Journal of Diseases Open access

Research Article

Canary in the Cardiac-Valve Coal Mine: Flow Velocity and Inferred Shear during Prosthetic Valve Closure – Predictors of Blood Damage and Clotting

Lawrence N Scotten[1*], Rolland Siegel[2], David J Blundon[3], Marcus-André Deutsch[4], Terence RP Martin[5]

[1]*Independent Consultant, Victoria, BC, Canada*
[2]*Independent Consultant, Portland, Oregon, USA*
[3]*Instructor (Retired), Environmental Technology Program, Camosun College, Victoria, BC, Canada*
[4]*Surgeon–Cardiothoracic, Klinik Fur Thorax-und Kardiovaskularchirurgie, Herz-und Diabeteszentrum NRW, Bad Oeynhausen, Germany*
[5]*Medical Engineer, Nottingham, UK*

[*]**Correspondence:** Lawrence N Scotten, Independent Consultant, Victoria, BC, Canada

Abstract

Objective: To demonstrate a clear link between predicted blood shear forces during valve closure and thrombogenicity that explains the thrombogenic difference between tissue and mechanical valves and provides a practical metric to develop and refine prosthetic valve designs for reduced thrombogenicity.
Methods: Pulsatile and quasi-steady flow systems were used for testing. The time-variation of Projected Open Valve Area (POVA) was measured using analog opto-electronics calibrated to projected reference orifice areas. Flow velocity determined over the cardiac cycle equates as instantaneous volumetric flow rate divided by POVA. For the closed valve interval, data from quasi-steady back pressure/flow tests was obtained.
Performance ranked by derived maximum negative and positive closing flow velocities, evidences potential clinical thrombogenicity via inferred velocity gradients (shear). Clinical, prototype and control valves were tested.
Results: Blood shear and clot potential from multiple test datasets guided empirical optimization and comparison of valve designs. A 3-D printed prototype valve design (BV3D) purposed for soft closure and reduced thrombogenic potential was assessed.
Conclusions: The relationship between leaflet geometry, flow velocity and predicted shear at valve closure illuminated an important source of prosthetic valve thrombogenicity. With an appreciation for this relationship and based on our experiment generated comparative data, we achieved optimization of valve prototypes with potential for reduced thrombogenicity.

Keywords: Prosthetic valve; Laboratory simulation, Projected open valve area, Valve closure, Thrombogenicity, Valve flow velocity. Rebound

Received date: Feb 04, 2024; **Accepted date:** Feb 11, 2024; **Published date:** Feb 21, 2024

Citation: Scotten LN, Siegel R, Blundon DJ, Deutsch MA, Martin TRP, Dutton JW, et al. (2024) Canary in the Cardiac-Valve Coal Mine: Flow Velocity and Inferred Shear during Prosthetic Valve Closure – Predictors of Blood Damage and Clotting. J Dis 3,2.

INTRODUCTION

Our interest in prosthetic valve dynamics was initially stimulated during formation of the cardiac research development laboratory tasked with supporting the newly opened cardiac surgery unit at Royal Jubilee Hospital in Victoria, BC, Canada. Incorporated as Vivitro Systems Inc. (VSI), our primary focus was research, design and development of cardiac valve implant devices and on the laboratory test systems required. During this phase we studied valve motion in an early pulse duplicator using highspeed cinematography and photogrammetric analysis [1]. Subsequently, an innovative simpler method was devised to determine Projected Open Valve Area (POVA) similar to planimetric quantification of POVA from 16 mm cinematography and was published in new laboratory technique measures projected dynamic area of prosthetic heart valves [2]. In 2009, work transitioned into a separate independent research and development enterprise, ViVitro Laboratories Inc.

(VLI) also based in Victoria, BC, Canada. Consistent with a focus on evaluation of various prosthetic valve models, our pulse duplicator was modified to include a unique opto-electronic subsystem which we named Leonardo. The addition of this subsystem redirected our interest in heart valve dynamics to the closure phase and associated supra-physiologic backflow fluid velocities. Driven by ongoing curiosity and armed with new data from Leonardo, we reported our findings through a series of preprints and publications [3-5]. In a recent broader application of our investigative technology, results from in silico computational modeling and in vitro experimental studies confirmed or verified the characteristics of leaflet spatial oscillations in bioprosthetic valves (flutter) throughout the open period of the cardiac cycle Lee, et al. and prompted peer commentary [6,7]. Given the arc of success with prosthetic valves over decades including initiation and progressive expansion of transcatheter devices, long-term durability and thrombosis issues persist. Thrombosis is a physics-based phenomenon that nature evolved to stem bleeding after an injury. For both transcatheter and surgically implanted bioprosthetic valves, limited durability related to multiple factors has stimulated introduction of a variety of "rescue devices". Intended to provide transcatheter based mitigation of complications in primary and valve-in-valve bioprosthetic valves implants, these devices are associated with their own unique complications.

The longer term consequences of a transcatheter based multiple valve approach for patient morbidity; mortality and overall cost are yet to be determined. In the current paper, our focus returns to identification and assessment of sources of thrombogenicity in contemporary clinical and also experimental mechanical and bioprosthetic heart valves with particular attention to the central role of conspicuous transient fluid velocities during valve closure. Flow velocity manifests shear via flow velocity gradients that can trigger blood damage and clot formation in vascular disease processes and cardiovascular implant devices [8,9]. When adjacent fluid layers bypass with speed differentials, shear forces increase and blood damage results. We have sought to assess and compare the dynamic behavior of clinical and experimental valves which stimulated provocative conclusions regarding development of less thrombogenic devices.

