Arterial Stiffness, Vascular Disease, and Risk of Cardiovascular Events

Jay N. Cohn, MD

Most cardiovascular morbid events are the consequence of a progressive vascular disease called atherosclerosis. This disease begins at an early age, probably initially with a defect or injury of the arterial endothelial protective function, and progresses with structural remodeling in the microcirculation and cellular and lipid accumulation in conduit arteries complicated by calcification, plaque formation, and, ultimately, plaque rupture as a precipitating factor for clot formation and acute morbid events. The rate of progression of this process is highly variable but may extend over many decades. Furthermore, aging changes, pressure effects, and atherosclerotic changes become inextricably intertwined.

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Because it is now possible to slow progression of this vascular disease with a number of pharmacological agents and possibly with lifestyle alterations, the discovery of markers that can identify the disease in asymptomatic individuals could facilitate appropriate intervention. The wall of the artery is the primary site of the disease process and has therefore become an attractive target for demonstrating functional or structural alterations that may precede the morbid events.

Noninvasive assessment of the arterial vasculature suitable for screening has been practiced since the development of the blood pressure cuff. Unfortunately, the ease of blood pressure measurement and the demonstration of its correlation with morbid events inhibited for many years the development of methods to more directly assess the arteries. Recently, there has been growing recognition that the disease of interest is in the arteries and that elevated blood pressure, although it may serve as a crude surrogate for arterial disease, is neither a sensitive nor a specific guide to its presence. Therefore, a number of noninvasive methods have been introduced to gain better insight into the abnormalities in the wall of the artery that can define the atherosclerotic process. It is important to begin with the recognition that atherosclerosis is a systemic vascular disease that results in functional and structural abnormalities in the entire arterial vasculature. Certain vascular areas, particularly the coronary and cerebral circulations, precipitate most morbid events, and the rate of progression may vary in different vascular beds in different individuals. The relative role of genes and environment in this variability is unclear, but abnormalities that mark the disease are usually discernible in any vascular area studied.

In this issue of Circulation, 2 European groups, the Rotterdam Study group and the Danish participants in the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) health survey, report that aortic pulse-wave velocity (PWV), a measure of aortic wall stiffness, provides prognostic information above and beyond that from traditional risk factors, including age, gender, blood pressure, cholesterol, diabetes mellitus, and smoking. These data provide further support for the concept that the biological process in the artery wall is a better guide to future cardiovascular morbid events than standard risk factors that epidemiologists have identified as statistically related to such events. These publications therefore raise important questions that must be addressed.

What Are the Determinants of PWV?

PWV as measured in these studies represents the velocity of the pulse wave transit from the carotid artery (equivalent to the aortic arch) to the femoral artery. Thus, it is a measure of stiffness of the aorta, an elastic artery with muscular contributions to its compliance. PWV is dependent not only on structural changes that alter stiffness or elastic modulus of the wall, which influences wave propagation, but also on caliber increases, which slow velocity, and on aortic pressure, which has a powerful direct relationship to stiffness. In general, thickening of the wall should reduce compliance, increase stiffness, and accelerate wave velocity. Thickening of the wall is characteristic of aging, of systolic hypertension, and of the increased intimal-medial thickness associated with atherosclerosis. Decreased compliance of the aorta results in higher systolic pressure, wider pulse pressure, and more rapid return of reflected waves to the root of the aorta, where they may further augment late systolic pressure.

The relationship between PWV and morbid cardiovascular events in these studies, therefore, could at least in part reflect the older age and higher blood pressure associated with increased PWV. The authors have attempted to correct for these influences and conclude that the PWV is an independent predictor of morbid events. Does that mean that aortic stiffness is contributing to the disease, as suggested by the Rotterdam Study group? Or does it merely imply that the vascular abnormality detected in the aorta is also present in other vascular beds and that its magnitude identifies the disease process better than chronological age, blood pressure,
胆固醇，以及其他因素，这些因素在统计学上与疾病有关。

**Is PWV the Best Measurement of Arterial Stiffness?**

结构变化可能在主动脉中是一个晚期表现，就如动脉粥样硬化疾病，这就是阻塞性斑块在传导动脉中代表了疾病，这种疾病可能更早被检测到。因为血管疾病可能有起源于内皮功能障碍，这种改变对微血管和小肌肉传导动脉有深远影响，评估动脉的血管功能，这种功能可以被检测到数周到数月。如果一个压力、一个狭窄的动脉评估，此外，这种测量可能比PWV更好检测早期疾病。

一个非侵入性方法已经被开发，而且有些在广泛使用。大多数依赖于动脉脉冲波分析，使用一个压电传感器被放在可触及的动脉上，通常在直径动脉。脉冲波所提供的“窗口”进入动脉系统，因此，这种假设是这种血管功能的改变是疾病的一种系统过程，依赖于它的表现和结构的整体血管内膜。

小动脉的硬化，作为血管内膜或结构改变的表现，改变的幅度和时间的反射波，在很大程度上依赖于计算机分析的收缩压下降。在某些情况下，这些方法是更容易被接受的用户，这种分析可以在5-10分钟完成，这种技术可以被广泛应用于大规模的筛选。初步的研究已经证明了小动脉内膜完整性和张力的独立性，与年龄和血压有关。

一个关于最佳方法的决定测量动脉僵硬度是临床问题。因为动脉硬化是一个标志疾病，它可能作为在欧洲队列中，作为预测性指标，预测新的5-10年事件。如果一个问题的早期识别血管异常的表现来启动预防性治疗的，那么，我们会在一个较小的动脉评估，这可以通过早期的标记，对血管疾病，识到它的预测价值是可以被改变的。如果一个兴趣在一个测量的僵硬度，这可能对有效治疗，独立于血压，这种功能是可改变的，根据长期的结构变化，可能被缓慢，但不一定被逆转通过药理学。

**Are Measures of Stiffness Useful Clinically?**

流行病学证据，对于一个测量对更显著性预测的事件来说，是与疾病不必要地渲染，那是一个有用的临床工具来管理个人病人。有用性依赖于敏感性和测量的特异性，以及在预测的和测量的风险的放大。事实上，年龄是最重要的预测者短期事件，以及血压提供不同的预测信息。这种测量，对于测量的僵硬度将是一个有用的临床工具，作为根据MONICA作者的建议。

欧洲队列的调查研究计算了受试者操作特征曲线，使用各种传统的风险标记和发现，增加PWV的区域下曲线从0.69到0.72。MONICA调查的观察者观察到，危险比被增加了，大约13%到15%。如果PWV被添加到传统的标记，风险的增加是显著的。PWV的增加，可能需要进一步的研究来确认这一假设。如果这样的研究，那么，这种方法可以在更大的人群中使用，通过监测疾病的进展，然后这种方法，可以建立在数据上，来识别早期的血管和心脏异常。

我们的方法在明尼苏达大学被开发，来利用更全面的筛查，来识别早期，但可能在单个测量，如PWV。数据来证实这个假设。如果这样的技术被应用，被要求，识别更精确，那么，可以在人群中使用，来启动预防性治疗，可能会放慢疾病进展，而不是后来的干预，以及应该增加一个示可能的内膜和血管疾病早期事件的减少，但需要一个更全面的筛查，来识别早期的改变，而不是依赖于风险因素，这样，可能会成为临床实践的标准。

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