We are IntechOpen, the world's leading publisher of Open Access books
Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Specific Features of Target Organ Damage in Patients with Arterial Hypertension and Coronary Artery Disease

Corina Şerban, Ruxandra Christodorescu, Alexandru Caraba,
Germaine Săvoiu, Carmen Cristescu and Simona Drăgan
*University of Medicine and Pharmacy "Victor Babeş" Timişoara,
Romania*

1. Introduction

Worldwide, nearly 8 million premature deaths, 54% of stroke cases and 47% of ischemic heart disease cases were attributable to high blood pressure (BP >115 mm Hg systolic) (Ruilope, 2011). It is widely known that arterial hypertension has effects on target organs like the brain, the heart and the kidney. Now a large body of evidence on the crucial role of subclinical organ damage in determining cardiovascular risk in individuals with and without high blood pressure is available. New evidence showed that inflammation and activation of immunity are central features in the pathogenesis of atherosclerosis and also in hypertension-induced target organ damage. Recent studies have demonstrated that macrophages and various T-cell subtypes play a pivotal role in the regulation of blood pressure and target organ damage (Muller, 2011). A powerful promoter of inflammation and one of the major mediators of hypertension-induced target organ damage is also Angiotensin (Ang) II (Kvakan, 2009). European guidelines for the management of arterial hypertension from 2007 defined target organ damage by the presence of any of the following:

- electrocardiographic left ventricular hypertrophy (LVH) (Sokolow–Lyon > 38 mm; Cornell >2440 mm x ms)
- echocardiographic LVH (left ventricle mass index in men ≥ 126 g/m² and in women ≥ 110 g/m²)
- carotid wall thickening (IMT > 0.9 mm) or plaque
- ankle/brachial index <0.9
- slight increase in plasma creatinine
- males: 115–133 µmol/l (1.3-1.5 mg/dl)
- females: 107–124 µmol/l (1.2-1.4 mg/dl)
- Low estimated glomerular filtration rate (< 60 ml/min/1.73 m²) or creatinine clearance < 60 ml/min
- Microalbuminuria 30-300 mg/24 h or albumin–creatinine ratio: ≥22 (males); or ≥31 (females) mg/g creatinine

Since then, other studies proposed *home blood pressure* to be as reliable as ambulatory monitoring in predicting hypertension-induced target-organ damage, because it is superior to carefully taken office measurements (Viazzi, 2002; Stergiou, 2007). Marinakis et al. have demonstrated a relationship between heart rate variability and TOD, thus highlighting its importance in the genesis of subclinical cardiovascular disease (Marinakis, 2003). Recently, inflammation, and in particular tumor necrosis factor-α (TNF-α), has been implied in the cascade leading to TOD in patients with essential hypertension (Navarro-Gonzalez, 2008). Another study proposed the maximum value of home blood pressure to be a novel indicator of target organ damage in hypertension (Matsui, 2011).

Remodeling of small resistance arteries is also considered an early sign of target organ damage in hypertension (Cheng, 2010). The microcirculation is recognized as the site where the earliest manifestations of cardiovascular disease, especially inflammatory responses, that may play a pivotal role in driving the atherosclerotic process in conduit vessels, occur (Lockhart, 2009). Endothelial dysfunction is a predictor of a series of cardiovascular diseases (Heitzer et al, 2001; Halcox et al, 2002), although data on hypertension are still scarce (Taddei et al, 2002). Furthermore, techniques available for investigating endothelial response to various stimuli are invasive, laborious and time consuming. Finally, methods are not yet standardized and no certainty exists, that endothelial function assessed in an organ is representative of other vascular territories. However, current studies on circulating markers of endothelial activity and on endothelial cell progenitors are promising (Werner et al, 2005). This could facilitate evaluation of their prognostic role on a larger scale for more widespread clinical use. Although not traditionally considered a target organ, arterial blood vessels represent the site for the development of the atherosclerotic process that causes cardiovascular events.

Remodeling of large arteries during essential hypertension is also an early sign of organ damage. There are a number of noninvasive screening tests to identify structural and functional abnormalities of large arteries in arterial hypertension. By the time symptoms develop or clinical signs of atherosclerosis can be detected in conduit vessels, the disease process is already at an advanced stage (McVeigh, 2004; Lockhart, 2009). Remodeling of large arteries is characterized by an increase in intima-media thickness (IMT) aimed for maintaining circumferential wall stress, lumen enlargement of proximal elastic arteries, and no change in the lumen diameter of distal muscular arteries. Measurement of IMT by ultrasound examination of carotid arteries, and identification of atherosclerotic plaques, are predictors of both stroke and myocardial infarction (Salonen et al, 1993, Bots et al, 1997; Hodis et al, 1998, O`Leary et al, 1999). There is evidence that in untreated hypertensive patients without target organ damage, these alterations are common and therefore carotid ultrasound examination can detect structural damage at an early stage by routine examination. The relationship between increased carotid IMT and cardiovascular events is known, and value of IMT in the common carotid artery > 0.9 mm is considered the cut-point to emphasize the existence of structural abnormalities also in coronary arteries (Graf, 2009). Increased carotid IMT may be related to intimal or medial hypertrophy or both, and may be an adaptive response to changes in flow, wall tension, or lumen diameter (Vaudo, 2000). It is likely that ultrasound examination limited to the common carotid artery measures vascular hypertrophy only, while the evaluation and examination of bifurcation atherosclerosis and/or internal carotid artery, where plaques are most common, are more reliable for IMT

estimation. The presence of atheromatous plaques can be identified by the presence of focal increased thickness of 0.5 mm or 50% of the surrounding IMT (Zanchetti et al, 2002; Zanchetti et al, 2004).

Low ankle-arm index below 0.9 indicates the presence of peripheral arterial disease and, in general, advanced atherosclerosis (Feringa et al, 2006), while the measurement of carotid IMT can detect early changes (Zanchetti et al, 2002). However, a low ankle-arm index correlates with further development of angina, myocardial infarction, heart failure, need for coronary bypass's, stroke, need for carotid surgery and peripheral vascular level (Hiatt et al, 2001, Vogt et al, 1993) and in patients with multivessel coronary involvement it confers additional risk (Burek, 1999).

