Quantifying the Effect of Aortic Valve Degradation Using Signal Processing Techniques

Reetu Singh, Michael D. VanAuker, Babu Joseph, Leo Ondrovic and Joel A. Strom
Department of Chemical Engineering, University of South Florida, Tampa, Florida

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1. Introduction

Aortic valve stenosis is a leading health problem in the United States, affecting about five out of every 10,000 people (Bonow et al. 1998). It is characterized by the valve leaflet thickening and stiffening, which results in the narrowing of valve orifice. An increase in the transvalvular pressure drop occurs, which can progress to a reduction in transvalvular flow or cardiac output, ultimately resulting in heart failure. Aortic valve stenosis is identified as an important cause of deaths resulting from exercise related heart failure. The rate of narrowing of the aortic valve in individual patients is highly variable and unpredictable, with the patient remaining asymptomatic for years despite progressive valve narrowing. Surgical valve replacement is the only effective therapy in the symptomatic patient. However, the timing of surgery is controversial in asymptomatic patients, a result of the long latency period between valve deterioration and the development of valve-related symptoms.

The current tools used for diagnosis include invasive (catheterization) and non-invasive (Doppler echocardiography) techniques. Catheterization is used to measure transvalvular pressure drops and flow rates, whereas velocities are obtained by Doppler echocardiography. Markers of aortic stenosis include effective orifice valve area (EOA), valve resistance, transvalvular pressure drop and velocities. Effective valve areas are calculated using catheterization data by with Gorlin and Gorlin equation (Gorlin and Gorlin, 1951) given by

$$AVA(cm^2) = \frac{CO}{51.6k\sqrt{\Delta P} * SEP * HR}$$

where CO is cardiac output (ml/min), SEP indicates systolic ejection period (s/beat), HR denotes heart rate (beats/min), and k is a constant that includes the discharge coefficient and empirically derived correction factors.

The American Heart Association in conjunction with the American College of Cardiology has promulgated guidelines to classify the degree of aortic stenosis as mild (area >1.5 cm^2), moderate (area >1.0 to 1.5 cm^2), or severe (area <=1.0 cm^2) (Bonow et al. 1998). Recently, it has been shown that the Gorlin equation and therefore the calculated valve areas have flow dependence (Bermejo et al. 1996).

Ford et al. (1990) proposed that hemodynamic resistance, defined as the ratio of mean transvalvular pressure drop to mean flow rate during systolic ejection, gives a better measure of stenosis as compared to valve areas.

$$\text{Resistance} = \frac{1333(TPG)_{mean}}{Q}$$

where TPG_{mean} is the mean transvalvular pressure gradient in mm Hg, and Q is the mean transvalvular flow rate in ml/s. The conversion factor of 1333 is used to convert pressure in mm Hg to dynes · cm^{-2}, in order to express resistance in metric units (dynes s cm^{-5}). It has been identified that valve resistance > 180 dyne-cm/s^5 indicates severe stenosis (Mascherbauer et al., 2004).

Aortic valve performance is the result of anatomic derangement of the valve itself coupled with the performance of the left ventricle and aorta-arterial system. The indicators of the severity of stenosis, e.g. transvalvular pressure drop and flow rate, and effective orifice area, can be confounded by other variables in the cardiovascular system, like the arterial compliance and hypertension, and left ventricular contractility. For example, coexistent hypertension, which is quite prevalent in patients with aortic stenosis (Antonini et al. 2003), can mask the severity of the stenosis due the increase in both arterial and vascular resistance (Kadem et al. 2005; Bermejo, 2005). Cannon et al. (1992) have shown that in some patients with relatively mild aortic stenosis, the calculated valve orifice areas can overestimate the severity of stenosis. Valve area depends on pressure drop and flow rate, which in turn are affected by other cardiovascular factors in addition to the aortic valve health. Hence, factors that manifest themselves as changes in pressure drop and flow through the valve would induce changes in indices of stenosis severity, thereby confounding the diagnosis of the same.

