

We Should Revise The Definition Of Venous Reflux: What Other Modality Should We Consider

Fedor Lurie, MD, PhD, RPVI, RVT

Research grants:
Janssen
IAC
Cardinal Health
Conrad & Caroline Jobst Foundation

Educational grants:
Servier
Conrad & Caroline Jobst Foundation

Consulting & Advisory Boards:
NIH – NHLBI
CMS – MEDCAC
Koya
Tactile Medical

Fedor Lurie, MD, PhD, RPVI, RVT

CVD: what is the Therapeutic target

Heart.org Medscape

“The primary goal of surgical or endovenous therapy is to improve the venous circulation by removing the major reflux pathways.”

Am J Occup Ther. 2013 Mar-Apr; 67(2): 162-170

An Ideal Therapeutic target

What makes a good drug target?
Isabella Gohar, Peter Ellinghaus, Anette Sommer, and Khawar Asadullah

Ideal Therapeutic Target	Valve incompetence	Reflux (current definition)
Is disease-modifying	Yes	Yes
Present in the disease and low prevalence in other diseases	Yes	No
High reliability, high PPV	Yes	No
Can be used to monitor therapeutic efficiency	Yes	No

Present in the disease and low prevalence in other diseases

Friedrich Trendelenburg
Über die Unterbindung der Vena saphena magna bei Unterschenkelvaricen. Beiträge zur klinischen Chirurgie, 1891; 7: 195-210.

Sir Benjamin Collins Brodie
Lectures Illustrative of Various Subjects in Pathology and Surgery. London, Longman, 1846.

Present in the disease and low prevalence in other diseases

Bauer G. *The etiology of leg ulcers and their treatment by resection of the popliteal vein. J Internationale de Chirurgie 1948;8:937-67.*

A method of performing descending venography

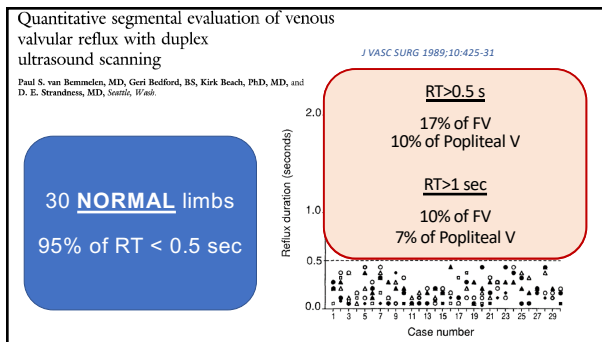
Deep venous reflux definitions and associated clinical and physiological significance

Robert L. Kistner, M.D., Eugene R. Ferris, M.D., Gurinder Randhawa, M.D., and Curtis Kamada, M.D., Honolulu, Hawaii

Ruh Hong Lim, MB ChB, BMed Sc (ONZCh), Genl Surg, MCh, Genl Surg, MB ChB, PhD, and Andre van Hil, MD, FRACS, The Netherlands, Nieuw-Zuidwijk

Level	Crude OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
None	1.1 (1.1 to 1.1)	NS	1.0 (1.0 to 1.0)	NS
1	1.2 (1.0 to 1.5)	NS	1.0 (0.8 to 1.4)	NS
2	2.2 (1.9 to 2.6)	<.0001	2.0 (1.7 to 2.4)	<.0001
3	3.7 (3.2 to 4.3)	<.0001	3.0 (2.5 to 3.6)	<.0001
Sign level	6.9 (6.7 to 7.2)	<.0001	5.9 (5.6 to 6.2)	<.0001
Reflex level	1.6 (1.5 to 1.6)	<.0001	1.7 (1.6 to 1.8)	<.0001

J VASC SURG 1986; 4:464-8.

