Journal of Biomechanics 44 (2011) 1367–1373

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

# Pulse wave velocity as a diagnostic Index: The pitfalls of tethering versus stiffening of the arterial wall

S. Hodis [a], M. Zamir [a,b]*

[a] Department of Applied Mathematics, University of Western Ontario, London, Canada N6A 5B7
[b] Department of Medical Biophysics, University of Western Ontario, London, Canada N6A 5B7

ARTICLE INFO

*Article history:*
Accepted 27 December 2010

*Keywords:*
Pulse wave velocity
Wave speed
Tethering
Arterial wall
Vascular stiffening
Hypertension
Age related hypertension

ABSTRACT

Pulse wave velocity (PWV) is often used as a clinical index of aging, vascular disease, or age related hypertension. This practice is based on the assumption that a higher wave speed indicates vascular stiffening. This assumption is well grounded in the physics of pulsatile flow of an incompressible fluid where it is fully established that a pulse wave travels faster in a tube of stiffer wall, the wave speed becoming infinite in the mathematical limit of a rigid wall. However, in this paper we point out that the physical principal of higher pulse wave velocity in a stiffer tube is strictly valid only when the wall is free from outside constraints, which in the physiological setting is present in the form of tethering of the vessel wall. The use of PWV as an index of arterial stiffening may thus lose its validity if tethering is involved. A solution of the problem of vessel wall mechanics as they arise from the physiological pulsatile flow problem is presented for the purpose of resolving this issue. The vessel wall is considered to have finite thickness with or without tethering and with a range of mechanical properties ranging from viscoelastic to stiff. The results show that, indeed, while the wave speed becomes infinite in the mathematical limit of a rigid free wall, the opposite actually happens if the vessel wall is tethered. Here the wave speed actually diminishes as the degree of tethering increases. This dichotomy in the effects of tethering versus stiffening of the arterial wall may clearly lead to error in the interpretation of PWV as an index of vessel wall stiffness. In particular, a normal value of PWV may lead to the conclusion that vessel wall stiffening is absent while this value may in fact have been lowered by tethering. In other words, the diagnostic test may lead to a false negative diagnosis. Our results indicate that the reason for which PWV is lower in a tethered wall compared with that in a free wall of the same stiffness is that the radial movements of the wall are greatly reduced by tethering. More precisely, the results show that PWV depends strongly on the ratio of radial to axial displacements and that this ratio is much lower in a tethered wall than it is in a free wall of the same stiffness.


## 1. Introduction

Mechanics of the arterial wall have often been pursued separately from the fluid flow problem within the arterial lumen. The fluid flow problem has generally been considered in full but, because of the inherent difficulties, it has so far been combined with only a thin wall as a boundary condition (Atabek, 1968; Womersley, 1957). More recently, the mechanics of a thick wall have been considered but, again because of the analytical difficulties involved, this was only possible with partial coupling at the fluid–wall interface in the sense of simply imposing the boundary conditions at the interface rather than allowing these conditions to emerge naturally from the dynamics of the two media (Humphrey and Na, 2002; Hodis and Zamir, 2008, 2009a, 2009b).

Solution of the pulsatile fluid flow problem fully coupled to a thick arterial wall is important because it represents the physiological situation more realistically and, in particular, because including the wall thickness makes it possible to deal with the issues of tethering and of mechanical stiffness of the wall more fully. One of the most important issues which has yet to be resolved is that of the wave speed in a stiff/rigid free wall versus that in a viscoelastic but fully tethered wall. While in a rigid free wall the wave speed is infinite, the corresponding wave speed in a non-rigid but fully tethered wall has yet to be determined. It has been suggested that it is in fact finite and small rather than infinite (Atabek, 1968; Cox, 1968; Misra and Choudhury, 1984; Taylor, 1959), thus leading to a wide dichotomy between the two situations.

Determination of the wave speed in these two situations is important because the wave speed is often used as a clinical index of aging or disease. The assumption on which this practice is based is that a higher wave speed indicates vascular stiffening. This assumption may lead to false negative results if tethering is involved because, as stated above, it is suspected that tethering may actually lower the wave speed. The purpose of the present paper is to

* Corresponding author at: Departments of Applied Mathematics and of Medical Biophysics, The University of Western Ontario, London, Canada N6A 5B7.
*E-mail address:* zamir@uwo.ca (M. Zamir).

