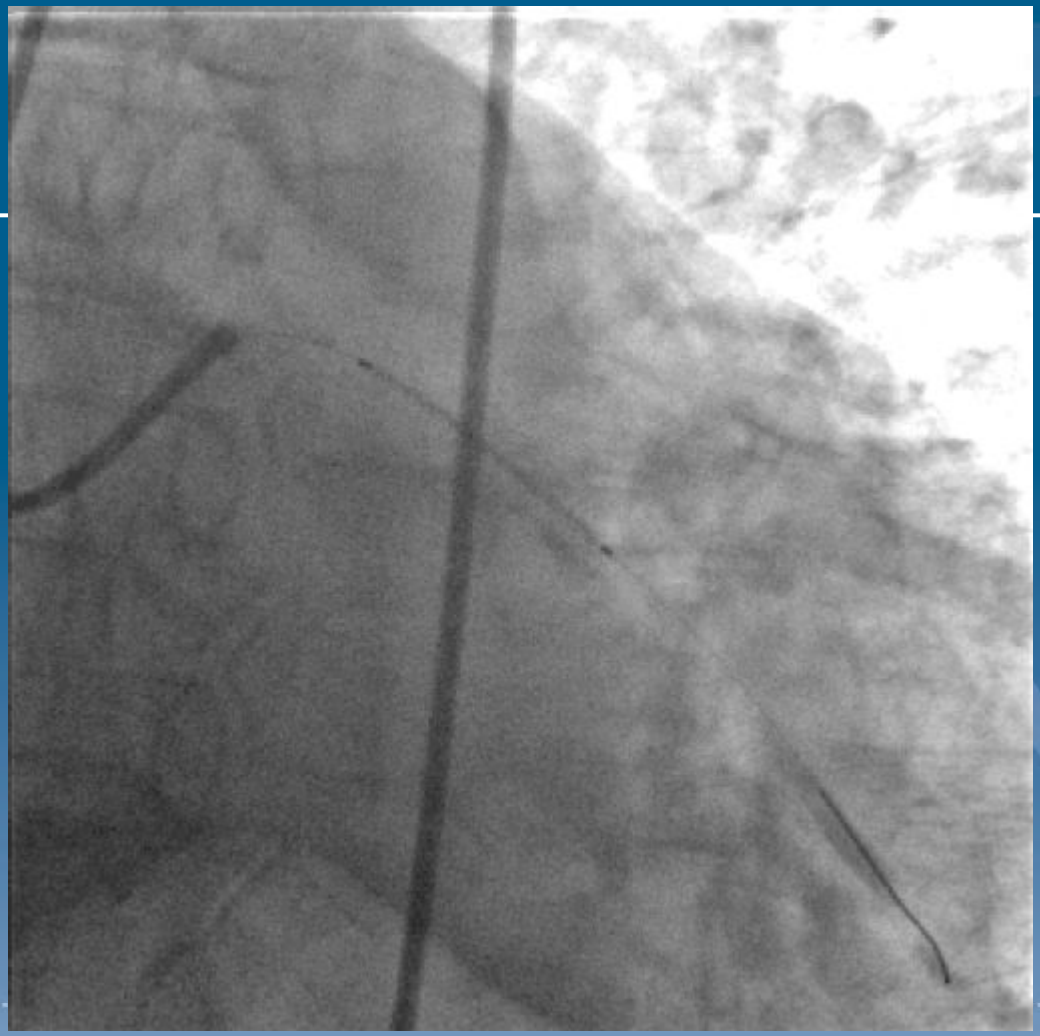


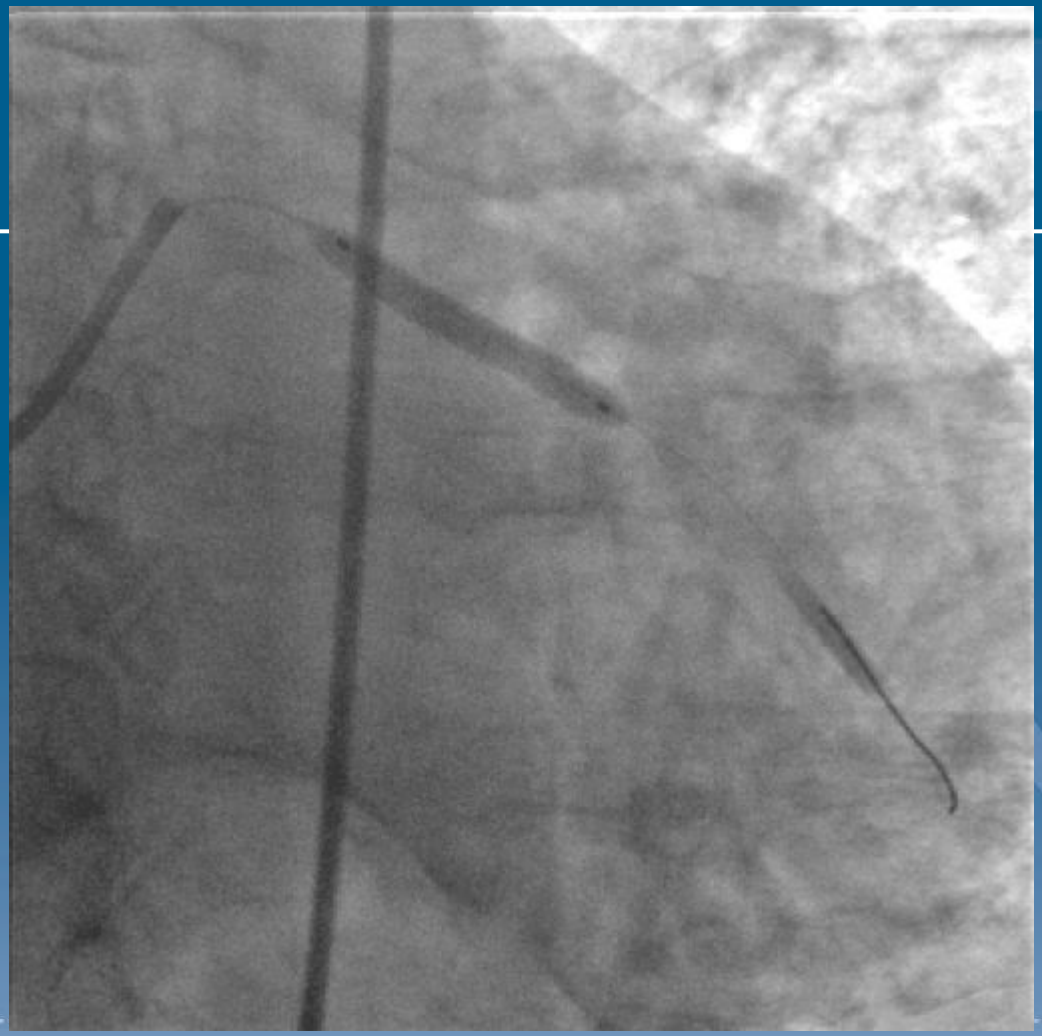


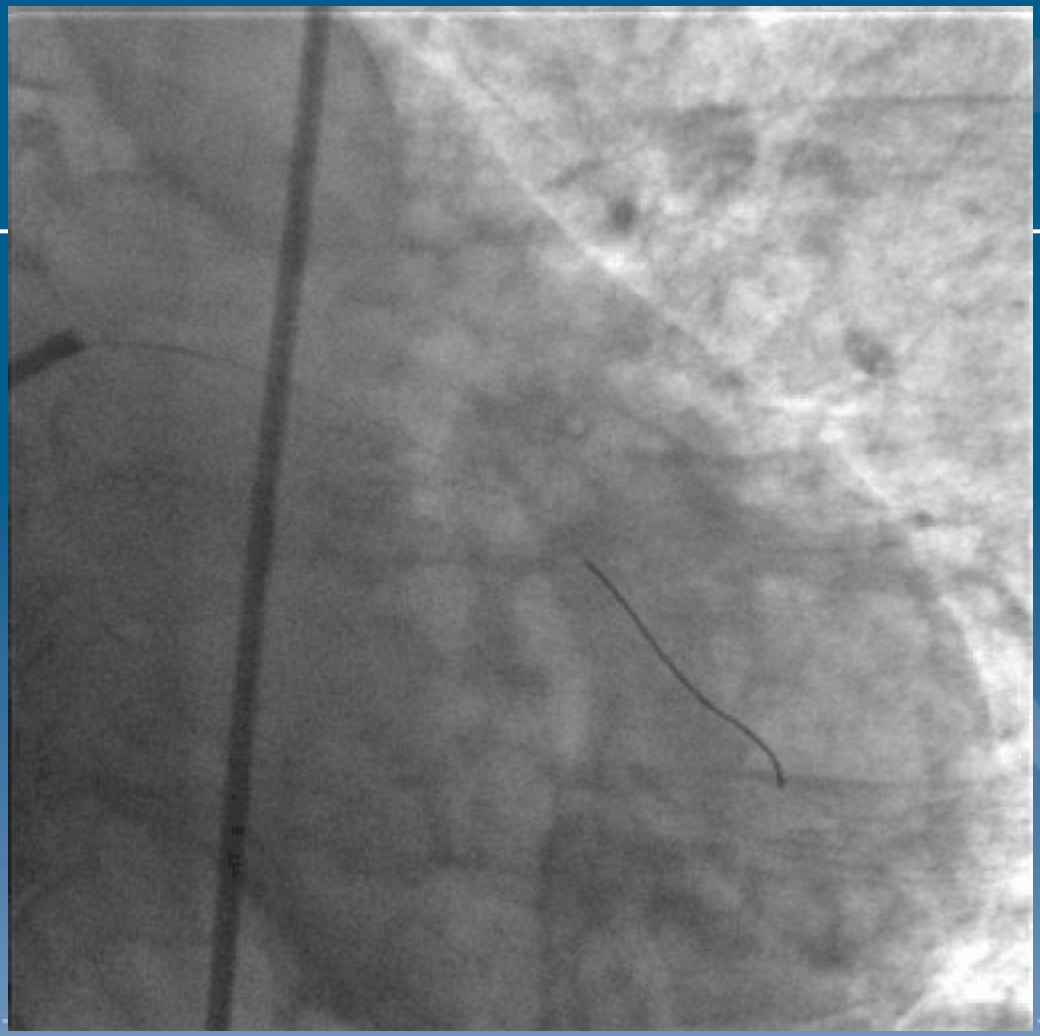

© Guidant Corporation 2006



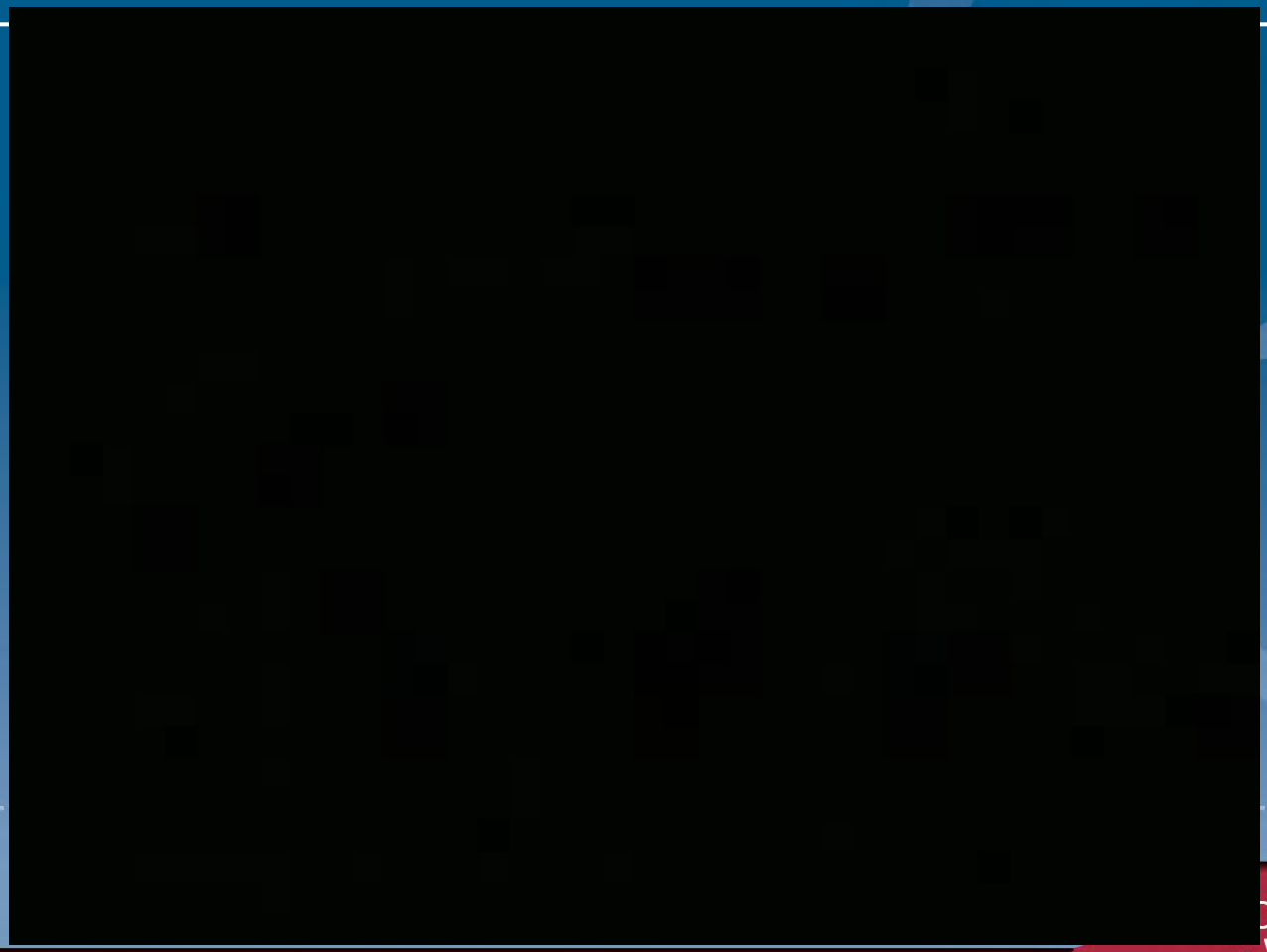








Death is Chasing Them

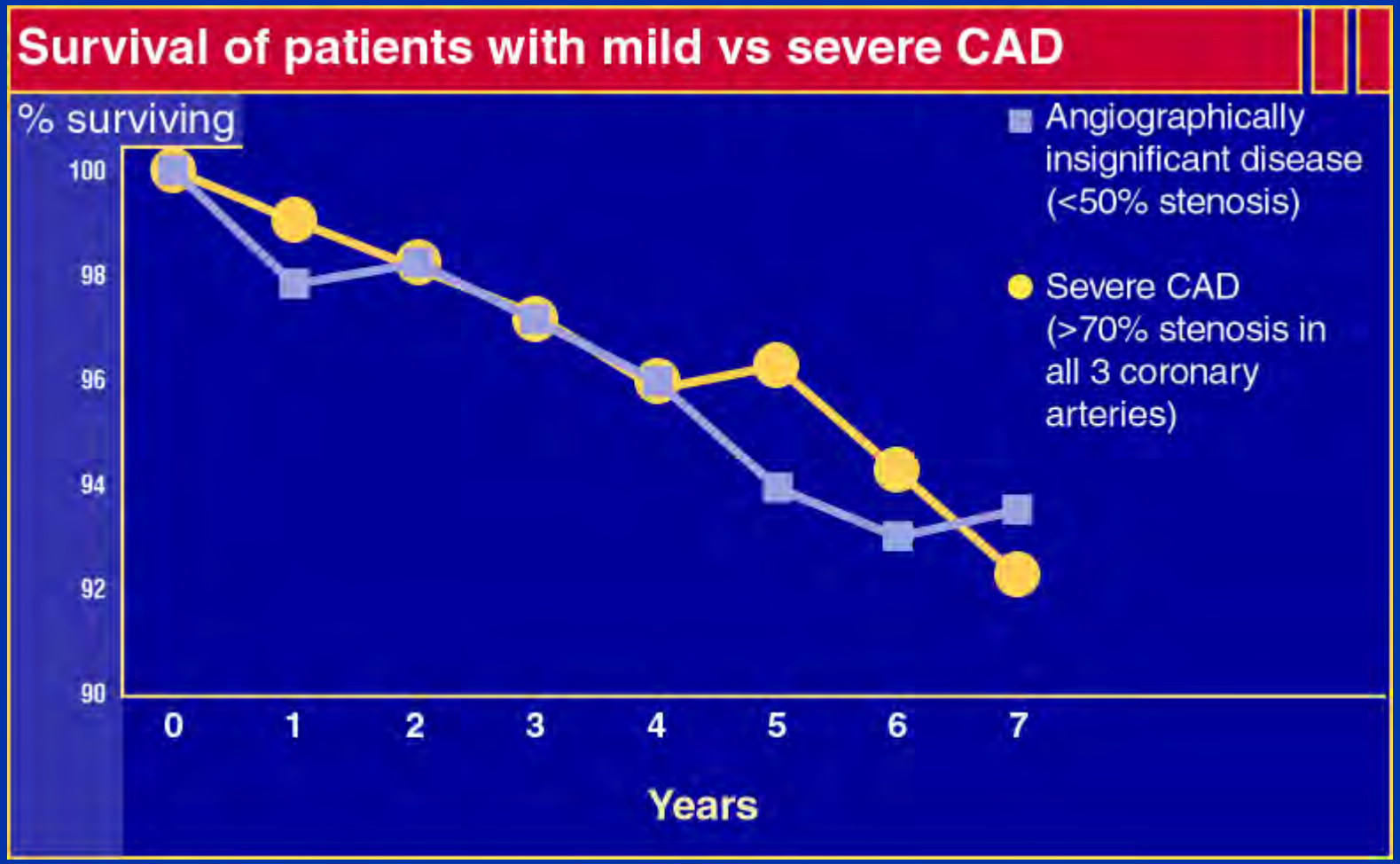


Current Concepts in Atherosclerosis

Richard C. Padgett, MD

Oregon Heart and Vascular Institute
Oregon Cardiology, PC
Eugene, Springfield & Florence

Lesion Severity: A Poor Predictor of Survival



From the Coronary Artery Surgery Study (CASS) as reported by Little et al.