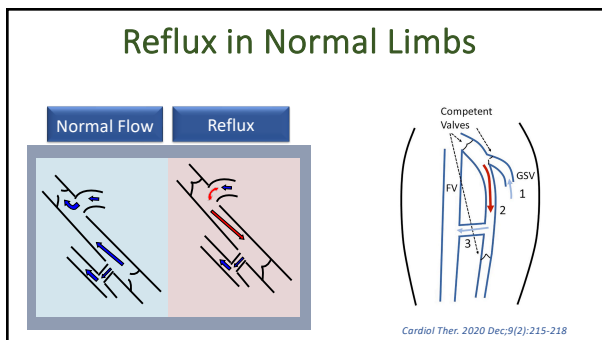


Prevalence of Reflux in CVD

Venous systems	C2 %(95%CI)	C5-6 %(95%CI)
Deep	18.8 (15.2-22.8)	54.5 (32.2-75.6)
GSV	28.9 (24.7-33.4)	57.1 (43.0-78.2)
GSV below knee	32.2 (27.7-36.9)	42.9 (21.8-66.0)
SSV	8.6 (6.2-11.7)	22.7 (7.8-45.4)

Bonn Populational Study

Maurins U, et al. *J Vasc Surg* 2008; 48(3):680-7



Prevalence of Reflux in athletes

ARTICLE IN PRESS
 For J Vasc Med Biol. Long (2024) vol. 36

High Physical Activity Volume Is Associated With an Increase in the Calibre of the Lower Limb Veins Without Impact on Functional Discomfort: the VARSPORT Study

Samuel Babiker^{1,2}, David Frenkel³, Andrew Thomas⁴, Laurent Herson⁵, Nicolas Noel⁶

Table 3. Comparison of lower limb vein diameter (measured as anteroposterior diameter (APD)) and presence or absence of reflux in high physical activity volume (HPAV) group and control group

Veins	HPAV group (n = 238)	Control group (n = 238)	OR (95% CI)	p value
APD - mm				
Deep veins				
FV				<.001
GSV				<.001
Superficial veins				
SSV				<.001
MSV				<.015
Presence or absence of reflux				
Deep veins				1.0
FV				1.0
MSV				0.0-5.00
SSV				0.0-5.00
Superficial veins				
MSV				1.94-8.30
SSV				<.001

Size and prevalence of reflux in are significantly larger in HPAV group

% of symptomatic patients is exactly the same (37%)

Present in other diseases

Duplex ultrasound abnormalities of the lower limb veins might precede clinical venous reflux signs in post-Fontan adolescents and young adults

Su Jin Kwon, MS¹, Yu-Mi Im, PhD², Jong Yoon Park, MD³, Dong-Hee Kim, MD, PhD⁴ and Tae-Jin Yum, MD, PhD⁵, Seoul, Cheonan and Wonyu-Si, Republic of Korea

• **Key Findings:** Among the 87 transplantation-free survivors who reached adolescence or young adulthood after the Fontan procedure, 66 (76%) showed venous reflux of the lower extremity on duplex ultrasound scanning. However, the CEAP (clinical, etiological, anatomical, pathophysiological) classification of the same cohort was mostly grade 0 (66 of 87; 76%).

High reliability, High PPV?

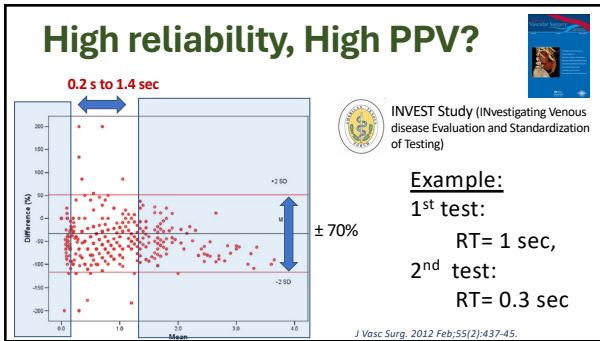
Definition of venous reflux in lower-extremity veins

J Vasc Surg 2003;38:793-8

Nicos Latsopoulos, PhD, DFC, RVT, Jay Tringoni, MD, Landon Pryor, MD, Apostolos K. Taniopoulos, MD, Steven S. Kang, MD, M. Akhtar Memon, MD, and William H. Baker, MD, Mayoool, IL

Duration of RF in the various normal veins varies, probably related to their size, valve location and number, tributary vessels uniting these veins, and wall compliance.