0021-9290/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2010.12.029

present the results of a solution of the problem of vessel wall mechanics as they arise from the physiological pulsatile flow problem. The vessel wall is considered to have finite thickness with or without tethering and with a range of mechanical properties ranging from viscoelastic to stiff, thus providing the grounds for resolving these issues. The words “stiff” or “stiffening” here and throughout the paper shall be used to describe a degree of elasticity or viscoelasticity in which the modulus of elasticity is high but finite. The word “rigid” shall be reserved for the mathematical limit in which the modulus of elasticity is infinite. In this paper we do not consider intermediate degrees of tethering, thus the word “tethered” shall mean fully tethered—the outer boundary of the vessel wall in this case is totally constrained by surrounding tissue.

## 2. Materials and methods

Our plan is to obtain a general solution for displacements within the vessel wall, then combine this with the classical solution for pulsatile flow within the vessel lumen, and finally apply compatibility conditions at the fluid–wall interface to determine the arbitrary constants. The process amounts to solving the so called “frequency equation” (Womersley, 1957; Zamir, 2000) which in the past has been solved for an infinitely thin wall but here is being solved for a wall of finite thickness. For simplicity, the analysis to follow is based on a single harmonic flow, but the final results presented in the figures are based on a generalization of the analysis to encompass 10 harmonics of a typical cardiac waveform (Zamir, 2005) and physiological parameters given in Table 1. The fluid is assumed to be Newtonian and incompressible, and the vessel wall material is assumed to be homogeneous and viscoelastic using the fractional derivative model of Craiem and Armentano (2007) in which the modulus of viscoelasticity $E^*$, normalized in terms of the static elastic modulus $E_0$ (=411 kPa), is given by

$$\overline{E}^*(\omega)=E^*(\omega)/E_0=E_f+\eta_1 e^{i\alpha\pi/2}\omega^{\alpha}+\eta_2 e^{i\beta\pi/2}\omega^{\beta} \tag{1}$$

where $E_f$ is a (constant) fraction of static elasticity, $\omega$ is frequency (rad/s), $\eta_1$, $\eta_2$ are viscous factors and $\alpha$, $\beta$ are derivative orders. In the results to follow we have taken $E_f$=0.1, 0.1, 1.0; $\alpha=0.11,0,0$; $\beta=0.8,0,0$; $\eta_1=0.13,0.16,0.73((\text{rad/s})^{-\alpha})$; and $\eta_2=0.003,0.16,0.73((\text{rad/s})^{-\beta})$ for viscoelastic, elastic, and stiff wall materials, respectively.

### 2.1. Wall displacements

Consider a straight thick-walled circular cylindrical segment of a blood vessel where the wall materials is assumed to be incompressible and viscoelastic. The analysis to follow is restricted to linear theory (small strains) but the stress–strain relationship is considered nonlinear. Using a cylindrical polar coordinate system with $x$ along the vessel axis, $r$ in radial direction and $\theta$ in circumferential direction, and assuming axisymmetry (no angular variation), then the general solution for displacements within the wall thickness is given by (Hodis, 2010)

$$\begin{cases}\xi(r,x,t)=[-i\gamma A_1 I_0(\gamma r)-i\gamma A_2 K_0(\gamma r)+\lambda_1 A_3 I_0(i\lambda_1 r)+\lambda_1 A_4 K_0(i\lambda_1 r)]e^{i(\omega t-\gamma x)}\\ \eta(r,x,t)=\gamma[A_1 I_1(\gamma r)-A_2 K_1(\gamma r)+A_3 I_1(i\lambda_1 r)+A_4 K_1(i\lambda_1 r)]e^{i(\omega t-\gamma x)}\end{cases} \tag{2}$$

where $\omega$ is the fundamental frequency, $t$ is time, $\xi$, $\eta$ are displacements in the $x$ and $r$ direction, respectively, $I_i$ and $K_i$ are the Modified Bessel functions of first and second kind, respectively, of order $i$ ($i$=0,1), $A_{1-4}$ are constants to be determined and

$$\begin{cases}\gamma=\dfrac{\omega}{c}\\ \lambda_1^2=\dfrac{\rho_w\omega^2}{E^*}-\gamma^2\end{cases} \tag{3}$$

with $c$ the fluid wave speed and $\rho_w$ is the wall density.

