

Venous ulcers: Pathophysiology and implications for management

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Faculty Disclosure
Nicos Labropoulos, Ph.D.

I hereby disclose that I:

- 1. Have no financial interest.**



Epidemiology of Venous Ulceration

European and Western Populations

0.5 to 1.5%

**USA : 600,000 patients treated and
2,000,000 workdays lost annually
>1 billion dollars spent**

Cornwall JV, Lewis JD. Br J Surg 1983;70:681

Callam JJ et al. Br Med J 1985;290:1855-6

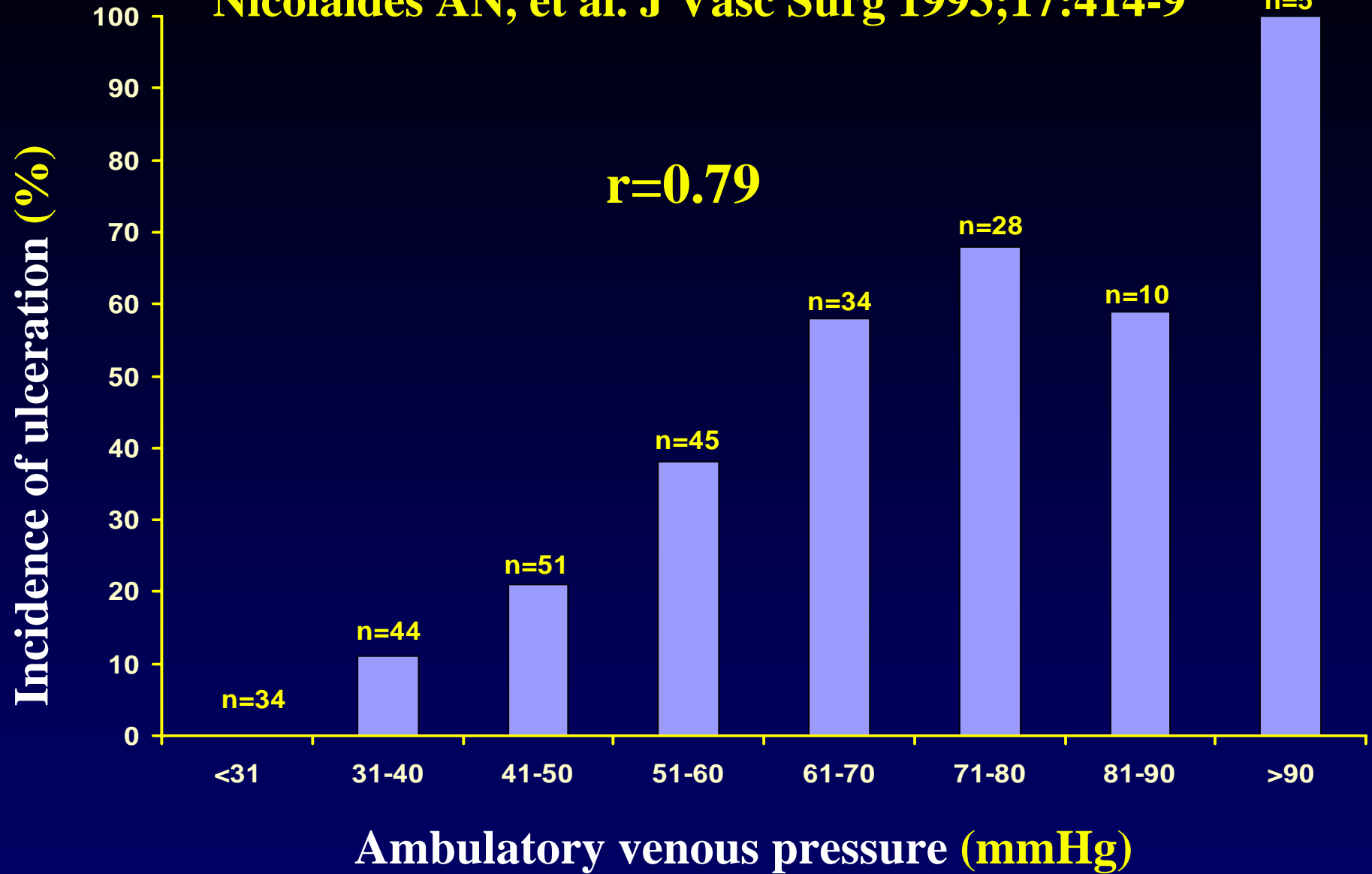
Stanley JC et al. J Vasc Surg 1996;23:172-81

12-14% of patients with CVI have
chronic venous ulceration (**C₅** or **C₆**)

Kistner et al. Mayo Clin Proc 1996;71:338-45

Labropoulos N. Vasc Surg 1997;31:224-5

Nicolaides AN, et al. J Vasc Surg 1993;17:414-9



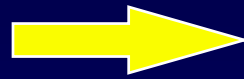
Deep vein thrombosis



Valvular damage



Venous reflux

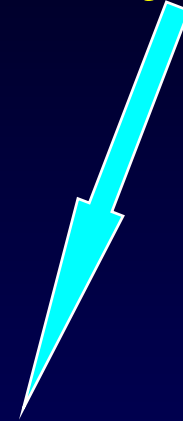
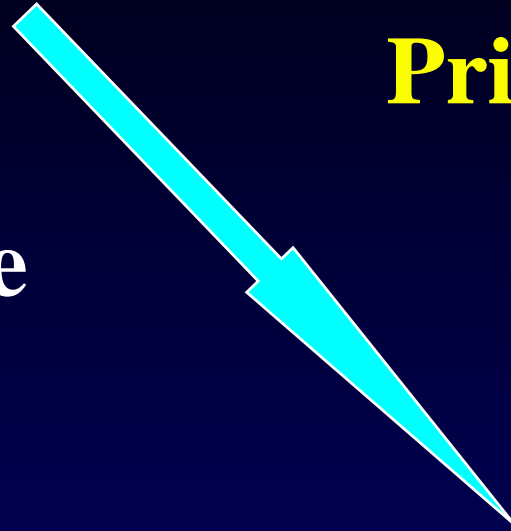


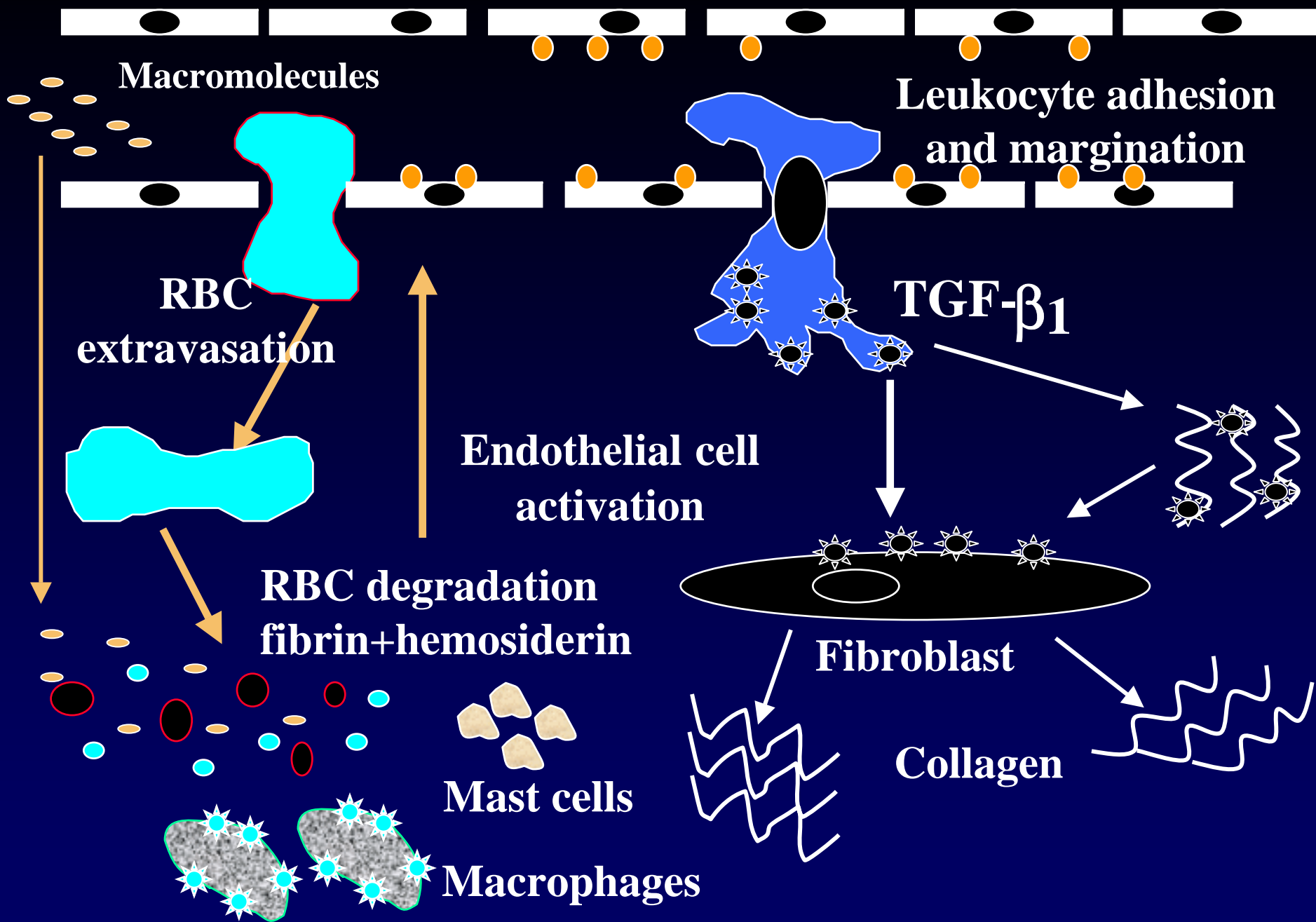
Venous hypertension



Skin damage

Primary Reflux





Macromolecules

Leukocyte adhesion and margination

RBC extravasation

TGF- β ₁

Endothelial cell activation

**RBC degradation
fibrin+hemosiderin**

Fibroblast

Collagen

Mast cells

Macrophages

Limitations of previous studies

The lack of an organized **classification system** made comparisons between reports difficult.

A **variety of diagnostic tests** were used by investigators to study patients with ulceration.

Even the larger studies due to the **complexity of venous disease** did not have adequate sample size for meaningful analysis.

AIM OF STUDY

To determine the **etiologic, anatomic and pathophysiologic characteristics** of chronic venous ulceration and to **promote uniform examination and report protocol.**

Loyola University Medical Center, Maywood, IL, USA
Leading Center PI Dr. Nicos Labropoulos

Edward Hines Jr VA, Maywood, IL, USA

West Suburban Hospital, Oak Park, IL, USA

Vascular Diagnostics Ltd., Park Ridge, IL, USA

Straub Foundation, Honolulu, HI, USA

**Imperial College of Science, Technology
and Medicine at St. Mary's, London, UK**

Chirurg/Gefäßchirurg/Phlebologe, Augsburg, Germany

University of Ferrara, Italy

University of Crete, Greece

University of Curitiba, PR, Brasil

Rio Imagem, Rio de Janeiro, Brasil

Angiolab, Vitoria, ES, Brasil

Methods

This was a **prospective multi-center** study

Protocol was created at LUMC; forms were sent to **12** participating centers in **6** different countries

Data were sent to the core center (**LUMC**) and entered into a customized database

All centers had **>3 yrs** experience with duplex ultrasound on venous disease prior to the study