In the last 10 years, a large amount of data has been accumulated on large artery compliance and pulse wave reflection phenomenon, which have been identified as the most important pathophysiological determinants of isolated systolic hypertension and increased pulse wave velocity (Safar et al, 2003). Measurement of arterial compliance by vascular diameter changes in relation to changes in blood pressure is complex and unsuitable for clinical use. On the other hand, pulse wave velocity measurement between femoral-carotid arteries provides detailed non-invasive assessment of arterial compliance, which is simple and rigorous enough to be considered a procedure (Laurent et al, 2006). This determination is an independent predictor for overall mortality and cardiovascular morbidity, coronary events and strokes in patients with uncomplicated essential hypertension (Laurent et al, 2001, Boutouyrie et al, 2002, Laurent et al, 2003; Willum-Hansen et al, 2006). Although the relationship between aortic stiffness and coronary events is continuous, a threshold value > 12 m/s for pulse wave velocity suggests significant alterations of aortic elastic function in middle-aged hypertensives (Mancia, 2007).

Several methods for detecting vascular lesions cannot be clinically used for a variety of reasons. An elevated media-to-lumen ratio of small resistance arteries dissected from gluteal subcutaneous tissue is an indicator of increased cardiovascular risk (Rizzoni et al, 2003). These measurements can demonstrate early changes in diabetes and hypertension (Korsgaard et al, 1993, Park et al, 2001; Rizzoni et al, 2001, Schofield et al, 2002) and have predictive value for cardiovascular morbidity and mortality (Rizzoni et al, 2003), but the invasive character of the method makes this approach unsuitable for general use. Increased calcium content in coronary arteries, measured by high resolution cardiac CT was also validated by prospective studies as predictor of cardiovascular disease but its availability is limited due to high costs (Greenland et al, 2003).

Other diagnostic procedures such as magnetic resonance, cardiac scintigraphy, coronary angiography and exercise testing are reserved for specific indications. Chest X-ray can be a useful additional diagnostic method, when dyspnea is the main symptom or when looking for information on large intrathoracic arteries of the pulmonary circulation. In recent years, an increased interest was given to assessment of cardiac fibrosis. Basic techniques have used echoreflectivity (Ciulla et al., 1997; Hoyt et al., 1984). Reversed dispersion method (backscattering signal) may reflect to some extent the contractile properties of the myocardium more than collagen content, while echoreflectivity more directly correlates with histologically measured fibrosis. Echoreflectivity showed that left ventricular hypertrophy may vary and that drugs that promote its regression may differ in

reducing fibrosis (Ciulla et al, 2004). Now, the most accurate method of assessing cardiac tissue composition is nuclear magnetic resonance, whose cost, however, prevents its widespread use. Also, tissue collagen component markers are currently under investigation (Ciulla et al, 2004), but they have been shown to only partially derive from cardiac tissue.

2. Hypertension-induced retinal damage

Hypertension, if not controlled, causes injuries to blood vessels and thereby causes alterations also in the retinal microcirculation. Advanced retinopathy is nowadays confirmed as hypertension-induced target organ damage (Cohuet, 2006). Signs of hypertensive retinopathy are frequently seen in adults 40 years and older, and are predictive for stroke, congestive heart failure, and cardiovascular mortality—independently from traditional risk factors (Wong, 2007). Mild hypertensive retinopathy signs, such as generalized and focal retinal arteriolar narrowing and arteriovenous kinking, are weakly associated with systemic vascular diseases. Moderate hypertensive retinopathy signs, such as isolated microaneurysms, hemorrhages and cotton-wool spots, are strongly associated with subclinical cerebrovascular disease and predict incident clinical stroke, congestive heart failure and cardiovascular mortality, independent from blood pressure and other traditional risk factors (Wong, 2005). Clinically, signs of hypertensive retinopathy were classified into four grades of increasing severity (Keith, 1974). The correlation between retinal vascular modifications and the severity of hypertension supports the importance of using fundus oculi to improve the diagnosis and to predict future cardiovascular events (Porta, 2005). In fact, assessment of hypertensive retinopathy signs for risk stratification is supported by international hypertension management guidelines, including the US Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) and the British Society of Hypertension (Williams, 2004; Chobanian, 2003).

The pathophysiological mechanism of hypertensive retinopathy is not completely established. It seems that elevated blood pressure and other pathogenic mechanisms may be involved, such as increased oxidative stress or low-grade inflammation. Retinopathy lesions have been associated with hyperglycemia, hypertension, endothelial dysfunction and inflammation in different studies (Wong, 2007). Many studies have linked signs of hypertensive retinopathy with cognitive decline, cerebral white-matter lesions identified by cerebral MRI, lacunar infarctions, cerebral atrophy, and stroke mortality (Wong, 2002; Kwa, 2002; Wong, 2003; Mitchell, 2005; Wong, 2007). Today, retinal examination offers an excellent way to study non-invasively the effects of common vascular risk factors on small vessels and possibly for gaining a better understanding of the pathophysiological processes involved in cerebral small vessel disease (Doubal, 2009).

3. Hypertension-induced cardiac damage

Electrocardiogram is part of all routine assessment of subjects with arterial hypertension. Left ventricular hypertrophy (LVH) is one of the earlier manifestations of TOD and constitutes a powerful predictor of cardiovascular events (Agabiti-Rose, 1998). This simple test provides useful information on conduction disturbances and ischemic heart disease, conditions that might urge the performance of additional investigations and influence the choice of antihypertensive drugs. A main advantage of ECG is to allow the detection of left

ventricular hypertrophy (LVH) (Larsen, 2002; Alfakih, 2006; Waeber, 2009). Sensitivity for identifying left ventricular hypertrophy is increased but still Sokolow-Lyon index (SV1 + RV5-6 > 38 mm) or the product of QRS duration times Cornell voltage (with adjustment of 6 mm in women and a partition value of > 2440 mm × ms) are independent predictors of cardiovascular events (Levy et al, 1994). Their use as markers of cardiac damage or regression induced by treatment appears to be valuable, at least in patients over 55 years (Okin et al, 2004, Fagard et al, 2004). ECG can also be used to detect patterns of ventricular overload (indicating a severe risk) (Levy et al, 1994), ischemia, conduction disturbances and arrhythmias, including atrial fibrillation, not rare in elderly hypertensive patients. Holter electrocardiographic monitoring is indicated to detect hypertension when arrhythmias or ischemic episodes exist. It may also provide evidence of reduced heart rate variability, which can occur in severe hypertension (Mancia et al, 1983). However, its negative prognostic significance is not established, although it has been demonstrated for heart failure and post infarction (Kleiger et al, 1987, Bigger et al, 1992, La Rovere et al, 2003).