Little WC et al, *Clin Cardiol*, 1991.

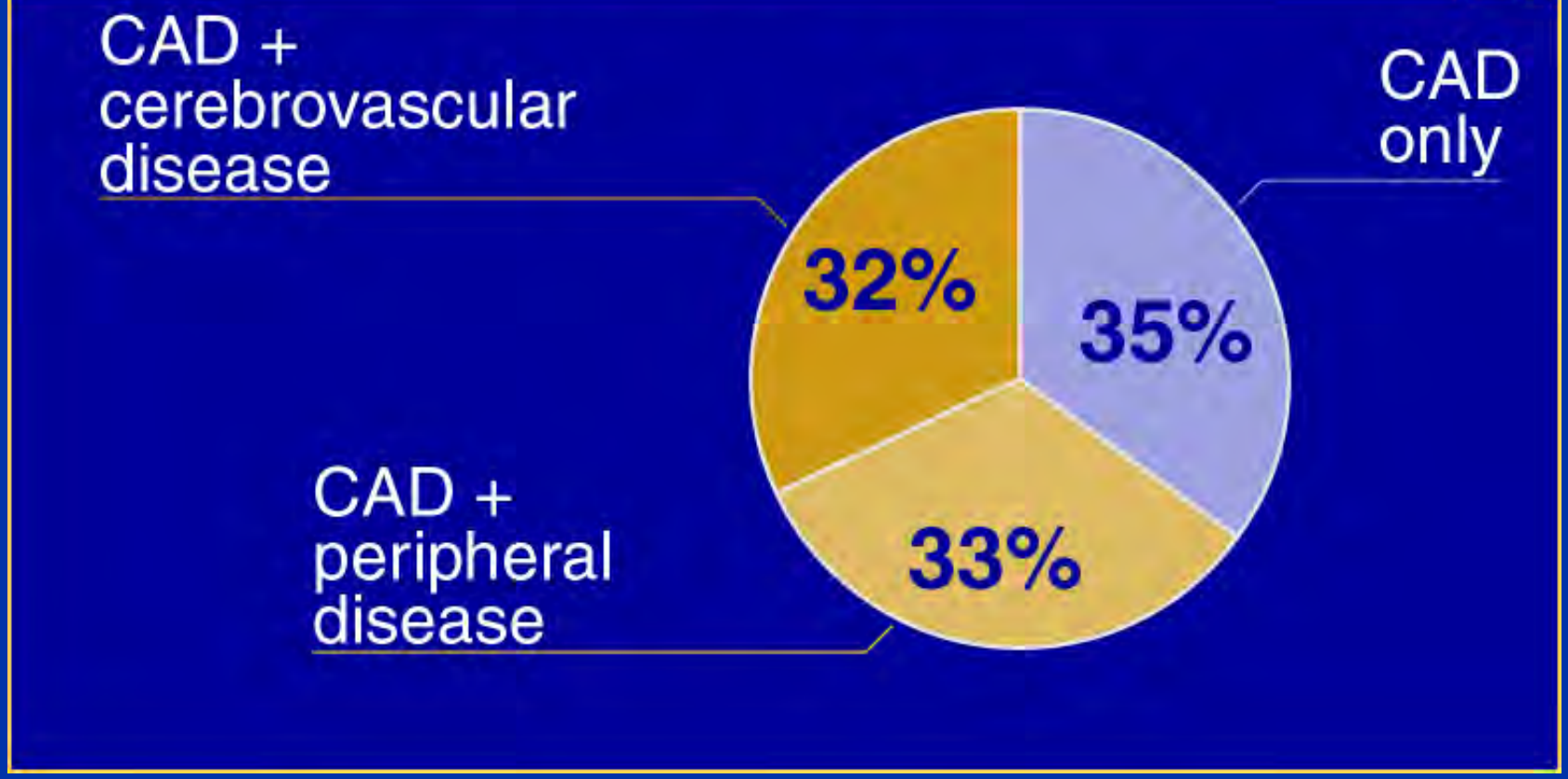
Vascular Disease: Scope of the Problem

- Vascular disease—and CAD in particular—is the leading cause of death in the US and other Western nations
- By 2020, cardiovascular disease will become the most common cause of death worldwide
- Due to the high initial mortality of vascular disease, the target of clinical practice must be aggressive risk factor management

American Heart Association®, *2000 Heart and Stroke Statistical Update*, 1999; Braunwald E, *N Engl J Med*, 1997; Kannel WB in *Atherosclerosis and Coronary Artery Disease*, 1996.

Atherosclerosis: A Systemic Disease

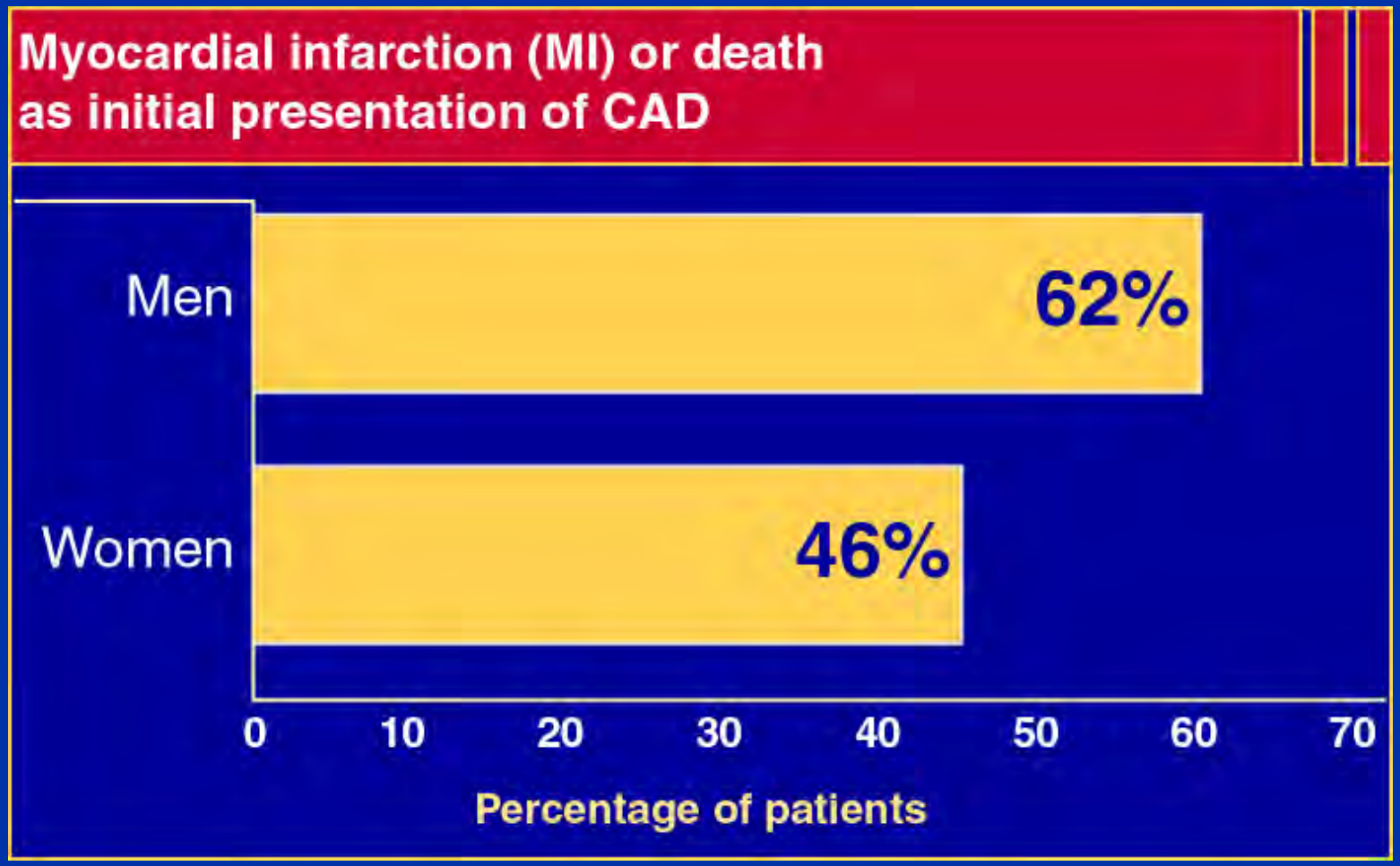
Most CAD patients have concomitant *symptomatic* peripheral or cerebrovascular disease



From a prospective analysis of 1886 patients aged ≥62 years, 810 patients were diagnosed with CAD as defined by a documented clinical history of MI, ECG evidence of Q-wave MI, or typical angina without previous MI. (Adapted from Aronow et al.)

Aronow WS et al, *Am J Cardiol*, 1994.

Coronary Artery Disease (CAD): The Diagnosis Often Comes Too Late



(Adapted from Levy et al.)

Levy D et al in *Textbook of Cardiovascular Medicine*, 1998.

Major Risk Factors for CAD

Modifiable risk factors

- Hypertension
- Dyslipidemia
- Diabetes
- Cigarette smoking
- Obesity
- Physical inactivity

Nonmodifiable risk factors

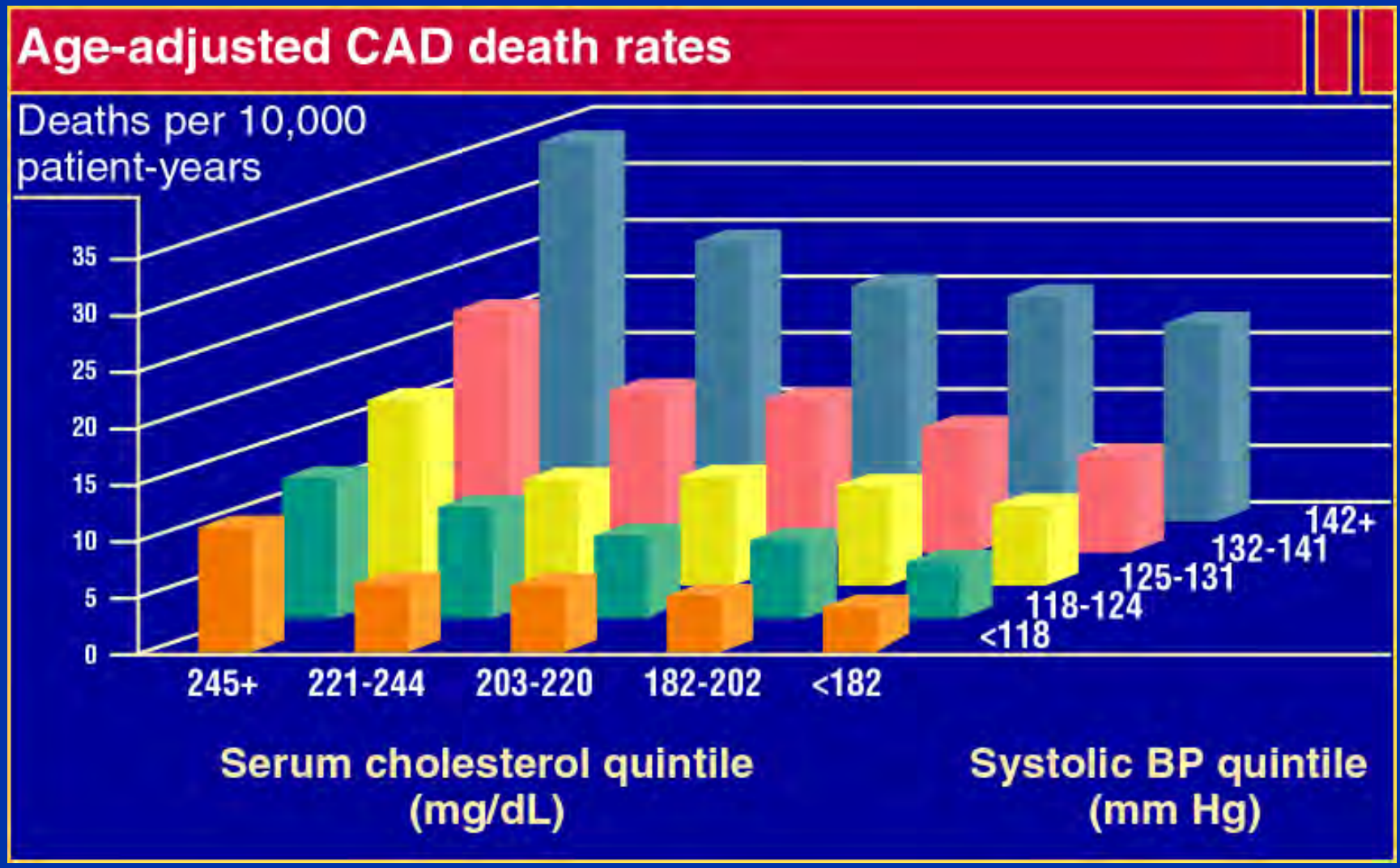
- Family history
- Age
- Gender

Grundy SM et al, *Circulation*, 1998; Grundy SM, *Circulation*, 1999.

New Risk Factors

- Homocysteine
- Lp(a)
- Small dense LDL
- Fibrinogen
- Hs-CRP Risk factor or Disease Identifier
- Coronary Calcium

