Peripheral Arterial Disease
Claudication

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Assumptions

• You know anatomy
• You know pathophysiology, biochemistry of atherosclerosis
• You are awake
Quiz

The best way to diagnose claudication is;

A. History and Physical Exam
B. Doppler Studies
C. CT scan
D. MRA
E. Contrast Angiography
Peripheral Vascular Disease

• Arterial
  – Obstruction
  – Thrombosis
  – Embolism
  – Aneurysm
  – Trauma/bleeding/malformations

• Venous

• Lymphatic
Obstruction

• The degree of narrowing at which pressure and flow begin to be affected.
• 75% cross sectional area or 50% reduction in diameter
• Assumes symmetry
• High-flow vs. low-flow
• Significance must be correlated clinically.
Normal Artery

- Arterial segment without turn, or narrowing.
- The pressure, or energy, in the blood at P1 is almost identical to that at P2.
- With exception of pulsatility, demonstrates energy loss predicted by Poiseuille’s law.
Poiseuille’s Law

- Describes a “parabolic profile”
- Velocities highest at the center.
- Shear rate (D) = \( \frac{\Delta v}{\Delta r} \)
- Tube must be long enough for profile to develop.
- Applies to each branch point and decrease in diameter.
Poiseuille’s Law

- Energy losses inversely proportional to fourth power of the radius
- Little effect until critical point reached
- Graphs then sharply curved
- Increased flow shifts to left
Poiseuille’s Law

- Energy losses related to the viscosity of blood
- Viscosity - friction existing between contiguous layer of fluid

\[
P_1 - P_2 = \frac{8L\eta}{V} \left( \frac{Q}{\pi r^4} \right) = \frac{8L\eta}{r^2} = Q\cdot \frac{8L\eta}{\pi r^4}
\]
Diseased Artery

- The blood has to speed up to get through the area of resistance.
- Pressure in P2 is lower than in P1.
- There is less pressure, or energy, left in the blood once it has got through the area of resistance because it had to do work to get through.
Pressure (energy) Loss at a Stenosis
Entrance and Exit

- Doubling the length of a lesion does not affect energy loss significantly.
- Two separate lesions of equal length and diameter will double resistance.
- Entrance and exit effects
- Two stenoses of unequal diameter in series, tighter of the two has greatest effect on resistance.
Turbulence

- Random velocity vectors
- Occur at branch points and after areas of narrowing.
- Short-lived
- Energy losses not accounted for by Poiseuille’s law.
Energy Loss

- Inertia
- Turbulence
- Pulsatility
- Poiseuille’s law defines *minimal* energy losses.
Exercise Induced Ischemia

Blood flow goes up but insufficiently to provide enough oxygen.

Ischemia

- Claudication
- Rest Pain
- Ulceration/Tissue Loss/Gangrene
CLAUDICATION

DEFINITION

REPRODUCIBLE PAIN WITH EXERCISE, RELIEVED BY CESSATION

FOUR THINGS
DIFFERENTIAL DIAGNOSIS

- MUSCULOSKELETAL
- NEUROLOGIC
- NEUROPATHIC
- VENOUS
- METABOLIC
CLAUDICATION

REPRODUCIBLE

PAIN IS REPRODUCED ALMOST EXACTLY THE SAME TIME AND PLACE UNDER THE SAME CONDITIONS

NOT LIKE ORTHOPEDIC PAIN WHICH IS VARIABLE OR NEUROLOGIC PAIN WHICH IS CONSTANT

“EVERY TIME I WALK A BLOCK AND I GET PAIN IN MY LEG”
CLAUDICATION

PAIN

CRAMPY, SHARP, TIGHTENING, SPASMIC, NUMBING IN A MUSCLE DISTRIBUTION BUT USUALLY NOT BURNING (NEURO-PATHY), DERMATOMAL (NEUROLOGIC), OR IN JOINTS.

OUCHY!
CLAUDICATION

EXERCISE

PAIN STARTS, CONTINUES DURING, AND STOPS WITH EXERCISE, IT DOESN’T JUST COME ON.