Echocardiography is more sensitive than electrocardiography in diagnosing left ventricular hypertrophy, in cardiovascular risk prediction and may help stratify global cardiovascular risk more precisely and establish therapy, although it has some technical limitations (differences between operators, poor image quality in obese patients and in patients with obstructive lung disease) (Reichek et al, 1981; Levy et al, 1990). A proper assessment includes measuring the dimensions of interventricular septum, posterior wall thickness and left ventricular end diastolic diameter of left ventricular to left ventricular mass calculation according to Devereux formula (Devereux et al, 1986). Although the relationship between left ventricular mass index and cardiovascular risk is linear, the estimates of left ventricular hypertrophy are widely used: > 134 g/m^2 for men and > 110 g/m^2 for women (Hammond, 1986). Concentric hypertrophy (increased left ventricular mass and relative wall thickness ratio >0.45), eccentric hypertrophy (relative wall thickness ratio < 0.42, with increased left ventricular mass) and concentric remodeling (relative wall thickness ratio ≥ 0.42, with normal left ventricular mass), are predictors for increased incidence of cardiovascular disease, but concentric hypertrophy is shown to provide the most cardiovascular risk increase (Jennings et al, 1997; Muiesan et al, 2004). A major advantage of echocardiography compared with ECG is better sensitivity, enabling the detection of milder degrees of LVH (Waeber, 2009). In addition, echocardiography provides a method to assess left ventricular systolic function. Ejection fraction, fractional shortening as medio-parietal endocardial and were proposed as possible additional predictors of cardiovascular events (De Simone, 1996; Aurigemma, 2001). Left ventricular diastolic filling (a measure of so-called "diastolic function") can be assessed by measuring the ratio wave Doppler E/A of transmitral blood flow, time to relax, protodiastolic pulmonary venous flow and left atrial enlargement (Swedberg, 2005). Useful information can be obtained by tissue Doppler at the mitral ring (Ogunyankin, 2006). All these determinations arouse great interest at present, because a considerable proportion (50%) of heart failures can be explained by "diastolic dysfunction" with an impaired systolic minimum and that the so-called „diastolic heart failure "is a condition with adverse prognosis. Alterations in diastolic function are common in hypertensive and elderly subjects with hypertension, at least one in four patients may be affected (Zanchetti, 2006). These changes may occur in the absence of systolic function alterations and even without left ventricular hypertrophy. There is evidence that diastolic dysfunction increases the

risk of atrial fibrillation (Tsang, 2004). Furthermore, two studies have reported that diastolic dysfunction is predictive factor for subsequent heart failure (Aurigemma, 2001) and is associated with an increased incidence of mortality (Redfield, 2003), although in another study it was shown that this combination is not independent (Bella et al, 2002). Echocardiography provides information about the presence and degree of left atrial dilation, which correlates with risk of atrial fibrillation, cardiovascular disease and death (Laukkanen, 2005; Verdecchia, 2003; Kizer, 2006). Also, data can be obtained by kinetic abnormalities of left ventricular segmentation, due to ischemia or previous infarction. A regression of left-ventricular hypertrophy on electrocardiography is indicative of substantial clinical benefit and should be an important objective of treatment (Devereaux, 2004; Okin, 2004).

4. Hypertension-induced renal damage

Diagnosis of hypertension-induced renal damage is based on the discovery of a reduced renal function and/or increased urinary albumin excretion detection (Stevens et al, 2006). Renal failure is now classified according to glomerular filtration rate, calculated by MDRD formula that includes age, gender, and race and serum creatinine of the patient (Hallan, 2004). Glomerular filtration rate values below 60 ml/min/1,73 m^2 indicate chronic kidney disease stage 3, while values below 30 ml min/l,73 m^2 indicate chronic kidney disease stage 4, and values below 15 ml/min/l,73 m^2 indicate chronic kidney disease stage 5 (Moe, 2005). Cockroft-Gault formula estimates creatinine clearance and is based on age, sex, weight and patient's serum creatinine (Cockroft and Gault, 1976). This formula is used for values > 60 ml/min, but it overestimates creatinine clearance in chronic kidney disease stage 3-5 (Moe et al, 2005). Both formulas are helpful in the detection of renal function slightly altered, where serum creatinine is still within normal limits (Moe et al., 2005). Reduced glomerular filtration rate and increased cardiovascular risk are also suggested by elevated levels of cystatin C (Shlipak, 2006). A slight increase in serum creatinine (up to 20%) can sometimes occur when initiating or changing antihypertensive therapy, but it should not be considered as a sign of progressive renal damage. Hyperuricemia is common in untreated hypertensives and has been shown to correlate with decreased renal flow and the presence of nephrosclerosis (Viazzi, 2007). While serum creatinine concentration increased or decreased estimated glomerular filtration rate shows a decrease in glomerular filtration rate, increased urinary excretion of albumin or protein indicates deterioration in the permeability of the glomerular filtration barrier.