Color Flow Duplex Ultrasound

Standing position

Saphenofemoral junction

GSV and SSV above knee segment

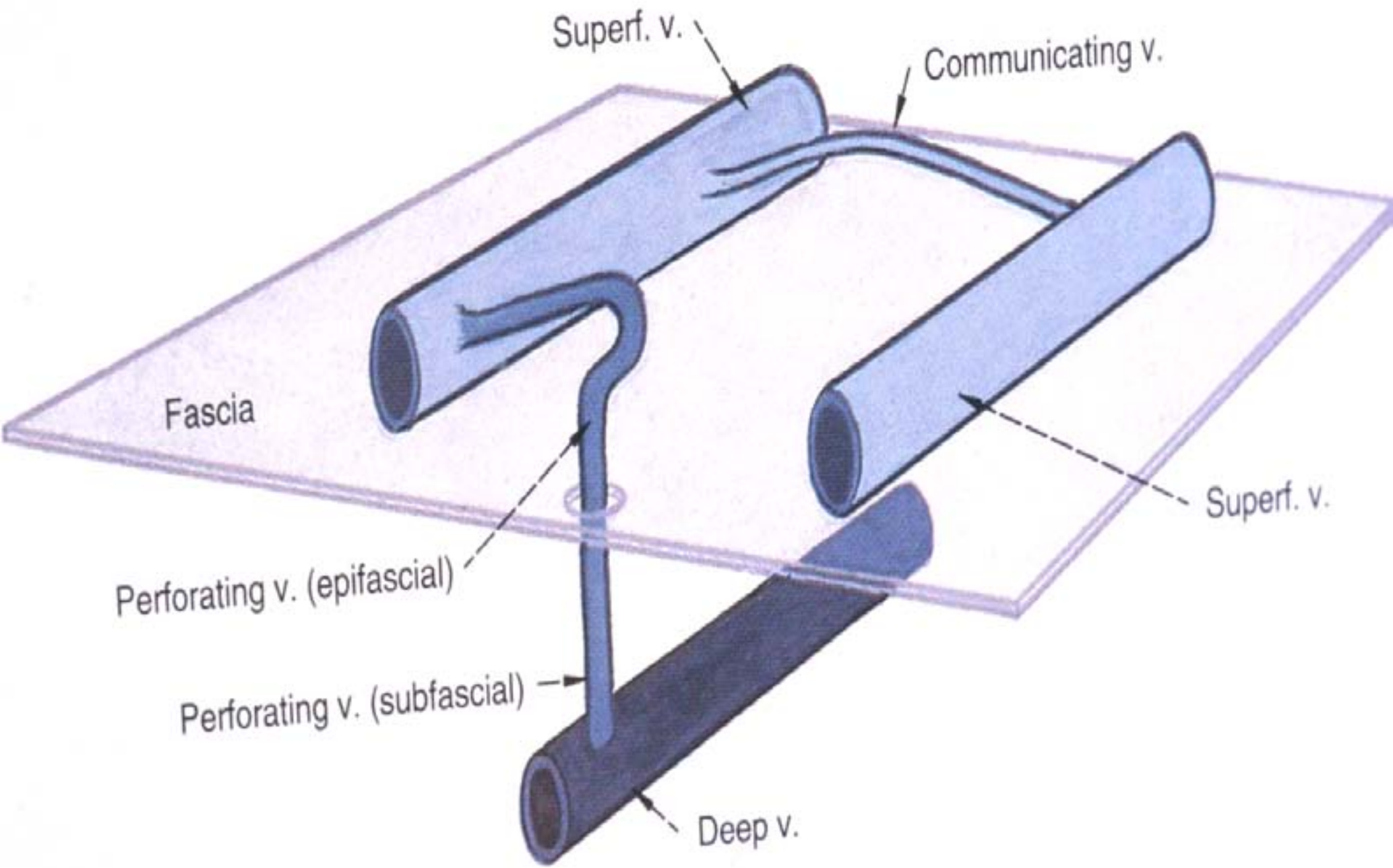
CFV, DFV, FV

Sitting position

GSV below knee segment

SSV, gastrocnemial veins

Popliteal and tibioperoneal veins



Etiology

P	531	71.3
S	166	22.4
P+S	46	6.2
C	2	0.27
Total	745	100

Patterns of reflux and obstruction

S	P	D	S+P	S+D	P+D	S+P+D	OBST	N	Total
99	8	32	278	73	20	215	9	12	745
13	1.1	4	37	9.8	2.7	28.9	1.075	2	100

S: superficial

P: perforator

D: deep

OBST: obstruction

N: normal

Overall system involvement

	Limbs	%
Superficial	664	89.973
Perforator	520	70.461
Deep	340	46.07

Pathophysiology

R	643	86.31
O	9	1.208
R+O	83	11.14
Normal	12	1.342
Total	745	100

CONCLUSIONS

The majority have a primary etiology (77.4%)

The superficial system is most frequently involved (88.7%)

Reflux is the most prevalent cause (97.5%)

CONCLUSIONS

Uncommon

Congenital disease
Isolated perforator vein reflux
Deep vein involvement alone
Obstruction alone

The prevalence of prior DVT is **25%**

Both reflux and obstruction are present in **11%**

Implications for treatment

Conservative treatment has a recurrence rate of **30 to 80%** at one year.

Fifty percent of patients with venous ulceration have **superficial venous reflux** with or without perforator vein involvement.

These are **ideal candidates for treatment** since the cause would be eliminated and recurrence would be reduced.

Echographic examination of the lower limbs

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Associate Professor of Surgery

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Loyola University Chicago

Distribution + extent of reflux

**Foot and calf muscle
pump efficiency**

Amount of reflux

Risk factors
**Genetic
predisposition**
**Rate of
progression**

C V I

**Venous wall and
soft tissue
cellular biology**

Severity of obstruction

**Lymphatic
compensation**

Distribution and extent of obstruction

Duplex scanning is superior to descending venography

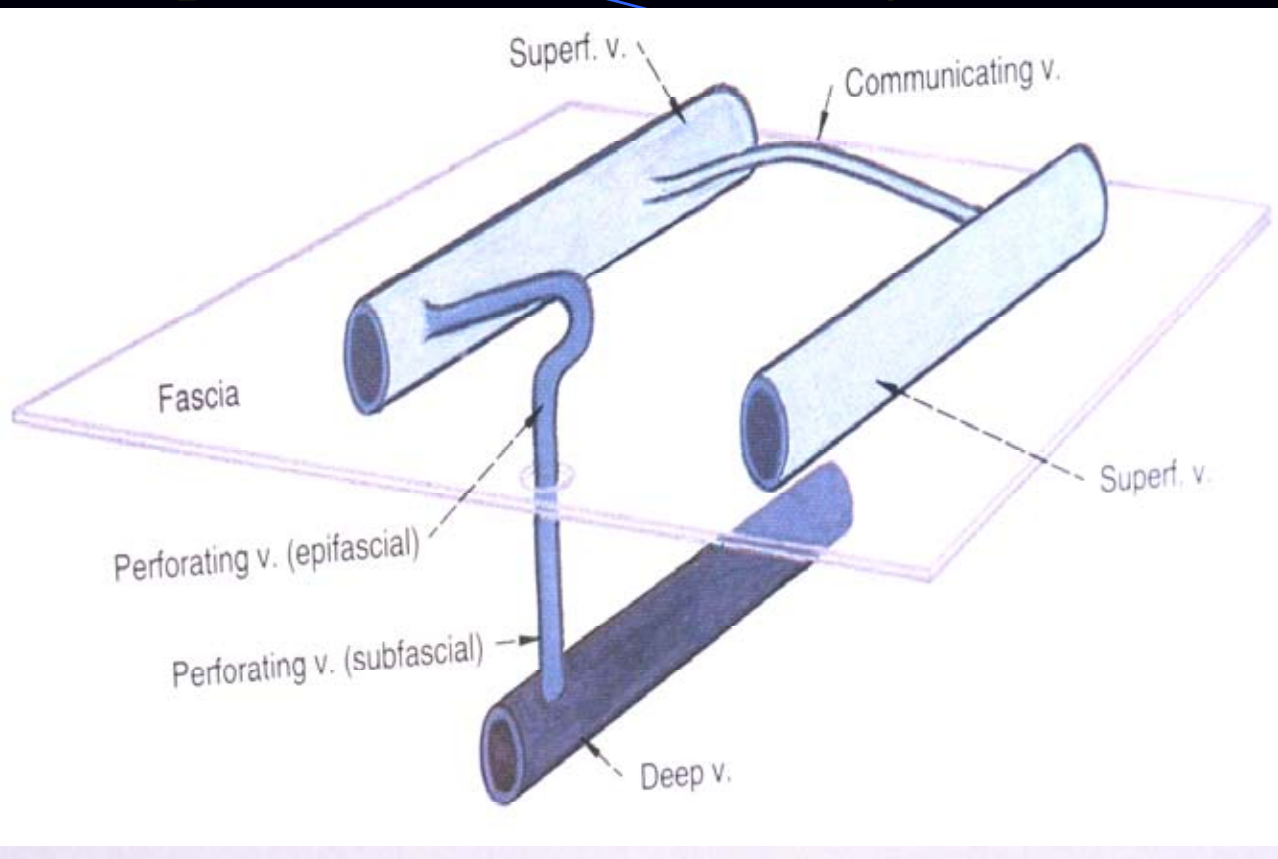
Neglen P, Raju S. J Vasc Surg 1992;16:687-93

Welch HJ et al. J Vasc Surg 1992;16:913-20

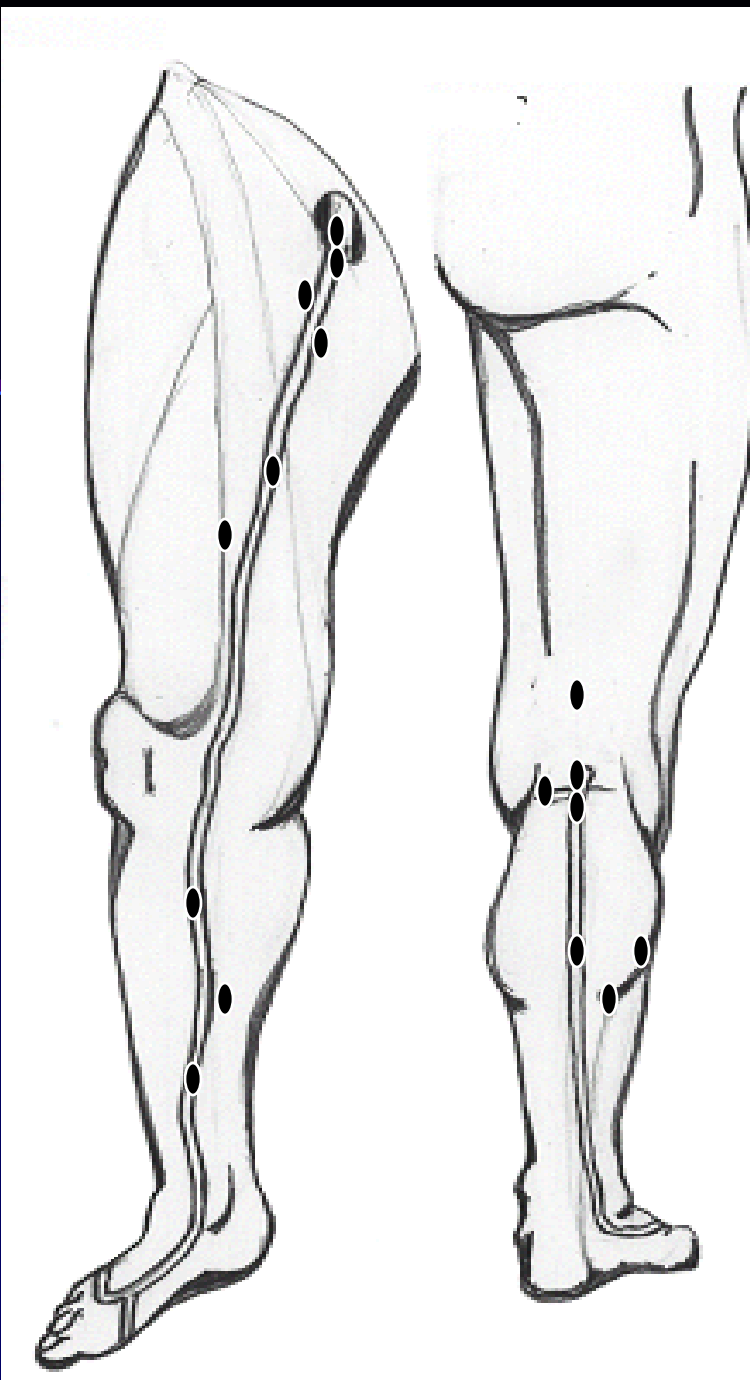
Valentin LI et al. Phlebology 1993;8:124-7

