Journal of
HYPERTENSION RESEARCH
www.hypertens.org/jhr

Review

J Hypertens Res (2018) 4(1):15–21

Hypertension and peripheral vascular damage assessment

Nicoleta Oprescu*, Nicoleta Monica Popa-Fotea, Miruna Mihaela Micheu

Department of Cardiology, Clinical Emergency Hospital of Bucharest, Bucharest, Romania

Received: February 14, 2018, Accepted: March 20, 2018

Abstract

Hypertension is the most prevalent cardiovascular risk factor and its relationship with atherosclerosis make this an uppermost factor to be taken into consideration in the overall evaluation of the patient. The early detection of atherosclerosis represents an ideal standard to be reached and is based mainly on the non-invasive evaluation of the peripheral arteries such as the carotid and femoral arteries. The overused echographic parameter intima-media thickness (IMT) proved to have a very poor sensitivity and specificity with no other supplemental advantage over the other classical cardiovascular risk factors such as sex, age, hypertension, dyslipidemia etc. All the meta-analysis against the utility of IMT urged the research for other parameters. Carotid artery plaque score (PS) and atherosclerosis burden score (ABS) are better to be used in the detection of atherosclerosis having improved correlation with the invasive detected of atherosclerosis as observed in various studies. Ankle-brachial index is a good test for the detection, prognosis and follow-up of the patients with peripheral arterial disease, although lack of standardization in the determination method is an issue to be considered. Arterial stiffness with pulse-wave velocity and arterial augmentation index as surrogate determinants seems to be highly related with vascular aging and even more with early arterial aging. Still there are black holes to be enlighten by large population clinical trials on hypertension and atherosclerosis.

Keywords: Hypertension; Atherosclerosis; detection; Intima media thickness (IMT); Carotid artery plaque score (PS); Atherosclerosis burden score (ABS); Arterial stiffness; Pulse-wave velocity

Hypertension is the most widely spread risk factor for premature cardiovascular diseases (CVD) as its incidence is higher compared with the other cardiovascular risk factors such as: cigarette smoking, dyslipidemia or diabetes. Among patients with a recent stroke or transit ischemic attack, the prevalence of hypertension is approximately 70% [1] and history of hypertension is present in 75% of patients with chronic heart failure (HF) [2]. Studies have demonstrated graded associations between higher systolic and diastolic blood pressure and increased CVD risk [3,4] from young to old individuals (from 30 to older than 80 years of age).

Observational and experimental studies show a link between hypertension and the development of atherosclerosis [5-7]. The most frequently cited pathophysiological mechanism of hypertension that may promote atherosclerotic disease is the increased arterial shear stress which promotes arterial smooth muscle hyperpla-

* Correspondence to: Nicoleta OPRESCU, MD
Department of Cardiology, Clinical Emergency Hospital of Bucharest, Floreasca street 8, 014461, Bucharest, Romania.
E-mail: nicoleta_m_oprescu@yahoo.com

sia and hypertrophy and increases endothelial permeability to plasma electrolytes by endothelial damage, that induces fibromuscular thickening of intima and media of large and small arteries [8]. Despite an unified concept of hypertension and atherosclerosis, these remain two separate disorders that cause similar, but distinct changes on the vascular tree; not every hypertensive individual shows extensive atherosclerosis and also not always atherosclerosis is accompanied by hypertension. Despite certain proves taken all together experimental, pathogenic and epidemiological studies does not clearly show that hypertension in the absence of other atherogenic factors causes atherosclerosis [9].

The early detection of atherosclerosis in subclinical stages currently represents a standard to be reached as the incidence and mortality rate of cardiovascular diseases is in continuous increase. Epidemiological studies have shown correlations between the atherosclerosis in one arterial territory and the involvement of other arteries such as coronary, carotid or femoral arteries [10]. Consecutively, early detection of arterial disease in an apparently healthy population has focused on arteries such as carotid and femoral arteries as they are easy to investigate and low cost. Many echographic parameters have been investigated, but none proved sufficient sensitivity and specificity.