Microalbuminuria was associated with a cluster of metabolic and nonmetabolic risk factors, suggesting that it might indicate the presence of generalized microvascular damage in patients with essential hypertension (Pontremoli, 1998). It was shown that microalbuminuria is also a predictor of diabetic nephropathy development in type 1 and 2 diabetes (Parving, 1996), while the presence of proteinuria indicates, in general, the existence of renal parenchymal lesions. In diabetic and non-diabetic hypertensive patients, microalbuminuria is a good predictor of cardiovascular events. It has been reported in some studies a linear relationship between non-cardiovascular mortality and cardiovascular and urinary protein ratio/creatinine > 3.9 mg/g in men and 7.5 mg/g in women. Thus the term microalbuminuria may be misleading (for falsely suggests a minor injury) and should be replaced with "low degree of albuminuria." Microalbuminuria can be measured by urinary

albumin concentration reporting urinary creatinine concentration (urine samples per 24 hours or the night should be discouraged because of lack of accuracy), type dipstick tests detect albuminuria above 300 mg/g creatinine and positive dipstick test for microalbuminuria in values above 30 mg/g creatinine. Microalbuminuria assessment is now recommended at the initial evaluation of a patient with hypertension. Two first-morning voided urine samples should be tested for the albumin/creatinine ratio (Redon, 2008). Microalbuminuria assessment is now recommended in a risk stratification strategy for hypertension management, since its presence indicates early organ damage and, rarely, a clustering of cardiovascular risk factors (Mancia, 2007).

5. Hypertension-induced brain damage

Until now, preclinical hypertensive lesions in the brain have not been well characterized. Microcirculation dysfunction may explain the deterioration in cognitive functions in hypertensive subjects (Cohuet, 2006). Cognitive deterioration and its end point overt dementia are, in brief, to be characterized by progressive memory loss, disorientation in time and space, loss of autonomy, and ultimately, depersonalisation/alienation (Birkenhäger, 2006). Consensus criteria recognize various syndromes, including multiple cerebral infarcts (large vessel infarcts), single infarcts, small vessel disease (multiple lacunes dementia), global hypoperfusion, and hemorrhagic dementia in the pathogenesis of vascular dementia (Cohuet, 2006). Silent brain infarction, which is cerebral target organ damage of hypertensive microangiopathies, is frequently seen in hypertensive patients (Kwon, 2007). Indeed, the degree of risk for hypertension-induced cerebrovascular disease increases progressively with the rise in BP levels (Wolf, 1991). An increased risk for cerebrovascular events in uncomplicated patients with hypertension and LVH diagnosed using both electrocardiography and echocardiography was demonstrated in the Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) study (Verdecchia, 2001). A close association has also been shown between silent stroke (evidenced by cerebral white matter lesions) and echocardiographic LVH in 62 asymptomatic middle-aged patients with hypertension (Sierra, 2002). Many epidemiologic studies have indicated a correlation between blood pressure level and cognitive decline or dementia later in life (Starr, 1993; Seux, 1998; Postner, 2002; Hanon, 2003; Piguet, 2003; Whitmer, 2005). The importance of lowering blood pressure in hypertensive subjects is well-known, but the relationship between hypertension and cognitive function is still controversial. It is believed that atherosclerosis resulting from long-standing hypertension, and cerebral hypoperfusion secondary to severe atherosclerosis may be major biological pathways linking both high blood pressure in midlife and low blood pressure in late-life to cognitive decline and dementia (Qiu, 2005).

6. Conclusion

Signs of target organ damage (TOD) should be carefully detected in all hypertensive patients because the likelihood of identifying high-risk individuals increases. Detection of any subclinical target organ damage in the coronary, peripheral, cerebral, and renal arterial beds requires therapeutic objectives and strategies in order to induce regression and improve patient prognosis.

7. References

Agabiti-Rosei E, Muiesan ML. (1998). Cardiac hypertrophy and hypertension. *Current Opinion in Nephrology and Hypertension,* Vol. 7, pp. 211–216.

Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. (2001). Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: The Cardiovascular Health Study. *Journal of the American College of Cardiology,* Vol. 37, No.4, (March, 2001), pp. 1042-1048.

Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK, Lee ET, Fabsitz RR, Howard BV, Devereux RB. (2002). Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults, The Strong Heart Study. *Circulation*, Vol. 105, No.16, (April, 2002), pp.1928-1933.

Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Kleiger RE, Rottman JN. (1992). Frequency domain measures of heart period variability and mortality after myocardial infarction. *Circulation,* Vol. 85, No.1, (January, 1992), pp. 164-171.

Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. (1997). Common carotid intima-media thickness and risk of stroke and myocardial infarction: The Rotterdam Study. *Circulation*, Vol. 96, (September, 1997), pp. 1432-1437.

Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, Laurent S. (2002). Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. *Hypertension,* Vol. 39, No.1, (January, 2002), pp. 10-15.

Burek KA, Sutton-Tyrrell K, Brooks MM, Naydeck B, Keller N, Sellers MA, et al. (1999). Prognostic importance of lower extremity arterial disease in patients undergoing coronary revascularization in the Bypass Angioplasty Revascularization Investigation (BARI). *Journal of the American College of Cardiology,* Vol. 34, No.3, (September, 1999), pp. 716-721.

Cheng, Cynthiaa; Daskalakis, Constantineb; Falkner, Bonitac, Alterations in capillary morphology are found in mild blood pressure elevation, *Journal of Hypertension,*Vol.28, No.11, (November, 2010), pp. 2258–2266.

Ciulla MM, Paliotti R, Esposito A, Diez J, Lopez B, Dahlof B, et al. (2004). Different effects of antihypertensive therapies based on losartan or atenolol on ultrasound and biochemical markers of myocardial fibrosis: results of a randomized trial. *Circulation,* Vol. 110, No.5, (August, 2004), pp. 552-557.

Ciulla MM, Paliotti R, Hess DB, Tjahja E, Campbell SE, Magrini F, Weber KT. (1997) Echocardiographic patterns of myocardial fibrosis in hypertensive patients: endomyocardial biopsy versus ultrasonic tissue characterization. *Journal of the American Society of Echocardiography,* Vol. 10, No.6, (July-August, 1997), pp. 657-664.

Chobanian AV, Bakris GL, Black H.R et al. (2003).The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC7 Report. *Journal of the American Medical Association,* Vol. 289, pp. 2560–2572.

Cockroft DW, Gault MH. (1976). Prediction of creatinine clearance from serum creatinine, *Nephron,* Vol. 16, No.1, pp. 31-41.

Cohuet G, Struijker-Boudier H. (2006). Mechanisms of target organ damage caused by hypertension: therapeutic potential. *Pharmacology and Therapeutics,* Vol. 111, No.1, (July, 2006), pp. 81–98.