Baker SR et al. Lancet 1993;341:400-3

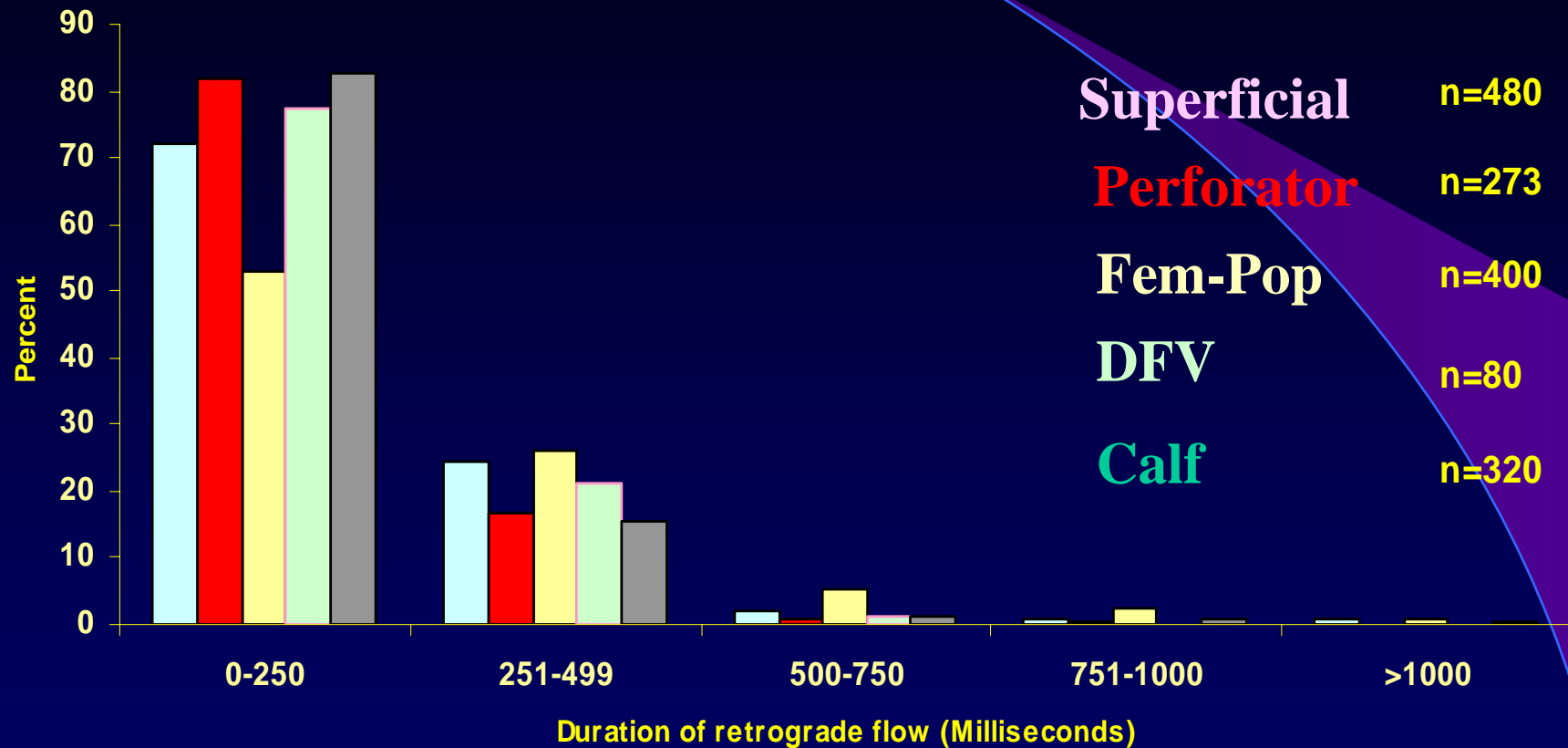
Labropoulos N et al. J Vasc Surg 2003;38:793-8



- DEEP**
- CFV, DFV, FVx2, POPVx2**
- GASTRV, ATV, PTV, PERV**
- SUPERFICIAL**
- SFJ, GSVx3, SPJ, SSV**
- PERFORATOR**



Distribution of retrograde flow in the different vein segments



Retrograde flow duration

	Mean	95% CI
Superficial	210ms	206 – 214
Fem-pop	280ms	375 – 385
Calf + DFV	190ms	188 – 192
Perforator	170ms	166 – 174

Femoropopliteal veins 400 segments

RF > 500ms

21/400 (5.25%)

RF: 510-2,600ms

RF >1,000ms

4/400 (1%)

	Supine > 500	Standing <500
Vein Segment	n	n
SFJ	1	1
GSV Thigh	3	2
GSV Upper calf	5	3
GSV Lower calf	10	5
SPJ	0	0
SSV calf	3	2
Perforator	2	1
Fem-pop	7	4
DFV	0	0
Calf veins	6	4
Total	37	22

48 segments with an **RF > 500ms** in standing position
the **RF < 500ms** in supine position in **6 (13%)**

RF Peak vein velocity

8 – 55cm/s

Segments with an RF **>500ms**

Mean peak velocity **23.5cm/s** **95% CI 20.2 – 26.8**

Segments with an RF **<500ms**

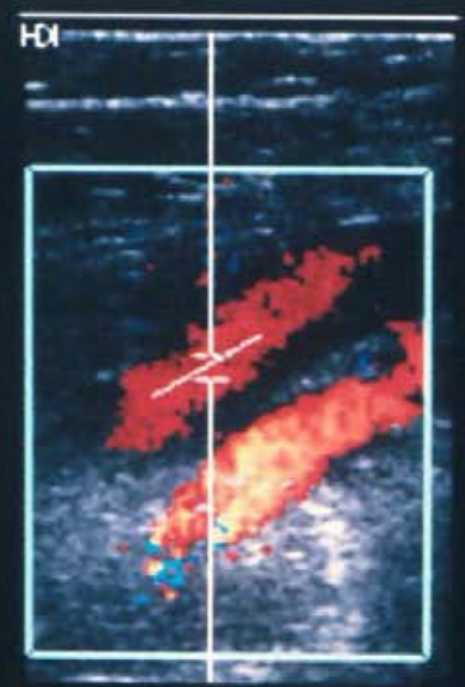
Mean peak velocity **15cm/s** **95% CI 14.8 – 15.2**

p<0.0001

Great variation in RF and peak vein velocity did not allow any meaningful cut-off value for the latter

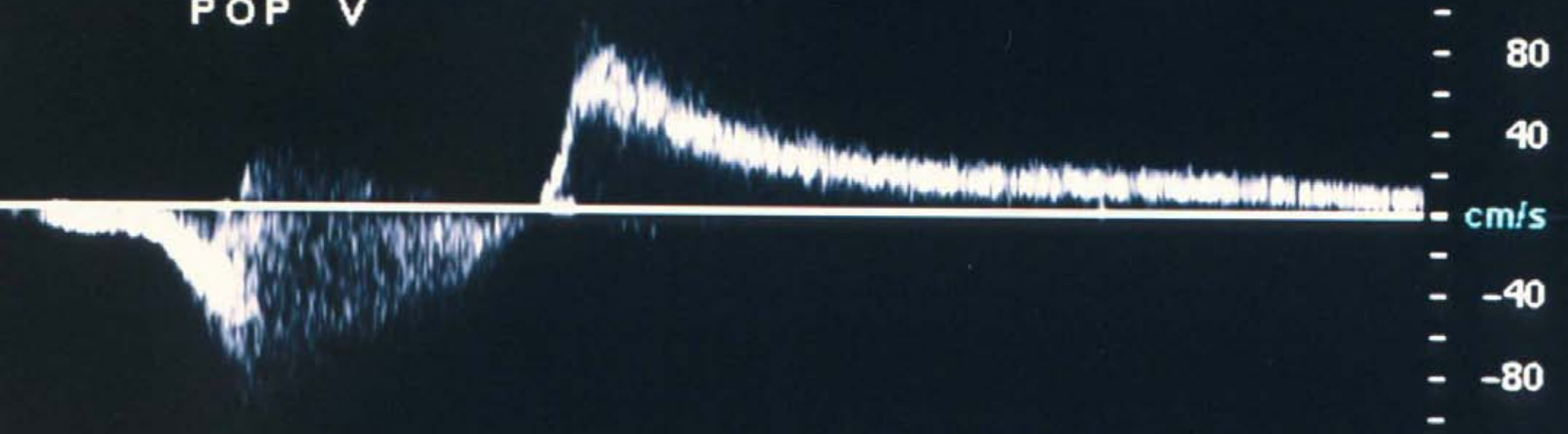
5
Rg 55dB
Dist Med
ate Med

73% Map 5
Low
2000 Hz



SV Angle 60°
Dep 3.2 cm
Size 2.0 mm
Freq 4.0 MHz
WF Low
Dop 65% Map 2
PRF 6250 Hz