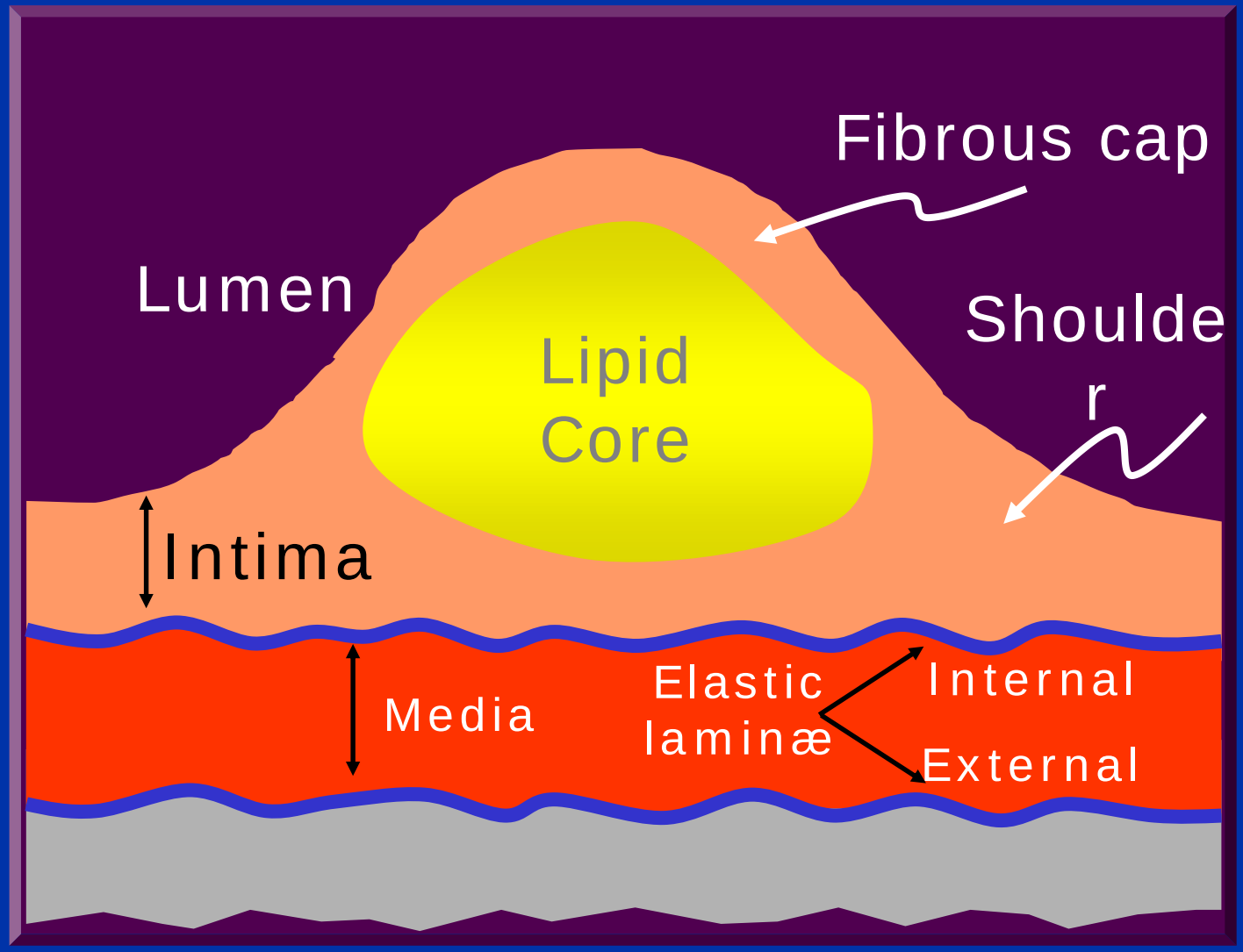
CAD Risk Is Incremental



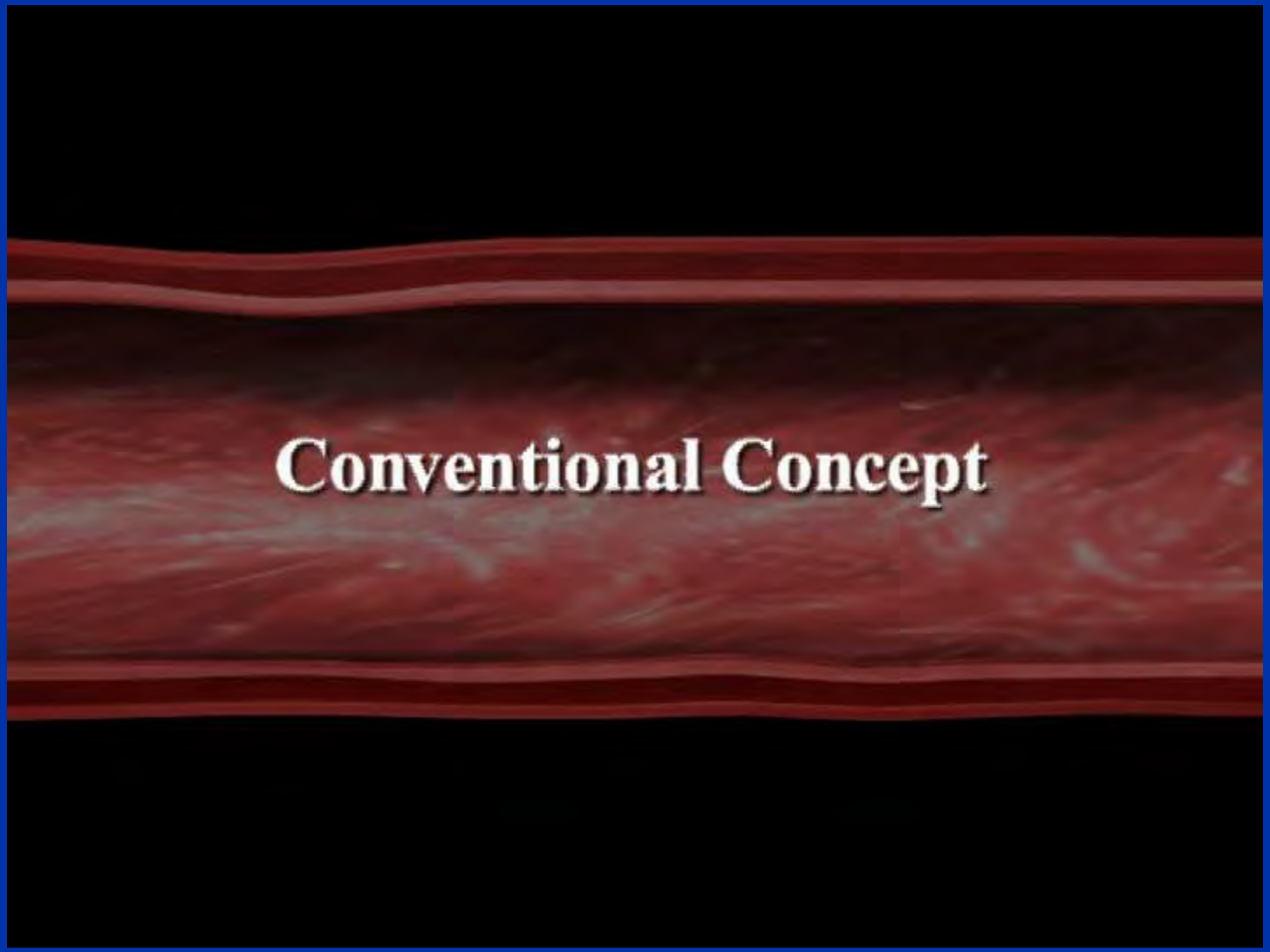
(Adapted from Neaton et al.)

Neaton JD et al, *Arch Intern Med*, 1992.

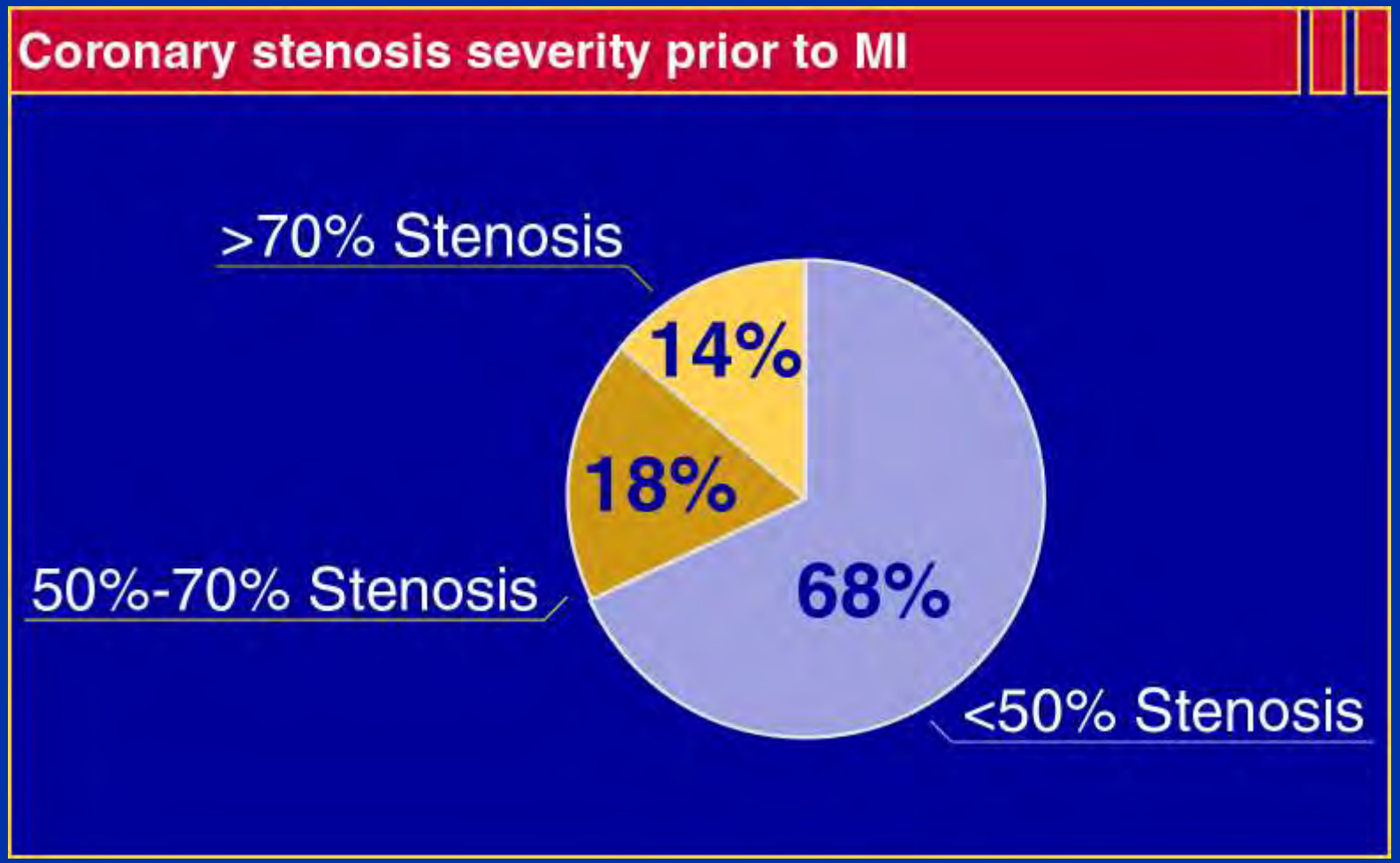
Anatomy of the Atherosclerotic Plaque




Development of Atherosclerotic Plaque


Conventional Concept

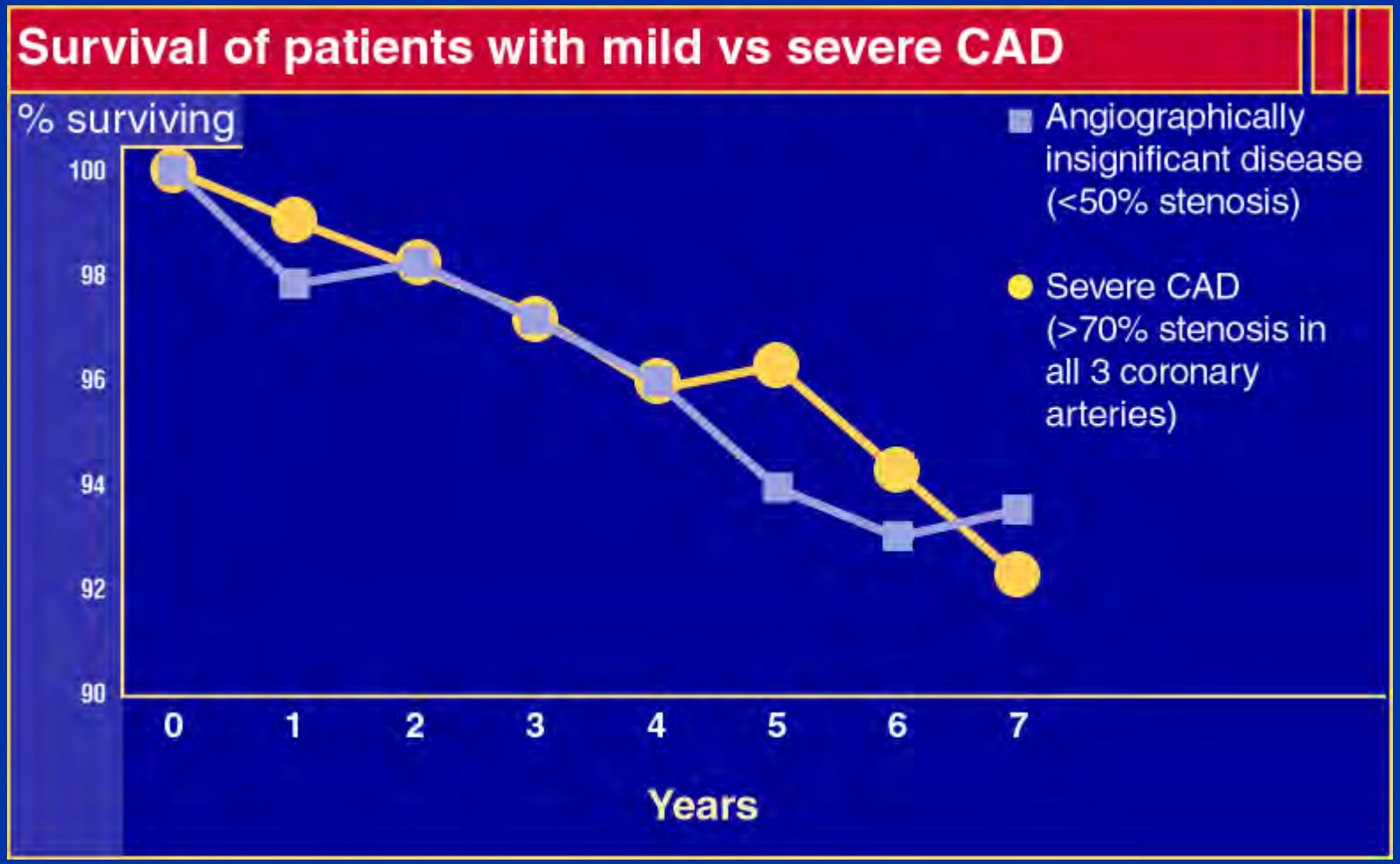
Most Myocardial Infarctions Are Caused by Low-Grade Stenoses



Pooled data from 4 studies: Ambrose et al, 1988; Little et al, 1988; Nobuyoshi et al, 1991; and Giroud et al, 1992.
(Adapted from Falk et al.)

Falk E et al, *Circulation*, 1995.

Lesion Severity: A Poor Predictor of Survival



From the Coronary Artery Surgery Study (CASS) as reported by Little et al.

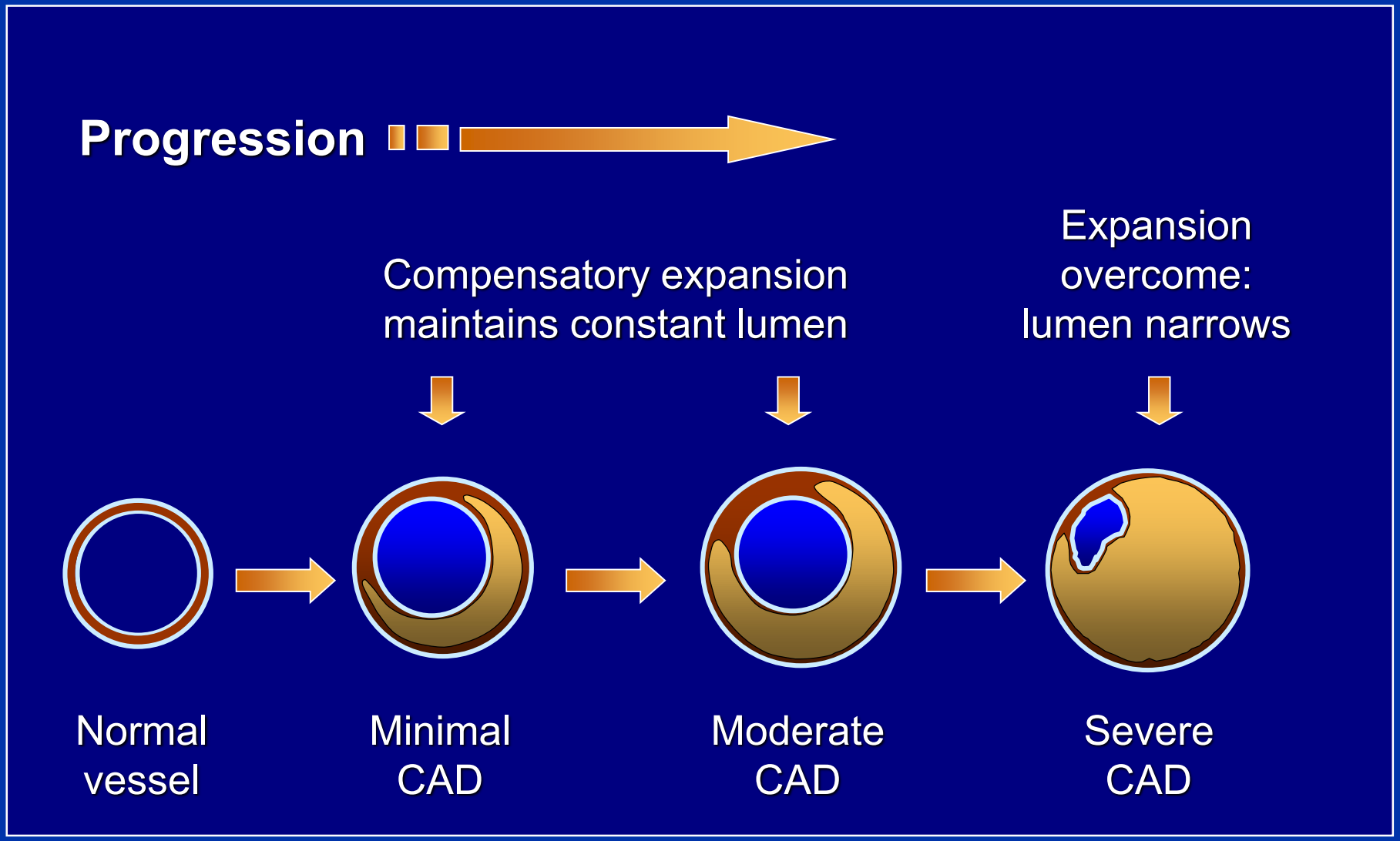
Little WC et al, *Clin Cardiol*, 1991.


Glagov's Model

Conventional vs Contemporary


IVUS Demonstration

Coronary Remodeling

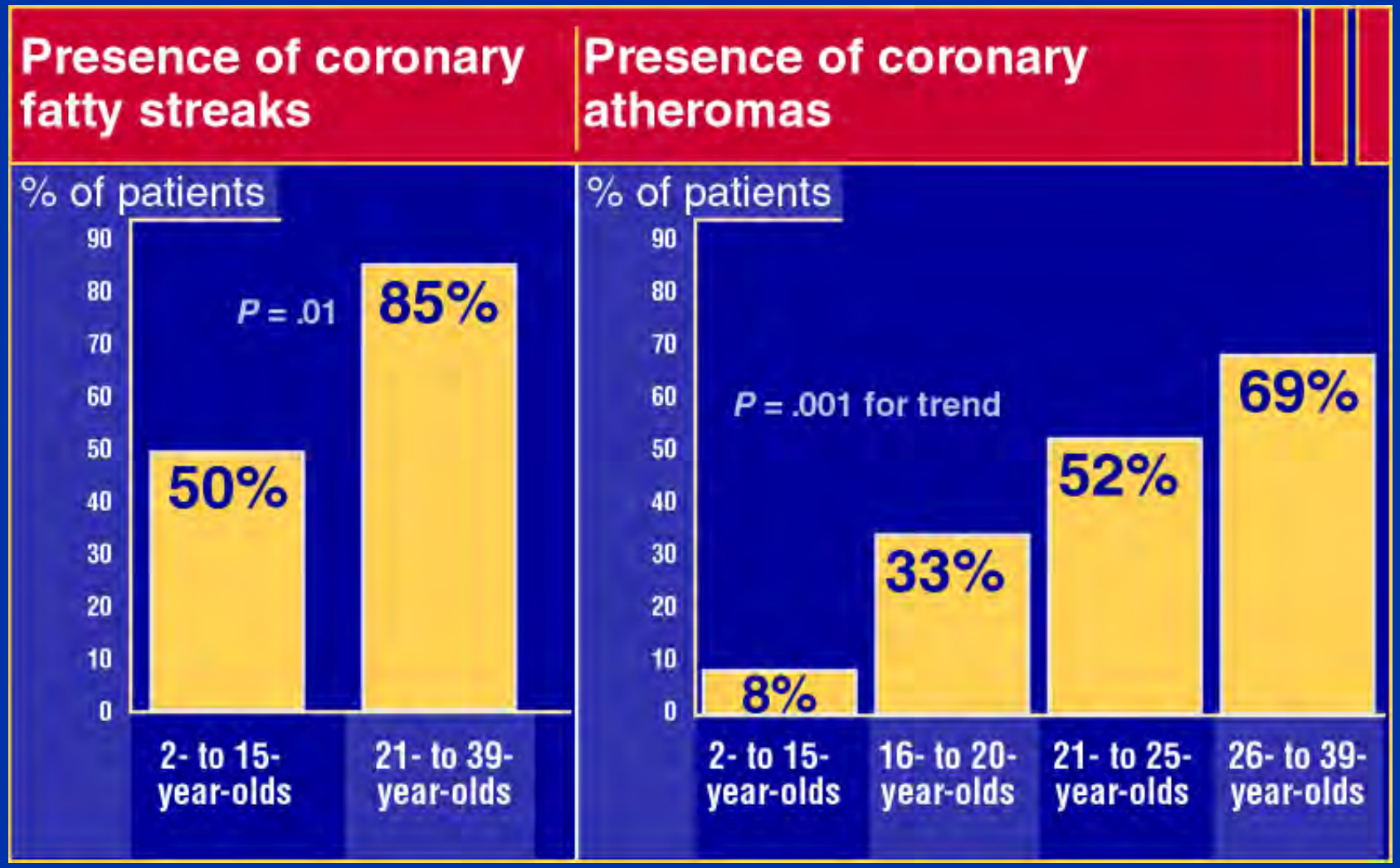


(Adapted from Glagov et al.)