De Simone G, Devereux RB, Koren MJ, Mensah GA, Casale PN, Laragh JH. (1996). Midwall left ventricular mechanics, an independent predictor of cardiovascular risk in arterial hypertension. *Circulation,* Vol. 93, No.2, (January, 1996), pp.259-265.

Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N.(1986). Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *American Journal of Cardiology,* Vol. 57, No.6, (February, 1986), pp. 450-458.

Devereux RB, K Watchell and E Gerdts, et al. (2004). Prognostic significance of left ventricular mass change during treatment of hypertension. *Journal of the American Medical Association,* Vol. 292**,** No.19, (November, 2004), pp. 2386–2388.

Doubal FN, Hokke PE; Wardlaw, JM. (2009). Retinal microvascular abnormalities and stroke: a systematic review. *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 80, No.2, (February, 2009), pp. 158–165.

Fagard RH, Staessen JA, Thijs L, Celis H, Birkenhager WH, Bulpitt CJ, et al. (2004). Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Prognostic significance of electrocardiographic voltages and their serial changes in elderly with systolic hypertension, *Hypertension,* Vol. 44, No.4, (October, 2004), pp. 459-464.

Feringa HH, Bax JJ, van Waning VH, Boersma E, Elhendy A, Schouten O, et al. (2006). The long-term prognostic value of the resting and post exercise ankle-brachial index. *Archive of Internal Medicine,* Vol. 166, No.5, (March, 2006), pp.529-535.

Graf IM, Schreuder, FHBM J.M. Hameleers, JM, Mess WH, Reneman RS Hoeks APG. (2009). Wall irregularity rather than intima-media thickness is associated with nearby atherosclerosis. Ultrasound in *Biology and Medicine,* Vol. 35, No. 6 (2009), (June, 2009), pp. 955–961.

Greenland P, Gaziano JM. (2003). Clinical practice, Selecting asymptomatic patients for coronary computed tomography or electrocardiographic exercise testing, *The New England Journal of Medicine,* Vol. 349, (July, 2003), pp. 465-473.

Halcox JP, Schenke WH, Zalos G, Mincemoyer R, Prasad A, Waclawiw MA, et al. (2002). Prognostic value of coronary vascular endothelial dysfunction, *Circulation*, Vol. 106, No.6, (August, 2002), pp. 653-665.

Hallan S, Asberg A, Lindberg M, Johnsen H. (2004). Validation of the Modification of Diet in Renal Disease formula for estimating GFR with special emphasis on calibration of the serum creatinine assay. *American Journal of kidney disease*, Vol. 44, (July, 2004), pp. 84-93.

Hammond IW, Devereux RB, Alderman MH, Lutas EM, Spitzer MC, Crowley JS, Laragh JH. (1986). The prevalence and correlates of echocardiographic left ventricular hypertrophy among employed patients with uncomplicated hypertension. *Journal of the American College of Cardiology,* Vol. 7, pp. 639–650.

Hanon, O., Seux, M. L., Lenoir, H., Rigaud, A. S., & Forette, F. (2003). Hypertension and dementia. *Current Cardiology Reports,* Vol. 5, pp. 435–440.

Heitzer T, Schlinzig T, Krohn K, Meinertz T, Munzel T. (2001). Endothelial dysfunction, oxidative stress, and risk of cardiovascular events in patients with coronary artery disease. *Circulation,* Vol. 104, pp.2673–2678.

Hiatt WR. (2001). Medical treatment of peripheral arterial disease and claudication. *The New England Journal of Medicine,* Vol. 344, pp. 1608-1621.

Hodis HN, Mack WJ, LaBree L, Selzer RH, Liu CR, Liu CH, Azen SP. (1998). The role of carotid arterial intima-media thickness in predicting clinical coronary events, *Annals of InternalMedicine,* Vol. 128, (February, 1998), pp. 262-269.

Houghton JL, Frank MJ, Carr AA, von Dohlen TW, Prisant LM. (1990). Relations among impaired coronary flow reserve, left ventricular hypertrophy and thallium perfusion defects in hypertensive patients without obstructive coronary artery disease. *Journal of the American College of Cardiology,* Vol. 15, No.1, (January, 1990), pp. 43–51.

Hoyt RM, Skorton DJ, Collins SM, Melton HE. (1984). Ultrasonic backscatter and collagen in normal ventricular myocardium, *Circulation*, Vol. 69, pp.775-782.

Jennings G, Wong J. (1997). Reversibility of left ventricular hypertrophy and malfunction by antihypertensy treatment. In: Hansson L, Birkenhager WH (editors). Handbook of Hypertension. Amsterdam: Elsevier Science; Vol. 18, pp. 184-223.

Keith NM, Wagener HP, Barker NW. (1974). Some different types of essential hypertension: their course and prognosis. *American Journal of Medical Science,* Vol.268, (December, 1974), pp. 336–45.

Kizer JR, Bella JN, Palmieri V, Liu JE, Best LG, Lee ET, et al. (2006). Left atrial diameter as an independent predictor of fi rst clinical cardiovascular events in middle-aged and elderly adults: the Strong Heart Study (SHS). *American Heart Journal,* Vol.151, No.2, (February, 2006), pp. 412-418.

Kleiger RE, Miller JP, Bigger JT Jr, Moss AJ, for the Multicentre Post-Infarction Research Group. (1987). Decreased heart rate variability and its association with increased mortality after acute myocardial infarction, *American Journal of Cardiology,* Vol. 59, No.4, (February, 1987), pp. 256-262.

Korsgaard N, Aalkjaer C, Heagerty AM, Izzard AS, Mulvany MJ. (1993). Histology of subcutaneous small arteries from patients with essential hypertension, *Hypertension* Vol. 22, No.4, (October, 1993), pp. 523-526.

Kvakan H, Luft FC, Muller DN. (2009). Role of the Immune System in Hypertensive Target Organ Damage. *Trends in Cardiovascular Medicine.* Vol. 19, No.7, (October, 2009), pp. 242-246.

Kwa VI, van der Sande JJ, Stam J, Tijmes N, Vrooland JL. (2002). Amsterdam Vascular Medicine G. Retinal arterial changes correlate with cerebral small-vessel disease. *Neurology,* Vol. 59, No.10, (November, 2002), pp. 1536–40.