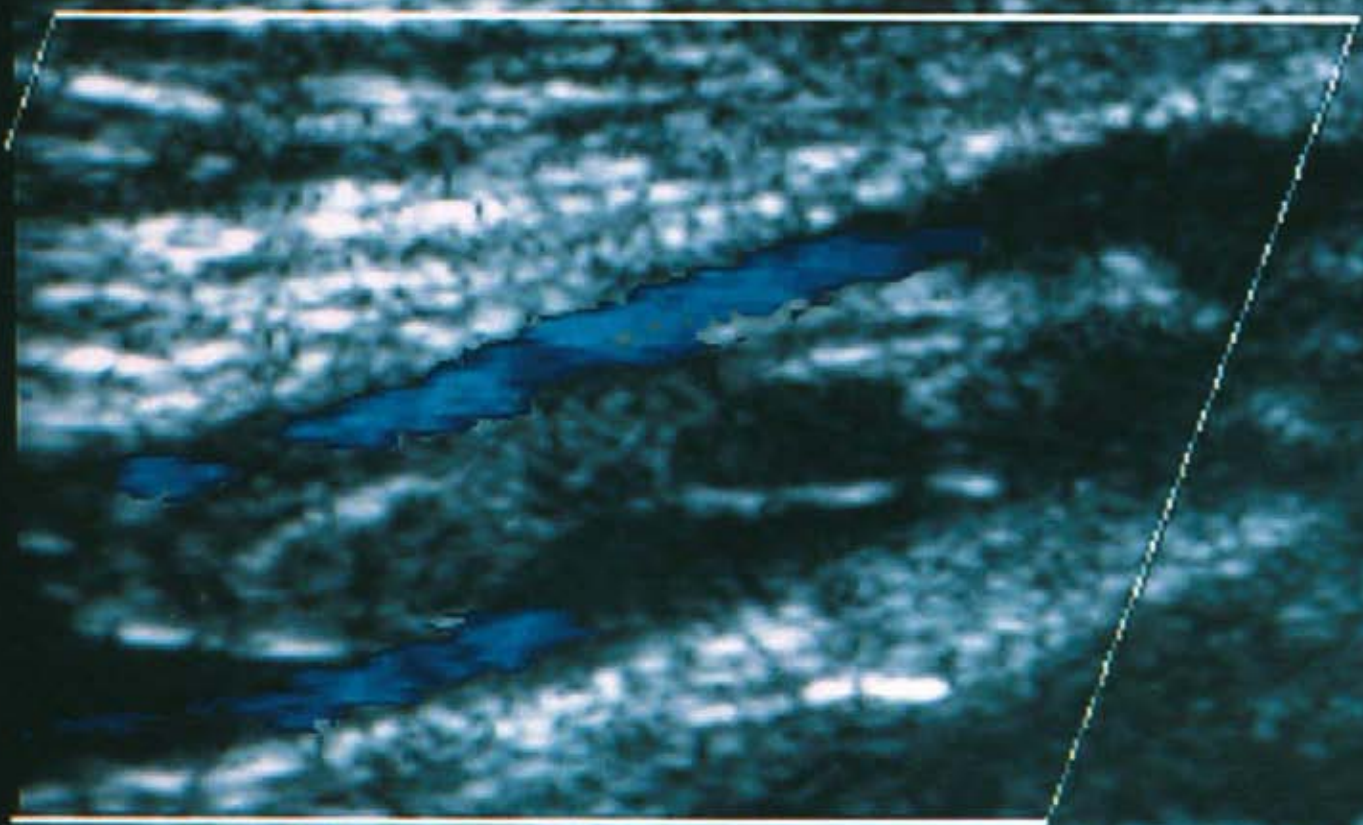
POP V



1774 38111 A
SPTAd 14M10.7
45DB C8 E3
HDI

CCULUR 68 7
MPLUR
MPLUR
PRF 205
2D RS 0000
PI 0000
DYN 0000

LEFT



1.5
2.0
2.5
3.0

THROMBUS LEFT POPLITEAL VEIN

19

2D CINE

PTS wall changes in CFV

LOYOLA MEDICAL CENTER

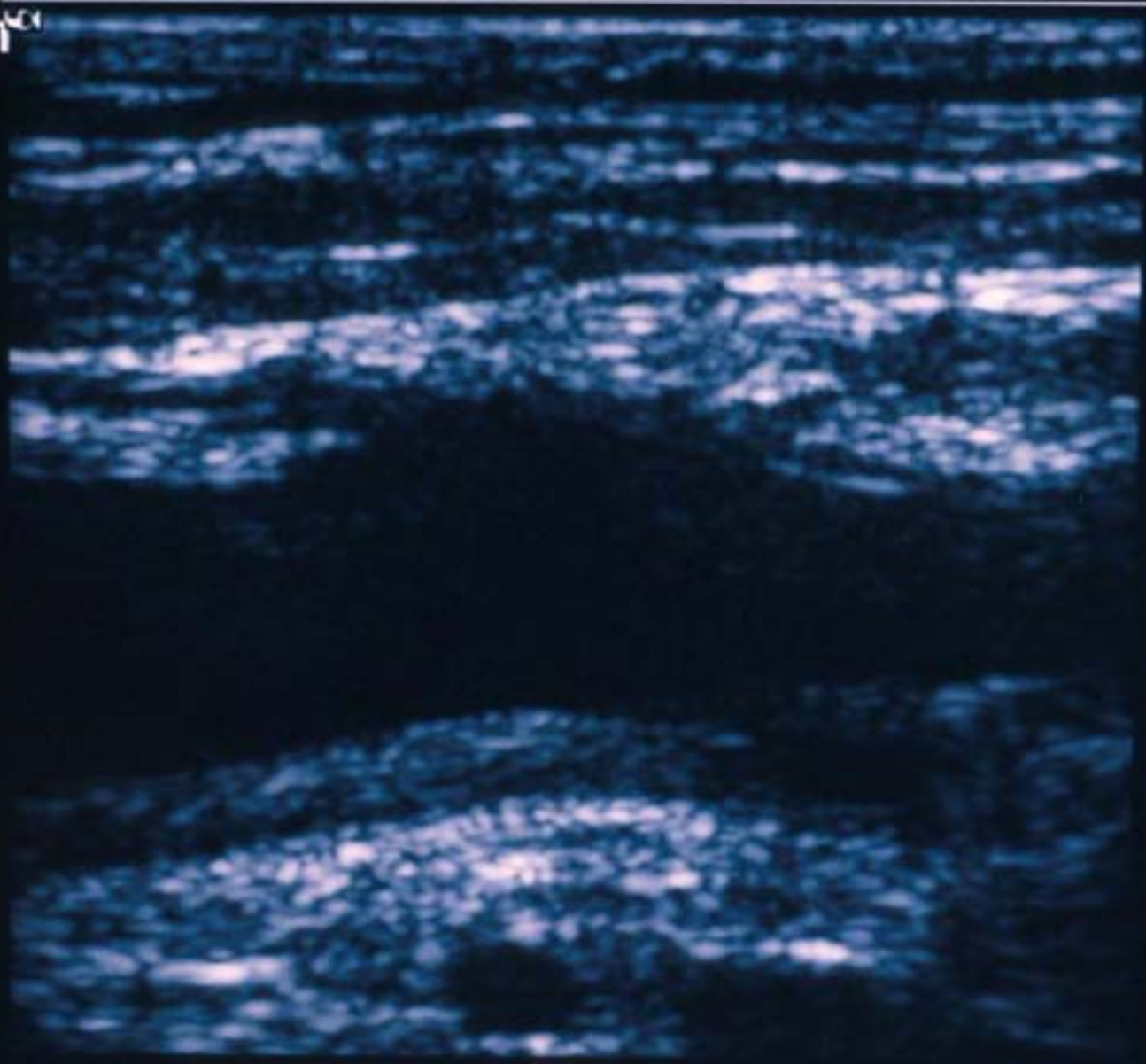
CL10-5 26mm VSurg/Vasc

8:55:23 am

Fr #98

S
g 50dB
st Low
te Med

LEFT



Prandoni P et al. Ann Intern Med 1996;125:1-7

355 patients with a **first** episode of DVT

Incidence of PTS was **22.8%** at **2y** and **28%** at **5y**

Ipsilateral recurrent DVT increased the risk for PTS Hazard ratio **6.4** **95% CI (3.1-13.3)**

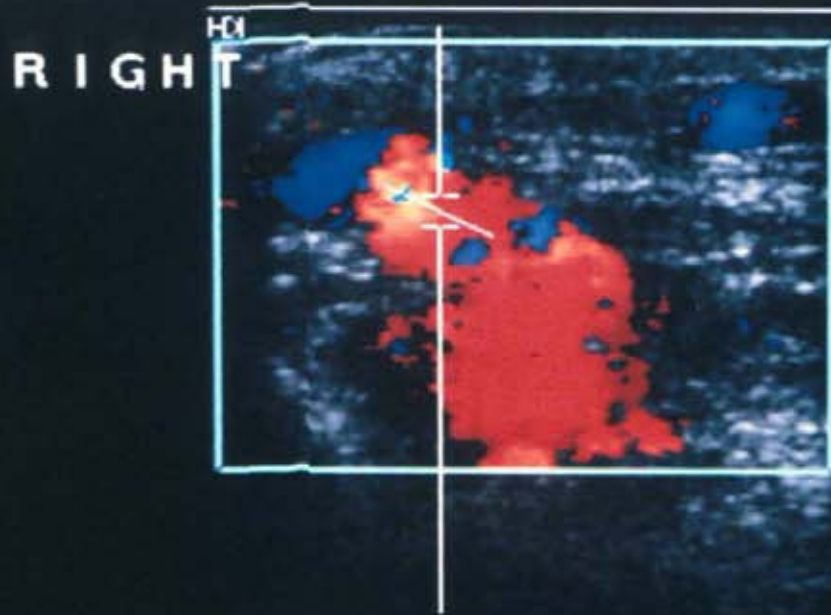
Survival at 8y was **70.2%** **95% CI (64.7-75.6)**

Lower calf posterolateral PV

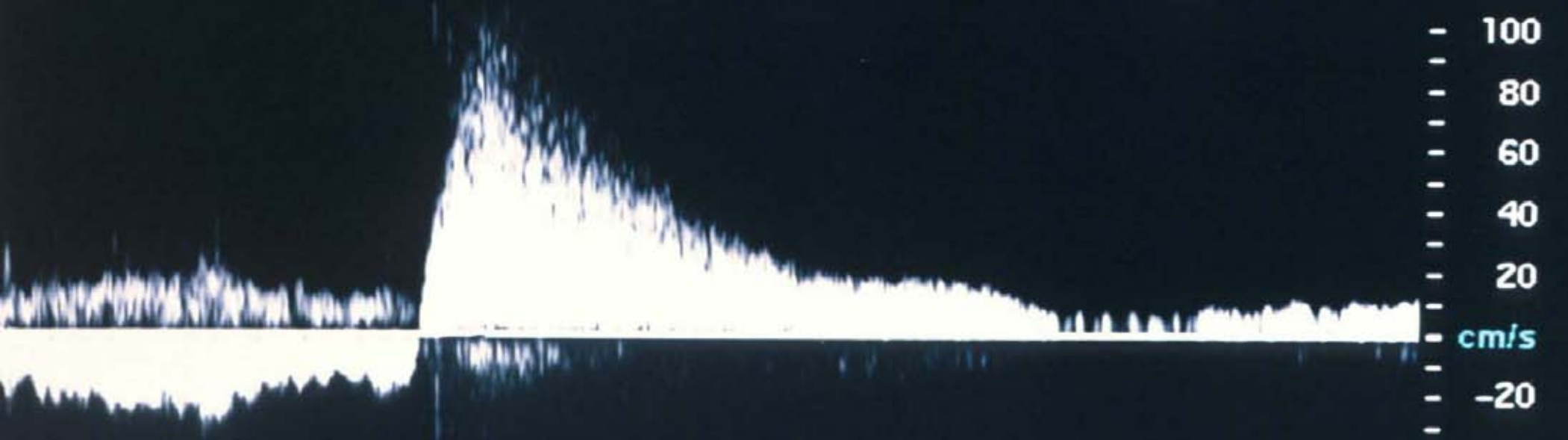
LOYOLA UNIVERSITY MEDI | L7-4 38mm PVasc/VEIN | 11:29:54 am | Fr #17 | 4.1 cm

Map 5
SynRg 55dB
Persist Med
Rate Med

Vol 78% Map 5
WF Low
RF 2000 Hz



SV Angle -60°
Dep 1.4 cm
Size 2.0 mm
Freq 4.0 MHz
WF Low
Dop 65% Map 2
PRF 3731 Hz



Labropoulos N et al. Eur J Vasc Endovasc Surg 1999;18:228-34

Mean duration of outward flow in incompetent PVs

Reflux

Deep

$0.9 \pm 0.3s$

$p < 0.001$

Superficial

$1.6 \pm 0.7s$

$p < 0.0001$

Superficial + deep

$2.4 \pm 0.9s$

Labropoulos et al. Am J Surg 1995;169:572-4

Labropoulos et al. J Vasc Surg 1996;23:504-10

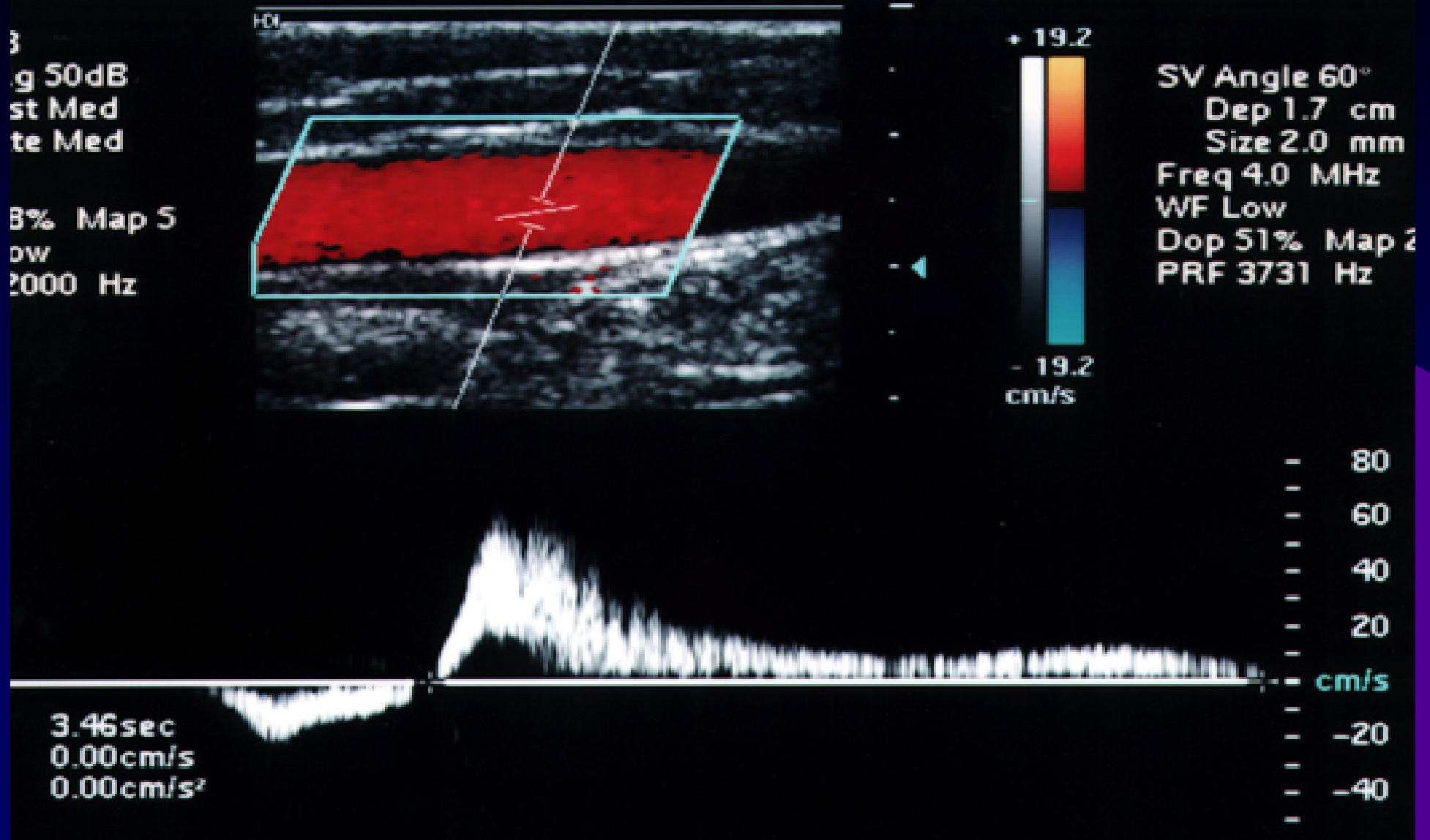
Superficial vein reflux is the most common abnormality in patients with chronic venous disease