Glagov et al, *N Engl J Med*, 1987.


Transition to Acute Coronary Syndrome

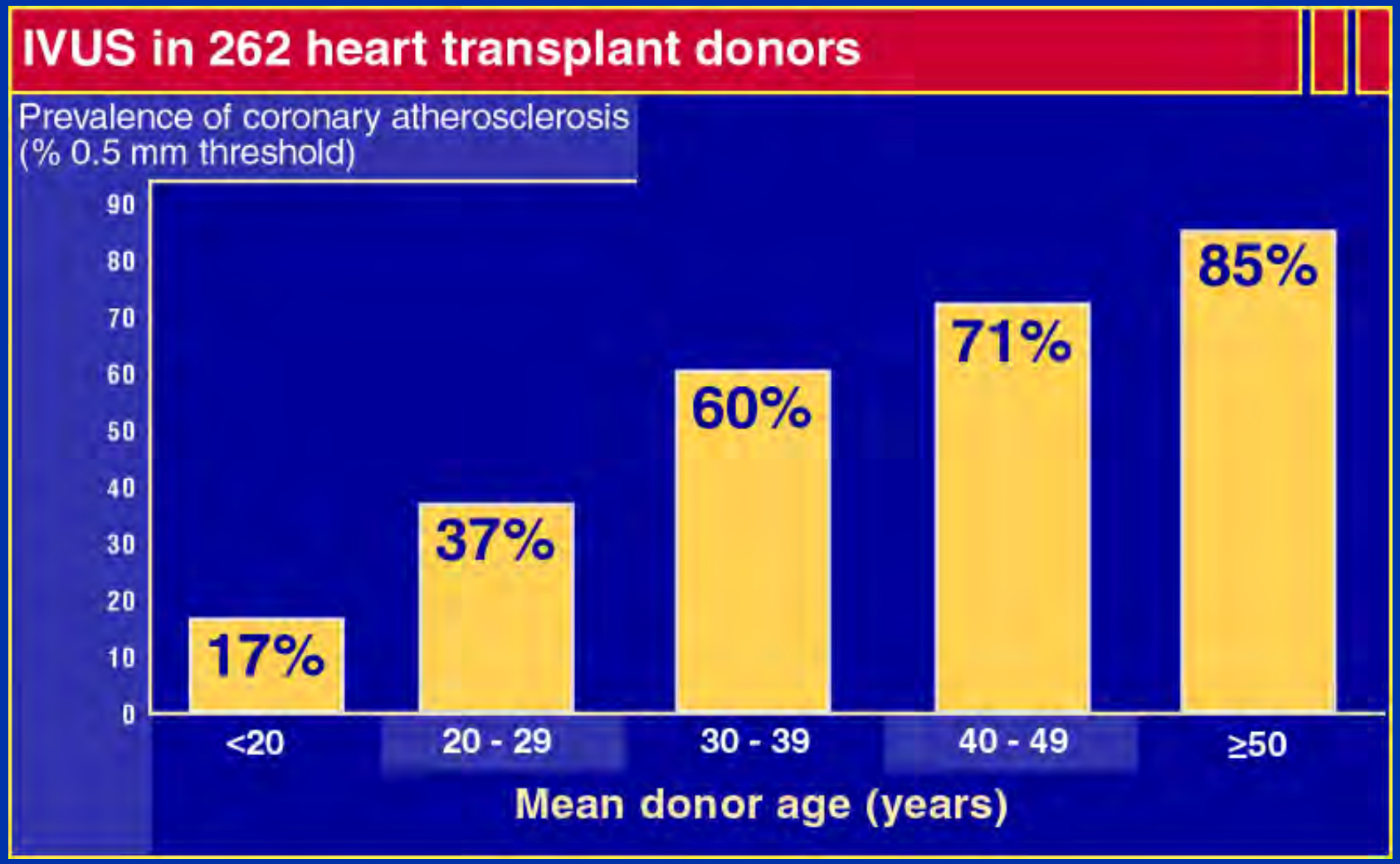
Atherosclerosis Begins in Childhood



(Adapted from Berenson et al.)

Berenson GS et al, *N Engl J Med*, 1998.

One in Six Teenagers Has Atheromas



(Adapted from Tuzcu et al.)

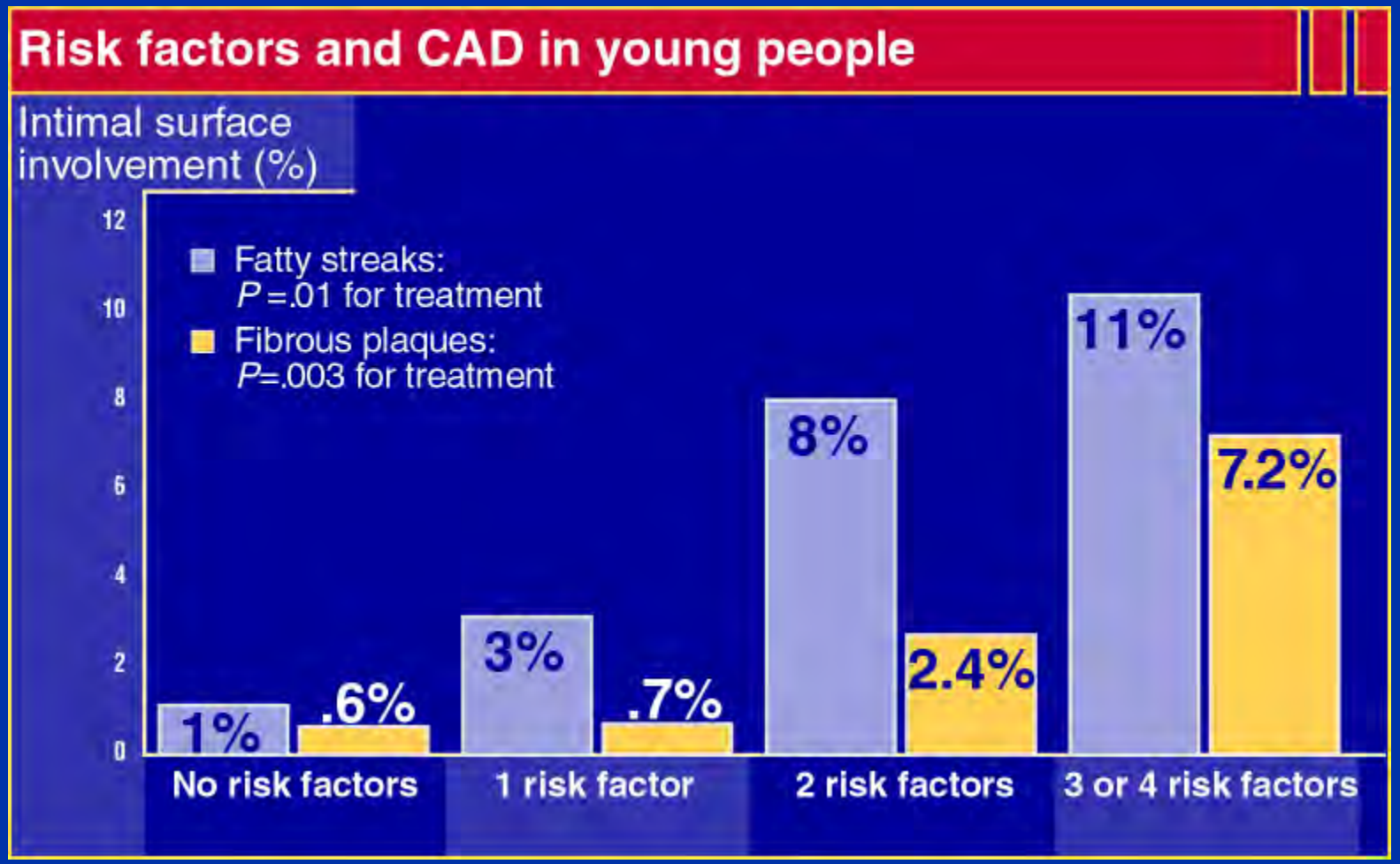
Tuzcu EM et al, in press.

CAD: Silent Disease Necessitates Aggressive Risk Factor Management

- IVUS corroborates necroscopy studies, proving that atherosclerosis begins in youth
- CAD progresses silently; the initial presentation is usually MI or sudden death
- Most atheromas are extraluminal, rendering them angiographically silent
- The only reasonable approach is early and aggressive risk factor management

Berenson GS et al, *N Engl J Med,* 1998; Tuzcu EM et al, in press; Levy D et al in *Textbook of Cardiovascular Medicine*, 1998; Yamashita T et al, *Progress in Cardiovascular Diseases*, 1999; Topol EJ et al, *Circulation*, 1995. Kannel WB in *Atherosclerosis and Coronary Artery Disease*, 1996.

The Correlation Between Atherosclerosis and Risk Factors Begins Early



(Adapted from Berenson et al.)

Berenson GS et al, *N Engl J Med*, 1998.

CAD: Not Just a Lipid Disease

- Half of all MIs occur in normolipidemic patients
- Smoking
  Accounts for 200,000 cardiovascular deaths annually
- Diabetes
  Affects 16 million Americans—and is growing
- Hypertension
  Confers as much risk for MI as smoking or dyslipidemia
  - Systolic hypertension is an even greater indicator of CAD risk than diastolic hypertension

Braunwald E, *N Engl J Med,* 1997; Grundy SM et al, *Circulation*, 1998; The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the National High Blood Pressure Education Program Coordinating Committee, *Arch Intern Med*, 1997.

Conclusions: Critical Lessons in Understanding Atherogenesis

- CAD is a ubiquitous, systemic disease that requires a systemic solution
- Most patients progress to MI or sudden death before a diagnosis of CAD is ever considered
- IVUS demonstrates that remodeling causes angiography to underestimate the extent of disease
- Extraluminal, angiographically silent atheromas are responsible for most acute coronary events, including sudden death

Aronow WS et al, *Am J Cardiol,* 1994; Levy D et al in *Textbook of Cardiovascular Medicine,* 1998; Nissen SE et al in *Textbook of Cardiovascular Medicine,* 1998; Falk E et al, *Circulation,* 1995.

"Awaiting overt signs and symptoms of coronary disease before treatment is no longer justified."

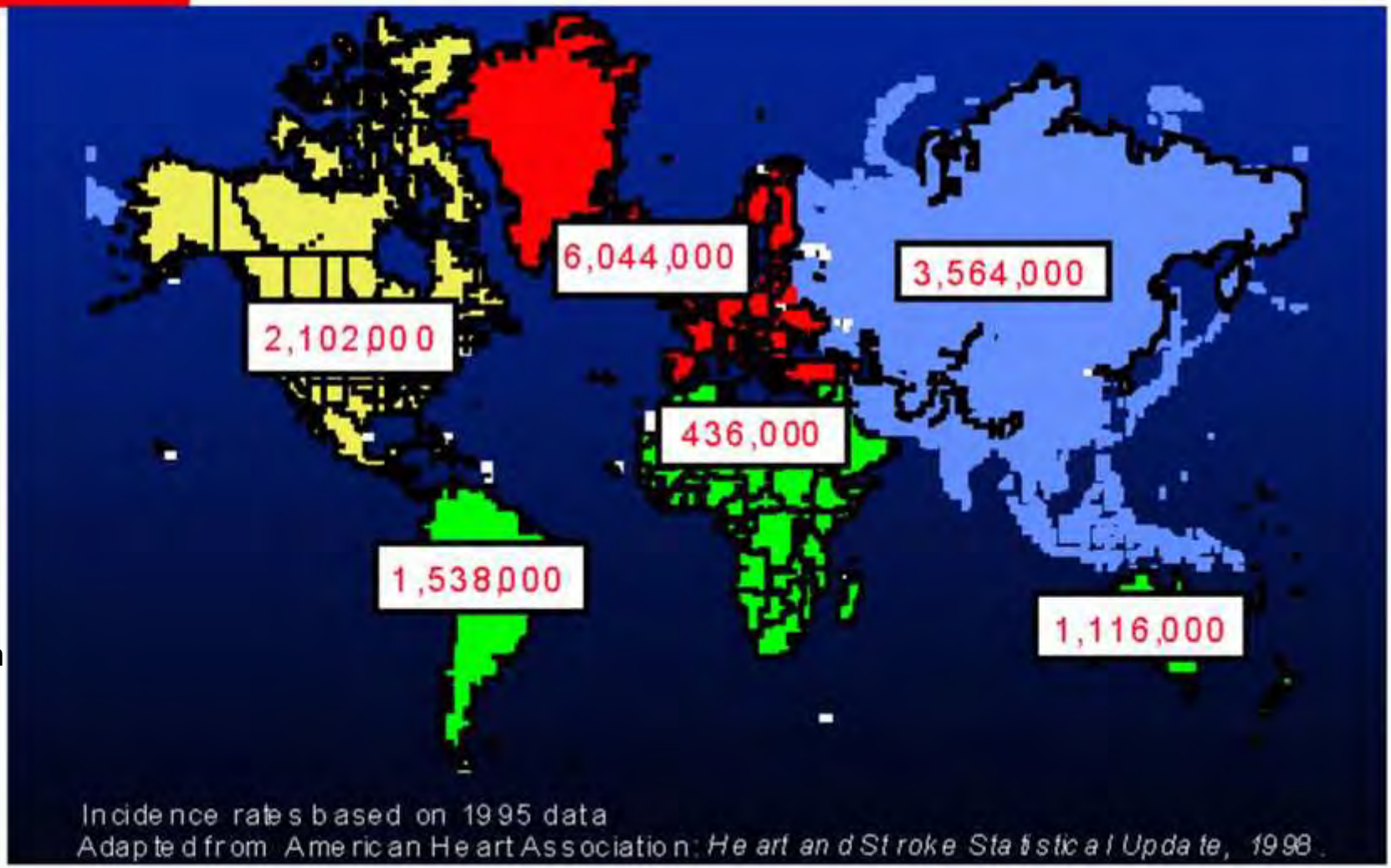
"In some respects, the occurrence of symptoms may be regarded more properly as a medical failure than as the initial indication for treatment."

—William B. Kannel, MD
Department of Medicine
Boston University Medical Center

Kannel WB in *Atherosclerosis and Coronary Artery Disease*, 1996.

The CVD Pandemic: Annual Incidence

> 15 Million Fatal Heart Attacks Each Year



Source:

World Heart Federation

Cardiovascular Disease

- Every 33 seconds, someone dies of a heart attack
- For 60% this is their first sign of Heart Disease
- The number-one killer in the United States since 1900, except during the 1918
- It has killed more Americans than all wars, infectious disease and cancer…Combined

But Who is at Risk?

Jim Fixx, 53 ✝ ♥

- Not Overweight
- Very Fit
- Non-Smoker

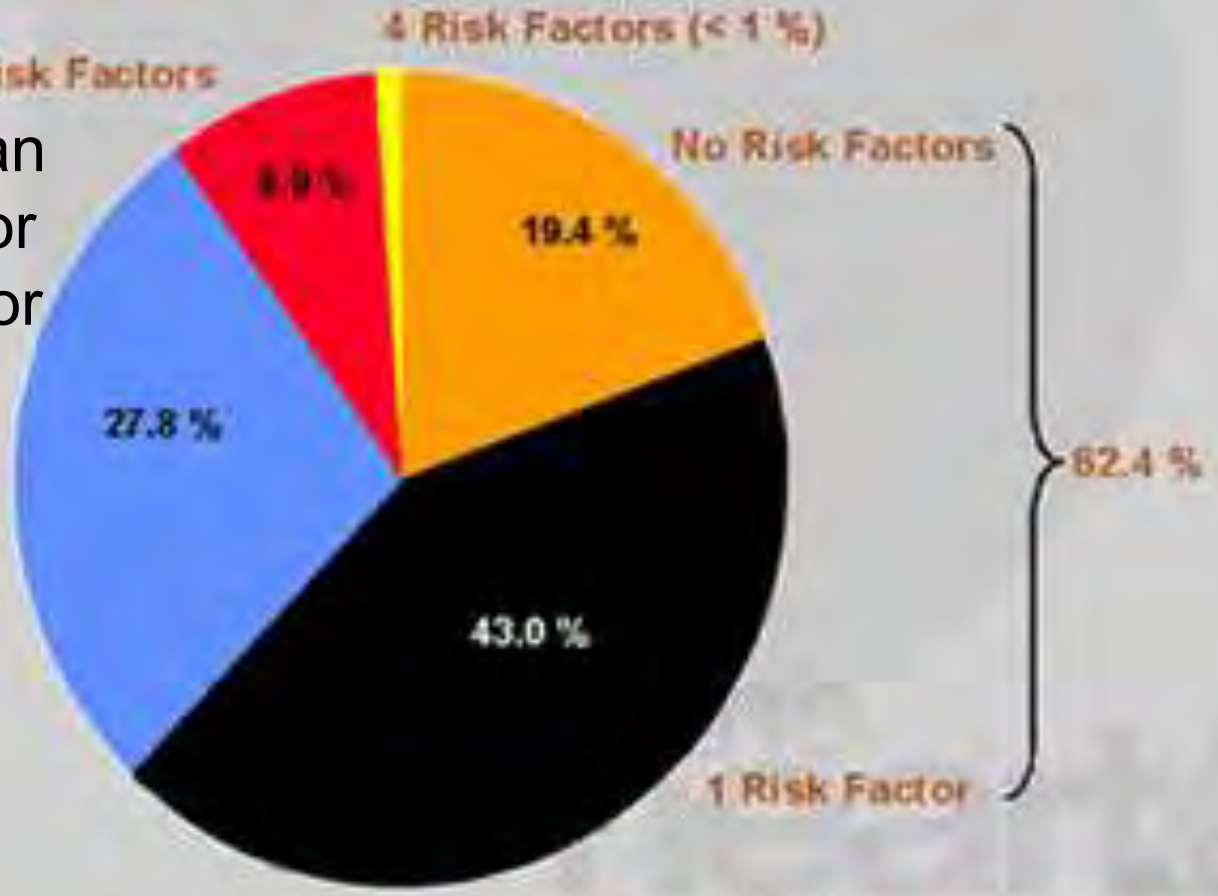
Sir Winston Churchill, 91 ✝

- Overweight
- Not Fit
- Heavy Smoker

Prevalence of Conventional Risk Factors in Patients with Coronary Heart Disease

N = 87,869

Risk factors: Smoking, Hypertension, Cholesterol, Diabetes mellitus



80.6% of American adults have one or more risk factor for heart attack!