There is a need to identify markers which would be unique to valve stiffness alone. Signal processing techniques, like Fast Fourier techniques, auto regressive moving average, moving average, and wavelets have been proposed as a tool to extract features from signals and identify variations (Güler İ., et. al, 2001, Güler İ. et. al, 1996). Previous studies by Kim and Tavel (2003) on 41 patients demonstrated the use of time-frequency analysis of the heart murmur to assess the severity of aortic stenosis. The wavelet technique may give better time and frequency domain resolution than other techniques, because it uses short time window for high frequency and vice versa (Aydin et al. 1999) Also, wavelet domain allows us to view information simultaneously in both time and frequency domain. Turkoglu et al. (2003) suggest the use of wavelet packet neural networks to analyze Doppler waveforms. Voss et al. (2005) used wavelet transform to separate stenotic subjects from normal ones. However, most previous studies have been preliminary and quantification of stenosis has not been addressed. In this work, we will report the effects of changes in hemodynamic variables on the performance of valves with varying stiffness. We have also used the wavelet signal processing technique to identify differences in valve performance in the frequency-time domain.

2. Materials and methods

Valves of similar size (25 mm annulus diameter) but varying stiffness used to simulate aortic valve degradation were synthesized using silastic 9280 series of liquid silicone rubber (Dow Corning, Kendallville, IN). The silastic rubber was available as a series of 5 elastomers, namely 9280-30, 9280-40, 9280-50, 9280-60, and 9280-70, each having different Shore A hardness and Young's modulus (Table 1).

A pulse duplicator (Figure 1) was used to simulate left ventricular pressure wave forms under different hemodynamic conditions, and to study their effects on the dynamics of the valves. The pulse duplicator consists of a ventricular chamber that houses a compressible bulb and is fed by an atrial reservoir. Solenoid valves allowed compressed air into the ventricular chamber bulb to

produce systole, and released the air to produce diastole. The air pressure was varied to change the pumping force, analogous to the contractility of the heart. The motion of the solenoid valves was controlled by a computer based control system, which can be used to set the heart rate and systolic ejection time. In our studies, systolic and diastolic cycles were set to 1/3 and 2/3 of the cardiac cycle duration, respectively. Afterload, simulated by varying the back pressure in the flow section downstream of the valve, affects the compliance of downstream section. Literature suggests that reduced arterial compliance gives rise to systemic hypertension (Kadem et. al, 2005) and hence, afterload is a measure of the same in our experiments.

The valves were mounted in the aortic position. The working fluid was a 40% (v/v) solution of glycerol in distilled water. Pressure was recorded using high fidelity pressure transducers (Millar Instruments, Houston, TX) located 2 cm upstream of the valve, 1.5 cm downstream near the vena contracta, and 8 cm further downstream at the site of recovered pressure. Flow through the valves was recorded using ultrasonic flow meter located downstream of the valve Transonic Flow Systems, Ithaca, NY). Pressure and flow data was collected using custom-built routines in LabView software (National Instruments, Austin, TX).

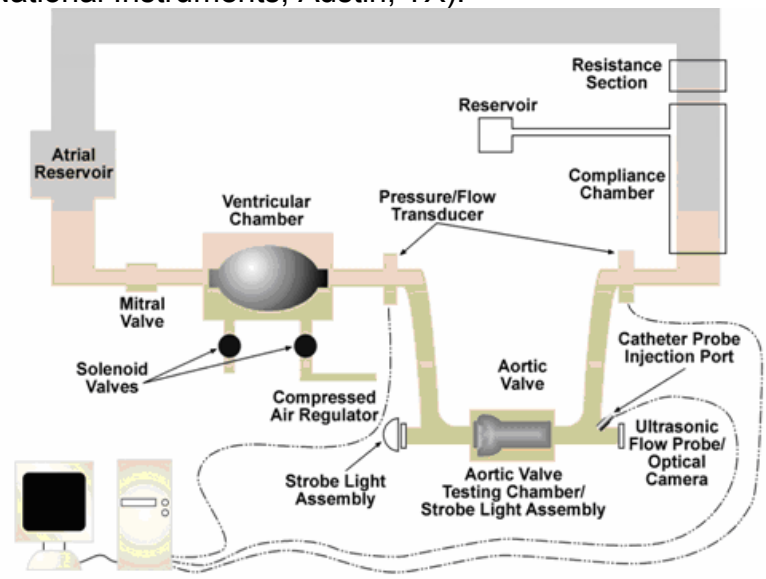

Figure 1. Pulse duplicator set-up

Each of the five valves was tested under conditions where either left ventricular contractility or back pressure was independently varied. The instantaneous pressures and flow, recorded at 1 ms intervals, were averaged over 30 or more beats to offset statistical variations. Instantaneous pressure drops were then obtained as the difference of downstream and upstream pressures for the averaged data. These values were used to calculate the instantaneous EOA using the Gorlin equation. Instantaneous Resistance was calculated as the ratio of the transvalvular pressure drop to the flow rate. The EOA and resistance employing the mean transvalvular pressure drop and mean flow during systole are also reported.