**Table 1**
Physiological parameters on which the results are based, with $E^*(\omega)$ based on a frequency of 10 rad/s.

| | |
|---|---|
| Viscoelastic material | $E^*/E_0$ =0.28+0.04$i$ |
| Elastic material | $E^*/E_0$= 0.41 |
| Stiff material | $E^*/E_0$ = 2.5 |
| Static elastic modulus | $E_0$= 411 KPa |
| Fluid pressure | P=13.3 KPa |
| Fluid viscosity | $\mu$=0.04 dynes s/cm$^2$ |
| Lumen radius | $a$=1 cm |
| Wall thickness | $h$=0.1$a$ |
| Fluid density | $\rho_f$=1.055 g/cm$^3$ |
| Wall density | $\rho_w$=1.1 g/cm$^3$ |

### 2.2. Fluid flow

The classical solution of the fluid flow problem in terms of pressure $p$ and axial and radial velocities, $u$ and $v$, respectively, is given by (Cox, 1968; Womersley, 1957)

$$\begin{cases}p(r,x,t)=AJ_0(i\gamma r)e^{i(\omega t-\gamma x)}\\ u(r,x,t)=[-i\gamma BJ_0(i\gamma r)-i\lambda_2 CJ_0(i\lambda_2 r)]e^{i(\omega t-\gamma x)}\\ v(r,x,t)=[-i\gamma BJ_1(i\gamma r)-i\gamma CJ_1(i\lambda_2 r)]e^{i(\omega t-\gamma x)}\end{cases} \tag{4}$$

where

$$\begin{cases}A=-i\rho_f\omega B\\ \lambda_2^2=\dfrac{i\rho_f\omega}{\mu}+\gamma^2\end{cases} \tag{5}$$

and $\rho_f$ is fluid density, $\mu$ is fluid viscosity and $B$ and $C$ are constants to be determined. $J_0$ and $J_1$ are Bessel functions of first kind of order 0 and 1, respectively.

### 2.3. Compatibility conditions

To provide compatibility between displacements within the wall thickness and flow within the vessel lumen, the following conditions are imposed:

(i) axial and radial fluid and wall velocities are equal at the fluid–wall interface;
(ii) axial (shear) and radial (normal) stresses within the fluid and the vessel wall are equal at the fluid–wall interface

These conditions can be expressed in terms of wall displacements $\xi$,$\eta$ and fluid velocities $u$, $v$ as follows:

$$\begin{cases}u=\dfrac{\partial\xi}{\partial t},\ r=a\\ v=\dfrac{\partial\eta}{\partial t},\ r=a\\ \mu\left[\dfrac{\partial v}{\partial x}+\dfrac{\partial u}{\partial r}\right]=E^*\left[\dfrac{\partial\eta}{\partial x}+\dfrac{\partial\xi}{\partial r}\right],\ r=a\\ -p+2\mu\dfrac{\partial v}{\partial r}=-\Omega+2E^*\dfrac{\partial\eta}{\partial r},\ r=a\end{cases} \tag{6}$$

where $\Omega$ is the so called mechanical pressure $=-(\sigma_{rr}+\sigma_{xx}+\sigma_{\theta\theta})/3$.

### 2.4. Outer boundary conditions

In the fully tethered case it is assumed that the displacements at the outer layer are zero, therefore the boundary conditions are

$$\begin{cases}\xi(a+h,x,t)=0\\ \eta(a+h,x,t)=0\end{cases} \tag{7}$$

In the case of a free wall, we use the approach introduced in Hodis and Zamir (2009b) which requires that if the wall thickness is extended to infinity, the following conditions must be satisfied in the limit:

$$\begin{cases}\lim\limits_{r\to\infty}\xi(r,x,t)=0\\ \lim\limits_{r\to\infty}\eta(r,x,t)=0\end{cases} \tag{8}$$

## 3. Results

The coupled fluid–wall equations (Eqs. (2) and (4)) with boundary conditions for a fully tethered wall (Eqs. (6) and (7)) lead to the homogeneous system of six equations (Eq. (17)) given in Appendix 1. Similarly, the boundary conditions for a free wall (Eqs. (6) and (8)) lead to the corresponding system in Eq. (18). There are six equations in each case for the six unknown constants $B$, $C$, $A_{1-4}$.

### 3.1. Fluid wave speed (PWV)

For nontrivial values of the unknown constants $B$, $C$, $A_{1-4}$ in Eqs. (17) and (18), the determinant of the coefficients in each system is set equal to zero, that is

$$\Delta_i=0,\quad (i=0,1) \tag{9}$$

where $\Delta_0$ is the determinant of the coefficients in Eq. (17) and $\Delta_1$ is the determinant of the coefficients in Eq. (18). The result in each case is the so called “frequency equation” for the complex wave speed $c$.