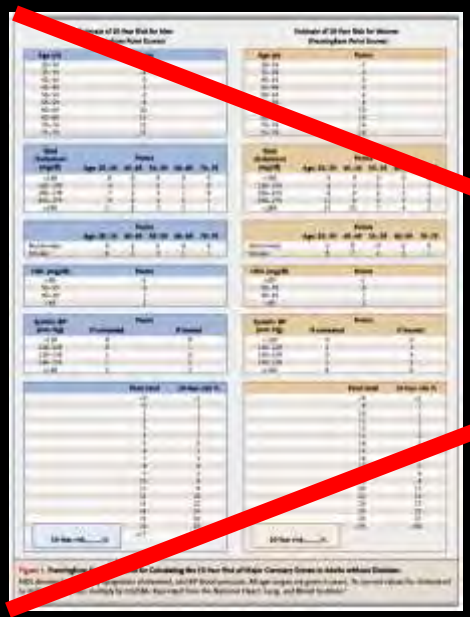
Khot U, et al. *JAMA* 2003;290:898–904.

Eradication of Heart Attack

dream or reality?

- **Most heart attack is preventable**
- **Heart attack remains the #1 killer**

Traditional approach has failed

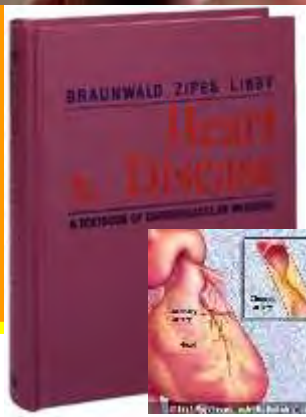


Age	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74		
(Low-risk level)*	(2%)	(3%)	(3%)	(4%)	(5%)	(7%)	(8%)	(10%)	(13%)	Abs... risk	Absolute Risk‡
Points †										Total CHD:	Hard CHD:
0	1.0									2%	2%
	1.5	1.0	1.0							3%	2%
2	2.0	1.3	1.3	1.0						4%	3%
3	2.5	1.7	1.7		1.0					5%	4%
4	3.5	2.3		1.8	1.4	1.0				7%	5%
5	4.0	2.6	2.6	2.0	1.6	1.1	1.0			8%	6%
6	5.0	3.3	3.3		2.0	1.4	1.3	1.0		10%	7%
7	6.5	4.3	4.3	3.3		1.9	1.6	1.3	1.0	13%	9%
8	8.0	5.3	5.3	4.0	3.2		2.0	1.6	1.2	16%	13%
9	10.0	6.7	6.7	5.0	4.0	2.9		2.0	1.5	20%	16%
10	12.5	8.3	8.3	6.3	5.0	3.6	3.1		1.9	25%	20%
11	15.5	10.3	10.3	7.8	6.1	4.4	3.9	3.1		31%	25%
12	18.5	12.3	12.3	9.3	7.4	5.2	4.6	3.7		37%	30%
13	22.5	15.0	15.0	11.3	9.0	6.4	5.6	4.5	3.5		35%
>14	26.5	>17.7	>17.7	>13.3	>10.6	>7.6	>6.6	>5.3	>4.1	>53%	

- **Prevention of heart attacks must be the primary goal.**

Treatment should be regarded as “locking the barn door after the horse is stolen”

Eugene Braunwald



Screening for Atherosclerosis

Risk Factors vs Disease

Numerous Risk Factors

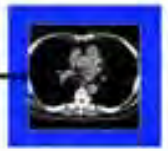
- High LDL
- Low HDL
- High BP
- Diabetes
- Smoking
- CRP
- Metabolic Syn
- Lp(a)
- Homocysteine
- Dense LDL
- Lp-PLA2
- ApoB/ApoA
- Family History
- Sedentary Life
- Obesity
- Stress
- ...
- ?

Over 200 risk factors have been reported.

Examples of Arterial Structure Tests

Carotid IMT and Plaque Measured by Ultrasound

Aortic and Carotid Plaque Detected by MRI



Coronary Calcium Score Measured by CT

Ankle Brachial Index

Brachial Vasoreactivity Measured by Ultrasound

Vascular Compliance Measured by Radial Tonometry

Examples of Arterial Function Tests

Microvascular Reactivity Measured by Fingertip Tonometry

AEHA

The Association for Eradication of Heart Attack

Leading the Way to Eradicate Heart Attacks

The Burden of Sudden Heart Attacks Today

19 million deaths every year

Era of Screening

Regular Screening & Interventions

Get in SHAPE

Screening for Heart Attack Prevention and Education

Era of "Polypill"

Chronic Prophylactic Drug Therapy

Combined Aspirin, Statin, ACE,...

Era of Vaccine

Prevention and Stabilization of Atherosclerosis by Vaccinationa and Immune Modulation Strategies

Learn about the AEHA Vaccine Initiative Mission 2020

$280 Billion / Year only in the USA

AEHA Calls for a Marriage between Fitness and Screening Centers to Proliferate SHAPE Compatible Clinics and Help Fight the Epidemic of Obesity, Diabetes, and Coronary Heart Disease

Shifting Cardiovascular Healthcare to >>>>> Out of Hospital

Produced By: AMERRA, Inc

Oregon Heart & Vascular INSTITUTE

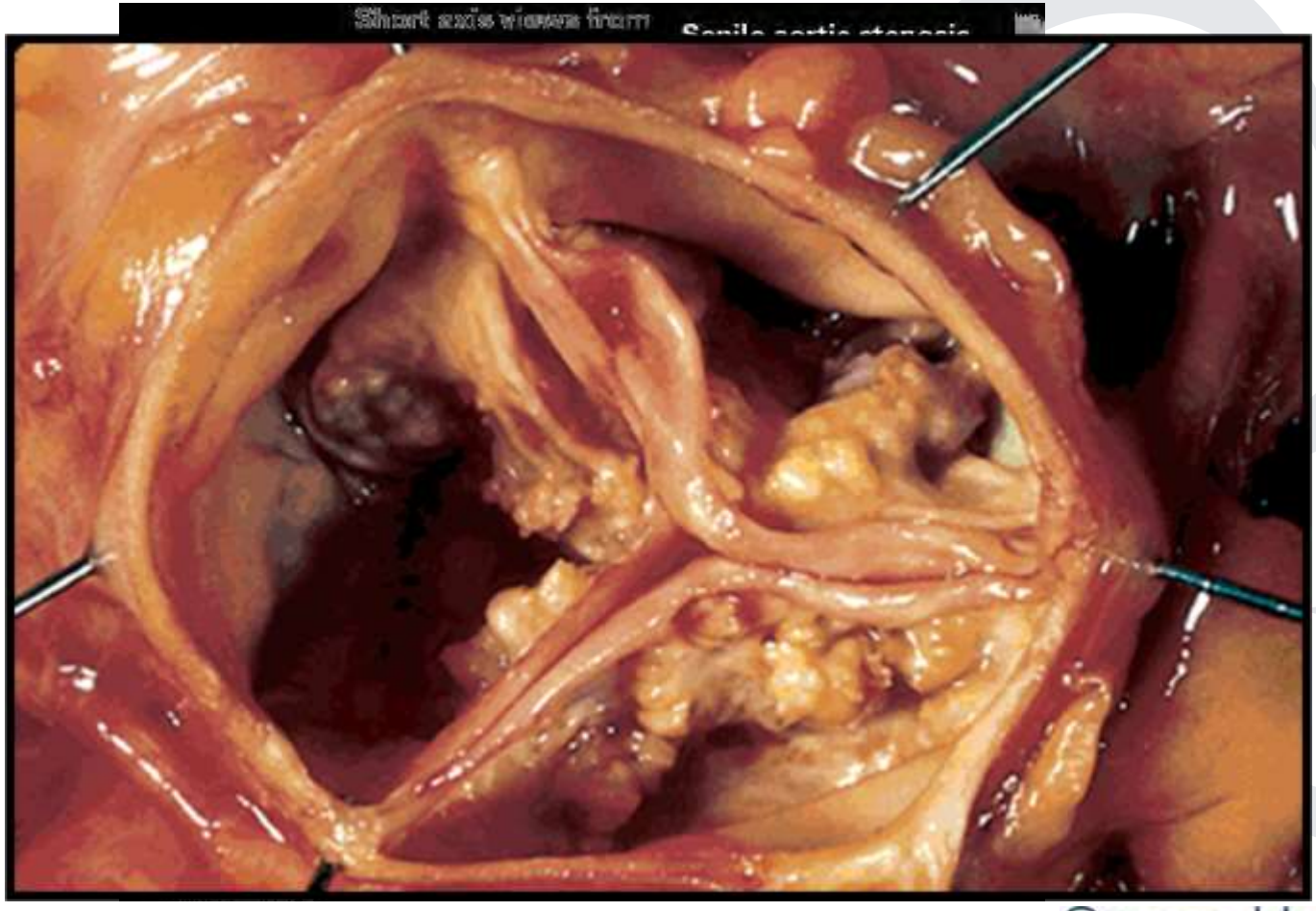
In Affiliation with Sacred Heart Medical Center

New technology to Valve Disease

Richard C. Padgett, MD

Executive Medical Director

Aortic Stenosis



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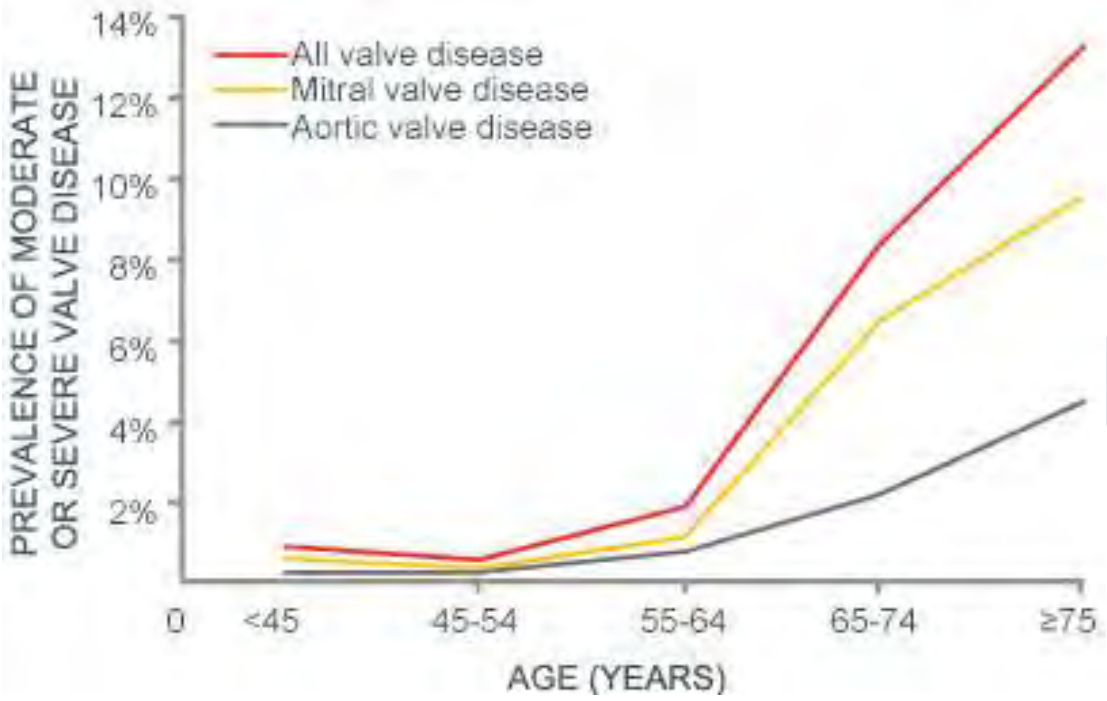
An Increasing Burden



Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005-11.

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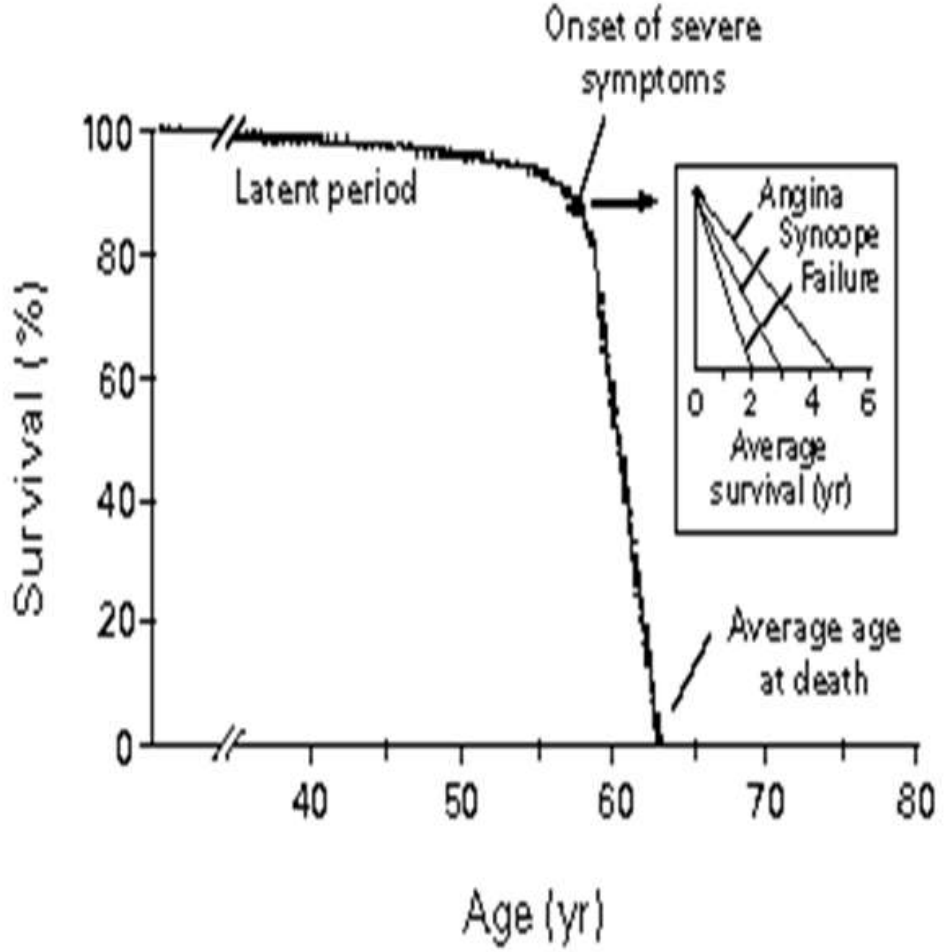
Burden of Valve Diseases in the US

Year	2000 → 2030
Disease	
AS	2.5 millions → 4.6 millions
MR	2.7 millions → 4.8 millions

Aortic Stenosis: Natural History



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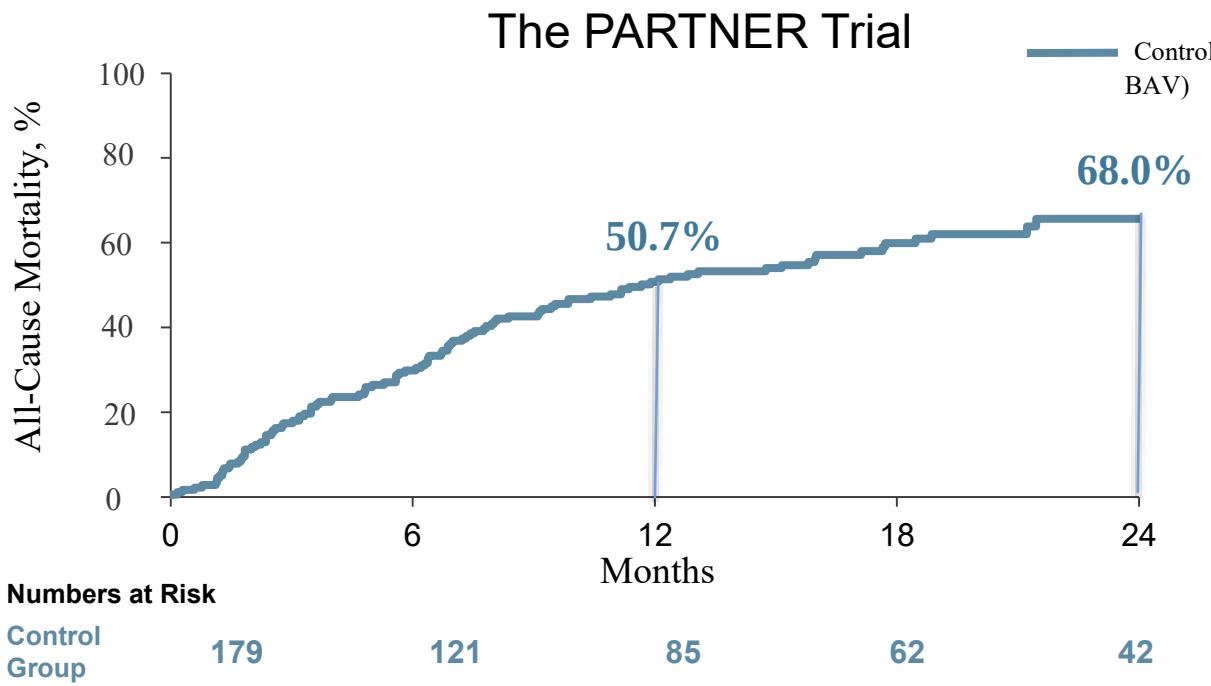
Aortic Stenosis