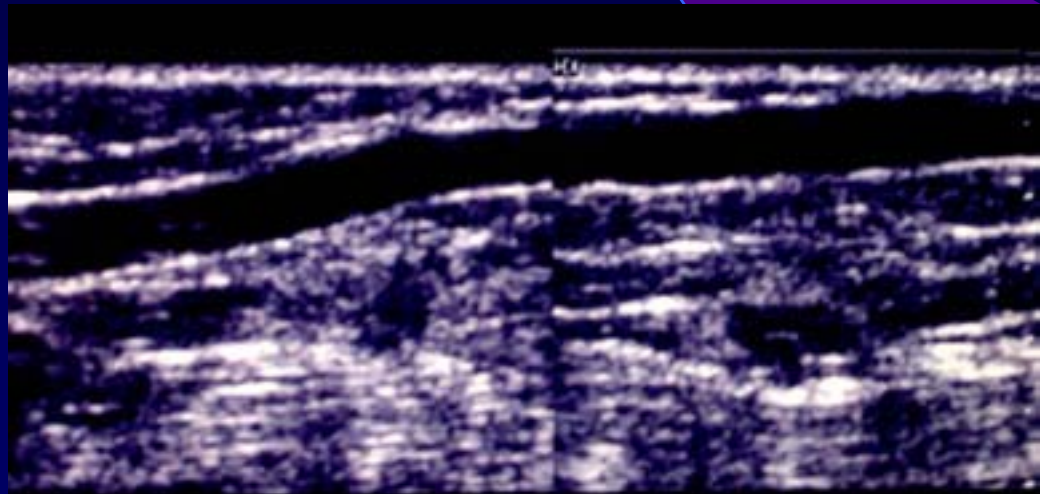
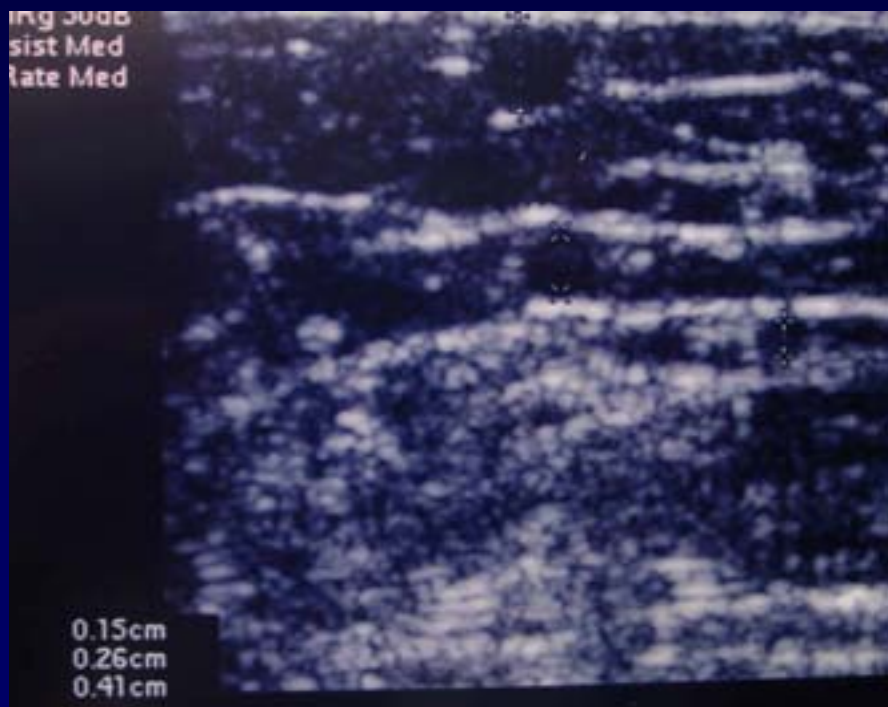
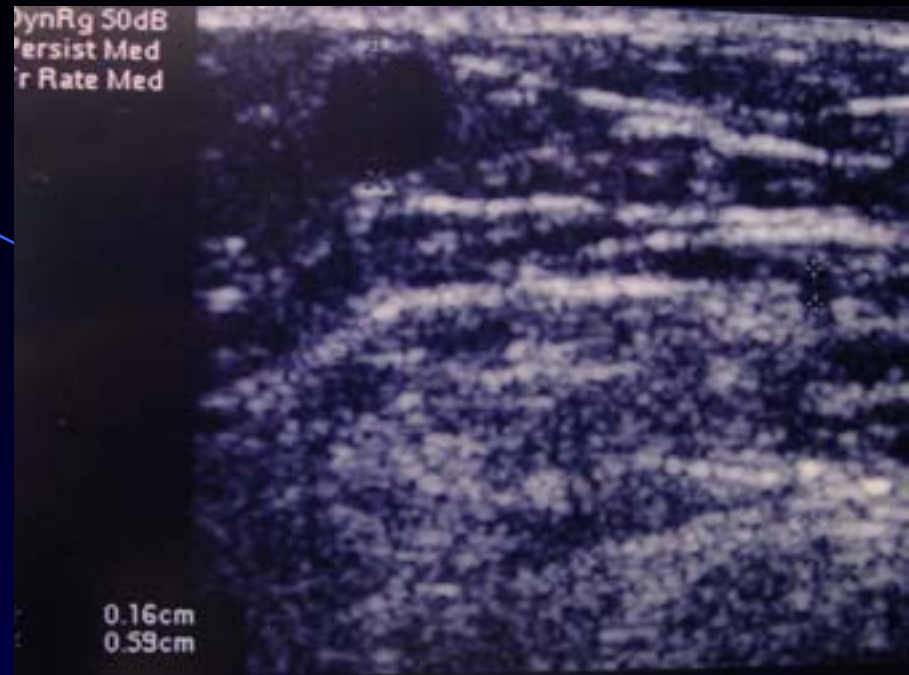
Labropoulos N,et al. J Vasc Surg 1997;26:736-42

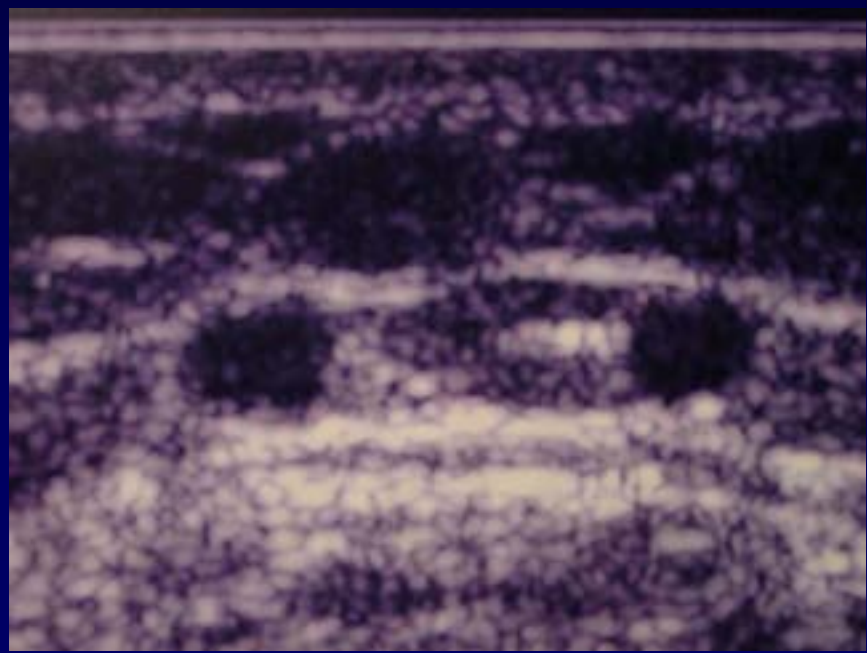
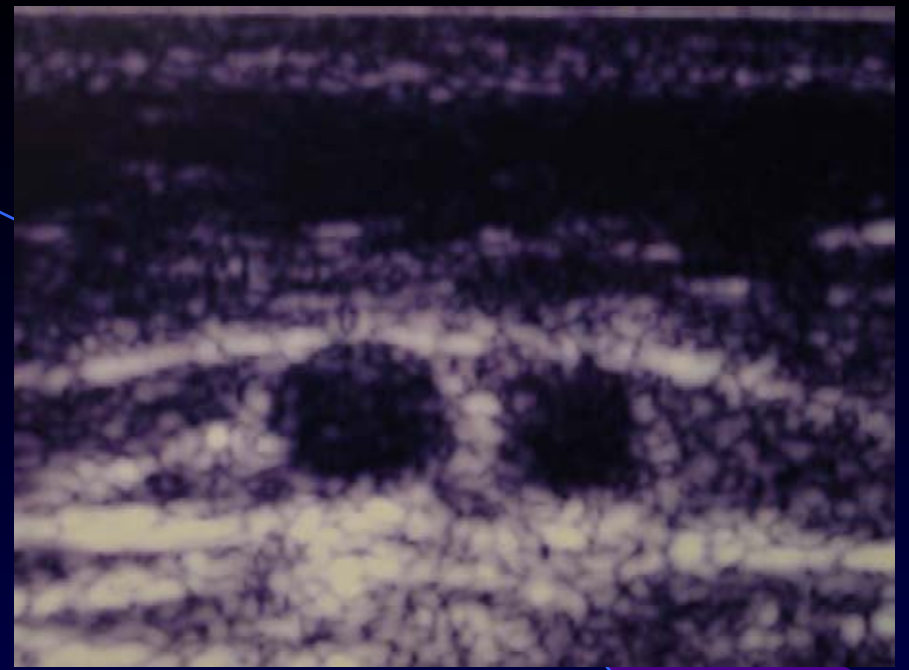
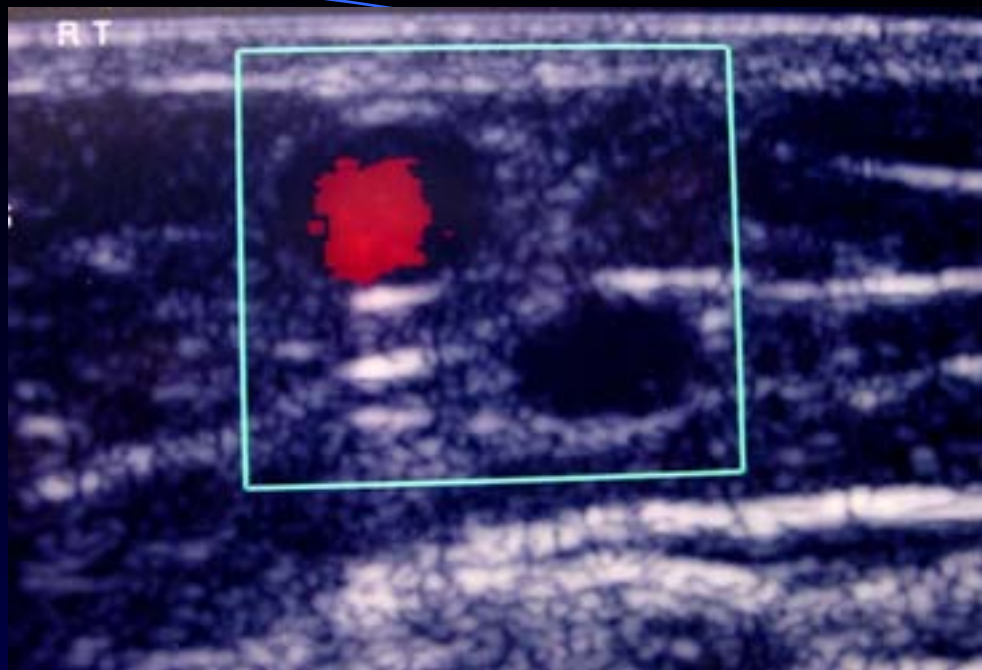
Reflux in the **saphenous veins** and their tributaries has the highest prevalence

GSV network has the highest prevalence

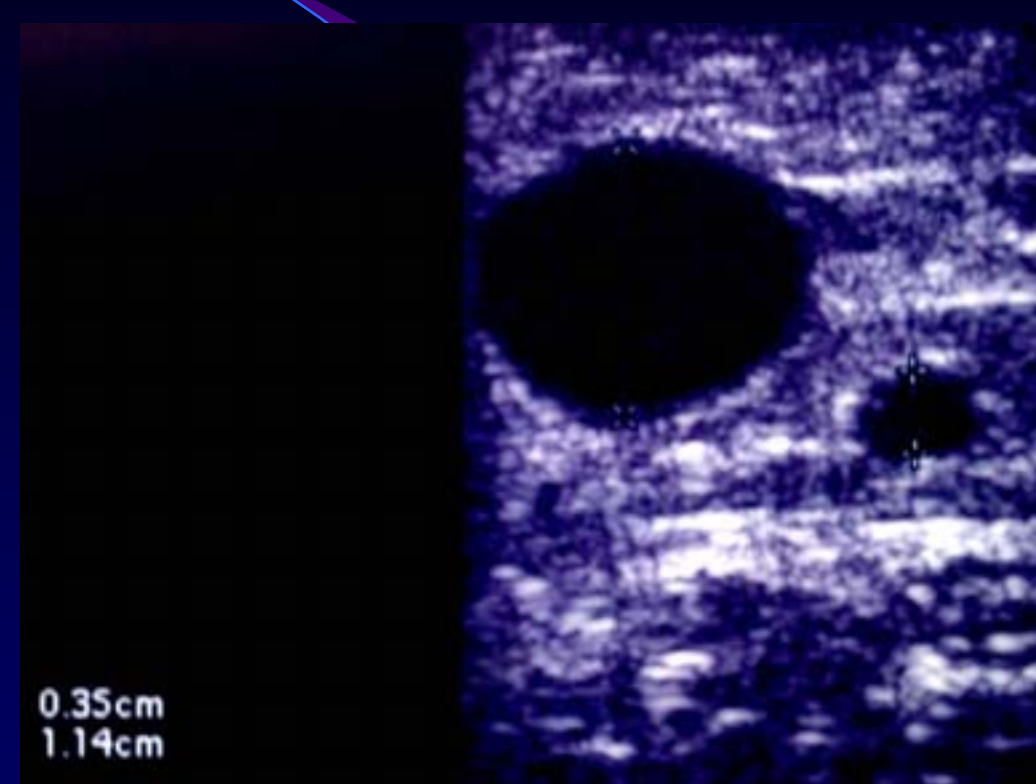
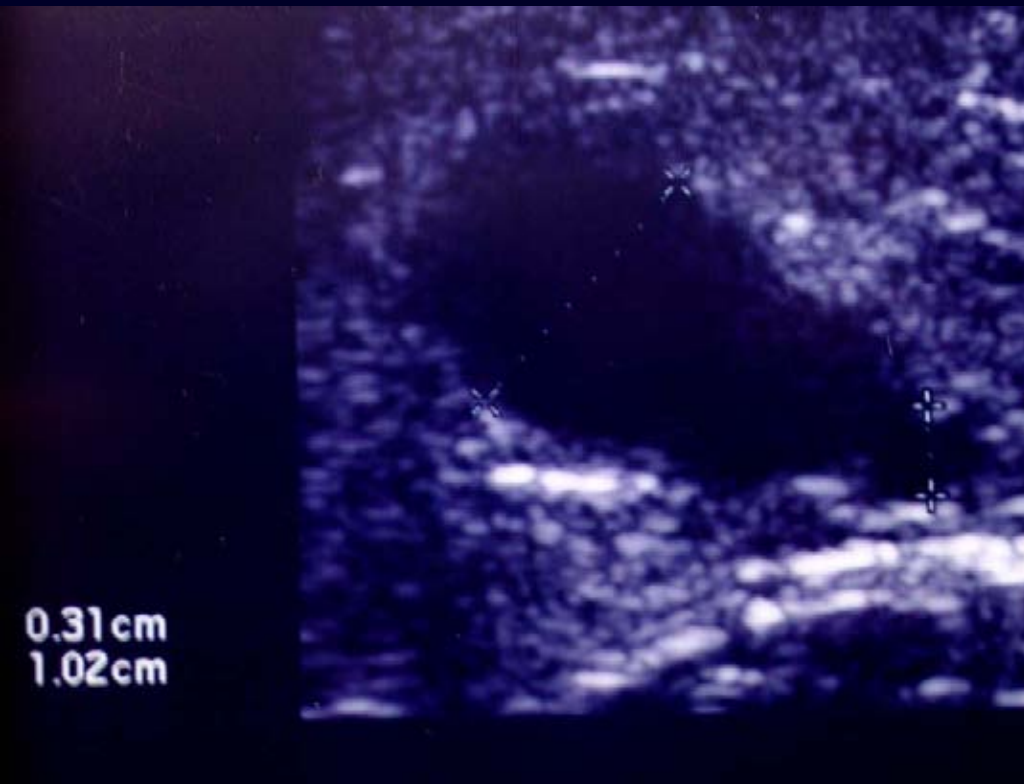
LOYOLA MEDICAL CENTER | L7-4 38mm PVasc/Ven | 9:52:12 am | F# 21 | 3.1 cm