Wavelet analysis was performed on the pressure drop data by subjecting it to one-dimensional wavelet analysis employing MatLab (The MathWorks, Inc., Natick, MA). The coefficients were then plotted in the time-frequency domain and they were color-coded to enhance the perception of differences in the frequency intensity patterns.

3. Results and Comments

Aortic flow waveforms result from the combined effects of a number of variables, e.g. valve leaflet stiffness, left ventricular contractility, and the downstream arterial impedance. In the present work, we have varied each the factors individually to study the effect of each on aortic valve dynamics and isolate the effect of valve stiffness from other factors. EOA is a dynamic quantity (VanAuker et al. 2004). Hence we have calculated instantaneous valve areas during the cardiac cycle, along with instantaneous transvalvular resistance.

The effects of valve stiffness on pressure drop, flow rate, valve area, and resistance are depicted in Figures 2a-c below.

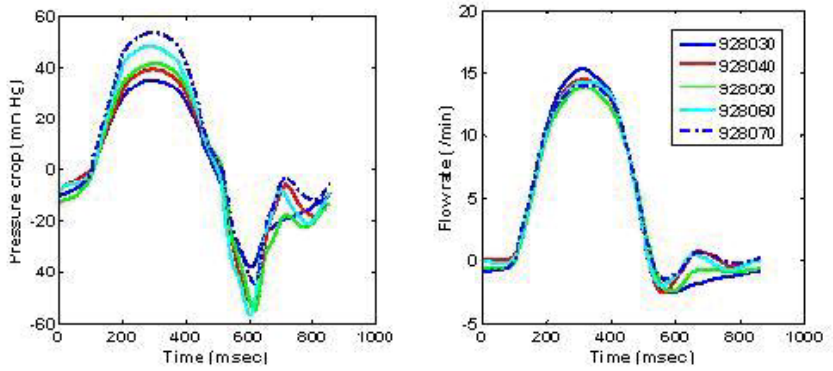

Figure 2a. Effect of valve stiffness on transvalvular pressure drop and flow

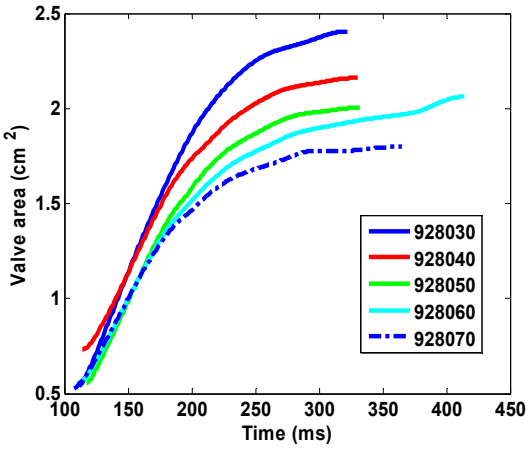

Figure 2b. Effect of valve stiffness on valve area

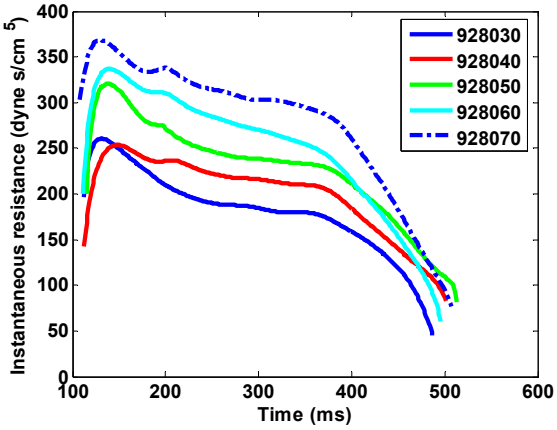

Figure 2c. Effect of valve stiffness on hemodynamic resistance

An increase in valve stiffness alone causes higher transvalvular pressure gradients coupled with reduced flow, thereby leading to smaller opening areas and higher resistances (Figure 2a-c, Table 1). Stiffer valves also show slower opening and higher fluctuations in pressure drop and flow in the valve closing phase. We also find that the percentage reduction in valve area is less (35%) as compared to that in resistance (59.5%) for changing stiffness.