Reflux can occur in any vein segment, irrespective of disease stage.¹⁵ This is supported by our study, which included patients without signs and symptoms of chronic venous insufficiency.



- ### Determinates of RT
- Size of the vein *J Vasc Surg: Venous and Lym Dis 2015;3:8-17.*
 - CSA of perforators *J Vasc Surg Venous Lym Dis 2022;10(1):69-74*
 - CSA of competent tributaries *J Vasc Surg Venous Lym Dis 2021;9(5):1282-1290*
 - Blood volume ejected by a maneuver *J Vasc Surg 2012;55:437-45*
 - Provoking maneuver, position, time of the day, etc.

An Ideal Therapeutic target

Drug Discovery Today Advances 8, November 2024, October 2021

What makes a good drug target?
 Isabella Gochava¹, Peter Ellinghaus², Anette Sommer³ and Khouri Asadullah⁴

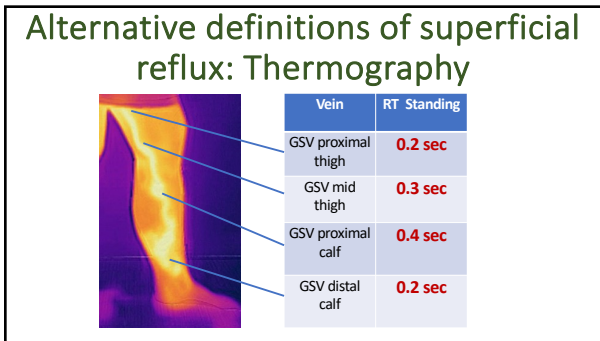
Ideal Target	Reflux
is disease-modifying	Yes
Present in the disease and low prevalence in physiological conditions or in other diseases	No
has a favorable 'assayability' (high reliability, high PPV)	No
target/disease-specific biomarker exists to monitor therapeutic efficacy	No

Alternative definitions of deep reflux: MRV

Relationships of Pelvic Vein Diameter and Reflux with Clinical Manifestations of Pelvic Venous Disorder
 Sergey Gerasimov^{1,2}, Anshu Kaulik, Nadezhda Mishkova, Oksana Efremova and Anastasiya Gerasimova

Quantitative two-dimensional phase-contrast magnetic resonance imaging characterization of lower extremity venous disease: venous reflux versus venous obstruction
 Yun-Kyoung Hong^{1,2}, Yun-Chae Han^{1,2}, Yoon-Hye Jeong^{1,2}, Chul-Chan Kim^{1,2}, Yuh-Gu Nyeo^{1,2}, Eun-Young Lee^{1,2}, Taehyun Yoon^{1,2}, Ayoung Chung^{1,2}, Jung-Hwa Chae^{1,2}, Suk-Kwang Wang^{1,2}, Seung-Yu Chae^{1,2}, Yu-Hui Lee^{1,2}, Chae-Woo Chae^{1,2}

Noncontrast MRI in assessing venous reflux of legs using QFlow analysis and radial basis function neural network technique
 Min-Ho Hong^{1,2}, Chae-Woo Chae^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}, Seung-Hye Jeong^{1,2}



- ### CONCLUSIONS
- Reflux time (RT) can not serve as a treatment target measure and/or the treatment outcome measure
 - RT may be used for description of segmental pathology in the context of anatomical extent of reflux (axial vs. segmental)
 - Current definition of reflux (by RT) became more a barrier than a benefit to the progress

It is time to move forward