Tributary reflux with normal GSV



Labropoulos N et al. J Vasc Surg 2000;32:954-60

Patterns of reflux in the SSV system

Pattern of reflux	n	%
Giac	7	3.1
Giac+SSV	10	4.4
Giac+SPJ+SSV	20	8.8
Giac+SPJ+SSV+Gastro	2	0.9
SPJ	4	1.8
SPJ+SSV	112	50
SPJ+Gastro	4	1.8
SPJ+SSV+Gastro	5	2.2
SSV	34	15
SSV+Gastro	4	1.8
Gastro	8	3.5
TRBs	9	4
nonSSV	7	3.1
Total	226	100

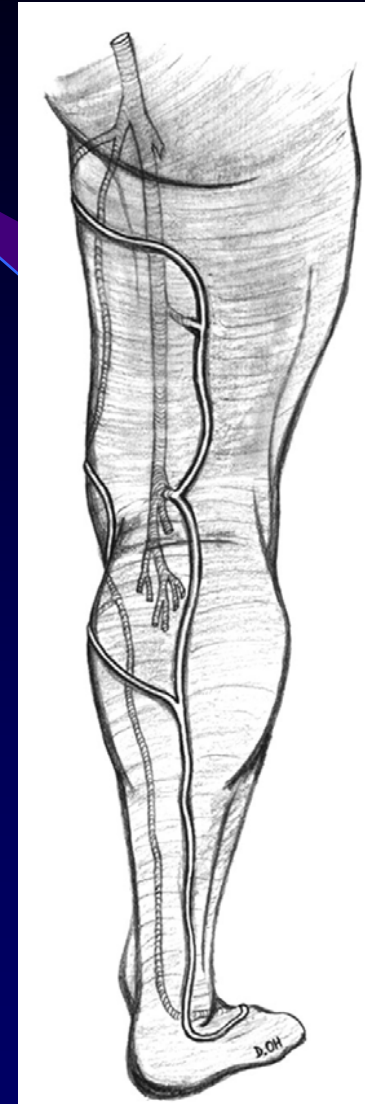
SPJ+SSV vs any other pattern, $p < 0.0001$

Four types of SSV termination
with at least **9 variations**

SSV duplication **2.2%**

Nonsaphenous reflux **3.1%**

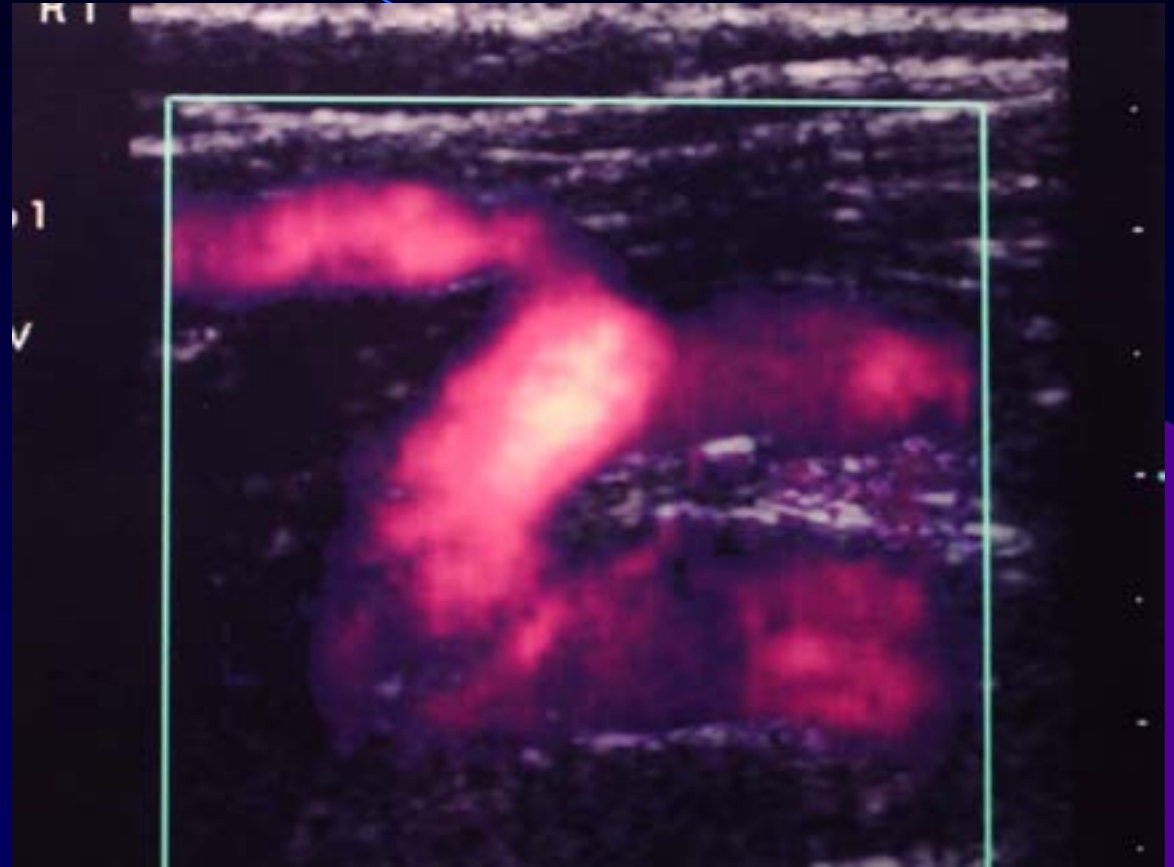
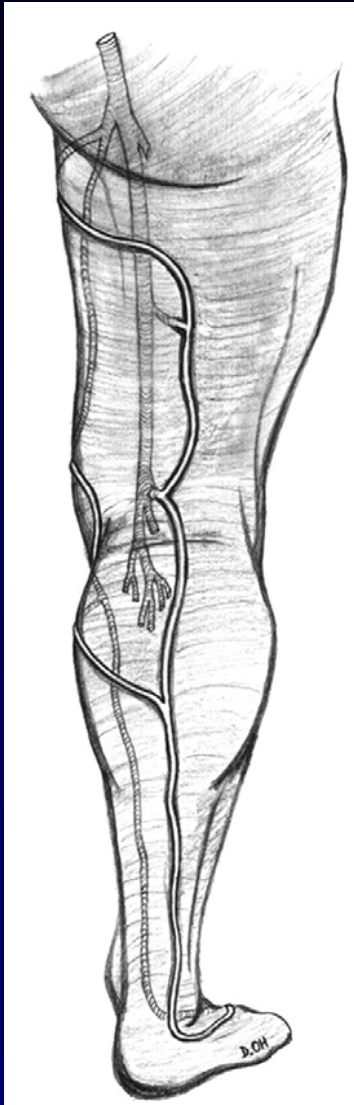
7%



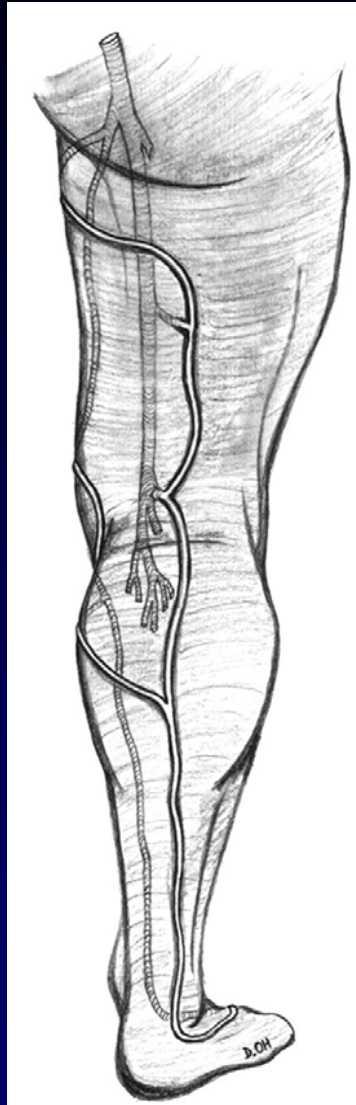
32%

61%

Connection with the popliteal vein 76%

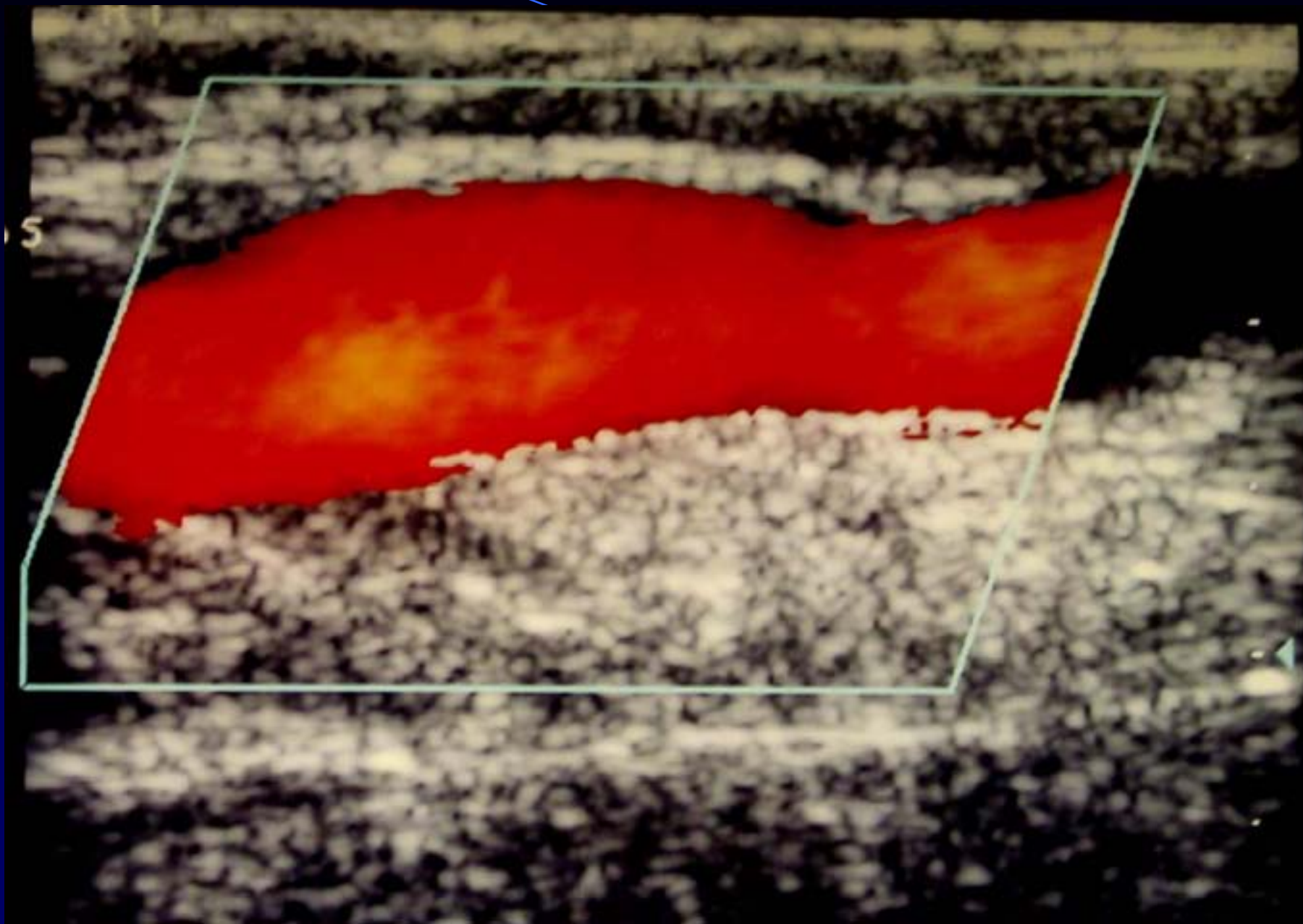


Above popliteal 32%



GSV	76%
Gluteal	5%
Vulvar	5%
SFV	16%
DFV	3%
Muscular	6%

MGV to SSV reflux



Labropoulos N et al. J Vasc Surg 2001;34:872-7

Superficial Nonsaphenous Vein Reflux

84 limbs in **72** patients had isolated nonsaphenous reflux

Prevalence: **84/835, 10%**

Female **67**

Male **5**

$p < 0.0001$

RESULTS

Number of pregnancies
Mean and **95% CI**

Nonsaphenous **3.2** **3.1-3.3**

Saphenous **2.2** **2.14-2.26**
(100 randomly selected females)