Carotid and Femoral ultrasound

Carotid ultrasound is mainly based on the measurement of intima – media thickness (IMT) and the presence and characteristics of plaques. Plaque thickness was showed to predict cardiovascular risk, reason for which intima-media thickness was included in many studies as a risk factor for cardiovascular risk [10]. However more recent studies pinpoint that IMT measured according to Mannheim consensus does not define atherosclerosis, as individuals with the same IMT can have totally different risk for cardiovascular events such as stroke, myocardial infarction etc [11]. IMT is not a sign of early atherosclerosis, but represents smooth muscle hypertrophy/hyperplasia induced by factors including hypertension. Several reasons may explain the impediment brought by IMT over traditional risk factors such as age, sex, blood pressure or hypercholesterolemia. It is measured in the common carotid artery, whereas the advanced lesions tend to appear in the bulb or in the proximal zone of the internal carotid artery. Another reason may be the poor axial resolution of usual carotid echography as the limit of significance is 200 μm outside the possibilities of accurate measurements. Algorithms that provide a more precise measurement or the 3D ultrasound with volumetric determinations may increase ultrasonographic performance. Despite all these drawbacks, ultrasonography remains a low-cost, non-invasive and easy to perform technique that can still have its place in the risk assessment and diagnosis of atherosclerosis. Meta-analysis showed that IMT alone without taking into account plaques, weakly predicts CV risk [12].

The need to study new novel risk factors is reiterated by large populations studies that show there is low correlation between traditional risk factors and carotid IMT. If the prevention ESC guide currently proscribes the determination of carotid ultrasound IMT in the CV risk assessment, there is a IIb recommendation for atherosclerotic plaque detection and ankle-brachial index [13].

Plaque is usually defined as the presence of a focal wall thickening at least 50% greater than the surrounding wall vessel or as a focal region with an IMT higher that 1.5 mm that protrudes into the lumen [14]. Plaques have to be characterized by their number, size, shape and echodensity. Plaques are related to both ischemic cardiac or cerebrovascular events, and echolucent much more than calcified plaques increase the risk for acute ischemic incidents. Many studies reveals the greater importance of variables that include plaque area and thickness, rather than IMT for CVD [15,16]. Despite the fact that formal indications have not been established as guideline recommendations, carotid artery plaque assessment with ultrasonography may be considered a risk modifier in CVD prediction.

Starting from the recommendations that indicate the importance of plaques in the CV risk assessment, an index denominated carotid artery plaque score (PS) was calculated by summing each plaque taking into account it maximum thickness in the ipsilateral carotid artery and by adding the bilateral carotid plaque scores is obtained a total PS. Terzi proved on more than 50.000 patients that plaque score (PS) had a higher diagnostic value for predicting future myocardial infarction events compared with IMT [17].

Another group [18] made use of another index of assessment, the atherosclerosis burden score (ABS), a