Kwon H-M, Kim BJ, Oh JY, et al. (2007). Retinopathy as an indicator of silent brain infarction in asymptomatic hypertensive subjects. *Journal of the Neurological Science,* Vol. 252, No.2, (January, 2007), pp. 159–162.

La Rovere MT, Pinna GD, Maestri R, Mortara A, Capomolla S, Febo O, et al. (2003). Short-term heart rate variability strongly predicts sudden cardiac death in chronic heart failure patients. *Circulation*, Vol. 107, No.4, (February, 2003), pp. 565-570.

Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. (2006). American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography. European Society of Cardiology. Recommendations for chamber quantification. *European Journal of Echocardiography,* Vol. 7, (March, 2006), pp. 79-108.

Larsen CT, Dahlin J, Blackburn H, Scharling H, Appleyard M, Sigurd B, et al. (2002). Prevalence and prognosis of electrocardiographic left ventricular hypertrophy, ST segment depression and negative T-wave; the Copenhagen City Heart Study. *European Heart Journal,* Vol. 23, No.4, (February, 2002), pp.315–324.

Laukkanen JA, Kurl S, Eranen J, Huttunen M, Salonen JT. (2005). Left atrium size and the risk of cardiovascular death in middle-aged men. *Archive of Internal Medicine,* Vol. 165, No.15, (August, 2005), pp. 1788-1793.

Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. (2001).Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension,* Vol. 37, (May, 2001), pp. 1236-1241.

Laurent S, Cockcrof J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. (2006). On behalf of the European Network for non invasive investigation of large arteries. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *European Heart Journal,* Vol. 27, pp.2588-2605.

Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. (1990). Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study, *The New England Journal of Medicine,* Vol. 322, (May, 1990), pp. 1561-1566.

Levy D, Salomon M, D'Agostino RB, Belanger AJ, Kannel WB. (1994). Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. *Circulation,* Vol.90, (October, 1994), pp. 1786-1793.

Lockhart CJ, Hamilton PK, Quinn CE and McVeigh GE. (2009). End-organ dysfunction and cardiovascular outcomes: the role of the microcirculation. *Clinical Science (London)* Vol. 116, (February, 2009), pp.175–190.

Mancia G, Ferrari A, Gregorini L, Parati G, Pomidossi G, Bertinieri G, et al. (1983). Blood pressure and heart rate variabilities in normotensive and hypertensive human beings. *Circulation Research,* Vol. 53, (July, 1983), pp. 96–104.

Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. (2007). Management of Arterial Hypertension of the European Society of Hypertension; European Society of Cardiology. 2007 guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Journal of Hypertension,* Vol.25, (June, 2007), pp.1105–1187.

Marinakis A.G., G.P. Vyssoulis and E.A. Karpanou, et al. (2003). Heart rate and blood pressure variability are predictors of target organ damage in arterial hypertension. *American Journal of Hypertension*, Vol. 16, p. 246A.

Matsui Y, Ishikawa J, Eguchi K, Shibasaki S, Shimada K, Kario K. (2011). Maximum value of home blood pressure: a novel indicator of target organ damage in hypertension. *Hypertension.* Vol. 57, No.6, (June, 2011), pp.1087-1093.

McVeigh, G. E., Plumb, R. and Hughes, S. (2004). Vascular abnormalities in hypertension: cause, effect, or therapeutic target? *Current Hypertension Reports,* Vol. 6, (June, 2004), pp. 171–176.

Mitchell P, Wang JJ, Wong TY, Smith W, Klein R, Leeder SR. (2005). Retinal microvascular signs and risk of stroke and stroke mortality. *Neurology,* Vol. 65, pp. 1005–09.

Moe S, Drueke T, Cunningham J, Goodman W, Martin K, Olgaard K, et al. (2005). Kidney Disease: Improving Global Outcomes (KDIGO). Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney International,* Vol. 67, (June, 2005), pp. 2089-2100.

Muiesan ML, Salvetti M, Monteduro C, Bonzi B, Paini A, Viola S et al. (2004). Left ventricular concentric geometry during treatment adversely affects cardiovascular prognosis in hypertensive patients. *Hypertension,* Vol. 43, No.4, (April, 2004), pp. 731-738.

Muller DN, Kvakan H, Luft FC. (2011). Immune-related effects in hypertension and target-organ damage. *Current opinion in nephrology and hypertension.* Vol. 20, No.2, (March, 2011), pp.113-117.

Navarro-Gonzalez J.F, C. Mora, M. Muros, A. Jarque, H. Herrera and J. Garcia, (2008). Association of tumor necrosis factor-alpha with early target organ damage in newly diagnosed patients with essential hypertension. *Journal of Hypertension,* Vol. 26, pp. 2168–2175.

O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. (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. *The New England Journal of Medicine,* Vol. 340, pp. 14-22.

Ogunyankin KO, Burggraf GW, Abiose AK, Malik PG. (2006). Validity of revised Doppler echocardiographic algorithms and composite clinical and angiographic data in diagnosis of diastolic dysfunction. *Echocardiography,* Vol. 23, pp. 817-828.

Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS. (2004). LIFE Study Investigators. Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events. *Journal of the American Medical Association,* Vol. 292, No.19, (November, 2004), pp. 2343-2349.

Park JB, Schiffrin EL. (2001). Small artery remodeling is the most prevalent form of target organ damage in mild essential hypertension. *Journal of Hypertension,* Vol. 19, (May, 2001), pp. 921-930.

Parving HH. (1996). Initiation and progression of diabetic nephropathy, *The New England Journal of Medicine,* Vol. 335, (November, 1996), pp. 1682-1683.

Piguet O, Grayson DA, Creasey H, et al. (2003). Vascular risk factors, cognition and dementia incidence over 6 years in the Sydney Older Persons Study. *Neuroepidemiology,* Vol. 22, (May-June, 2003), pp. 165–171.

Porta, M., Grosso, A., & Veglio, F. (2005). Hypertensive retinopathy: there's more than meets the eye. *Journal of Hypertension,* Vol. 23, (April, 2005), pp. 683–696.