Symptom/Sign	Live expectancy
Angina	5 years
Syncope	2-3 years
Congestive Heart Failure	1-2 years

Therapy: Valve replacement for severe aortic stenosis
Operative mortality (elderly) ~ 4-24%/Morbidity ~ 3-11%
Event rate in asymptomatic severe AS ~ 1%/year

Standard Therapies are Inadequate



- Despite frequent BAV, **standard therapy did not alter the dismal course of disease for inoperable patients** in The PARTNER Trial
  - 50% died within 1 year
  - 68% died within 2 years

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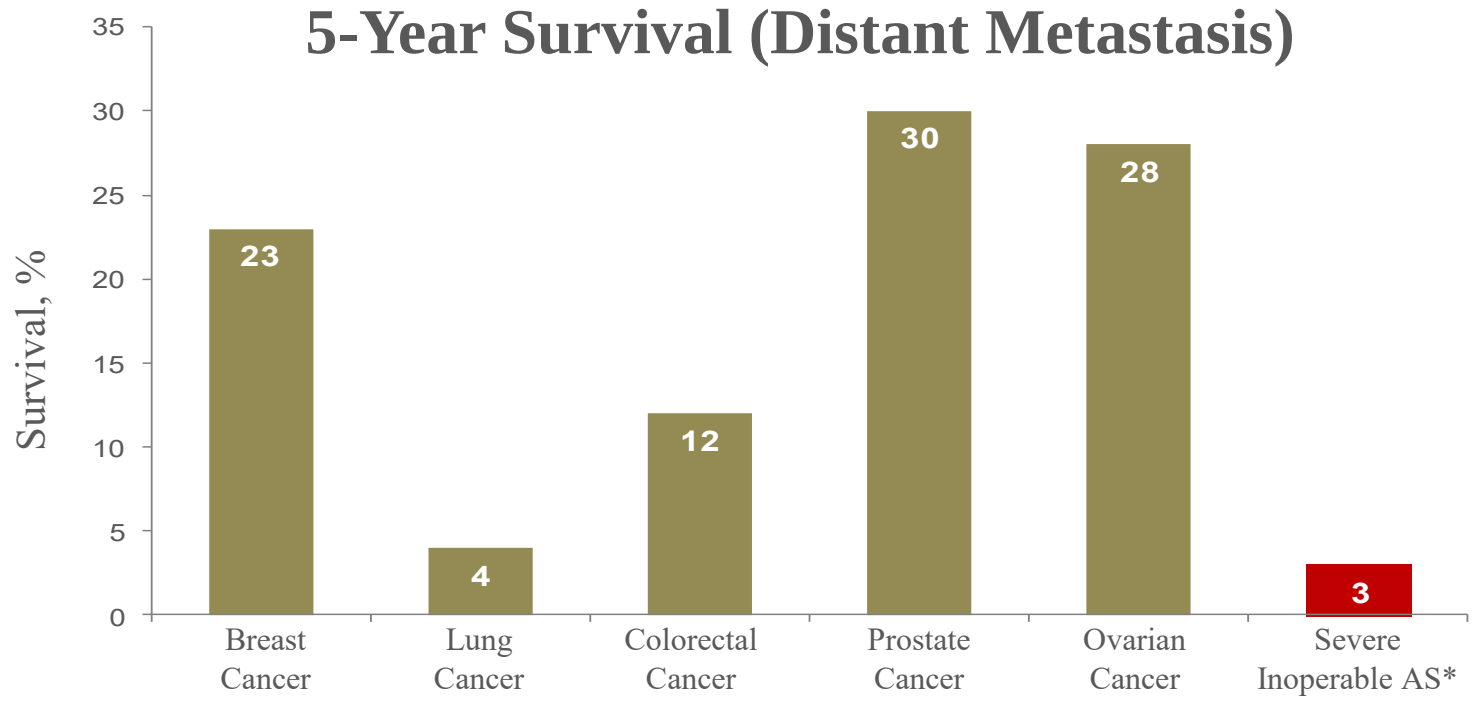
Worse Prognosis than Many Metastatic Cancers



*Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic

- 5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis

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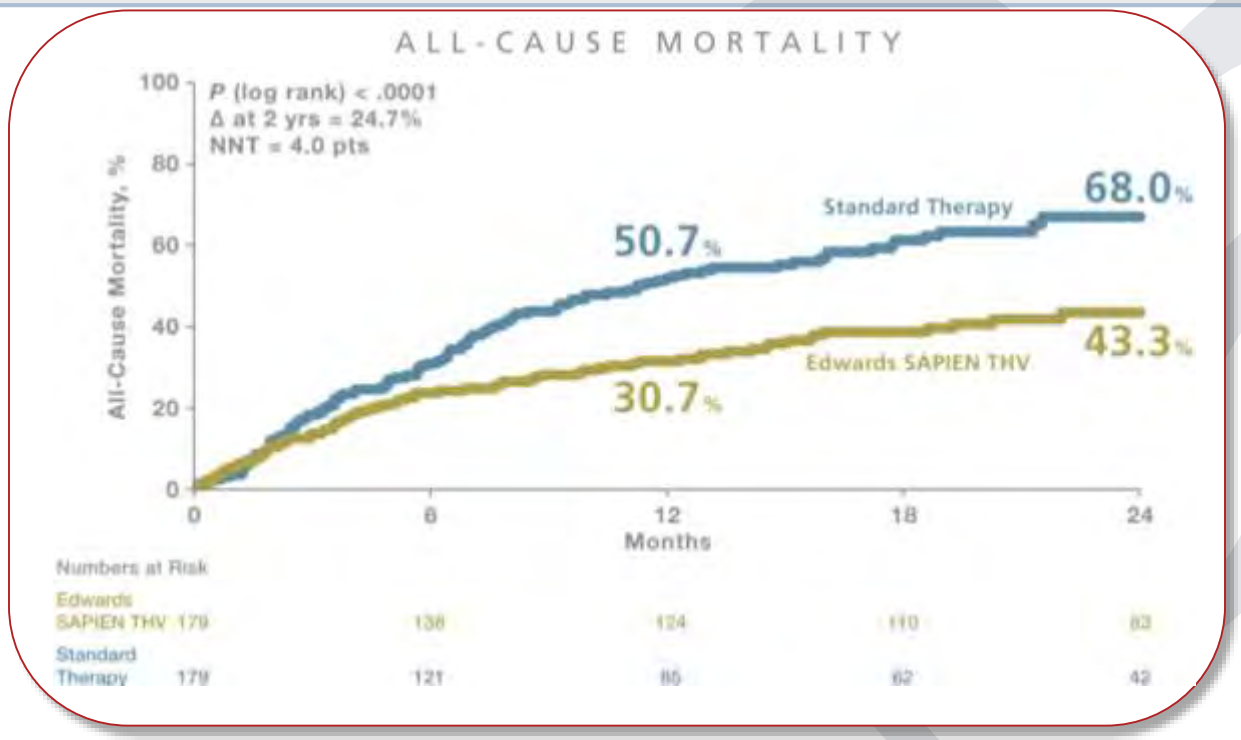
Absolute Reduction in Mortality in Inoperable Patients

The Edwards SAPIEN valve significantly improves survival



24.7% absolute reduction in mortality

Despite expert care and frequent BAV, standard therapy failed to alter the dismal natural course of disease

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• Tri-leaflet
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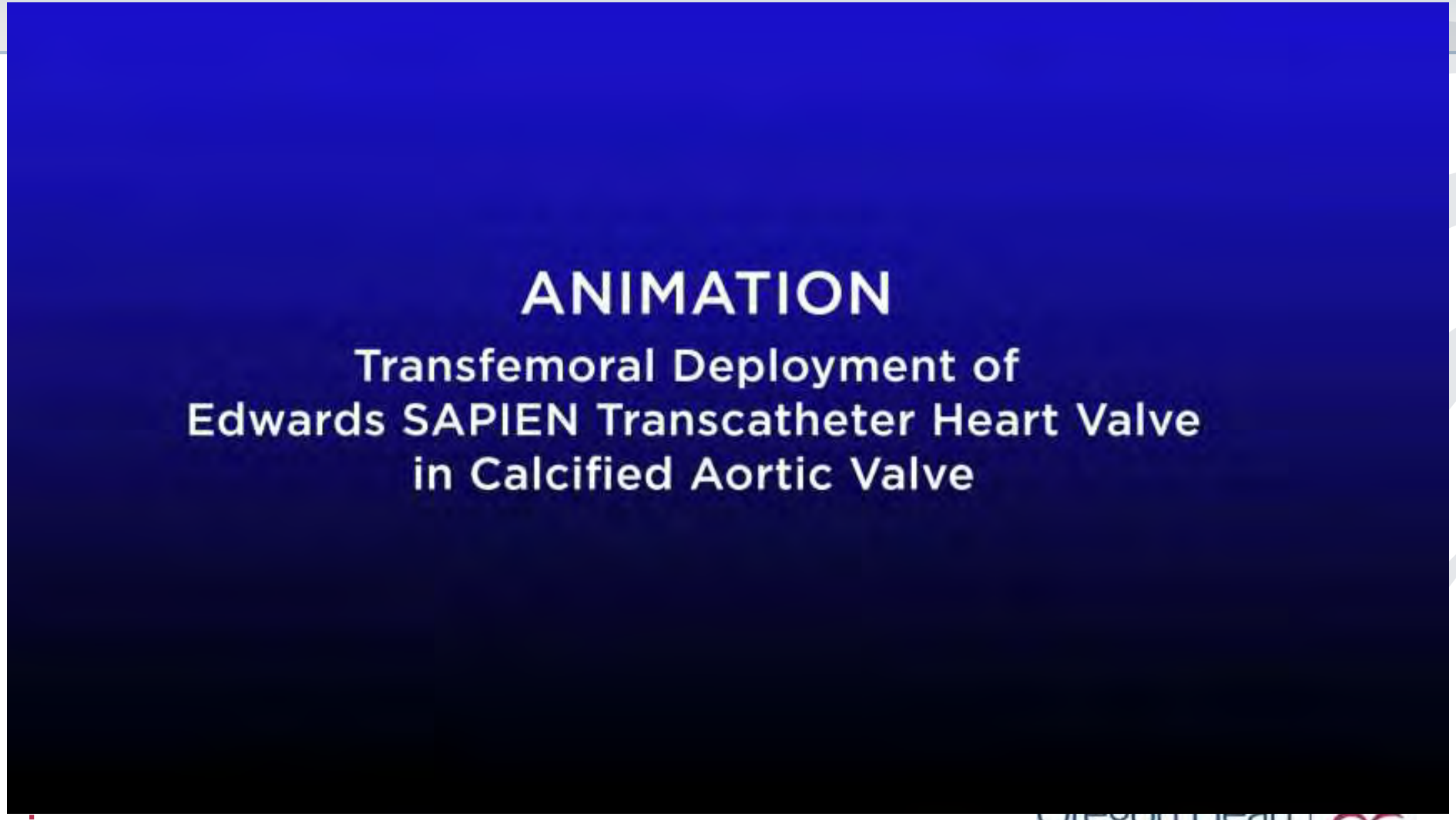

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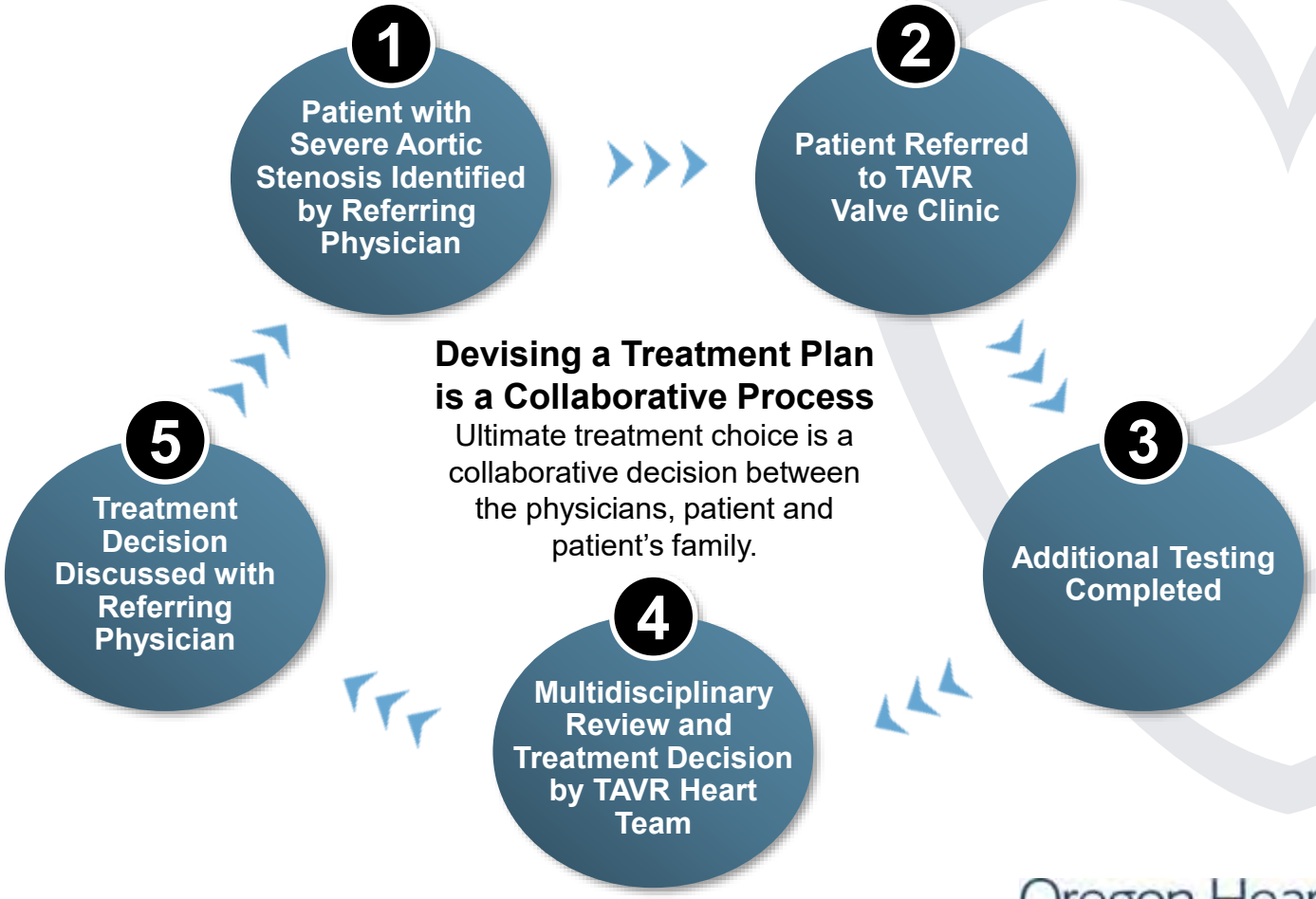
A Collaborative Treatment Decision



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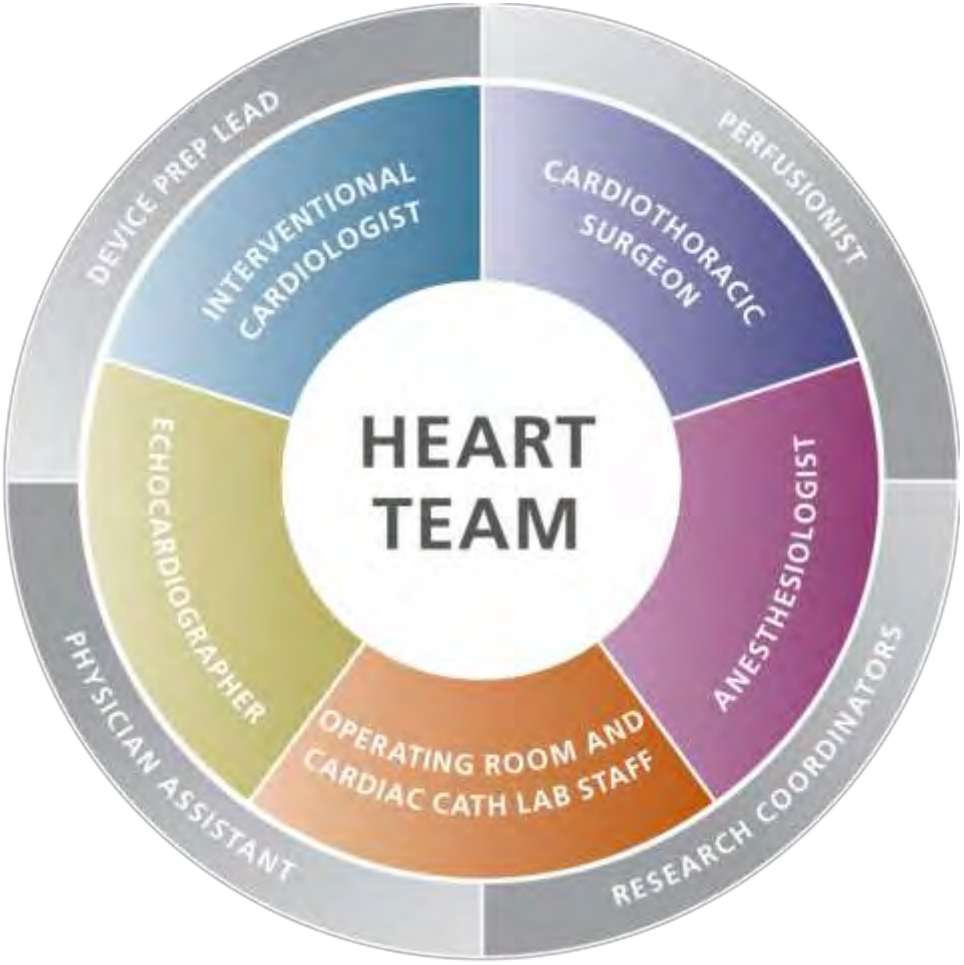
A Dedicated Heart Team