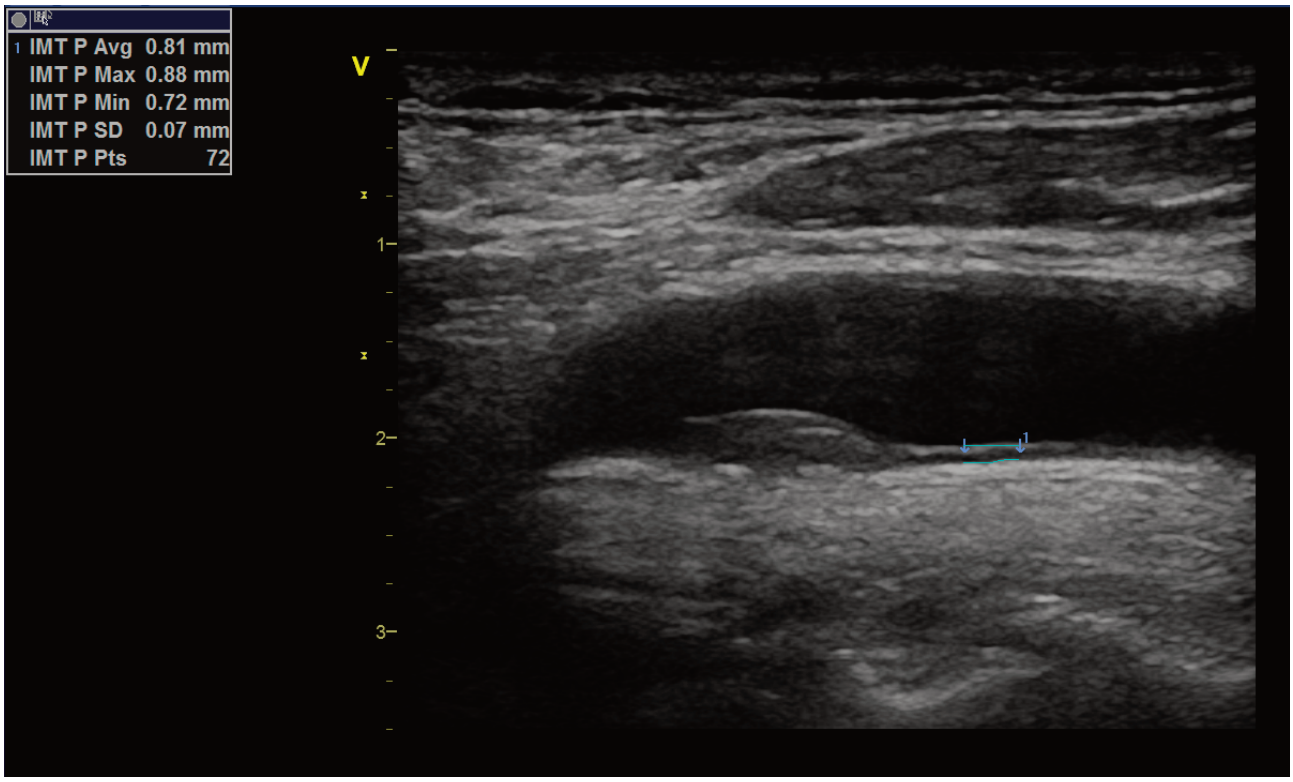

Figure 1. Carotid bifurcation with a large plaque (2.6 mm in its maximum diameter)

score that sums the number of carotid and femoral bifurcations with plaques. The predictive value of ABS surpassed IMT, carotid/femoral plaque scores in the detection of coronary artery disease in a cohort of patients with coronary angiography. In the ABS study mentioned above both left and right carotid and femoral arteries were examined (four arterial sites). Carotid investigation included common carotid artery (CCA), bulb, and the origin of the internal and external branches. Femoral arteries were examined from 4 cm above bifurcation to 4 cm in the superficial branch as well as the origin of the profound branchial branch. All in all, ABS proved to be a better predictor of peripheral atherosclerosis as it takes into account not only a short segment of the common carotid artery that may be free of plaques, but a wider area throughout multiple locations of the arterial tree increasing the likelihood to accurately detect atherosclerosis. The hypothesis that the presence of atherosclerosis on carotid arteries is associated with plaques on other arterial branches such as femoral was infirmed in the CAFES-CAVE study, where 30% of the patients with normal carotid arteries had significant plaques on femoral arteries [19], observations confirmed also by other studies [20].

To exemplify the lack of clinical significance of IMT, we report the case of two patients with the value of IMT within the normal range, although one has important plaques at carotid (figure 1) and femoral bifurcations (figure 2), and implicitly a high ABS, while the other has no plaques at the same arterial zones investigated (figure 3 and 4). In the case of the patient with numerous plaques, aortic PWA and augmentation indexes sustained the high cardiovascular risk.