OUCHY!
CLAUDICATION

CESSION

PAIN GOES AWAY WHEN YOU STOP EXERCISING WITHIN MINITS

DON’T HAVE TO RAISE THE LEG AS IN VENOUS DISEASE

ALL GONE!
CLAUDICATION DIFFERENTIAL DIAGNOSIS-REPRISE

- VENOUS CLAUDICATION
- SPINAL CORD COMPRESSION
- OSTEOARTHRITIS
- PERIPHERAL NERVE COMPRESSION
- CHRONIC COMPARTMENT SYNDROME
- POPLITEAL ENTRAPMENT, CYST OR ANEURYSM
- SPASMS OR METABOLIC
Claudication

Harbinger of more severe systemic disease

People who are over 50 and smoke or have diabetes have a 30% chance of having secret PAD
CLAUDICATION

NATURAL HISTORY

AT FIVE YEARS  %

MORTALITY  30

OF THE SURVIVORS

NONFATAL MI/CVA  20

STABLE  73

WORSE  16

BYPASSED  7

AMPUTEE  4
OVERLAP AMONG PAOD, CAD AND CVD

CEREBRAL

25%

7%

30%

CARDIAC

3%

12%

PAOD

4%

19%

PAD

CAPRIE, Lancet 1996;348:1349
ABI (Ankle/Brachial Index)

\[
\frac{\text{Ankle Pressure}}{\text{Brachial Pressure}} = 1.0-1.2
\]

By Doppler*
ABI: Predictor of CAD Events and Survival

- Epidemiological studies have confirmed the ABI’s prognostic value:
  - Relative risk of cardiovascular mortality was 5.9 times higher in group with ABI $\leq 0.8^1$
  - 5-year survival was only 44% in patients with ABI $< 0.4^2$
  - Prognostic value of ABI measurement in patients with PAD is analogous to that of ejection fraction or left ventricular end-diastolic diameter in patients with heart failure

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**PAD and All-Cause Mortality***

*Kaplan-Meier survival curves based on mortality from all causes.
*Large-vessel PAD.

Mortality in Patients With Severe PAD

Relative 5-Year Mortality

Patients (%)

Breast Cancer\(^2\)
Colon/Rectal Cancer\(^2\)
PAD\(^1\)
Non-Hodgkin’s Lymphoma\(^2\)

15
38
44
48

\(^{1}\)McKenna M et al. *Atherosclerosis*. 1991;87:119-128.
HOW AWARE ARE WE?

PARTNERS STUDY (UTMCK)

ROUTINE ABI DETECTED PAD IN 29% OF 6,979 PTS

44% NOT BEEN PREVIOUSLY DIAGNOSED

6% OF NEW CASES (11% OF ALL) HAD CLAUDICATION

49% OF PHYSICIANS AWARE OF EXISTING PAD IN THEIR PTS

33% OF NEW PAD PTS, 71% OF CVD PTS PLACED ON ANTIPLATELET Rx

JAMA 2001 286:1317
MAKE AN ANATOMIC DIAGNOSIS

- BASED ON HISTORY AND PHYSICAL

- THINK OF LEVELS OF DISEASE

- FOUR STANDARD LEVELS

AORTO-ILIAC

FEM-POP

TIB-PERONEAL

PEDAL
HISTORY

AREA

HIP, THIGH, BUTTOCK  AORTOILIAC
CALF  AORTOILIAC OR
FOOT  FEM-POP

BUERGER’S
DISEASE
<table>
<thead>
<tr>
<th>Distance</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; TWO BLOCKS</td>
<td>ONE LEVEL</td>
</tr>
<tr>
<td>&lt; TWO BLOCKS</td>
<td>TWO LEVELS</td>
</tr>
<tr>
<td>REST PAIN OR TISSUE</td>
<td>THREE LEVELS</td>
</tr>
<tr>
<td>LOSS</td>
<td></td>
</tr>
</tbody>
</table>
PHYSICAL EXAM

- **PULSES**: 0,1,2 PLUS ONE LEVEL ABOVE
- **BRUITS**: STENOSIS VS OCCLUSION
- **ELEVATION PALLOR/DEPENDANT RUBOR**: THREE LEVELS
- **ONYCHOGRYPHOSIS**: CHRONICITY
THE PATIENT WITH > TWO BLOCK CALF CLAUDICATION WHO HAS A FEMORAL PULSE HAS:

FEM-POP DISEASE AND IF HE HAS A BRUIT IN HUNTERS’ S CANAL HE HAS:

FEM-POP STENOSIS
ADD PHYSICAL EXAM

OR IF HE HAS AN ABSENT OR DIMINISHED FEMORAL PULSE HE HAS:

AORTOILIAC DISEASE

ILIAC OR FEMORAL BRUIT?

