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NOTE

On the maximum operating frequency of prosthetic heart valves

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Abstract

A criterion is presented to evaluate the maximum pulsating flow frequency beyond which prosthetic heart valves cease to properly operate. The idea is tested with the experimental measurements obtained with an biological Edwards-Carpenter valve type model. It is found that beyond a certain characteristic frequency, the valve is no longer capable of fully operating in a cyclic manner. Furthermore, based on data recently reported by other authors, this preliminary comparison suggests that for a wide range of materials, leaflet sizes and operating conditions prosthetic heart valves might fail to properly operate for frequencies beyond 4.5 Hz (or 240 ppm).

1. Introduction

According to the World Health Organization cardiac deceases are still the leading causes of death worldwide (World Health Organization 2016). In particular, valvular heart disease (VHD) is notably common (Nkomo *et al* 2006), since it affects nearly 2.5% of the global adult population. In spite of the uncertainties related with its clinical diagnosis (Iung *et al* 2003, Marijon *et al* 2007), valve replacement has become the second most frequent kind of surgery in western countries (Korossis *et al* 2000). It is further believed that VHD will continue to be an important public-health problem in the years to come in many countries (e.g d'Arcy *et al* 2010, Domenech *et al* 2016).

Projects aimed at developing prosthetic heart valves receive significant funding from both governments and health organizations. However, despite the degree of refinement achieved since the first mechanical models were introduced, there remain certain aspects concerning the performance of prosthetic heart valves which are still poorly understood. The relevance of the problem becomes clear when the function of the valve is considered. Valvular prostheses serve the important function of preserving the directionality of the stream of blood through the heart. In order to fulfill this function, the leaflets must behave as 'check-valves' that deform passively under the loading action of the flow itself (Sotiropoulos *et al* 2016). This implies that the leaflets' tissue ought to sustain continuous stretching and bending over a life span of order 10^9 cycles (Sacks *et al* 2009). Hence, besides the functional capabilities, artificial valves must also comply with high durability requirements. In the specific case of biological prostheses, some studies indicate that the periodic mechanical loading may eventually alter the tissue structure and mechanical properties (Hasan *et al* 2014).

In comparison with their mechanical counterparts, biological prostheses exhibit superior hemodynamic flow properties. The reason is that pericardium leaflets have properties similar to those of native tissue (Hasan *et al* 2014). Globally speaking, pericardium leaflets tend to induce much lower shearing stresses in the flow and, as a result, their blood cell damaging potential is significantly lower (López-Zazueta *et al* 2011). Nevertheless, a new generation of sophisticated polymeric materials are currently engineered to create more natural flow patterns around them, while retaining their almost unlimited life spans (Butterfield *et al* 2001).

An important issue deserving attention concerns valve testing. All prostheses must be subjected to extended testing, prior to their use in humans. This occurs in accordance with well defined norms and standards (Nolan 1994). For example, biological valves must be able to withstand 200 million cycles before failure (Lu *et al* 2003). Also, the prosthesis must fully open and close during each cycle, while the mean transvalvular pressure must be at least 100 mmHg at closure. In order to accomplish the testing program within reasonable periods of time, the tests are carried out in pulsatile flow simulators at accelerated pulsation rates (Fettel *et al* 1980, Lu *et al* 2003). Surprisingly enough, there seems to be no critical assessment reported in the literature, about the mechanical limitations of artificial valves subjected to this kind of testing regimes.

In view of the forgoing discussion, we present a mechanical argument that aims to define the maximum flow pulsation frequency at which a valve operates correctly. In essence, we argue that beyond certain pulsating frequency a valve made of flexible leaflets ceases to respond dynamically: the valve can no longer close at each cycle because the flow changes more rapidly than the elastic response of the leaflets. Our theoretical analysis is tested by proof-of-concept experiments conducted with the prosthetic valve model most commonly used in Mexico but also confirmed by considering other published data (Hasan *et al* 2014).