Requires marriage of OR & Cath Lab staff

- Cardiothoracic Surgeon
  Learns: Large bore catheter technology and wire techniques
- Interventional Cardiologist
  Learns: Structural heart & aortic stenosis
- OR and Cath Lab staff both have to learn new equipment and processes

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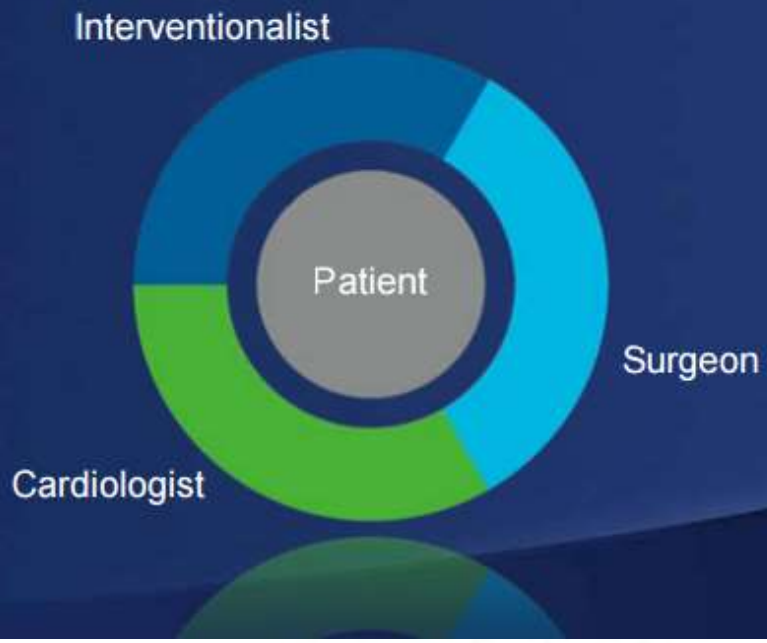
Multidisciplinary Cardiovascular Team

- To ensure the success of the hybrid approach, the multidisciplinary team approach has developed
  - Facilitates joint pre-operative decision-making and intra-operative collaboration between surgery and cardiology



Reference: Maisano 20120

Summary JS

- 85 y.o. male
- STS 10%
- EuroSCORE 3%
- NYHA III

- Creatinine 1.2 BUN 14
- Hgb 12.9
- PLT 130 BNP 422

Clinical History

- Increasing fatigue and exercise intolerance
- Work-up for total knee replacement; echocardiogram shows progression of aortic stenosis, now severe.
- Alzheimer's dementia.
- CAD - moderate
- Chronic kidney disease.

- Hypertension
- Hyperlipidemia,
- Diabetes/ Diabetic neuropathy.
- Obesity.
- History of osteomyelitis of the ankle/ foot.
- BPH./ prostate cancer
- Arthritis.
- Gout.
- Suspected carrier of methicillin-resistant Staph aureus.

Echocardiography – JS

- TTE performed on 6/12/2015

Required Measurements			
Peak Velocity	4.29 m/s		
Mean Gradient	44.4 mmHg	**Annulus Diameter**	**21 mm**
AVA	0.80 cm	Ejection Fraction	65 %

Findings
• Severe aortic stenosis
• Mild aortic regurgitation. • Trace mitral regurgitation • Trace tricuspid regurgitation

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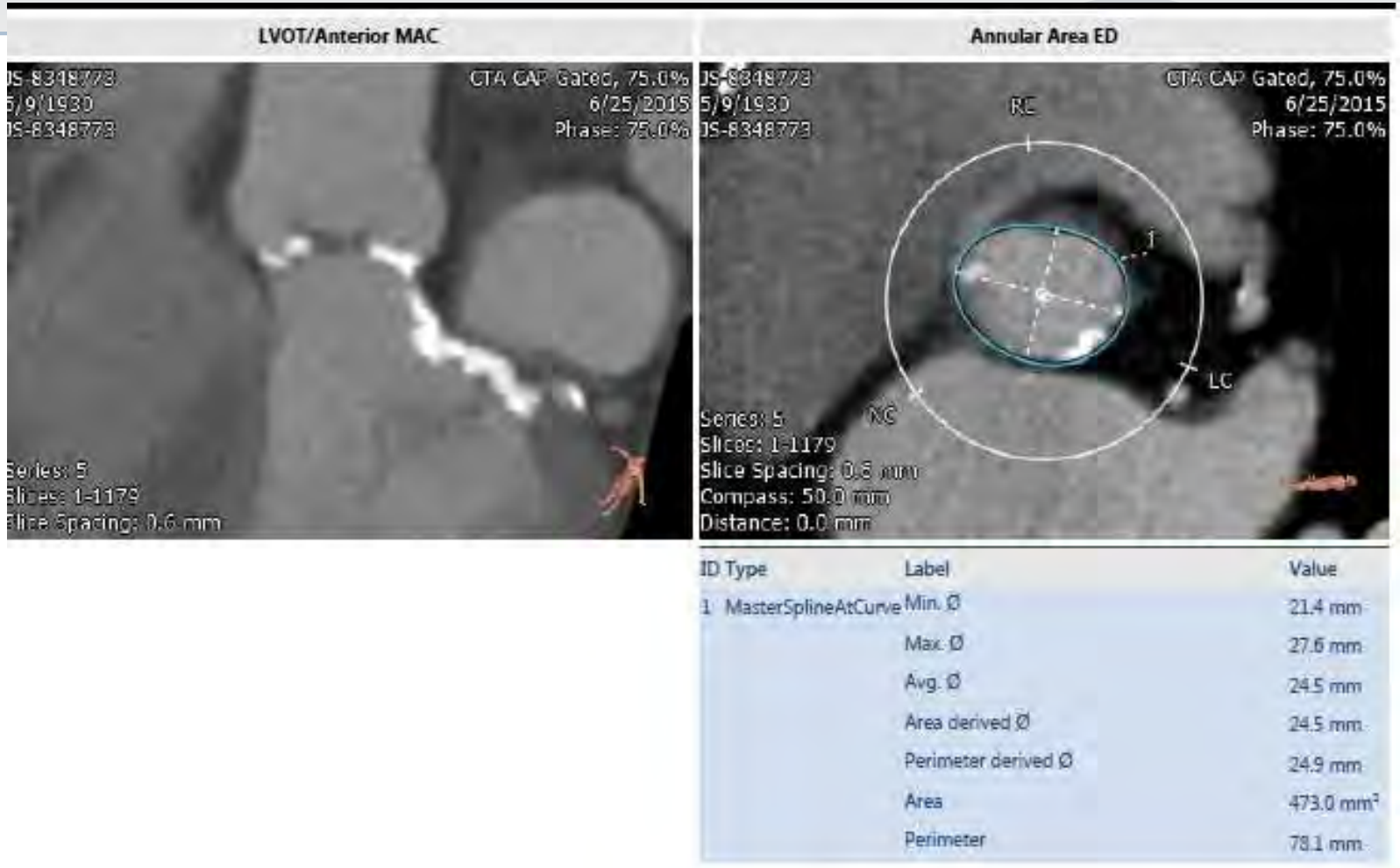
3Mensio – area 473.0 (26 Valve)



ID	Type	Label	Value
1	MasterSplineAtCurve	Min. Ø	21.4 mm
		Max. Ø	27.6 mm
		Avg. Ø	24.5 mm
		Area derived Ø	24.5 mm
		Perimeter derived Ø	24.9 mm
		Area	473.0 mm²
		Perimeter	78.1 mm

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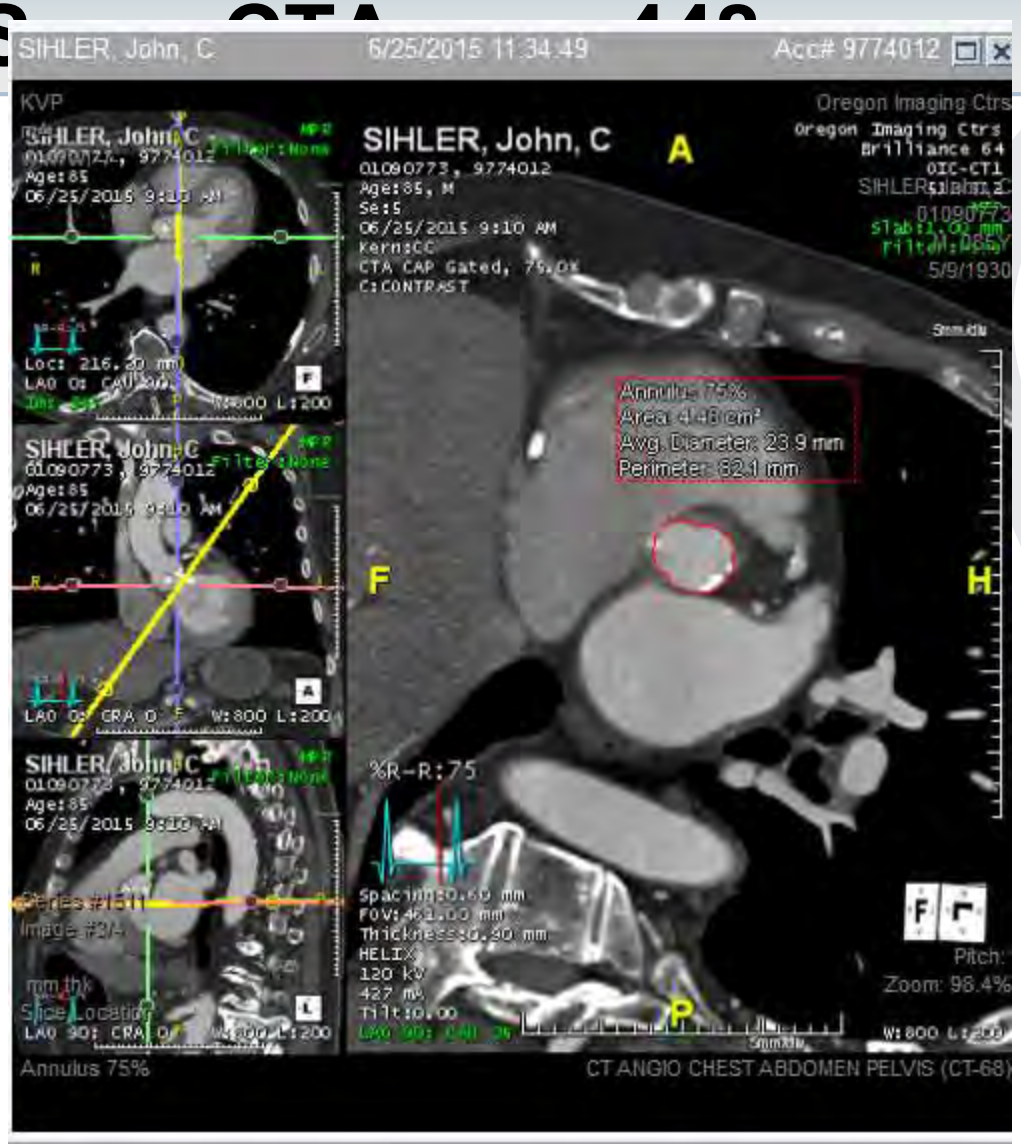
JS CTA 442



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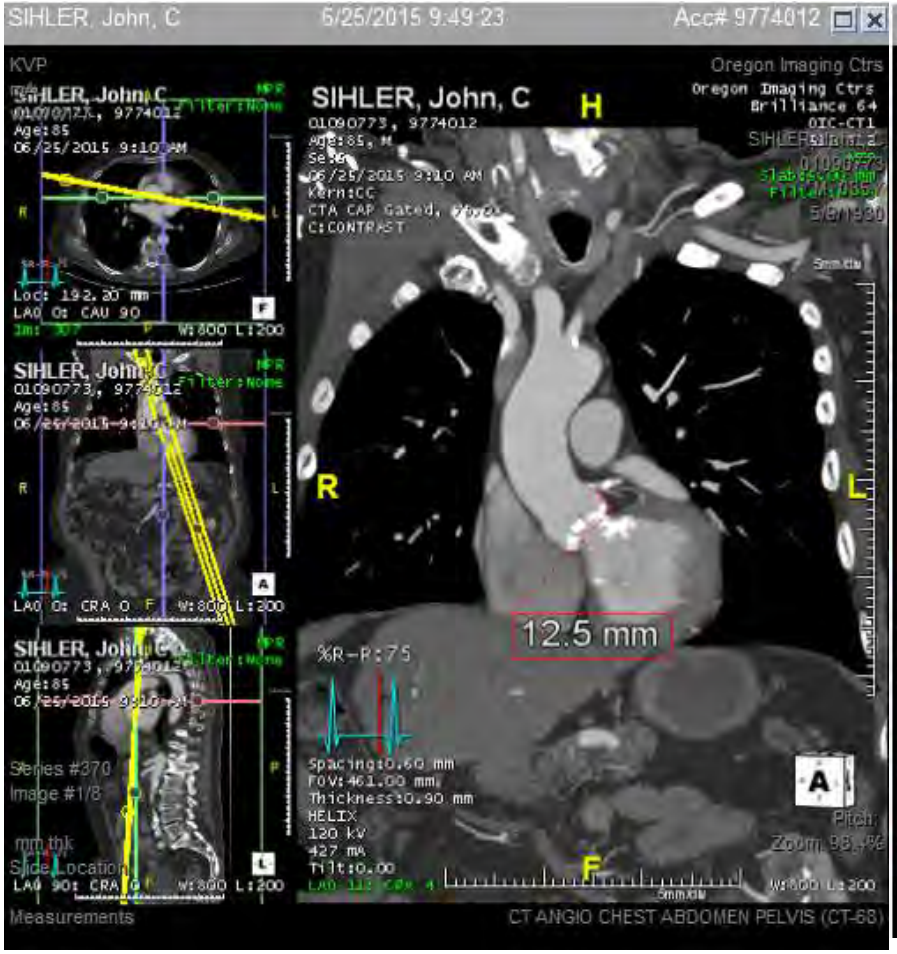
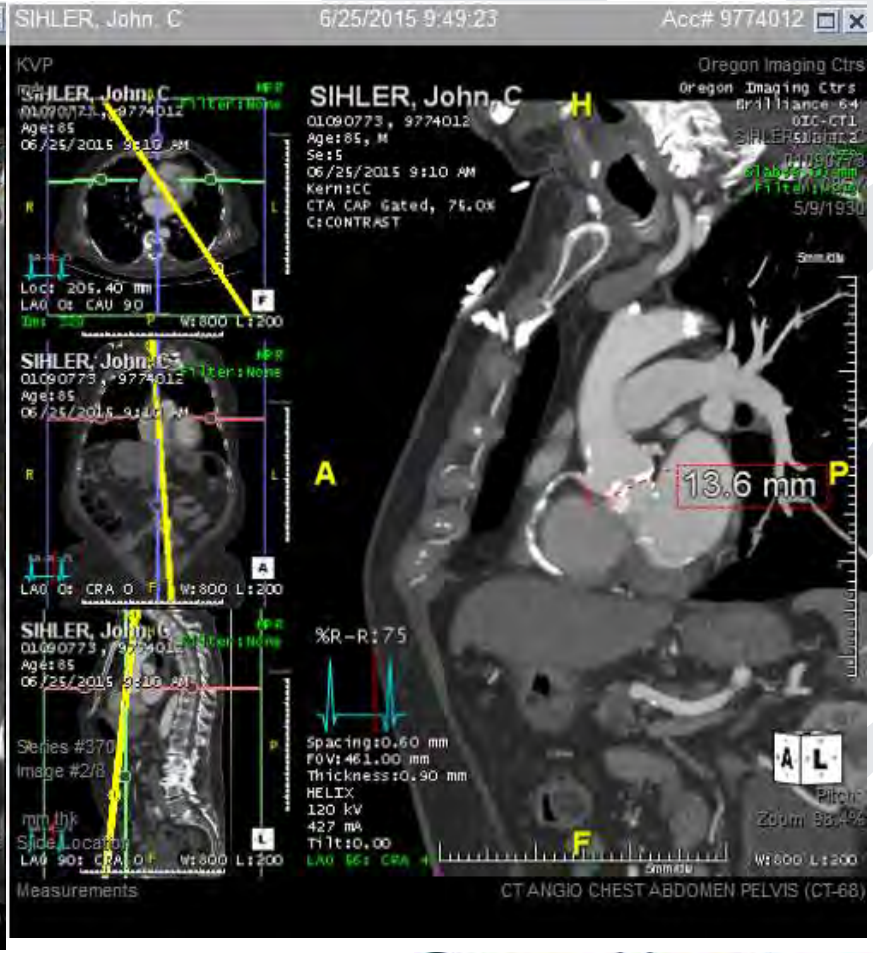
Ostial heights Lt: 12.5 Rt: 13.6