Pontremoli R, Nicolella C, Viazzi F, Ravera M, Sofia A, Berruti V, et al. (1998). Microalbuminuria is an early marker of target organ damage in essential hypertension. *American Journal of Hypertension,* Vol. 1, (April, 1998), pp. 430–438.

Posner, H. B.; Tang, M. X.; Luchsinger, J., Lantigua, R., Stern, Y., & Mayeux, R. (2002). The relationship of hypertension in the elderly to AD, vascular dementia, and cognitive function. *Neurology,* Vol. 58, No. 8, (April, 2002), pp. 1175– 1181.

Qiu C, Winblad B Fratiglioni, L. (2005). The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurology*, Vol. 4**,** No.8, (August, 2005), pp. 487–499.

Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. (2003). Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *Journal of the American Medical Association,* Vol. 289, No.2, (January, 2003), pp. 194-202.

Reichek N, Devereux RB. (1981). Left ventricular hypertrophy: relationship of anatomic, echocardiographic and electrocardiographic findings. *Circulation*, Vol. 63, No.6, (June, 1981), pp. 1391-1398.

Rizzoni D, Porteri E, Boari GE, De Ciuceis C, Sleiman I, Muiesan ML, et al. (2003). Prognostic significance of small-artery structure in hypertension. *Circulation,* Vol. 108, No.18, (November, 2003), pp.2230-2235.

Rizzoni D, Porteri E, Guelfi D, Muiesan ML, Valentini U, Cimino A, et al. (2001). Structural alterations in subcutaneous small arteries of normotensive and hypertensive patients with non-insulin-dependent diabetes mellitus. *Circulation*, Vol. 103, (March, 2001), pp. 1238-1244.

Ruilope LM. (2011). Normotension, blood pressure variability and early target organ damage. *Hypertension research.* Vol. 34, No.10, (July, 2011), pp. 1075.

Safar ME, Levy BI, Struijker-Boudier H. (2003). Current perspectives on arterial stiffness and pulse pressure in hypertension and cardiovascular diseases, *Circulation,* Vol. 107, No.22, (June, 2003), pp. 2864-2869.

Salonen JT, Salonen R. (1993). Ultrasound B-mode imaging in observational studies of atherosclerotic progression, *Circulation*, Vol. 87 (Suppl II), (March, 1993), pp. II56-II65.

Schofield I, Malik R, Izzard A, Austin C, Heagerty A. (2002). Vascular structural and functional changes in type 2 diabetes mellitus: evidence for the roles of abnormal myogenic responsiveness and dyslipidemia. *Circulation*, Vol. 106, No. 24, (December, 2002), pp. 3037-3043.

Seux, M.L.; Thijs, L.; Forette, F.; Staessen, J. A.; Birkenhager, W.H.; Bulpitt, C.J.; et al. (1998). Correlates of cognitive status of old patients with isolated systolic hypertension: The Syst-Eur Vascular Dementia Project. *Journal of Hypertension,* Vol. 16, (July, 1998), pp. 963–969.

Sierra CA. de la Sierra, J.C. Pare, E. Gomez-Angelats and Coca A. (2002). Correlation between silent cerebral white matter lesions and left ventricular mass and geometry in essential hypertension. *American Journal of Hypertension,* Vol. 15**,** No.6, (June, 2002), pp. 507–512.

Shlipak MG, Katz R, SarnakMJ, Fried LF, Newman AB, Stehman- Breen C, et al. (2006). Cystatin C and prognosis for cardiovascular and kidney outcomes in elderly persons without chronic kidney disease, *Annals of Internal Medicine,* Vol. 145, (August, 2006), pp. 237-246.

Starr, J. M., Whalley, L. J., Inch, S., & Shering, P. A. (1993). Blood pressure and cognitive function in healthy old people. *Journal of the American Geriatrics Society,* Vol. 41, No.7, (July, 1993), 753– 756.

Stergiou GS, Argyraki KK, Moyssakis I, Mastorantonakis SE, Achimastos AD, Karamanos VG, Roussias LG. (2007). Home blood pressure is as reliable as ambulatory blood pressure in predicting target-organ damage in hypertension. *American Journal of Hypertension*, Vol. 20, pp.616–621.

Stevens LA, Coresh J, Greene T, Levey AS. (2006). Assessing kidney function measured and estimated glomerular filtration rate. *The New England Journal of Medicine,* Vol. 354, pp. 2473-2483.

Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M et al. (2005). Task Force for the Diagnosis, Treatment of Chronic Heart Failure of the European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005). The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *European Heart Journal,* Vol. 26, No.11, (June, 2005), pp.1115-1140.

Taddei S, Salvetti A. (2002). Endothelial dysfunction in essential hypertension: clinical implications. *Journal of Hypertension,* Vol. 20, No.9, (September, 2002), pp. 1671-1674.

Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. (2004). Risks for atrial fibrillation and congestive heart failure in patients > 65 years of age with abnormal left ventricular diastolic relaxation, *American Journal of Cardiology,* Vol. 93, No.1, (January, 2004), pp.54-58.

Verdecchia, P. Porcellati, C., Reboldi, G. Gattobigio, R. Borgioni, C. Pearson T.A.Ambrosio, G. (2001). Left ventricular hypertrophy as an independent predictor of acute cerebrovascular events in essential hypertension. *Circulation*, Vol. 104**,** No.17, (October, 2001), pp. 2039–2044.

Verdecchia P, Reboldi G, Gattobigio R, Bentivoglio M, Borgioni C, Angeli F, et al. (2003). Atrial fibrillation in hypertension: predictors and outcome. *Hypertension,* Vol. 41, No. 2, (February, 2003), pp. 218-223.

Viazzi, F. Leoncini G. Parodi, D. et al. (2002). Pulse pressure and subclinical cardiovascular damage in primary hypertension. *Nephrology Dialysis and Transplant*, Vol. 17**,** No.10, (October, 2002), pp. 1779–1785.

Viazzi F, Leoncini G, Ratto E, Falqui V, Parodi A, Conti N, et al. (2007). Mild hyperuricaemia and subclinical renal damage in untreated primary hypertension. *American Journal of Hypertension*, Vol. 20, No.12, (December, 2007), pp. 1276–1282.