2. Maximum operation criterion

To investigate the limits of correct open-close performance of a valve made of flexible leaflets, we can consider a generalized beam equation

$$A_{ij}\frac{\partial^2\delta_j}{\partial t^2}+B_{ij}\frac{\partial\delta_j}{\partial t}+D_{ij}\frac{\partial^4\delta_j}{\partial x_i^4}=0. \tag{1}$$

where the δ_j represent the deflections undergone by the leaflets. The physical properties of the surrounding fluid and leaflets are combined in the mass, damping and stiffness coefficients: A_{ij}, B_{ij} and D_{ij}. For simplicity we consider the one-dimensional deflection of a single leaflet moving in a Newtonian incompressible fluid. Neglecting the added mass effect (Brennen 1982) and the internal damping (Maringer 1966), the equation reduces to

$$\frac{\partial^2\delta}{\partial t^2}\approx\frac{C'EI}{\rho hx}\frac{\partial^4\delta}{\partial x^4}, \tag{2}$$

where the constant C' absorbs the numerical coefficients, ρ is the leaflet density, E is the modulus of elasticity and I is the area-moment of inertia; h and δ are, respectively, the thickness and the deflection of the leaflet. For valves with leaflets of characteristic size L, that can be subjected to maximum deflections of size H, the relevant scales are

$$\delta\sim H,\qquad x\sim L,\qquad t\sim t_v=f_v^{-1}. \tag{3}$$

where t_v represents the characteristic time of the valve (the inverse of the characteristic frequency, f_v). Note that a leaflet has width and length, but in most cases their are of the same of the same order; hence, it is sufficient to only consider a single size L. With these scales the dimensionless leaflet deflection equation reads

$$\frac{\partial^2\tilde{\delta}}{\partial\tilde{t}^2}\approx\frac{C'EI}{f_v^2\,\rho\,h\,L^5}\frac{1}{\tilde{x}}\frac{\partial^4\tilde{\delta}}{\partial\tilde{x}_i^4}, \tag{4}$$

with the tildes denoting dimensionless quantities.

Therefore, one may conclude that

$$\mathcal{O}\left(\frac{C'EI}{f_v^2\,\rho\,h\,L^5}\right)\sim 1. \tag{5}$$

This estimation implies that the characteristic frequency of the leaflets must scale as

$$f_v^2\sim\frac{C'EI}{\rho\,h\,L^5}. \tag{6}$$

Now, writing this expression as an equality we have

$$f_v=C\left[\frac{EI}{\rho\,h\,L^5}\right]^{1/2}. \tag{7}$$

where C is a free parameter that can be adjusted. This factor could also account for other secondary effects that influence the valve performance (e.g. material imperfections, misalignments, etc.)

We can compare the valve's characteristic frequency, f_v, with the flow pulsation frequency, f_p,

$$f_p=\frac{U_p}{L} \tag{8}$$

where U_p is the average flow speed. Considering the ratio of these two frequencies, we have

$$f^*=\frac{f_p}{f_v}=\frac{1}{C}\left[\left(\frac{\rho\,U_p^2}{E}\right)\left(\frac{hL^3}{I}\right)\right]^{1/2}. \tag{9}$$

The quantity f^* may be used as a criterion to determine when the valve will cease to operate properly. If we arbitrarily set the value of $f^*=1$, as the critical condition, f^*_{crit}, two possible situations can be identified. If $f^*<1$ then the valve will be capable of adjusting to the imposed dynamic loading, and will open and close effectively at each cycle; on the other hand, if $f^*\geqslant 1$ the elastic capacity of the valve will not be sufficient to respond to the changes in the flow and, therefore the valve will fail to fully close during each pulsation.

Note that the first factor in the square bracket of equation (9) can be interpreted as a pseudo-Weissenberg number, which compares inertial fluid stresses with the elastic stresses on the leaflet. The second factor in the bracket is a geometrical measure of the slenderness of the leaflets. Hence, in a sense, the frequency f^* determines the extent to which the interplay between the elastic and the geometrical properties influence the dynamical response of the valve.