NO! AORTOILIAC OCCLUSION

YES! AORTOILIAC STENOSIS
ANKLE/BRACHIAL INDEX (ABI)

• OFFICE PROCEDURE (NURSE CAN DO IT)
  BLOOD PRESSURE CUFF
  HAND HELD DOPPLER (5MHz)

• DIAGNOSE OCCULT PAOD

• CONFIRM SUSPECTED DISEASE
  
  >0.7   > 2 BLOCK CLAUDICATION
  0.5-0.7 1-2 BLOCK CLAUDICATION
  <0.4   REST PAIN, TISSUE LOSS
SEGMENTAL PRESSURES

The Rules

- The thigh pressure is 1.0-1.2x the arm and the same on each side.
- A difference of greater than 20 mm between segments is significant.
- The toe pressure is 70% of the ankle.
SEGMENTAL PRESSURES

- ANKLE/BRACHIAL or TOE/BRACHIAL INDEX
- SEGMENTAL CUFFS
- FEMORAL WAVEFORMS
- EXERCISE
- PVR
DIABETIC VESSELS

- UNCOMPRESSIBLE VESSELS
- CIRCUMFERENTIAL CALCIFICATION
- USE TOE/BRACHIAL PRESSURE OR PVR
SEGMENTAL PRESSURES

• CONFIRMS ANATOMIC DIAGNOSIS BY PHYSIOLOGIC MEANS

• PRETTY GOOD WAY TO FOLLOW OR SHOW THE PATIENTS HARD DATA

• B-MODE ULTRASOUND OF QUESTIONABLE VALUE AND ADDS EXPENSE

• IN THE NONINVASIVE VASCULAR LAB
TREATMENT
## Claudication Risk Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk (Odds Ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>2.5</td>
</tr>
<tr>
<td>Age (per 10 yrs)</td>
<td>2.1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.0</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.1</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.9</td>
</tr>
<tr>
<td>Homocysteinemia</td>
<td>7.0</td>
</tr>
<tr>
<td>ETOH</td>
<td>-2.0</td>
</tr>
</tbody>
</table>

Coexistence of more than one - more than additive

JVS 2000; 31:S17
MEDICAL THERAPY

- CONTROL RISK FACTORS - PROLONG LIFE (LIPIDS, DIABETES, HTN)
- SMOKING CESSATION
- ANTIPLATLET THERAPY - REDUCE CARDIAC AND VASCULAR RISK
- DIET AND WEIGHT LOSS
- EXERCISE THERAPY
- PHARMACOLOGIC THERAPY
CONTROL RISK FACTORS

• LIPIDS “TRY DIET FIRST”
  – LDL CHOL<100 mg/dl, better < 70 mg/dl for high risk PAD pts
  – Niacin side effects
  – Fibrates for low HDL and high TG
  – Statins (simvastatin)-check liver enzymes, rhabdomyolysis

• HTN
  – Controlled according to joint committee IV guidelines 140/90
  – Beta blocker (atenolol) and ACE inhibitor

• HOMOCYSTEINEMIA
  – For level >5mmole/L, folic acid, B12, B6
CONTROL RISK FACTORS

DIABETES
- FBS RANGE 80-120 mg/dl
- POSTPRANDIAL <180 mg/dl
- HEMOGLOBIN A1C <7.0%
- FOOT CARE
  • Orthotics
  • Inspection
ANTIPLATELET THERAPY

• ASA, 75-350 mg/d, REDUCES CARDIAC AND VASCULAR DEATH, NONFATAL MI AND PERIPHERAL ARTERY SURGERY

• TICLOPIDINE REDUCES MI AND STROKE

• CLOPIDOGREL REDUCES STROKE, MI OR VASCULAR DEATH

• COST BENEFIT NOT AVAILABLE, CONSIDER SIDE EFFECTS
PHARMACOTHERAPY

• PENTOXIFYLLINE
  RBC DEFORMITY, DECREASE FIBRINOGEN,
  PLATELET AGGREGATION
  VARIED IMPROVEMENT/SIDE EFFECTS

• PROSTAGLANDINS
  PGE-1, PGI-1 (UTMCK DEPT. SURGERY TRIAL)
  SIDE EFFECTS

• CARNITINE-SMALL TRIALS

• VASODILATORS-NOT A STITCH OF INDICATION

• CILOSTAZOL
  PHOSPHODIESTERASE III INHIBITOR,
  VASODILATOR, ANTIPLATELET ACTIVITY
  IMPROVEMENT/SIDE EFFECTS
MEDICAL THERAPY

![Graph showing mean % change over weeks for Placebo, Pentoxifylline, and Cilostazol.]

