Prevention Suite



"Atherosclerosis is a systemic disease that remains asymptomatic for decades. With the integration of heart-vessel study (carotid IMT and stiffness with cardiac deformation index and coronary flow) we could draw a new roadmap to diagnose an early and personalized CVD risk assessment"

Dr. Fausto Rigo, Cardiac Diagnostic Imaging Department, Dell'Angelo Hospital, Mestre-Venice (Italy)

In the global effort to reduce suffering and death from CVD, the World Heart and Stroke Forum (WHSF) Guideline Task Force of the World Heart Federation (WHF) recommends that every country should develop a policy on CVD prevention¹

Therefore, the primary prevention of atherothrombosis diseases represents an increasing challenge worldwide². So far, the atherosclerosis risk in asymptomatic patients has been weighed up by applying scores that take some risk factors into account and concern a general risk predisposition.

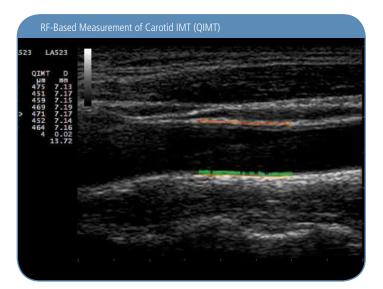
However, the risk for an individual within a population is not just a function of their absolute ranking in relation to others but of the overall risk of the population in which they live. An individual's risk should always be judged in the context of the CVD risk of the population as a whole^{2,3}.

A large number of tools for estimating risk of CHD or other atherosclerotic disease have been developed over the past decades, including risk score charts, risk assessment algorithms, and computer software programs, but these could fail to identify the single subject with a real vascular risk for developing an ischemic disease^{4,5}.

Whatever technology we apply to detect asymptomatic subjects, we should strive for further refinements in risk prediction to identify intervention procedures⁶.

However, before screening technology is used in routine clinical practice, the following screening criteria should be met^{1,3}: the noninvasive tool for detecting CHD or other atherosclerotic disease is valid, precise, easy, and acceptable. Furthermore, this kind of technical screening should be employed by trained and expert operators, without biologically adverse effects and with an affordable cost, appropriate for the healthcare system, and justified by the outcome³.

Although imaging approaches hold great appeal, they may remain too expensive and/or entail too high a radiation exposure to prove cost-effective or cost-beneficial for screening of unselected populations of unknown cardiovascular risk⁶. Endothelialdependent vasodilatation assessed by a variety of techniques correlates with many risk factors, but not with complete fidelity⁷. Imaging approaches, both anatomical and functional, have generated great interest for cardiovascular risk prediction.

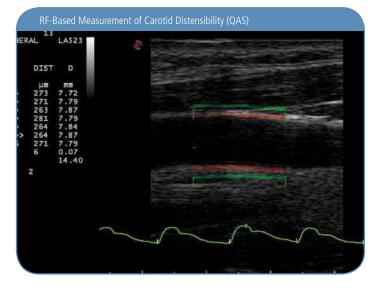


An optimal alignment of ultrasound probe across the longitudinal section of carotid artery is mandatory for accurate IMT measurement. With RF-based Esaote system, adequately depicted segments of IMT are indicated in green, the average IMT thickness is displayed beat-to-beat on the screen, and the mean value (MED) and standard deviation (SD) are continuously calculated. These inherent quality feedbacks allow achieving a correct probe position, optimal and stable IMT delineation and thus the correct and repeatable measurements.

Carotid IMT and stiffness

Carotid IMT has been shown to correlate with the degree of carotid atherosclerosis measured by autopsy⁸ that, in turn, has been found to correlate with atherosclerotic burden in other arterial beds⁹⁻¹⁰. Consequently, carotid IMT is considered a surrogate marker of subclinical atherosclerosis. Increased carotid IMT is associated with CV risk factors¹¹⁻¹², prevalent CV diseases¹³ and coronary artery atherosclerosis¹⁴⁻¹⁵.