Prevalence of Reflux

	n	%
Posterolateral thigh	42	47
Vulvar	18	20
Gluteal	11	12
Sciatic nerve	9	10
Popliteal fossa	7	8
Knee	3	3
<hr/>		
Total	90	100

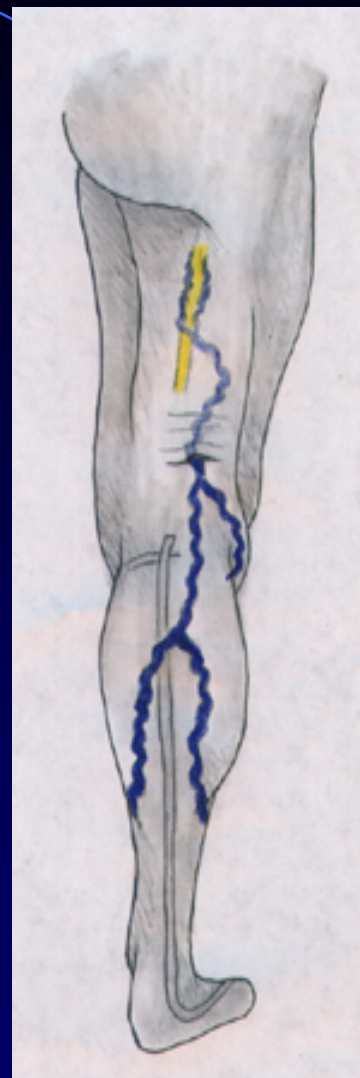
Gluteal



L P thigh



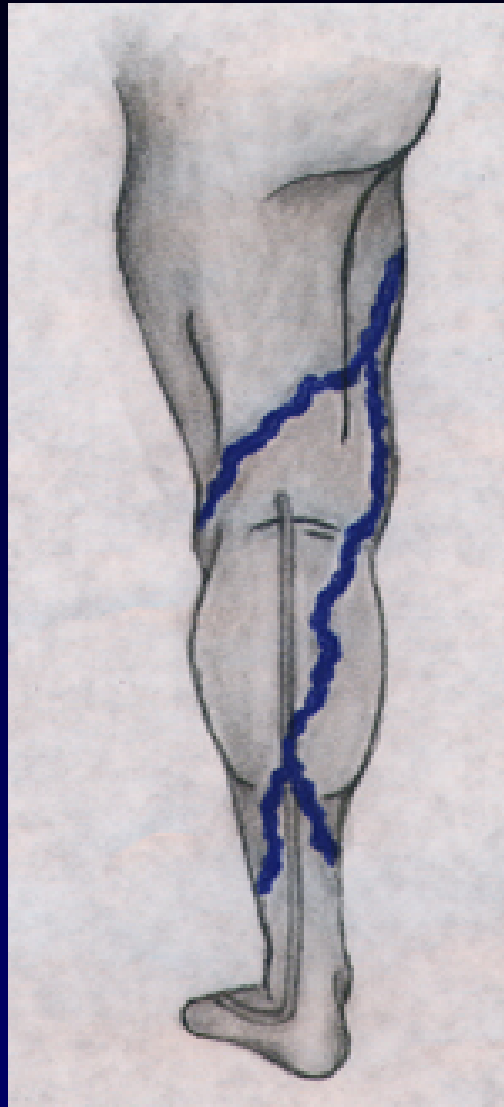
Sciatic N



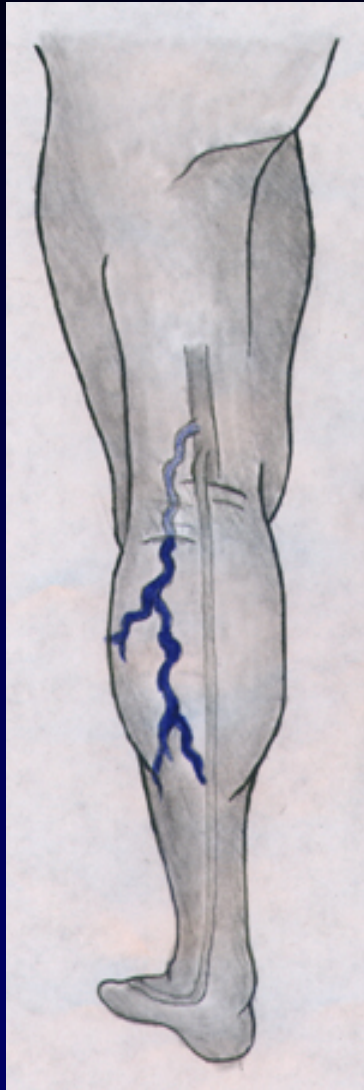
PLTP



Vulvar



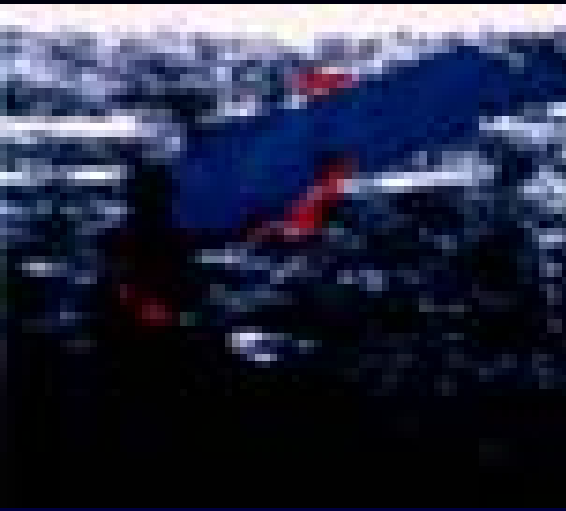
V. Popliteal fossa



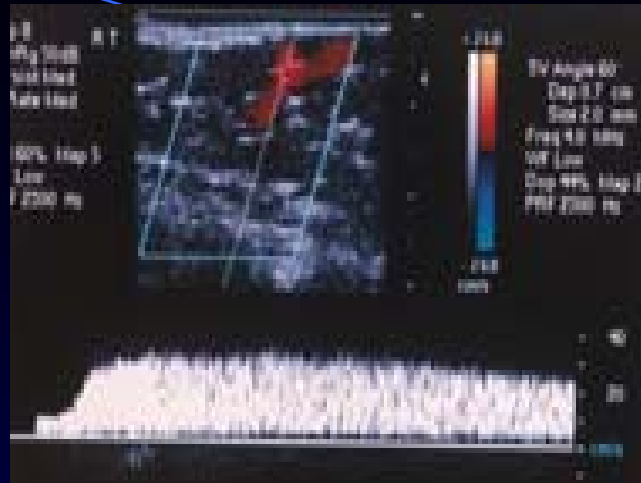
Knee PV



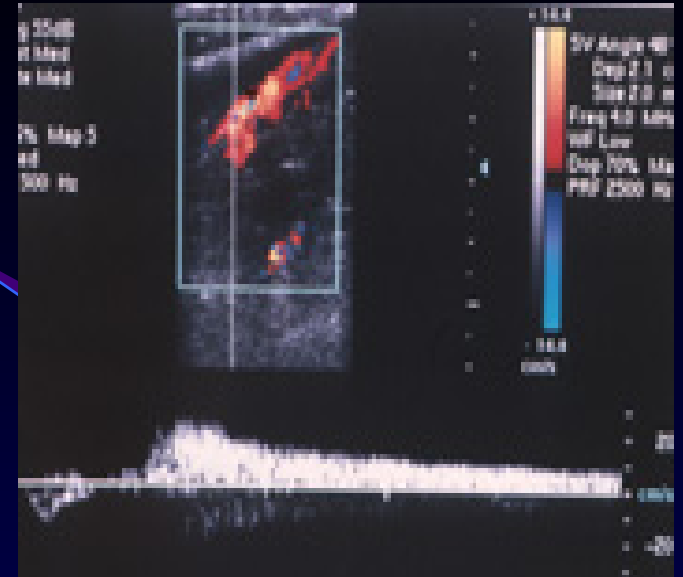
Gluteal V



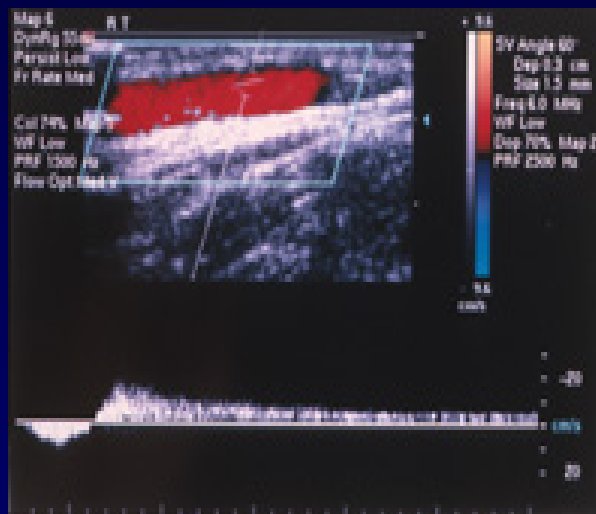
Vulvar V



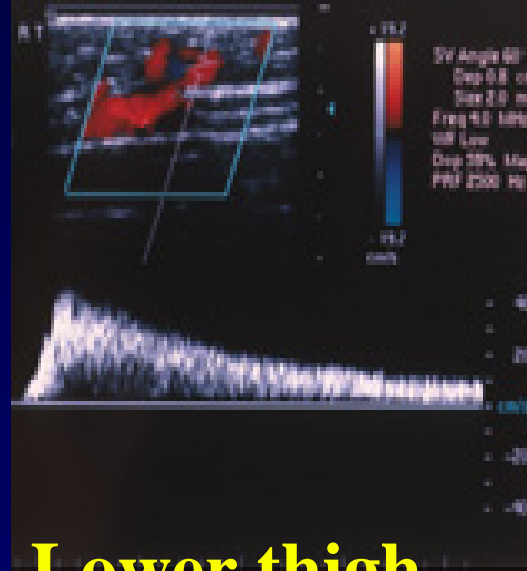
Sciatic nerve V



PLTP



PLTP Tributary



Lower thigh posterior



Knee perforator

**Duplex scanning is a great method for
the diagnosis of recurrent varicose veins**

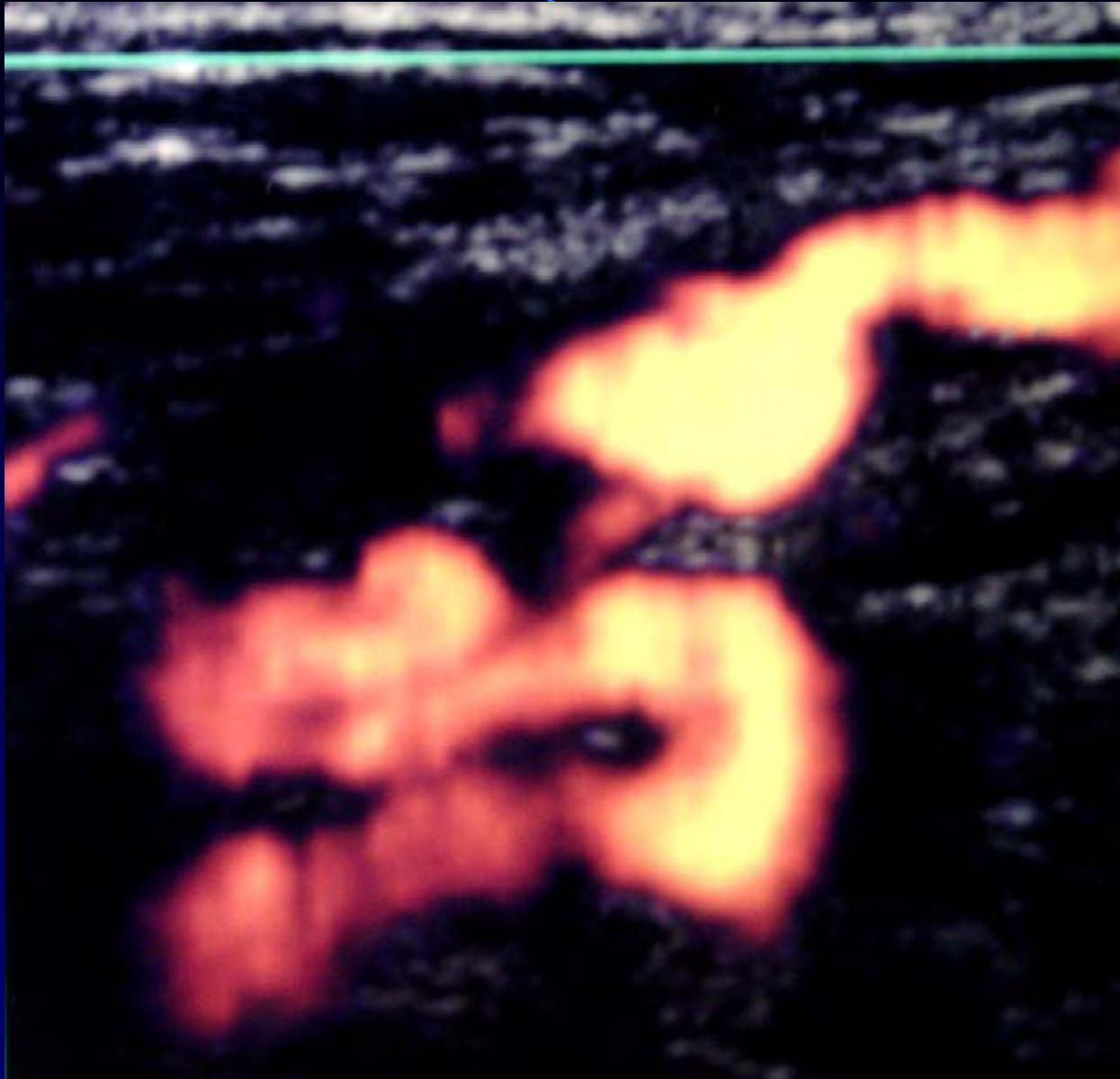
Thibault and Lewis. J Dermatol Surg Oncol 1992;18:618-24

Redwood and Lambert. Br J Surg 1994;81:1450-1

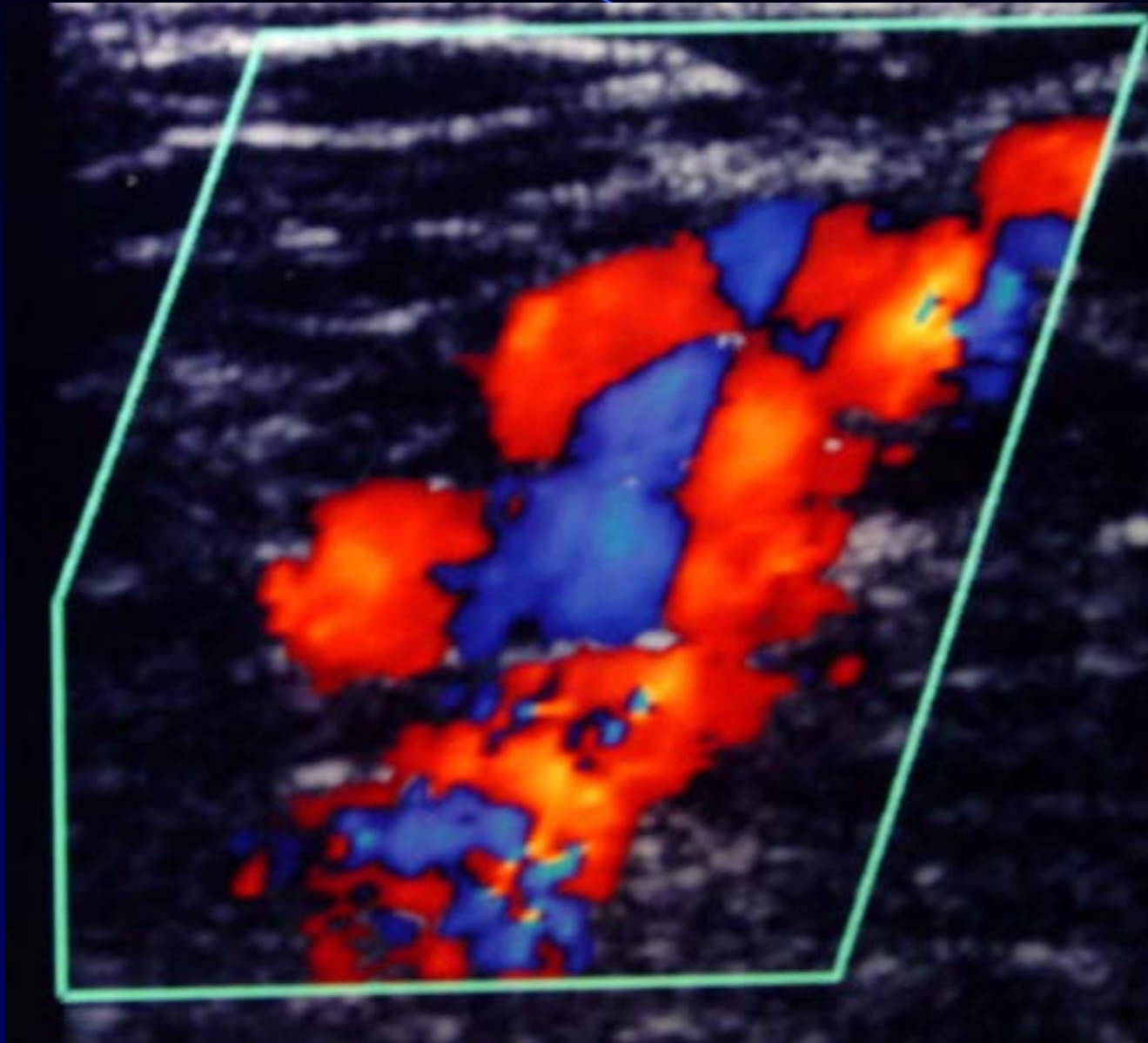
Myers K, et al. American Venous Forum, Florida 1995

Labropoulos N, et al. Surgery 1996;119:406-9

Recurrent venous reflux at SFJ due to incomplete ligation



Neovascularization after SFJ ligation



Reporting standards in venous disease

J Vasc Surg 1995;21:635-45

Hugh G. Beebe

John J. Bergan

David Bergqvist

Bo Eklof

Ingvar Erikson

Mitchel P. Goldman

Lazar J. Greenfield

Robert W. Hobson II

Claude Juhan

Robert L. Kistner

Nicos Labropoulos

Mark Malouf

James Menzoian

Gregory L. Moneta

Kenneth A. Myers

Peter Neglen