Ankle–brachial index

The ankle–brachial index (ABI) is an easy to perform and reproducible screening test available even in the early stages of atherosclerotic disease, when it can be considered an surrogate marker for atherosclerosis. ABI was found to have important prognostic information for future cardiovascular events [21]. An ABI of less than 0.9 indicates a stenosis of more than 50% between the aorta and the distal arteries of the inferior

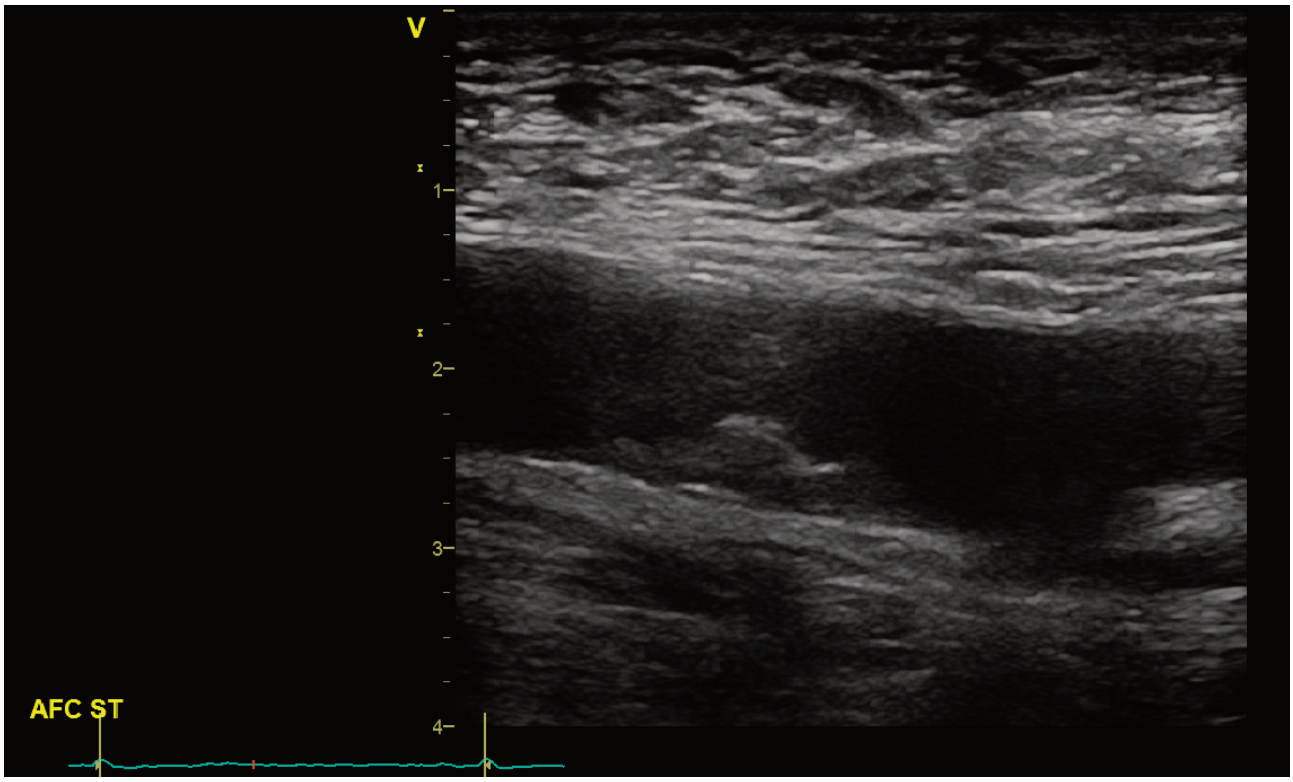

Figure 2. Femoral bifurcation displaying a large plaque (3.2 mm in its maximum diameter) with a thin fibrous cap