Table 1: EOA and Resistance for valves of varying stiffness under same conditions

Valve material	Modulus (100%) (Psi)	EOA (cm^2)	Resistance (dyne s/cm^5)
928030	130	1.36	178.84
928040	200	1.25	204.69
928050	370	1.16	229.40
928060	530	1.13	252.84
928070	760	1.06	285.27

Figures 3a-c depict the effects of afterload on valve performance for a valve of constant stiffness.

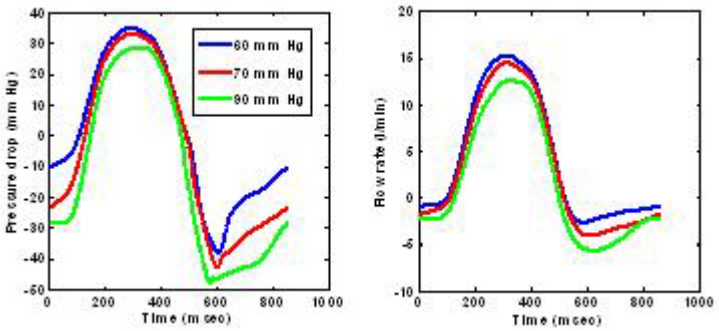

Figure 3a. Effect of systemic hypertension on transvalvular pressure drop and flow for constant stiffness

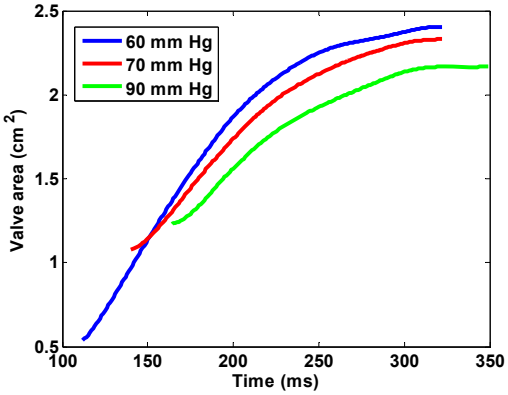

Figure 3b. Effect of systemic hypertension on valve area

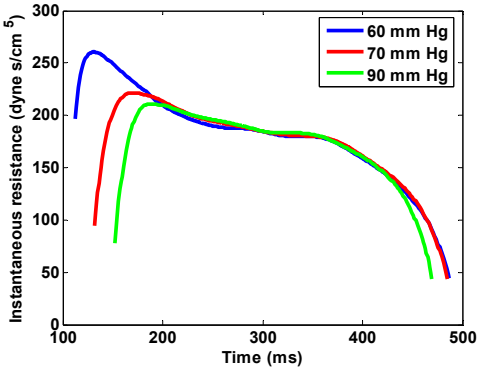

Figure 3c. Effect of systemic hypertension on hemodynamic resistance

Table 2: Variation in EOA and resistance with aortic compliance or hypertension

Aortic pressure (mm Hg)/hypertension	EOA (cm^2)	Resistance (dyne s/cm^5)
60	1.36	204.69
70	1.31	203.56
90	1.18	202.78

Figure 3a indicates that for a valve of given stiffness, systemic hypertension leads to a concomitant decrease in transvalvular pressure drop and flow, in accordance with the finding of Chambers (1998). We also observe a reduction in EOA (13.86+/-0.64 % over a set of 5 valves) under increased hypertension (Table 2), contrary to the findings of Kadem et al (2005). This might be due to the fact that in our experiments, the compliant aortic root, to which the authors attribute the increase in the anatomic EOA, is absent. The increased afterload due to hypertension causes a reduction in transvalvular pressure drop and flow, and consequently EOA (Figure 3b). However, the instantaneous hemodynamic resistance is not significantly altered (0.96 +/- 0.3 % change) although it peaks initially before the valve opens (Figure 3c).

Figures 4a and b reflect the coupled effects of hypertension and valve stiffness.