Andrew N. Nicolaides

Thomas F. O'Donnell

Hugo Partsch

Michel Perrin

John M. Porter

Seshadri Raju

Norman M. Rich

Graeme Richardson

Harry Schanzer

Philip Coleridge Smith

D. Eugene Strandness

David S. Sumner

Patient Characteristics

CVI is seen in all decades of life

Prevalence **25-33%** of females
10-20% of males

Incidence **2.6%** per year females
1.9% per year males

CVI classes **0-3** **47y**

CVI classes **4-6** **58y**

p<0.0001

C E A P

Varicose veins are present in >80%

Skin changes 20-25%

Healed or active ulcers 12-14%

Symptoms 70-80%

C E A P

Primary	65%
Secondary	27%
Primary and secondary	8%
Congenital	<1%

C E A P

Superficial		>85%
GSV	LSV	Nonsaphenous
70-80%	15-20%	10%
Perforator		25-35%
Calf >Thigh		
Deep		30%

Prevalence of skin damage increases with the extent of reflux and obstruction

C E A P

Reflux 81%

Obstruction 2%

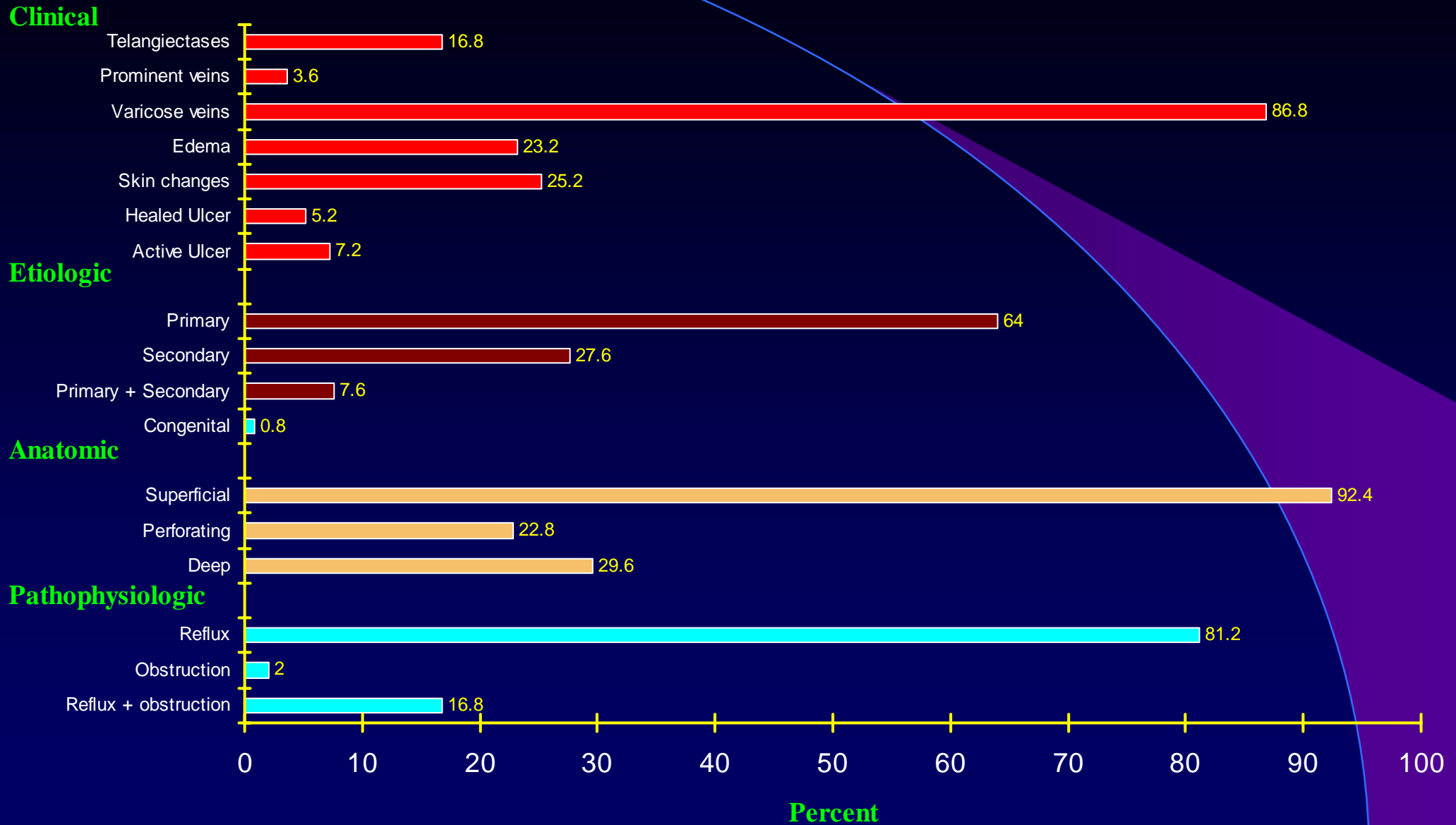
Reflux + Obstruction 17%

Combined reflux and obstruction **increase the odds** for development of signs and symptoms **3.5 times**

The prevalence of thrombosis **increases** with the severity of CVI but is **<35%** in patients with ulcers

Labropoulos N. Vasc Surg 1997;31:224-5

Clinical, etiologic, anatomic and pathophysiologic data (n= 250 limbs)



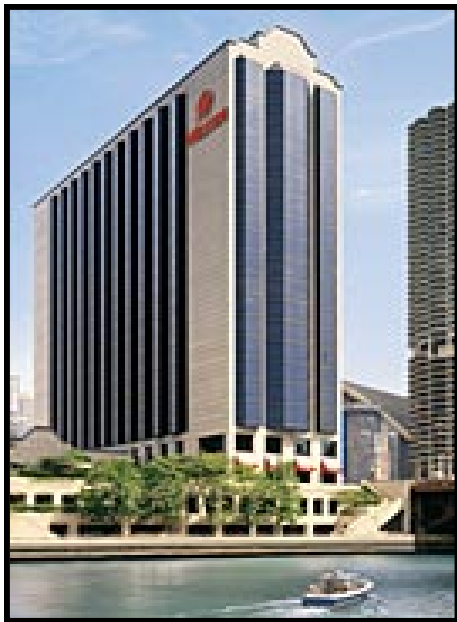
Thank you





Welcome to the

**13th Annual MIIT Interventional Radiology
and Endovascular Therapy Seminar**



October 28-30, 2004

**Chicago Westin River North Hotel
Downtown Chicago**