AM. J. Cardiology 2001 87;19D
Tobacco Dependence

• Reduction does not reduce all causes mortality (Am. J Epidem 2002;156:194)
• Behavior therapy-20% quit rate in a program
• Nicotine replacement therapy (gum, patch etc) 40-60% quit rate when combined with behavior modification but 25-30% at 1 yr
Tobacco Dependence

- Bupropion SR-(Zyban) antidepressant, dopaminergic and adrenergic effects, 7-12 wks, twice as good as placebo, side effects
- Varenicline-(Chantrix) a4B2 nicotinic acetylcholine receptor partial agonist, 12 wks, reduces side effects of withdrawal
Risk Factor Reduction

Reduces risks of death and other cardiovascular complications
## EXERCISE THERAPY

<table>
<thead>
<tr>
<th>EXERCISE</th>
<th>N</th>
<th>CHANGE ACD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUPERVISED/ASA</td>
<td>10</td>
<td>+105</td>
</tr>
<tr>
<td>ASA</td>
<td>10</td>
<td>-----</td>
</tr>
<tr>
<td>SUPERVISED/PTSFN</td>
<td>15</td>
<td>+371</td>
</tr>
<tr>
<td>TM</td>
<td>10</td>
<td>+74</td>
</tr>
<tr>
<td>HOME</td>
<td>41</td>
<td>+61</td>
</tr>
<tr>
<td>SUPERVISED</td>
<td>59</td>
<td>+99-195</td>
</tr>
<tr>
<td>HOME/PGI</td>
<td>123</td>
<td>+69-142</td>
</tr>
</tbody>
</table>

INDICATIONS FOR INVASIVE INTERVENTION

- LIFESTYLE OR OCCUPATIONAL INTERFERENCE
- FAILURE OF MEDICAL THERAPY
- PROGRESSION
- UNTOWARD EVENT
- ASSOCIATED DISEASE
- SURGICAL RISKS REASONABLE
DIAGNOSTIC TESTS

- ANGIOGRAPHY
- 3-D CAT SCAN
- MAGNETIC RESONANCE ANGIOGRAPHY
- CARDIAC STRESS TEST

CTA
Angio
MRA
Invasive Treatment

• Surgery
  – Traditional
  – Durability
  – Higher mortality, LOS

• Angioplasty, stent
  – Percutaneous
  – Lower LOS, mortality
  – Durability
PRIMARY ILIAC PTA AND STENT PATENCY-METAANALYSIS

Stenosis-Stent
Stenosis-PTA
Occlusion-Stent
Occlusion-PTA

Radiology 2001 221:137
PRIMARY STENT AND PTA PATENCY
UT DATA

Timeran et al JVS
PRIMARY STENT PATENCY

Time (months)

Primary Stent Patency

Men

Women

P = 0.02

Timeran et al JVS
PRIMARY STENT PATENCY IN WOMEN

Primary Stent Patency

Time (months)

CIA

EIA

P < 0.001

Timeran et al JVS
**PRIMARY STENT PATENCY**

AHA Category 1 and 2 Lesions

Time (months)

Primary Patency

Non-HRT users

HRT users

$P = 0.003$

Timeran et al JVS
## PRIMARY STENT PATENCY

Univariate Analysis - Kaplan-Meier

<table>
<thead>
<tr>
<th>Variable</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone replacement therapy</td>
<td>0.020</td>
</tr>
<tr>
<td>EIA stenting</td>
<td>0.001</td>
</tr>
<tr>
<td>Renal insufficiency (creatinine ≥ 1.6)</td>
<td>0.199</td>
</tr>
<tr>
<td>Hyperlipemia</td>
<td>0.061</td>
</tr>
<tr>
<td>Diabetes (IDDM or NIDDM)</td>
<td>0.881</td>
</tr>
<tr>
<td>Smoking history</td>
<td>0.134</td>
</tr>
<tr>
<td>Indication (claudication vs. critical ischemia)</td>
<td>0.582</td>
</tr>
<tr>
<td>Type of stent (Palmaz vs. Wallstent)</td>
<td>0.663</td>
</tr>
<tr>
<td>Runoff score &lt; 5</td>
<td>0.161</td>
</tr>
<tr>
<td>Disease severity (AHA categories)</td>
<td>0.182</td>
</tr>
</tbody>
</table>