In the last years, a growing interest has been focused on arterial stiffening that reflects a loss of elasticity of the arterial wall, either due to atherosclerosis or arterial ageing. Increase in aortic stiffness, estimated by measuring carotid-femoral pulse wave velocity (PWV), has been shown to be associated with CV risk factors¹⁶⁻¹⁷, with the presence and extent of atherosclerotic load in



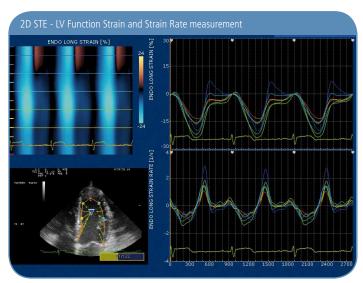
Continuous red lines indicates an adequate detection of carotid adventitia. Continuous green lines display dynamically the amplified vessel wall movement. Real.time distension waveform is displayed at the bottom (yellow line). The average carotid distention and diameter are displayed beat-to-beat on the screen, and the mean value (MED) and standard deviation (SD) are continuously calculated. From distention waveform, standard indices of carotid stiffness are automatically calculated.

the coronary arteries $^{\rm 18}$ and with cardiovascular events in different populations $^{\rm 19-20}.$

Emerging evidence from cohort studies affirms that a calcium score derived from electron beam computed tomography may also add information regarding cardiovascular risk to traditional algorithms^{21,22}.

Cardiac deformation index

2D STE, resolving the multidimensional components of LV deformation, is another very promising imaging approach, that can play an important and incremental role in cardiovascular prevention field as the study of myocardial contractility function provides useful and predictive values against traditional LV Global Function assessment (Global EF) for determining subclinical cases



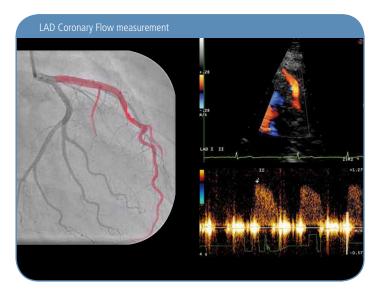
that are likely to progress into Heart Failure. A growing body of evidence are reporting the presence of marked impairment of cardiac longitudinal and circumferential mechanics are reported in presence of preserved/minimal impaired Global LV function²³.

CT scan angiography shows promise for probing coronary anatomy non-invasively⁶. Molecular imaging aims to interrogate functional aspects of atherosclerotic lesions that go beyond mere anatomical features, including aspects of inflammation directly implicated in plaque stability and thrombogenic potential²⁴.

At least in the mid-term, cost-effectiveness and risk benefit analyses will probably favor a tiered approach for the deployment of imaging in cardiovascular risk assessment in apparently well individuals⁶.

Coronary flow imaging

Recently, we were able to obtain important information regarding the influence of atherosclerotic coronary narrowing in a large number of patients, with the opportunity of validating this technique by matching data with those obtained by Doppler flow wire. We have already validate the coronary flow velocity mapping on left anterior descending coronary artery by matching this data with coronary angiography²⁵.



Doppler-derived coronary flow assessment on left anterior descending coronary artery (LAD) could represent an effective diagnostic modality in highlighting the presence of a pathological coronary narrowing.

The usual risk factors for CAD were little use in predicting obstructive CAD at angiography.

Each carotid parameter (c-IMT and c-plaques) had increased diagnostic value. A LAD velocity > 70 cm/sec, found at any site, was the most predictive parameter, building a significant additional diagnostic value for the prediction of CAD.

Integrated ultrasound investigations

The integrated ultrasound study represents a faster and easier way to investigate those asymptomatic patients with an intermediate risk for atherosclerosis.

The novelty could be represented by the possibility of investigating the subject during a single cardiovascular investigation by the same physician who, through the application of innovative technology, is able to assess the carotid artery, cardiac function by analyzing the left ventricle deformation indexes and coronary flow velocity mapping on the left anterior descending coronary artery.

From this combined evaluation we could get important and complementary information in order to stratify and to individualize personal risk and therefore to apply an individual and tailored prevention strategy.

