Central blood pressure is dependent on the stiffness of large arteries and pulse wave reflection. These parameters are very important in the development of hypertensive target organ disease. Moreover, recent clinical studies have shown their independent predictive value for cardiovascular morbidity and mortality. Therefore, 2007 guidelines for the management of hypertension inserted the evaluation of central arterial stiffness as an important component for assessing total cardiovascular risk. Differences in the way various antihypertensive drugs affect arterial stiffness and central hemodynamics may explain the greater cardiovascular protection provided by newer drugs (eg, renin-angiotensin system blockers or calcium channel blockers) independent of peripheral blood pressure reduction, as shown by recent clinical studies. However, the predictive value of the attenuation of arterial stiffness, wave reflections, and central blood pressure still needs to be confirmed in prospective, long-term, large-scale therapeutic trials. Thus, whether these measurements should be routinely performed as a diagnostic or therapeutic indicator remains debatable.

Introduction
The treatment of hypertension is based on brachial artery blood pressure (BP) values [1•]. This behavior is supported by a meta-analysis involving almost 1 million persons enrolled in 61 prospective observational studies, which demonstrated a relationship between cuff systolic and diastolic BP and cardiovascular mortality in middle-aged and elderly adults without previous overt vascular disease [2]. Moreover, clinical trials indicated that lowering brachial BP with antihypertensive drugs effectively reduces the risk of cardiovascular outcomes [3,4]. Regarding the benefits of individual drug classes, clinical trials did not show significant differences in total cardiovascular events among regimens based on angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, diuretics, or β-blockers, as long as similar brachial BP reductions were achieved, although there were some differences in specific outcomes [3,5]. Nevertheless, the recent guidelines for the management of essential hypertension inserted the evaluation of central arterial stiffness among the quantification of target organ damage, as an important component for assessing the total cardiovascular risk in hypertensive patients, because of its proven prognostic value [1•,6••].

Large-artery arterial stiffness and pulse wave reflection influence central BP, which is the pressure exerted directly on the brain and on the heart [7]. Beyond their pathophysiologic importance in determining the development of cardiovascular disease, knowledge of central pressure and pulse wave characteristics may be important to fully assess optimal cardiovascular drug therapy [8]. Indeed, some clinical studies have shown greater cardiovascular protection by newer drugs than by β-blockers [9,10], independently of brachial BP reduction, suggesting that they may have a different effect on central hemodynamics.

Arterial Stiffness, Wave Reflection, and Central Blood Pressure
According to the “Windkessel” model, which distinguishes the “conduit” and “cushioning” functions of the arterial tree, hypertension is characterized by an increase in peripheral resistance and a decrease in arterial compliance. When peripheral resistance is increased, mean BP rises, with an increment in systolic and diastolic BP. When arterial compliance is reduced, mean BP is unchanged, but BP oscillations...
heterogeneity, which is caused by the molecular, cellular, and histologic structure of the arterial wall [15•], has important physiologic and pathophysiologic consequences. The pressure wave is progressively amplified from central to distal conduit arteries because peripheral arteries are smaller and stiffer and reflection sites are closer, leading the reflected waves to be added onto the forward wave. The result is that the amplitude of the pressure wave is higher, the so-called amplification phenomenon [16,17]. For this reason, it is actually inaccurate to use brachial pressure as a measure of central pressure, particularly in young subjects. The usual stiffness gradient between central and peripheral arteries can be reduced or even reversed with aging or disease [18].

Methods of assessment
As already mentioned, the 2007 Guidelines for the Management of Arterial Hypertension of the European Societies of Cardiology and of Hypertension included arterial stiffness, measured as carotid to femoral pulse wave velocity (PWV), as an intermediate end point in evaluating target organ damage [1•]. Carotid–femoral PWV is considered to be the “gold standard” measurement of arterial stiffness, as it is the simplest noninvasive and reproducible method and has the largest amount of clinical evidence, providing the predictive value of aortic stiffness for cardiovascular events [6••]. Indeed, the aorta is a major vessel of interest when determining arterial stiffness because it makes the largest contribution to the arterial buffering function [6••,7] and is responsible for most of the pathophysiologic effects of central pressure and arterial stiffness on the left ventricle, brain, and kidney.

PWV can be measured from various different waveforms, including pressure, distension, and flow [6••]. Waveforms are usually obtained transcutaneously at the common carotid artery and the femoral artery. The distance (D) covered by the waves is assimilated to the surface distance between the two recording sites, and the time delay (Dt or transit time) measured between the feet of the two waveforms. PWV is then calculated as the ratio of the distance to the time delay: \( \text{PWV} = \frac{D}{Dt} \) (seconds). The waveforms can be recorded simultaneously (with the Complior System [Colson; Les Lilas, France], for example) or sequentially, with an electrocardiogram as reference point (using a system such as the SphygmoCor System [ArtCor; Sydney, Australia]).

As previously described, the arterial pressure waveform is a composite of the forward pressure wave, created by ventricular contraction, and a reflected wave—actually a composite of many reflected “wavelets.” When vessels are elastic, PWV is low and the reflected wave arrives back to the aortic root during late systole, adding mostly to the diastolic part of the wave. When arteries are stiff, however, PWV rises and the reflected wave arrives back at the central arteries earlier, adding to the forward wave and augmenting the systolic pressure (Fig. 1). This phenomenon can be quantified through the augmentation index (Alx), defined as the difference between the second

![Figure 1. The effect of arterial stiffening on systolic blood pressure (top), which is increased by reduction of systolic expansion, increase in forward wave, and reflected wave velocity along the aorta (bottom).](image)