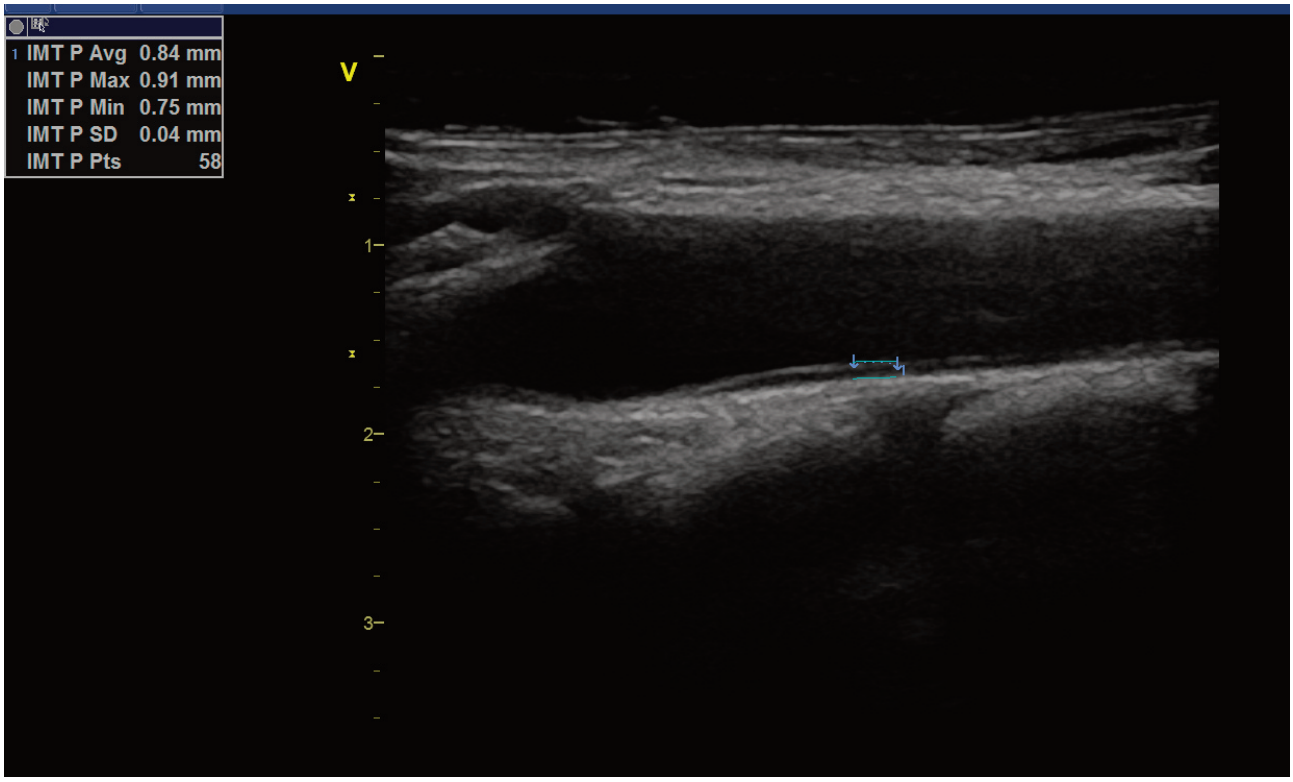

Figure 3. Carotid bifurcation with no plaques

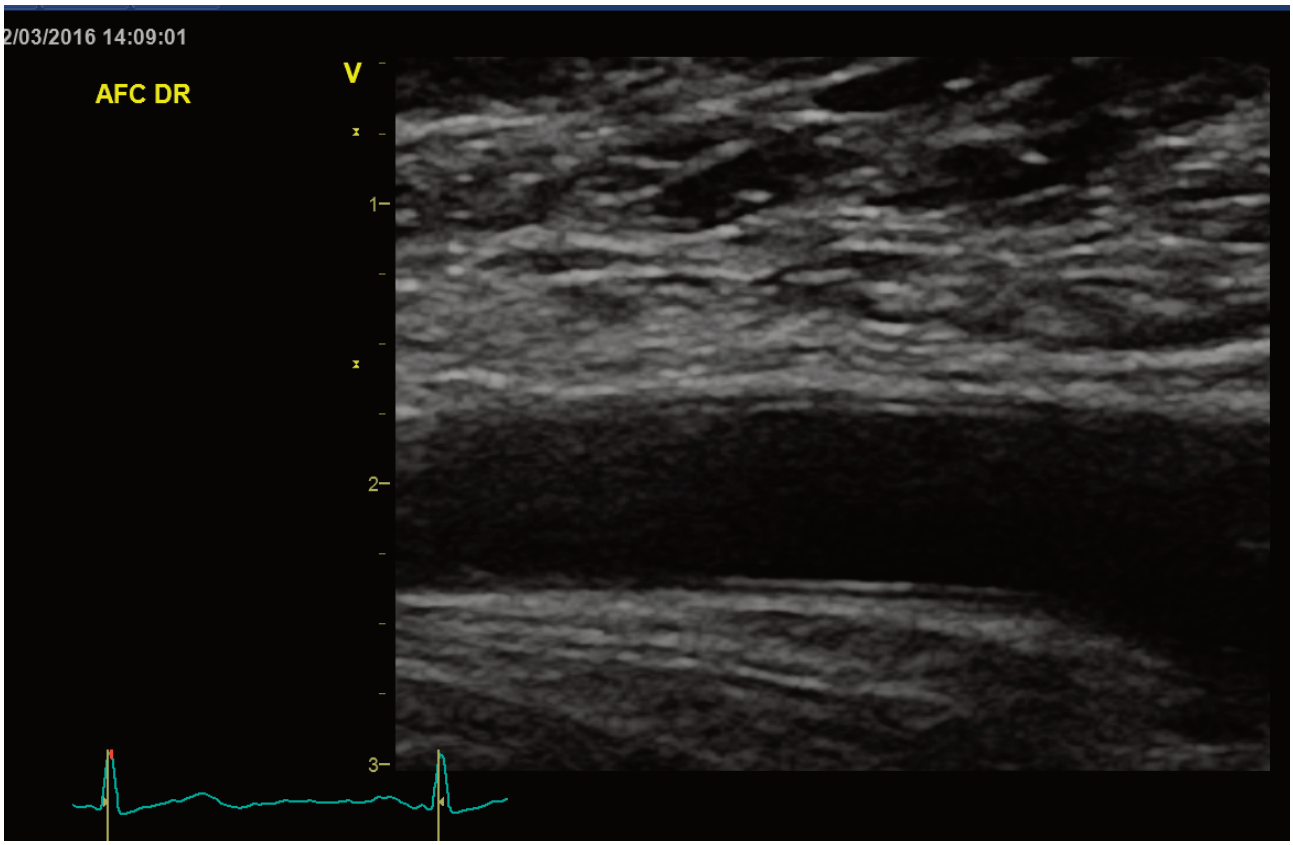

Figure 4. Femoral bifurcation with no plaques

limb. With a sensitivity of 79% and a specificity of 90% an ABI of less than 0.90 is considered to be a reliable marker of peripheral artery disease (PAD) [22]. An abnormal ABI in an asymptomatic individual would reclassify into a new higher risk category for future CVD. There are controversial studies regarding the potential of ABI to reclassify patients in different risk categories [23]. Future research must fill the gaps to determine the benefits and harms of aggressive treatment of persons reclassified from low or intermitted into high risk category and the effects of reclassifying from high or intermediate. ABI is recommended as part of the management of the patient with recent lower extremity revascularization as an ABI improvement of 0.15 post percutaneous transluminal angioplasty had 67% sensitivity and 100% specificity for patency of post-surgery artery. Different methods and values of cut-off have been used in different population studies which decreases its value as confident marker. Therefore is a need to define a uniform method to be used worldwide.

Arterial stiffness

The aging of the large artery wall is characterized by a reduction in the elastin content, along with an increased amount of collagen and changes between cells and matrix leading to increased arterial stiffness defined by an increased rigidity of the artery wall that can occur in association with increased age and/or various other CV risk factors. Arterial stiffness is commonly measured using either aortic pulse wave velocity (PWV) or arterial augmentation index. The concept of vascular aging can be motorized through changes in arterial stiffness. The predictive value of arterial stiffness for CV events has been well demonstrated in various trials with the largest amount of evidence for aortic stiffness, measured through carotid-femoral pulse wave velocity (cfPWV). Many studies and reviews consistently showed the independent predictive value of aortic stiffness for fatal and nonfatal CV events taking a PWV threshold of 12 m/s has the point from where increases the arterial damage [24]. The Sixth Joint Task Force of

the European Society of Cardiology suggests to use PWV as marker of CV risk only for individuals close to cut-off, but regular use in all patients to improve CV risk classification is not recommended [13].