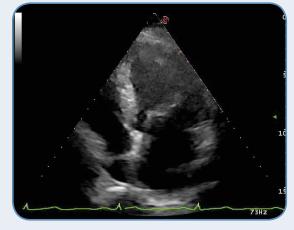
References

- 1. World Health Organization. The world Health report 2002: reducing Risks, Promoting Health Life. Geneva, Switzerland: World Health Organization;2002:248
- Pyoorala K, de Backer G, Graham I, et al Prevention of coronary artery heart disease in clinical practice: recommendations of the Task Force of the European society of Hypertension. Eur Heart J 1994;15:1300-1331
- 3. Smith SC, Jackson R, Pearson TA, eta al. Principles for National and Regional Guidelines on cardiovascular Disease Prevention. A scientific Statement From the World Heart and Stroke Forum. Circulation;109:3112-3121
- Ramsay LE, Haq IU, Jackson Pr, et al. Targeting lipid-lowering drug therapy for primary prevention of coronary artery disease: am update Sheffield table.Lancet 1996;348:387-388
- British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, endorsed by British Diabetic Association. Joint British recommendations on prevention of coronary heart disease in clinical practice.Heart.1998:80 (suppl(2):1-29
- LibbY P, Crea F. Clinical implications of inflammation for cardiovascular primary prevention. Eur Heart J 2010:31:777-783
- Sudano I, Spieker LE, Hermann F, Flammer A, Corti R, Noll G, Luscher TF. Protection of endothelial function: targets for nutritional and pharmacological interventions. J Cardiovasc Pharmacol 2006;47(Suppl. 2):S136– S150.
- Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R, Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging, Circulation (1986), 74: pp. 1399-1406.
- Mitchell JR, Schwartz CJ, Relationship between arterial disease in different sites. The study of the aorta, coronary, carotid and iliac arteries, Br Med J. (1962), 1: pp. 1293-1301.
- Finn AV, Lolodgie FD, Virmani R, Correlation between carotid intima/ medial thickness and atherosclerosis: A point of view from pathology, Arterioscler Thromb Vasc Biol. (2010), 30: pp. 177-181.
- Polak JF, Person SD, Wei GS, Godreau A, Jacobs DR, Harrington A, Sidney S, O'Leary DH, Segment-specific association of carotid intima-media thickness with cardiovascular risk factors. The Coronary Artery Risk development in Young Adult (CARDIA) Study, Stroke (2010), 41: pp. 9-15.
- Schott LL, Wildman RP, Brockwell S, Simkin-Silverman LR, Kuller LH, Sutton-Tyrrell K, Segment-specific effect of cardiovascular risk factors on carotid intima-medial thickness in women at midlife, Arterioscler Thromb Vasc Biol. (2004), 24: pp. 1951-1956.
- Burke GL, Evans GW, Riley W, Sharrett AR, Howard G, Barnes RW, Rosamond W, Crow RS, Rautaharju PM, Heiss G, Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study, Stroke (1995), 26: pp. 386-91.

- Kablak-Ziembicka A, Tracz W, Przewlocki T, Pieniazek P, Sokolowski A, Konieczynska M, Association of increased carotid intima-media thickness with the extent of coronary artery disease, Heart (2004), 90: pp.1286-90.
- Davis PH, Dawson JD, Mahoney LT, Lauer RM, Increased carotid intimalmedial thickness and coronary calcification are related in young and middle-aged adults. The Muscatine study, Circulation (1999), 100: pp. 838-42.
- 16. Ferreira I, Henry RM, Twisk JW, van Mechelen W, Kemper HC, Stehouwer CD; Amsterdam Growth and Health Longitudinal Study. The metabolic syndrome, cardiopulmonary fitness, and subcutaneous trunk fat as independent determinants of arterial stiffness: the Amsterdam Growth and Health Longitudinal Study. Arch Intern Med. 2005;165:875-882.
- Schram MT, Henry RM, van Dijk RA, Kostense PJ, Dekker JM, Nijpels G, Heine RJ, Bouter LM, Westerhof N, Stehouwer CD. Increased central artery stiffness in impaired glucose metabolism and type 2 diabetes: the Hoorn Study. Hypertension. 2004;43:176-181
- McLeod AL, Uren NG, Wilkinson IB, Webb DJ, Maxwell SR, Northridge DB, Newby DE, Non-invasive measures of pulse wave velocity correlate with coronary arterial plaque load in humans, J Hypertens. (2004), 22: pp. 363-368.
- Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM, Havlik R, Lakatta EG, Spurgeon H, Kritchevsky S, Pahor M, Bauer D, Newman A; Health ABC Study, Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults, Circulation (2005), 111: pp. 3384-3390.
- 20. Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, Laurent S, Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study, Hypertension (2002), 39: pp. 10-15.
- Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. J Am Med Assoc 2004;291:210–215
- Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. J Am Coll Cardiol 2005;46:158–165.
- 23. Geyer et al. "Assessment of Myocardial Mechanics Using Speckle Tracking Echocardiography: Fundamentals and Clinical Applications" J Am Soc of Echocardiogr 2010, Volume 23 Number 4, April 2010
- 24. Jaffer FA, Libby P, Weissleder R. Optical and multimodality molecular imaging:insights into atherosclerosis. Arterioscler Thromb Vasc Biol 2009;29:1017–1024.
- 25. Rigo F, TonaF, Grolla E, et al. Coronary flow velocity assessment on left anterior coronary artery as marker of atherosclerosis: fesibility and accuracy of transthoracic echocardiographic study compared to Doppler flow wire investigation. Eur Heart J abs 2010