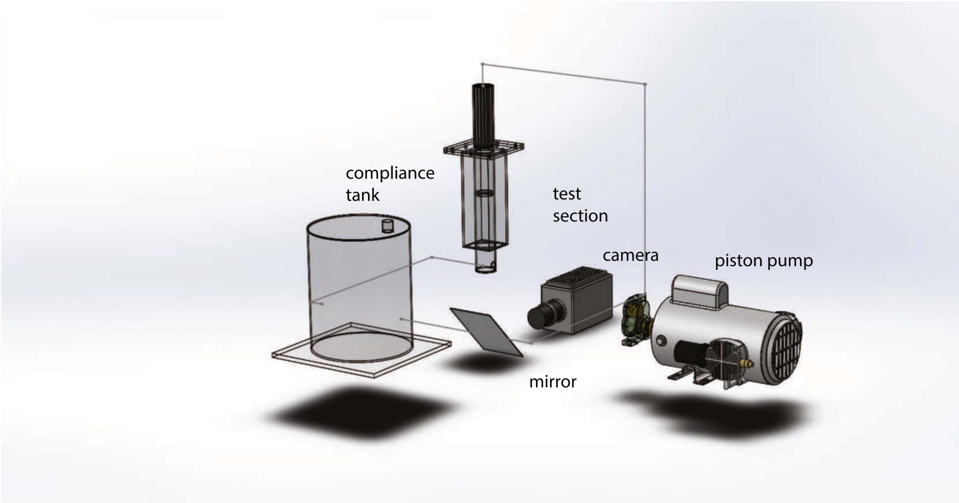

Figure 1. Experimental setup. The flow circuit is based on a Windkessel model.

3. Proof-of-concept validation

A series of experiments were conducted to test the proposed idea: a flexible leaflet valve should cease to operate correctly beyond a certain critical frequency. In the context of previous investigations, the tests were conducted with the prosthetic valve that is most extensively used in Mexican hospitals.

3.1. Flow loop

Figure 1 shows a diagram of the apparatus. The test section consisted of a 400 mm long plexi-glass cylindrical channel, with an internal diameter of 50.8 mm. The entire flow circuit was configured after the Windkessel model to emulate the basic characteristics of the human cardiovascular system (Fung 1997, Diourté *et al* 1999). Water was selected as the working fluid for two main reasons: (a) the viscosity of the blood flowing through large vessels is essentially determined by the blood plasma, which behaves as a Newtonian fluid (Sequeira and Janela 2007), and (b) a transparent fluid enables direct visualization of the operation of the valve in the open-close cycle. Aimed at reducing the optical distortions caused by the curved surfaces, the channel was enclosed by a rectangular box (of the same transparent material), and the space between the cylinder and the box was filled with water. Two rings located at the center of the cylinder held in place the prosthetic valve. The compliance tank reproduced, to some extent, the elastic behavior of the human circulatory system. A specific dynamic response was determined by the compression and decompression rates of a fixed amount of air contained in its interior (figure 1). Meanwhile, a pulsatile flow was produced by means of a diaphragm pump designed to operate at high frequencies (Gónzalez-Téllez 2011). Various frequencies were selected within the interval ($3.65 \leqslant f_p \leqslant 7.15$) Hz. The pump was set to operate in such a way that, as the pulsatile frequency increased, the flow rate decreased in an inversely proportional manner. For these validation tests the flow rates were varied within the interval ranging from 14.1 ml/s (at 7.15 Hz) to 52.7 ml/s (at 3.65 Hz) (Sánchez-Ríos 2014).