Gaps in evidence

The lack of homogeneity in the definition and measurement of ultrasound or hemodynamic parameters for the assessment of CV risk urged the development of new standardized scores with less variability and higher intra and inter individual reproducibility such as carotid artery plaque score (PS), atherosclerosis burden score (ABS). Although continuous improvement is made in the field there are still gaps to be filled through large clinical trial.

Acknowledgement

This work was supported by CREDO Project - ID: 49182, financed through the SOP IEC -A2-0.2.2.1-2013-1 cofinanced by the ERDF.

Conflicts of interest

The authors confirm that there are no conflicts of interest.

References

1. Cushman WC, Reda DJ, Perry HM, Williams D, Abdellatif M, Materson BJ (2000) Regional and racial differences in response to antihypertensive medication use in a randomized controlled trial of men with hypertension in the United States. Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. Arch Intern Med 160:825–31
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA, McBride PE, Peterson PN, Stevenson LW, Westlake C (2017) 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol 70:776–803
3. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R (2002) Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 360:1903–1913
4. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, White IR, Caulfield MJ, Deanfield JE, Smeeth L, Williams B, Hingorani A, Hemingway H (2014) Blood pressure and incidence of twelve cardiovascular diseases: Lifetime risks, healthy life-years lost, and age-specific associations in 1 25 million people. Lancet 383:1899–1911
5. Nakanishi R, Baskaran L, Gransar H, Budoff MJ, Achenbach S, Al-Mallah M, Cademartiri F, Callister TQ, Chang H-J, Chinnaiyan K, Chow BJW, DeLago A, Hadamitzky M, Hausleiter J, Cury R, Feuchtner G, Kim Y-J, Leipsic J, Kaufmann PA, Maffei E, Raff G, Shaw LJ, Villines TC, Dunning A, Marques H, Pontone G, Andreini D, Rubinshtein R, Bax J, Jones E, Hindoyan N, Gomez M, Lin FY, Min JK, Berman DS (2017) Relationship of Hypertension to Coronary Atherosclerosis and Cardiac Events in Patients With Coronary Computed Tomographic Angiography. Hypertens (Dallas, Tex 1979) 70:293–299
6. Ninomiya T, Perkovic V, Turnbull F, Neal B, Barzi F, Cass A, Baigent C, Chalmers J, Li N, Woodward M, MacMahon S (2013) Blood pressure lowering and major cardiovascular events in people with and without chronic kidney disease: meta-analysis of randomised controlled trials. BMJ 347:f5680
7. Dzau VJ (1990) Atherosclerosis and hypertension: mechanisms and interrelationships. J Cardiovasc Pharmacol 15 Suppl 5:S59-64
8. Hollander W (1976) Role of hypertension in atherosclerosis and cardiovascular disease. Am J Cardiol 38:786–800
9. Hollander W (1976) Role of hypertension in atherosclerosis and cardiovascular disease. Am J Cardiol 38:786–800
10. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK (1999) Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med 340:14–22
11. Satiroglu O, Kocaman SA, Karadag Z, Temiz A, Cetin M, Canga A, Erdogan T, Bostan M, Cicek Y, Durakoglugil E, Vural M, Bozkurt E (2012) Relationship of the angiographic extent of peripheral arterial disease with coronary artery involvement. J Pak Med Assoc 62:644–649
12. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M (2007) Prediction of clinical cardiovascular events with carotid intima-media thickness: A systematic review and meta-analysis. Circulation 115:459–467
13. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, Van Der Worp HB, Van Dis I, Verschuren WMM, Binno S, De Backer G, Roffi M, Aboyans V, Bachl N, Carerj S, Cho L, Cox J, De Sutter J, Egidi G, Fisher M, Fitzsimons D, Franco OH, Guenoun M, Jennings C, Jug B, Kirch-