Case Study

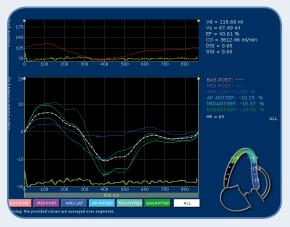
63 year-old male, Hypertension, LDL 164 mg/dl, ECG: SR LVH RA, No symptoms



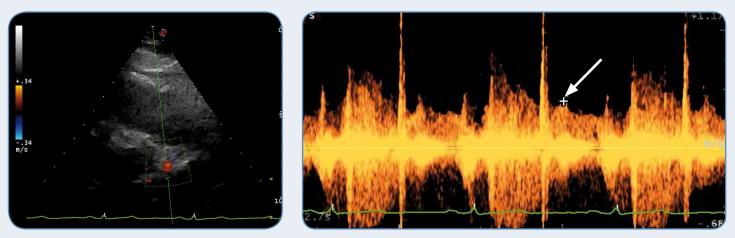
Echo TTE approach apical 4 chamber view during diastolic phase displaying a hypertrophic and slightly dilated left ventricle.



Echo TTE approach apical 4 chamber view during systolic phase displaying left ventricle with decreased global contractility (EF 40%).

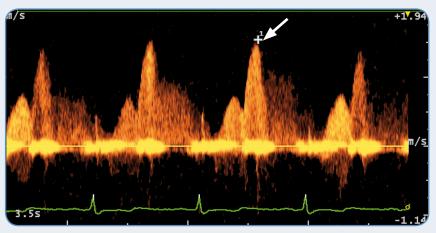


Longitudinal Strain reduced in all segments falling into LAD Territories , particularly depressed are Apical Lateral (-1,59) and Antero-septal (-10,29).

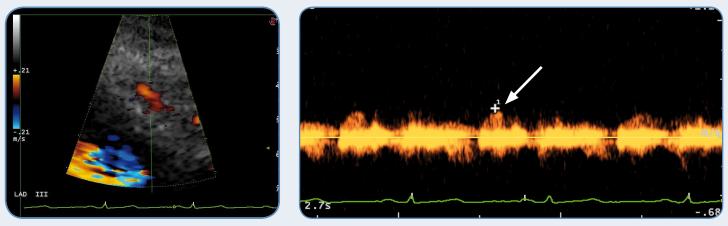


To the left - Color Doppler approach which allows to identify left anterior descending (LAD) coronary artery tract. To the right - Doppler spectral recording of LAD's first section with a flow rate of 40 cm/s, a normal velocity for this coronary segment.





To the left - middle tract of LAD with aliasing demonstrating high sampling rate. To the right - equivalent Pulse Doppler spectral recording displays a clear pathological flow rate between first and second LAD tracts demonstrating that this segment's flow undergoes a clinically significant sudden acceleration.



To the left - The red color signal of LAD's distal portion with Color Doppler approach witnessing that flow rate is within physiological sampling range as evidenced, to the right, by the equivalent Doppler spectral recording displaying normal flow rates.

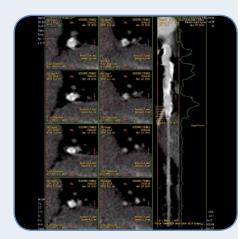
Case Study

Left panel: A CT Scan multislice heart examination addressed to the first tract of left anterior descending coronary artery which shows a narrowing poorly quantifiable for the presence of a higher value of calcium score (> 400 CS)

Right panel: same image acquired with multislice CT displaying anterior coronary vessel stenosis, probably > 50%, where an accurate diagnostic assessment of stenosis' severity is not possible due to calcification.

Left and right panels: A coronary angiography addressed to LAD, from different approaches, that highlights a critical stenosis of the first tract of LAD.

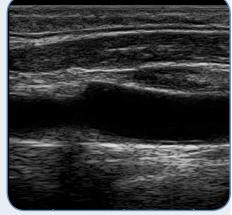






Left panel: Two-dimensional echocardiographic image displaying a significant amount of a plaque at the entrance of the left common carotid

Right panel: Two-dimensional echocardiographic image displaying a pathological increase in right common carotid IMT and intermediate plaques in the same segment.



Esaote S.p.A.

International Activities: Via di Caciolle 15 - 50127 Florence, Italy - Tel. +39 055 4229 1 - Fax +39 055 4229 208 - international.sales@esaote.com - www.esaote.com Domestic Activities: Via A. Siffredi, 58 16153 Genoa, Italy, Tel. +39 010 6547 1, Fax +39 010 6547 275, info@esaote.com