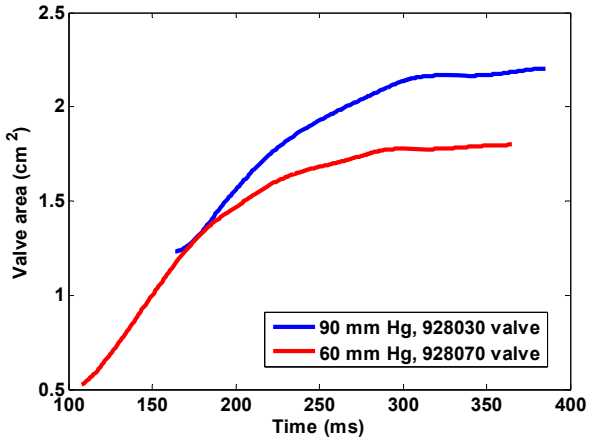

Figure 4a. Coupled effect of hypertension and valve resistance on valve area.

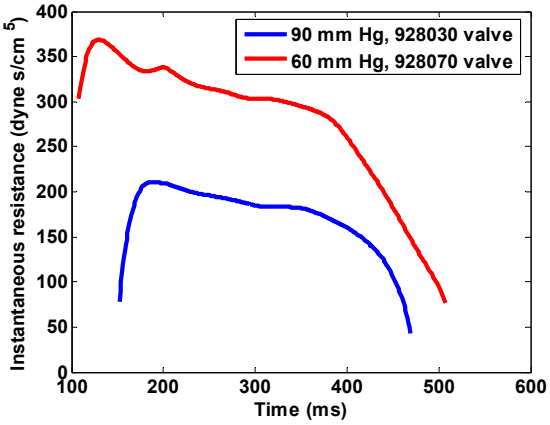

Figure 4b. Coupled effect of hypertension and valve resistance on valve area.

Figure 4a suggests that although increased hypertension brings about considerable reduction in area, it does not overcome the effect of stenosis. Hence, even under increased hypertension, a less stiff valve shows greater EOA and lesser resistance (Figs. 4a-b). The effect of hypertension and valvular stenosis being complimentary to each other, an increase in both would show reduced areas and high resistance, as found in our studies. Thus, hypertension affects EOA in a manner similar to stenosis explaining the overestimation of disease severity in hypertensive individuals.

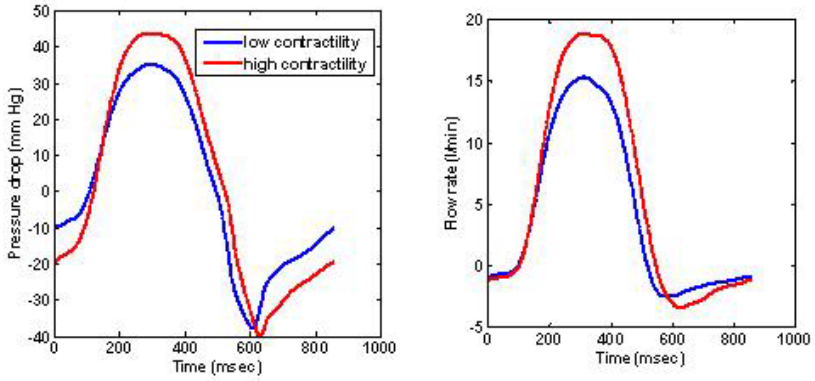

Figure 5a: Variation in transvalvular pressure drop and flow under changing contractility (valve stiffness constant)