3.2. Prosthetic heart valve specimen

The valve used in this validation was designed and manufactured at the Instituto Nacional de Cardiología in Mexico City. It was a Carpentier-Edwards valve type, with three bovine pericardium leaflets attached to rigid posts on a titanium ring (see figure 2). The valve's external diameter and height were, respectively, $D = 34.0$ mm and $H = 18.2$ mm. Internally, the valve bore diameter was 24.4 mm. The leaflets had a length, width and thickness of $L \approx 23.0$ mm, $W \approx 30.0$ mm and $h \approx 0.6$ mm, respectively. Two different valves of the same nominal dimensions were used.

3.3. High speed video recording

The aperture and closure of the valve throughout the cycle was recorded with a Motion Pro X4 high speed camera. A mirror inclined at 45° was placed at the bottom of the cylindrical channel, in order to visualize the valve in the axial direction. The image resolution was set to 512×512 pixels, with a sampling rate of 1,500 fps (frames per second).

The valve was observed during 3 s for each pulsatile flow condition. Fifteen different frequencies in the range $3.65 \leqslant f_p \leqslant 7.15$ Hz were considered. Depending on the frequency, a different number of open-close cycles were obtained from each case, ranging from 10 to 20 complete cycles.

4. Results

The sequence of images shown in figure 3 portrays the behavior of the prosthetic heart valve. From top to

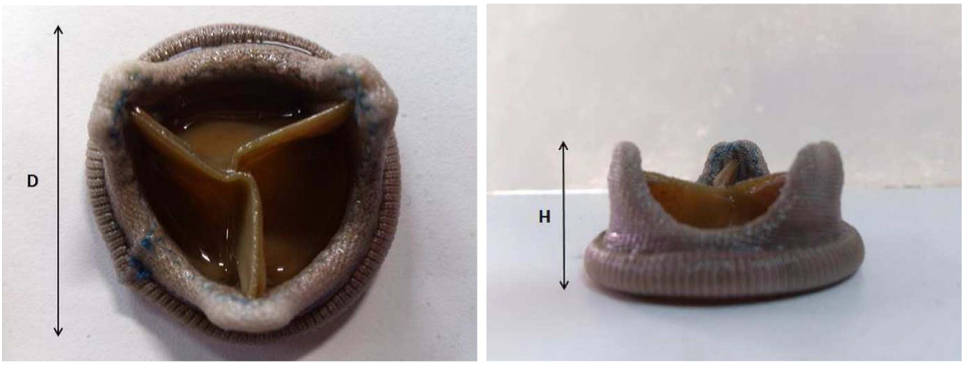

Figure 2. Top and side views of the valve used in the experiments. The valve is based on an bovine pericardium Edwards-Carpenter model, produced at the Instituto Nacional de Cardiologia in Mexico City (Sánchez-Arévalo *et al* 2010).

bottom, the three depicted pulsation frequencies correspond to $f_p = 4.65$, 5.65, and 6.65 Hz, respectively. The time is normalized in terms of the cycle period, T; hence, $t^* = t/T$. Also, from left to right the images correspond to the instants $t^* = 0$, $t^* \approx 0.2$ and $t^* = 0.9$.

In the case corresponding to the pulsation frequency $f_p = 4.65$ Hz (first row of figure 3) the valve is observed to operate correctly throughout the entire cycle. This means that for relatively small frequencies the valve opens and closes satisfactorily at all times. However, as the pulsation frequency is increased, the leaflets cease to properly close towards the end of the cycle (see the snapshot for $t^* = 0.9$ in the second row of images). This particular case corresponds the critical frequency $f_p = 5.65 \pm 0.4$ Hz (obtained from two valves with the same nominal size and properties), and marks the onset of the unwanted behavior of the valve. Beyond this frequency the valve clearly fails to properly close at the end of the cycle, as it is depicted by the last row of images in figure 3 (in particular note that the valve remains opened at $t^* = 0$). The corresponding frequency in this last case is $f_p = 6.65$ Hz. Interestingly, an erratic behavior is also observed for frequencies around the critical value, thereby indicating the incipient appearance of unstable modes. The valve thus appears to close only from time to time. Furthermore, distinctive cross-sectional areas result with each one of the frequencies in the neighborhood of f^*_{crit}.