Timeran et al JVS
# METAANALYSIS OF WEIGHTED PRIMARY PATENCY (%)

<table>
<thead>
<tr>
<th>PTA AND STENTS</th>
<th>AFB</th>
<th>FPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>YRS TS 1 3 5</td>
<td>5 10</td>
<td>5</td>
</tr>
</tbody>
</table>

## ILIAC PTA

| STENOSIS | 95 78 66 61 |
| OCCLUSION | 83 68 60 - |

## ILIAC STENT

| STENOSIS | 99 90 74 72 |
| OCCLUSION | 82 75 64 - |

## FEM-POP

| STENOSIS | 90 61 51 48 |
| OCCLUSION | 88 67 - - |

TASC Consensus Data JVS 2000 31
FEM-POP PRIMARY GRAFT PATENCY

Time (months)

Patency Rate (%)

Non-HRT users

HRT users

$P = 0.004$

Timeran et al JVS
## FEM-POP MULTIVARIATE ANALYSIS

### (COX REGRESSION)

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary patency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRT</td>
<td>0.914</td>
<td>2.5</td>
<td>1.3-4.8</td>
</tr>
<tr>
<td>Estrogen alone</td>
<td>0.916</td>
<td>2.5</td>
<td>1.3-5.0</td>
</tr>
<tr>
<td>HRT + PTFE</td>
<td>1.191</td>
<td>3.3</td>
<td>1.4-7.5</td>
</tr>
<tr>
<td><strong>Assisted primary patency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRT</td>
<td>1.044</td>
<td>2.8</td>
<td>1.4-5.6</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.784</td>
<td>2.2</td>
<td>1.1-4.3</td>
</tr>
</tbody>
</table>

Timeran et al JVS
Effects of Estrogen, Progesterone, and Combination Exposure on Interleukin-1β Induced Expression of VCAM-1, ICAM-1, PECAM, and E-Selectin by Human Female Iliac Artery Endothelial Cells

K.T. Piercy, MD, R.L. Donnell, DVM, PhD, ACVP, S. Kirkpatrick, BS,
S.D. Pappas, BS, S.L Stevens, MD, FACS, M.B. Freeman, MD, FACS,
M.H. Goldman, MD, FACS
Department of Surgery
University of Tennessee Medical Center,
Knoxville
Luminal Flow

Loose Rolling Adhesion
- E-selectin
- P-selectin
- L-selectin

Firm Adhesion
- ICAM-1
- ICAM-2
- VCAM-1

Migration
- PECAM-1
- ICAM-1
- VCAM-1
Hormonal Effects on Adhesion Molecule Expression

VCAM-1

Mean FI

Control  Est  Prog  Est/Prog

ICAM-1

Mean FI

Control  Est  Prog  Est/Prog
HORMONE REPLACEMENT THERAPY

• MAY AFFECT CARDIAC RISK IN PATIENTS WITH PREEXISTING DISEASE

• AFFECTS PATENCY OF VASCULAR INTERVENTIONS

• MAY BE RESULT OF INDUCED HYPERCOACUABLE STATE OR INTIMAL HYPERPLASIA
VASCULAR SURGERY
A NEW PARADIGM “ONE STOP SHOPPING”

A PHYSICIAN FIRST-WITH THE PRIMARY MD

RISK MANAGEMENT

DIAGNOSTIC METHODS

MEDICAL THERAPY

INTERVENTIONAL SKILLS “NOT ROCKET SCIENCE”

SURGERY

FOLLOW UP-WITH PRIMARY MD

QUALITY ASSESSMENT-OBJECTIVE LOOK BACK
REVIEW-CLAUDICATION

- DIAGNOSIS BY HISTORY AND PHYSICAL
- CONFIRM BY ANKLE/BRACHIAL INDEX
- TREAT RISK FACTORS
- MEDICAL THERAPY
- REFER FOR INVASIVE INTERVENTION
- LONG TERM FOLLOW UP