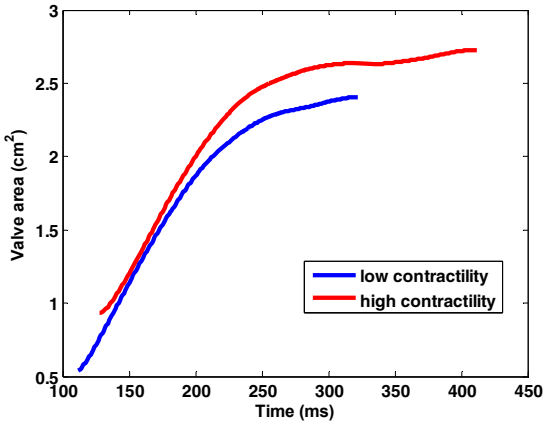

Figure 5b: Valve area changes with contractility

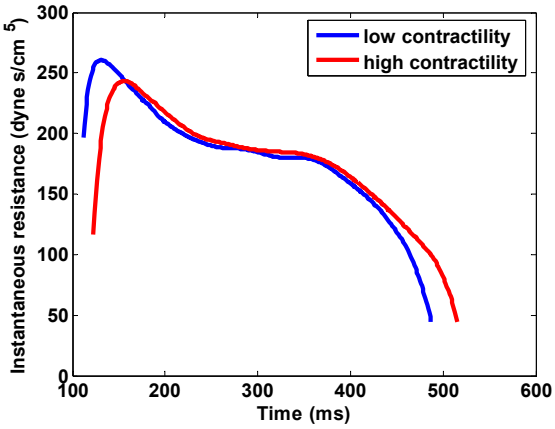

Figure 5c: Resistance variation with contractility

Figures 5a-c and Table 3 indicate the effects of changing heart contractility on valve dynamics when the stiffness is unchanged. Decreased contractility leads to reduced pressure drop, flow and EOA (13.3 +/- 2.5 %) but valve resistance was less affected (variation 3.5 +/- 2.5%). When assessing the stenotic severity using EOA, reduced left ventricular contractility might overestimate the severity of stenosis. Our studies also show that for stiff valves, an increase in contractility leads to a smaller EOA and a higher resistance. Clearly, a stiff valve will show similar behavior under low contractility as well because both the factors have analogous effect of valve dynamics.

Table 3: Variation in EOA and resistance with contractility

Contractility	EOA (cm^2)	Resistance (dyne s/cm^5)
Low	1.36	178.84
High	1.56	177.63

3.1. Wavelet analysis of pressure drop profiles

Wavelet transforms deal with separating data into different frequency components and studying each component with a resolution in accordance with its scale or frequency. Scale is inversely proportional to frequency. Discrete wavelet transformation (DWT) of a function f(t) involves its inner product with a wavelet at discrete values of dilation and translation. Dilation changes the frequencies and translation moves the signal in the time domain, thereby mapping a time domain function onto a time-frequency domain (Palavajjhala et al. 1994). At each dilation and translation, the inner product of the mother wavelet with the signal gives an estimate of the strength of the signal at that localization in terms of a coefficient. A high coefficient at a particular frequency and time indicates the presence of that frequency in the signal at that instant.

In the present work, the pressure drop profiles were subject to 1D wavelet analysis to obtain wavelet coefficients.

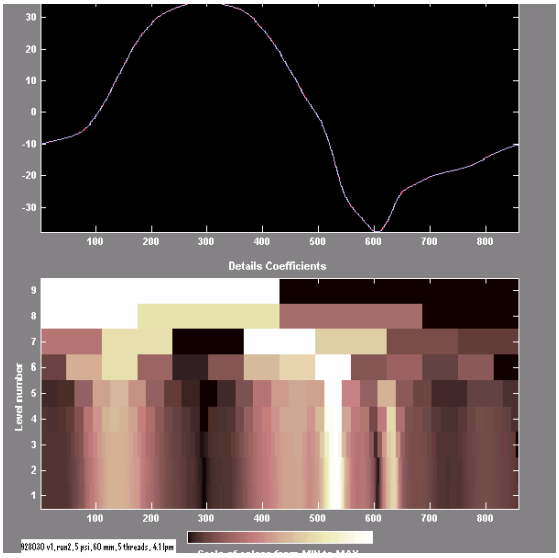

Figure 6: Wavelet decomposition (928030 valve, 60 mm Hg afterload)

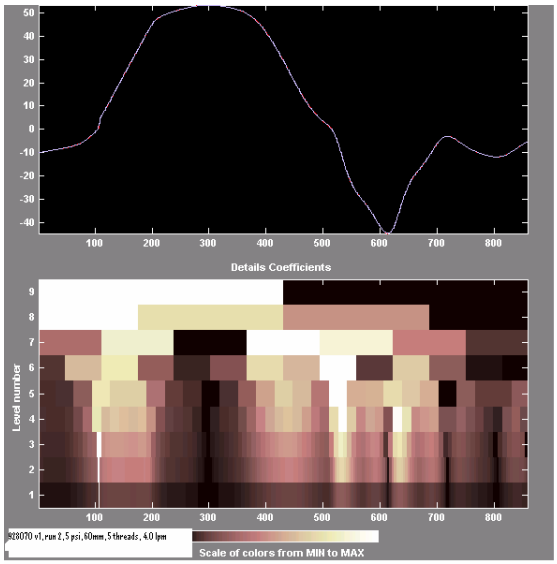

Figure 7: Wavelet decomposition (928070 valve, 60 mm Hg afterload)