For the particular case analyzed here, the value of the constant C can be calculated. The physical properties of this type of leaflets can be obtained from Hernández-Badillo *et al* (2015) who have shown that $I \sim 10^{-12}$ m^4 for flexible plates whose curvatures are within the interval $1.0 \leqslant \kappa \leqslant 4.0$ m^{-1}; Sánchez-Arévalo *et al* (2010) reported values for density, thickness and length of $\rho \sim 10^3$ kg/m^3, $h \sim 10^{-3}$ m, $L \sim 10^{-2}$ m and, more importantly, E for bovine pericardium to be of order 10^6 Pa. Considering these values and assuming that the critical frequency is $f_p = 5.65$ Hz, then $C = 0.056$ for $f^*_{crit} = 1$.

5. Discussion and conclusions

A criterion to determine the bounds for correct operation of prosthetic heart valves was derived. This criterion determines the maximum pulsating frequency (f_p) at which a given valve may be subjected, before it stops effectively sealing the transvalvular bore during the cardiac cycle. Relevant material properties, as well as geometrical properties, appear explicitly in the functional form of the criterion. Hence, if the materials and the geometry are changed, the corresponding value of the critical frequency f^*_{crit} can be readily computed.

Validation experiments were conducted to test the predicted value of f^*_{crit}. In the framework of a broader investigation, these tests involved the valve type most extensively used in Mexican hospitals. The prosthesis in question corresponds to an Edwards-Carpenter valve type made with bovine pericardium. It was found that this particular valve sustains a maximum frequency $f_p = 5.3$ Hz, prior to the onset of an inadequate operation. Already at $f^*_{crit} \approx 1$ a series of small amplitude motions of the leaflets' edges are observed, which may hinder the full closure of the valve at all times. If an additional 30% safety margin is considered, the upper limit of the maximum operating frequency is at around $f_p = 4.5$ Hz (or 240 ppm). This margin would account for factors which may be difficult to evaluate, or which are not directly taken into account in the criterion (e.g. inhomogenities of the material properties, assembly imperfections and secondary flow effects in the vicinity of the valve). Interestingly, similar values of f_p can be obtained from considering changes in the mechanical properties and dimensions of other materials used to manufacture other bioprostheses (Hasan *et al* 2014). Therefore, we can argue that most biological and flexible leaflet valves will not operate correctly beyond this limit.

Considering equation (9), the only possibility for a valve to work correctly under such large pulsation frequencies would be reducing the mean flow speed, U_p, as discussed by Ledesma-Alonso *et al* (2014). Since, $U_p \sim f_p V/D^2$ (V being the displaced volume per