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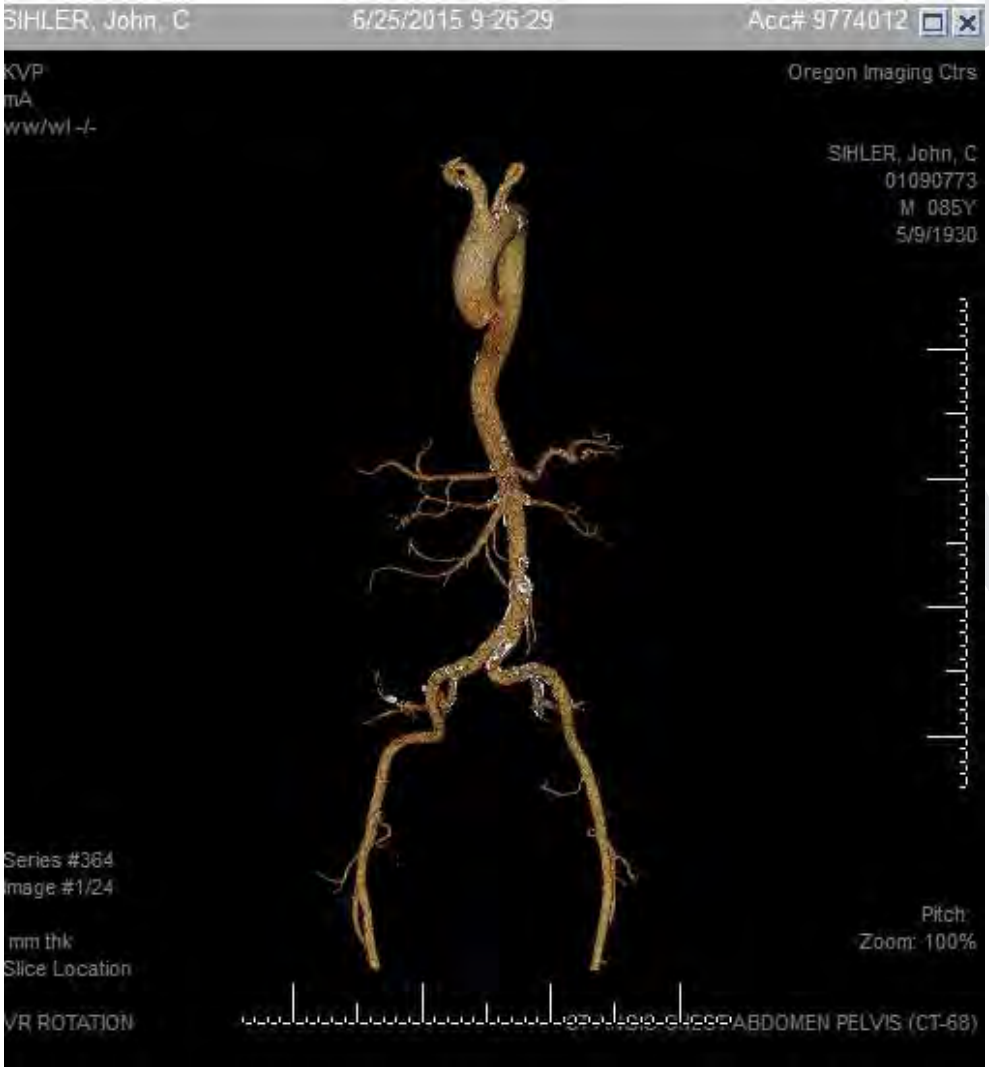
DL access



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Deployment angle RAO 3 Cranial 2

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JS Peripheral Sizing

Minimal Luminal Diameters			
Right		Left	
Common Iliac	8.0 mm	Common Iliac	6.9 mm
Prox external Iliac	8.8 mm	Prox external Iliac	8.6 mm
Mid external iliac	9.0 mm	Mid external iliac	8.5 mm
Common Femoral	8.8 mm	Common Femoral	8.2 mm

JS Procedural Plan

This patient is suitable for transfemoral TAVR with Sapien XT

- Concern of calcium extending into LVOT
- Plan B - Dr. Koh – support only

Annulus Diameter Measurement	THV Valve Size Proposed	Femoral Access Side Proposed	Smallest Vessel Diameter Measurement
24.7 cm	26 mm	Right	8.0 mm

First TAVR @ OHVI Sept 12th 2012


PHILIPS
09/12/2012 10:05:43 TIS0.1
JPEG CR 15:1
X7-2t/Adult
FR 28Hz
13cm
M4
135
-25
xPlane
68%
68%
51dB
P Off
Gen
G
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R
PAT T: 37.0C
TEE T: 38.8C
JPEG
62 bpm

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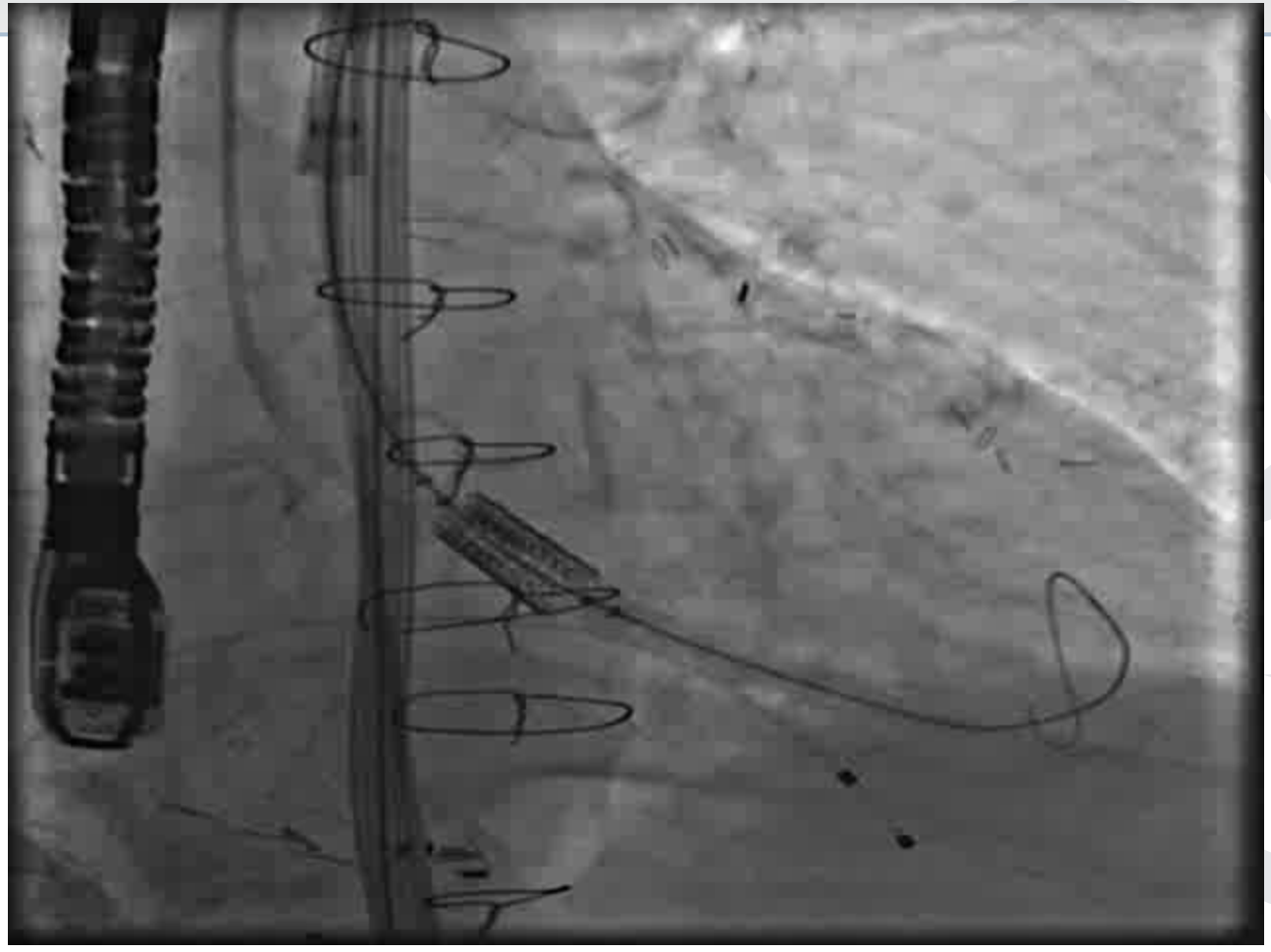

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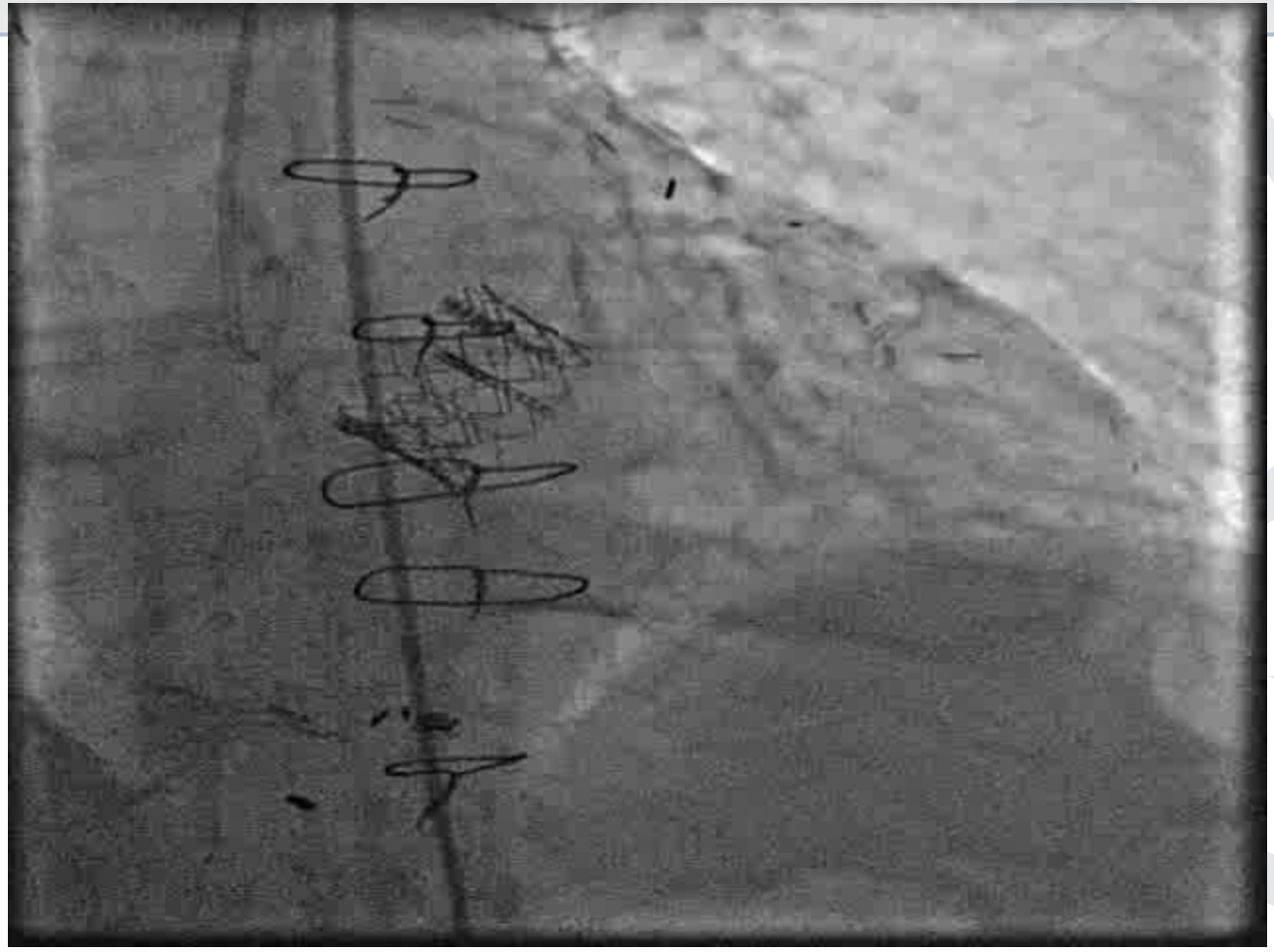

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PHILIPS
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12cm
2D
67%
C 51
P Off
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P R
JPEG
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TEE T: 39.1C
61 bpm


PHILIPS
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PAT T: 37.0C
TEE T: 39.0C
62 bpm

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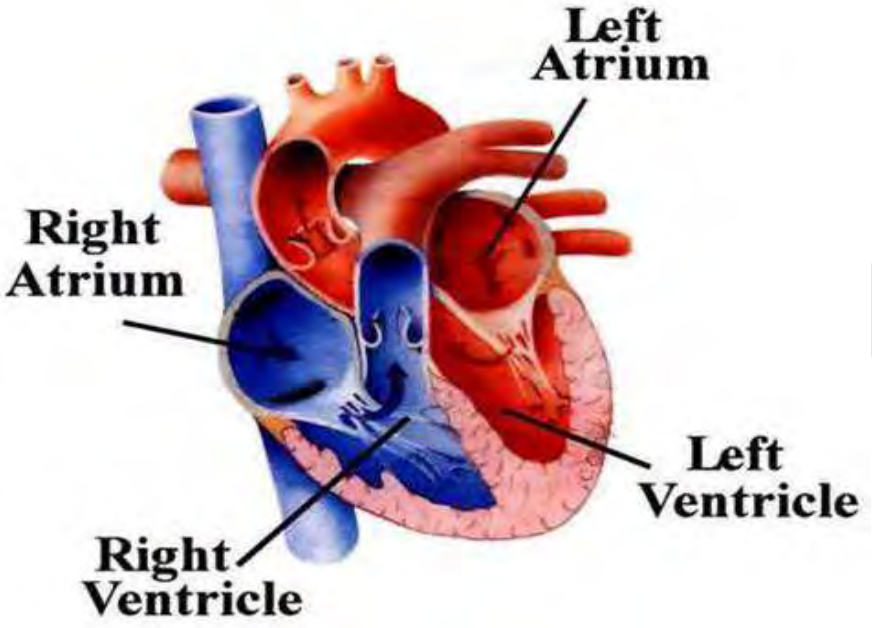
Percutaneous treatment of Mitral Regurgitation

The Mitra Clip procedure

The four chambers of the Heart



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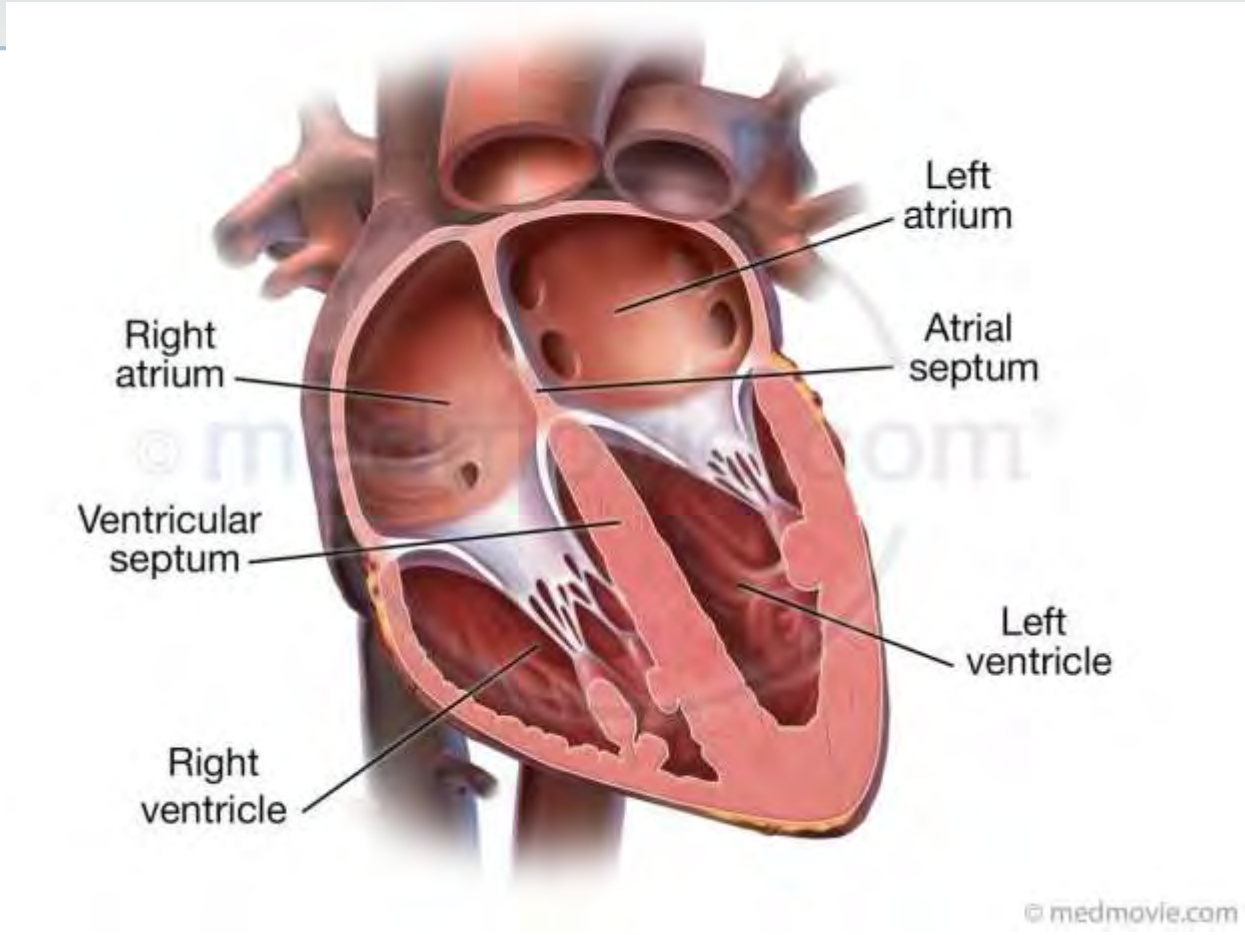

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