Figures 6 and 7 show the wavelet decomposition for valves of two different stiffnesses under similar hemodynamic conditions. At aproximately 300 ms (the time when systole ends), the stiffer valve shows the absence of high frequencies for a greater time as compared to the valve of lesser stiffness. Clearly, the wavelet decompositions show significant differences. In comparison to Fig. 6, Figs. 8 and 9 show that for the same valve, an increase in either left ventricular contractility or hypertension does not significantly affect the wavelet decomposition. Therefore, wavelet analysis can be used to separate intrinsic valve performance from confounding variables.

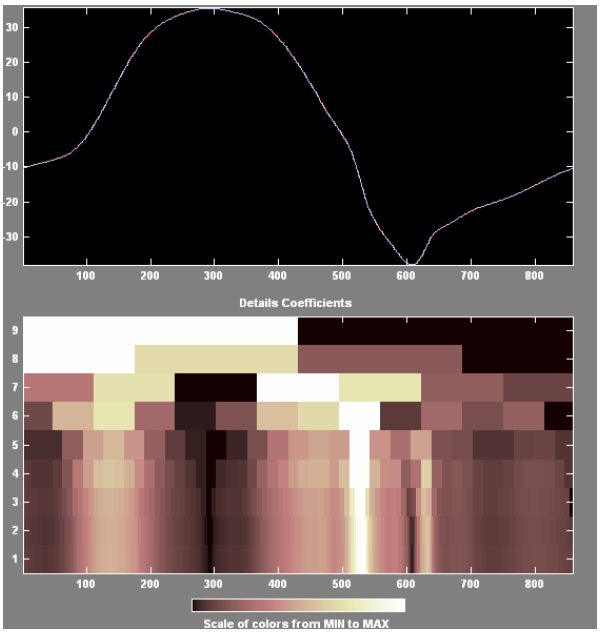

Figure 8: 928030 valve, high contractility

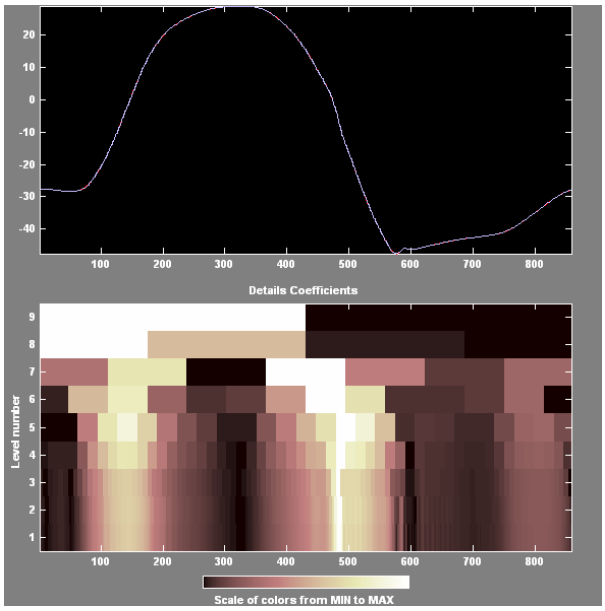

Figure 9: 928030 valve, increased Hypertension (90 mm Hg afterload)

4. Conclusions

The effects of various hemodynamic factors affecting the assessment of stenotic severity were studied on valves of varying stiffness. As valve stiffness increases, the EOA and the hemodynamic resistance increases. Our studies indicate that increased hypertension brings about a reduction in EOA even for a valve of constant stiffness and when combined with stenosis, it affects the assessment of severity of the same. Decreased contractility of the heart also brings about reduction in EOA and also affects the assessment of stenosis severity when both are present concomitantly. To isolate the effect of one variable from another, a 1D wavelet analysis of the pressure drop signals was performed. Results indicate that the wavelet decompositions are more reflective of valve conditions and other factors like hypertension and contractility have less bearing on the time frequency resolution of the signals. Efforts to quantify the effect of each factor based on wavelet coefficients are underway.

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