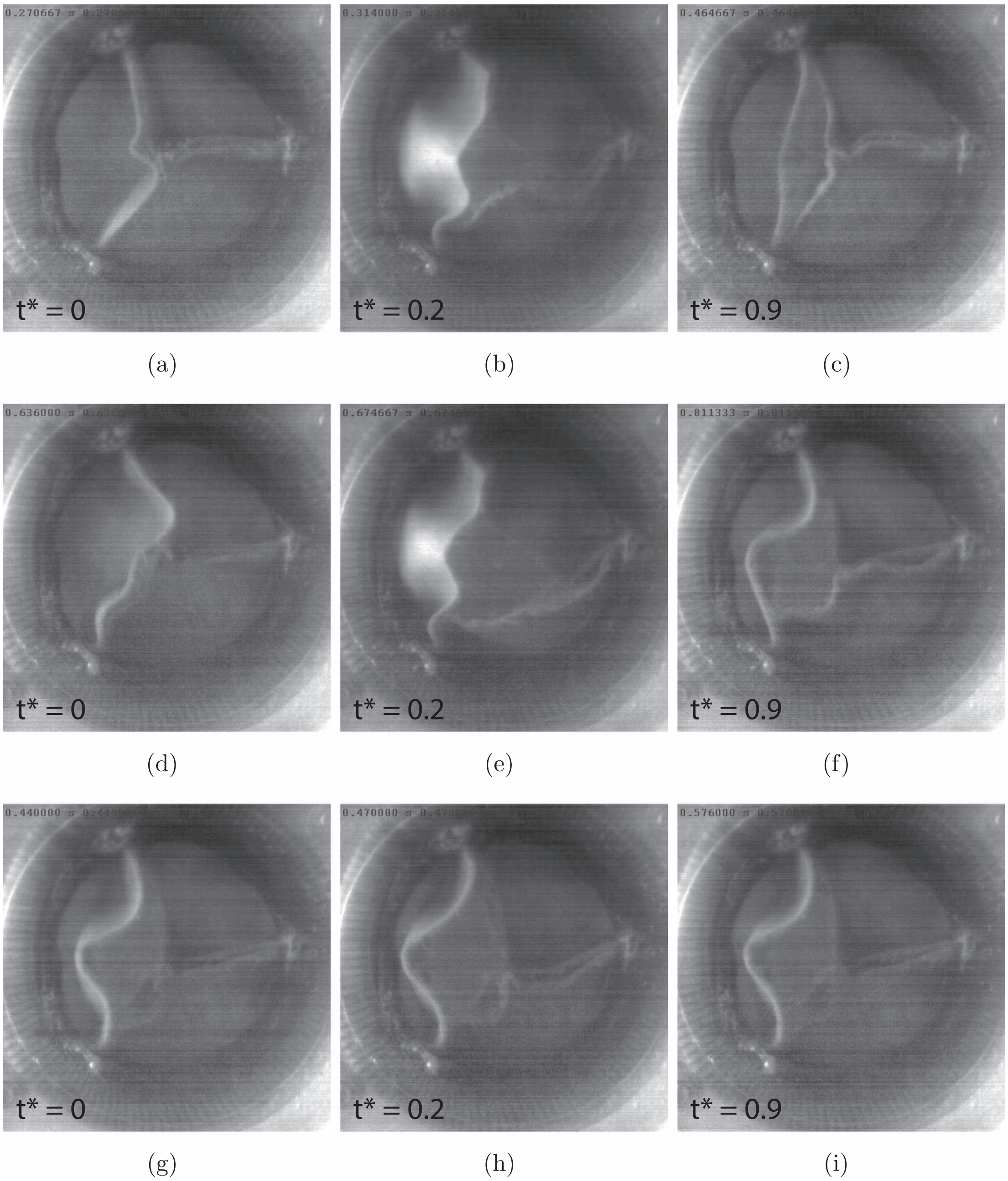

Figure 3. Valve frontal view for three different times and frequencies: images (a)–(c) are for $f = 4.65$ Hz; images (d)–(f) are for $f = 5.65$ Hz; images (g)–(i) are for $f = 6.65$ Hz. The time is normalized in terms of the cycle period: $t^* = t/T$.

stroke), decreasing U_p would imply reducing the volume per stroke which would then fail to comply with the established normed tests (Nolan 1994).

From a survey of the published literature on the subject, a critical discussion of the mechanical limits of correct operation of flexible leaflet valves does not exist. The present study provides the basis for this discussion. It is important to ensure that the valves that are tested under accelerated conditions function correctly and within their mechanical limits.

As a final remark, it is pointed out that the criterion could be used for other purposes. For example, if a new material is under consideration, the correct geometry could be established in order to fulfill the requirement $f^* \leqslant f^*_{crit}=1$. On the other hand, if the geometry factors were to be determined *a priori*, then the material could be selected to have suitable values of E and ρ. In addition, the accelerated test protocols could be revised and adjusted in accordance with the effects here discussed. It would also be of significant interest to determine the flow structure for valves operating near the critical frequency. Most likely the velocity field changes in a significant manner; this fact would also influence both the valve operation and the stress level imposed onto the fluid across the valve. We plan to pursue such study in the future.

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