hof P, Kotseva K, Lip GYH, Mach F, Mancia G, Bermudo FM, Mezzani A, Niessner A, Ponikowski P, Rauch B, Stauder A, Turc G, Wiklund O, Windecker S, Zamorano JL, Achenbach S, Badimon L, Barón-Esquivias G, Baumgartner H, Bax JJ, Dean V, Erol Ç, Gaemperli O, Kolh P, Lancellotti P, Nihoyannopoulos P, Torbicki A, Carneiro AV, Metzler B, Najafov R, Stelmashok V, De Maeyer C, Dili M, Gruev I, Mili i D, Vaverkova H, Gustafsson I, Attia I, Duishvili D, Ferrières J, Kostova N, Klimiashvili Z, Hambrecht R, Tsioufis K, Szabados E, Andersen K, Vaughan C, Zafrir B, Novo S, Davletov K, Jashari F, Kerimkulova A, Mintale I, Saade G, Petrulioniene Z, Delagardelle C, Magri CJ, Rudi V, Oukerraj L, Çölkesen BE, Schirmer H, Dos Reis RP, Gherasim D, Nedogoda S, Zavatta M, Giga V, Filipova S, Padial LR, Kiessling A, Mahdhaoui A, Ural D, Nesukay E, Gale C (2016) 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur. Heart J. 37:2315–2381

14. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, Najjar SS, Rembold CM, Post WS (2008) Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force Endorsed by the Society for Vascular. J. Am. Soc. Echocardiogr. 21:93–111
15. Zhang H, Liu M, Ren T, Wang X, Liu D, Xu M, Han LF, Wu Z, Li H, Zhu Y, Wen Y, Sun W (2015) Associations between carotid artery plaque score, carotid hemodynamics and coronary heart disease. Int J Environ Res Public Health 12:14275–14284
16. Morito N, Inoue Y, Urata M, Yahiro E, Kodama S, Fukuda N, Saito N, Tsuchiya Y, Mihara H, Yamanouchi Y, Saku K, Urata H (2008) Increased carotid artery plaque score is an independent predictor of the presence and severity of coronary artery disease. J Cardiol 51:25–32
17. Terzi S, Sayar N, Bilsel T, Enc Y, Yildirim A, Cilo lu F, Yesilcimen K (2007) Tissue Doppler imaging adds incremental value in predicting exercise capacity in patients with congestive heart failure. Heart Vessels 22:237–244
18. Yerly P, Marquès-Vidal P, Owlya R, Eeckhout E, Kappenberger L, Darioli R, Depairon M (2015) The Atherosclerosis Burden Score (ABS): a Convenient Ultrasound-Based Score of Peripheral Atherosclerosis for Coronary Artery Disease Prediction. J Cardiovasc Transl Res 8:138–147
19. Belcaro G, Nicolaides AN, Ramaswami G, Cesarone MR, De Sanctis M, Incandela L, Ferrari P, Geroulakos G, Barsotti A, Griffin M, Dhanjil S, Sabetai M, Bucci M, Martines G (2001) Carotid and femoral ultrasound morphology screening and cardiovascular events in low risk subjects: A 10-year follow-up study (the CAFES-CAVE study). Atherosclerosis 156:379–387
20. Postley JE, Perez A, Wong ND, Gardin JM (2009) Prevalence and Distribution of Sub-Clinical Atherosclerosis by Screening Vascular Ultrasound in Low and Intermediate Risk Adults: The New York Physicians Study. J Am Soc Echocardiogr 22:1145–1151
21. Vogt MT, McKenna M, Anderson SJ, Wolfson SK, Kuller LH (1993) The relationship between ankle-arm index and mortality in older men and women. J Am Geriatr Soc 41:523–30
22. Hiatt WR (2001) Medical Treatment of Peripheral Arterial Disease and Claudication. N Engl J Med 344:1608–1621
23. U.S. Preventive Services Task Force (2009) Using nontraditional risk factors in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 151:474–82
24. Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of Cardiovascular Events and All-Cause Mortality With Arterial Stiffness: A Systematic Review and Meta-Analysis. J Am Coll Cardiol 55:1318–1327