Vogt MT, Cauley JA, Newman AB, Kuller LH, Hulley SB. (1993). Decreased ankle/arm blood pressure index and mortality in elderly women. *Journal of the American Medical Association,* Vol. 270, No.4, (July, 1993), pp. 465-469.

Vaudo G, Schillaci G, Evangelista F, Pasqualini L, Verdecchia P, Mannarino E. (2000). Arterial wall thickening at different sites and its association with left ventricular hypertrophy in newly diagnosed essential hypertension. *American Journal of Hypertension*, Vol. 13, (April, 2000), pp. 324-331.

Waeber B, de la Sierra A, Ruilope LM. (2009). Target organ damage: how to detect it and how to treat it? *Journal of Hypertension,* Vol. 27 (Suppl 3), (June, 2009), pp.S13 – S18.

Werner N, Kosiol S, Schiegl T, et al. (2005). Circulating endothelial progenitor cells and cardiovascular outcomes. *The New England Journal of Medicine,* Vol. 353, No.10, (September, 2005), pp. 999–1007.

Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, Jeppesen J. (2006). Prognostic value of aortic pulse wave velocity as index of arterial stiff ness in the general population. *Circulation,* Vol. 113, (February, 2006), pp. 664-670.

Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS, Thom SM. (2004). British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *British Medical Journal,* Vol. 328, (March, 2004), pp. 634–640.

Whitmer RA, Sidney S, Selby J, Johnston SC, Yaffe K. (2005). Midlife cardiovascular risk factors and risk of dementia in late life. *Neurology,* Vol. 64, No.2, (January, 2005), pp. 277–181.

Wong TY, McIntosh R, Wong TY, McIntosh R. (2005). Hypertensive retinopathy signs as risk indicators of cardiovascular morbidity and mortality. *British Medical Bulletin.* Vol.73–74, (September, 2005), pp. 57 -70.

Wong TY, Klein R, Sharrett AR, et al. (2002). Retinal microvascular abnormalities and cognitive impairment in middle-aged persons: the Atherosclerosis Risk in Communities Study. *Stroke,* Vol. 33, No.6, (June, 2002), pp. 1487–1492.

Wong TY, Klein R, Sharrett AR, et al. (2002). Cerebral white matter lesions, retinopathy, and incident clinical stroke. *Journal of the American Medical Association,* Vol. 288, No.1, (July, 2002), pp. 67–74.

Wong TY, Mosley TH Jr, Klein R, et al. (2003). Retinal microvascular changes and MRI signs of cerebral atrophy in healthy, middle-aged people. *Neurology*, Vol. 61, (September, 2003), pp. 806–811.

Wong TY, Klein R, Nieto FJ, et al. (2003). Retinal microvascular abnormalities and 10-year cardiovascular mortality: a population-based case-control study. *Ophthalmology,* Vol. 110, (May, 2003), pp. 933–940.

Zanchetti A, Agabiti-Rosei E, Ambrosioni E, Chiariello N, Leonetti G, Mancia G, et al. (2006). Left ventricular diastolic dysfunction in a cohort of hypertensive patients attending hospital outpatient clinics in Italy, the APROS-DIADYS project. *Journal of Hypertension,* Vol. 25, No.10, (suppl 6), (October, 2007), pp. 2158-2167.

Zanchetti A, Bond MG, Hennig M, Neiss A, Mancia G, Dal Palu C. (2002). European Lacidipine Study on Atherosclerosis investigators. Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis: principal results of the European Lacidipine Study on Atherosclerosis (ELSA), a randomized, double-blind, longterm trial. *Circulation*, Vol. 106, No.19, (November, 2002), pp. 2422-2427.

Zanchetti A, Bond MG, Hennig M, Tang R, Hollweck R, Mancia G. et al. (2004). ELSA Investigators. Absolute and relative changes in carotid intima-media thickness and atherosclerotic plaques during long-term antihypertensive treatment: further results of the European Lacidipine Study on Atherosclerosis (ELSA). *Journal of Hypertension*, Vol. 22, No.6, (June, 2004), pp. 1201-1212.
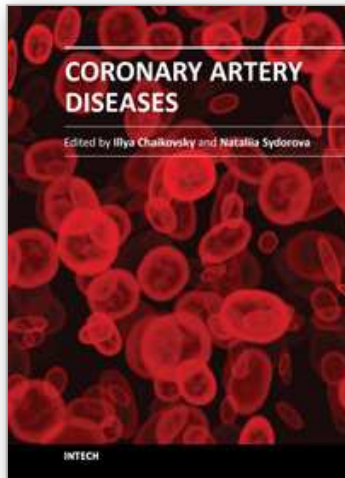
Coronary Artery Diseases

Edited by Dr. Illya Chaikovsky

This book has "wide geography" both literally and figuratively. First of all, this book brings together contributions from around the world, both from post-industrial countries and developing world. This is natural, because coronary artery disease is becoming pandemic worldwide. CAD is the single most frequent cause of death in developed countries, causes about 1 in every 5 deaths. Mortality from cardiovascular disease is predicted to reach 23.4 million in 2030. Moreover, in the developing world, cardiovascular disease tends to affect people at a younger age and thus could negatively affect the workforce and economic productivity. The morbidity, mortality, and socioeconomic importance of CAD make its diagnosis and management fundamental for all practicing physicians. On another hand, the book widely represents "geography" of CAD itself, i.e. many various aspects of its pathophysiology, epidemiology, diagnosis, treatment are touched in this book. This book does not pretend on complete and integral description of the Coronary artery disease. Rather, it contains selected issues on this complex multifactorial disease. Nevertheless, we hope that readers will find Coronary Artery Disease useful for clinical practice and further research.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Corina Şerban, Ruxandra Christodorescu, Alexandru Caraba, Germaine Săvoiu, Carmen Cristescu and Simona Drăgan (2012). Specific Features of Target Organ Damage in Patients with Arterial Hypertension and Coronary Artery Disease, Coronary Artery Diseases, Dr. Illya Chaikovsky (Ed.), ISBN: 978-953-51-0238-0, InTech, Available from: http://www.intechopen.com/books/coronary-artery-diseases/specific-features-of-target-organ-damage-in-patients-with-arterial-hypertension-and-coronary-artery-

INTECH
open science | open minds