MATERIALS AND METHODS

Pulse duplicator experiments and computational modeling

Over time, progressive adaptations to the pulse duplicator and experiment outcomes have been reported [10]. This included the optical measurement of valve POVA kinematics and non-trivial in silico evaluations [11]. Test conditions, FSI parameters, and boundary conditions used in this study are reported in the Figure 1.

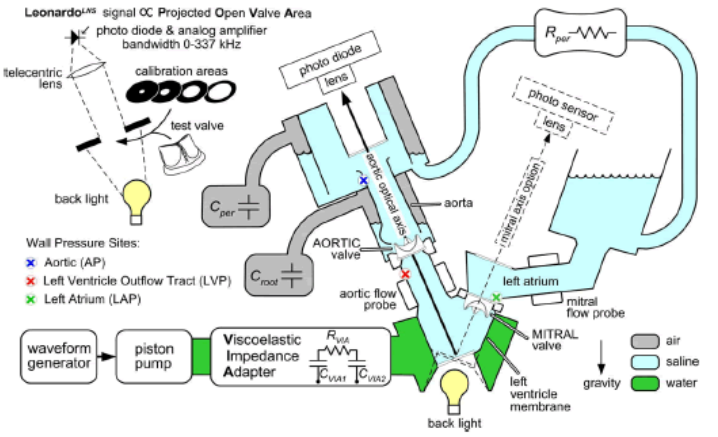

Figure 1: Leonardo^LNS pulse duplicator system includes reduced models of compliance and resistance: C_{VIA1} 120 mL; C_{VIA2} 50 mL; C_{per} 615 mL; C_{root} 640 mL; R_{per} adjusted for normal mean aortic pressure of 100 mmHg; R_{VIA} 200 c.g.s. units test fluid saline; Cardiac output ~5 L/min.

Valve name	Description
St. Jude Medical Regent™ (SJM)	Mechanical bi-leaflet
mock-TAVR (PVL pre-adjusted)	Simulated TAVR with preset trivial Paravalvular Leak (PVL)

Valve name	Description
On-X™ Life Technologies	Mechanical bi-leaflet
BV3DLNS	Printed prototype, bi-leaflet
Lapeyre-Triflo™-F6 (circa 2004)	Prototype, mechanical tri-leaflet
Edwards-Perimount™	Bioprosthetic, pericardial tri-leaflet

Note: Valve seat size (TAD) ~25 mm. (A)ortic, (M)itral; Non-test valve Mitroflow** pericardial size 29 mm. **Sorin, Milan, Italy

Test valves are listed in Table 1. Flow and pressure signals are filtered by analogue circuitry (bandwidth BW ~0-100 Hz). The POVA signal was unfiltered and had a measured rise time ~1.04 μs (BW ~0-337 KHz). Saline was used as an accepted test fluid per ISO 5840-3 with density ρ=1.0 g/cm3 and dynamic viscosity μ=1.0 Cp.

Assessment of dynamic flow velocity The Leonardo system enables assessment of dynamic flow velocity through test valves using measurements from an electromagnetic magnetic flow probe together with photodiode detection of POVA. Mathematically, flow velocity equates to the ratio of these two quantities as: Flow velocity (cm/s)=volumetric flow rate (cm3/s)/POVA (cm2) The assumption is POVA has a uniform flow profile but this may not hold true when valve occluder motion and flow are irregular. Experiments indicate that as POVA decreases, valve flow velocity increases and conversely, decreases when POVA increases. This behavior is governed by Bernoulli's principle.

Pressure measurement

Left atrial, left ventricle aortic outflow tract, and aortic sites pressures measured via short catheters (~7.5 cm length) have internal diameter of ~1.8 mm connected to disposable pressure transducers (DeltranTM, model PT43-604)*** (***: Utah Medical Products Inc., Midvale, Utah 84047-1048, USA). Catheter ports measured wall pressures referenced to the mid-plane of the test valve. In Figure 1, aortic transvalve pressure is measured between the left ventricular outflow tract (LVP) and the aorta (AP). Mitral transvalve pressure is measured between the left atrium (LAP) and the left ventricular outflow tract (LVP).

Significant waveform characteristics Several traits are clear in Figures 3-5. All signals were sampled synchronously. Regions relevant to the valve closure moment are near the dashed red line. Of importance are: Initial minimum valve POVA values and initial peak negative values attained in transvalve pressure, volume flow rate, and closure flow velocities. For bioprosthetic valves, we observed an upward-downward movement of both the valve frame and leaflets demonstrative of compliance reactivity. Hydrodynamic oscillations are also present post valve closure as seen in the unadjusted volume flow rate in some of the waveforms. Comparing the phasing of volume flow rate and POVA near valve closure, regional components having compliance influence hydrodynamic patterns.

Signal synchronicity

As indicated in Figures 3 and 4, in the aortic and mitral valve sites, instantaneous minimum regurgitant volume flow rate and minimum POVA are synchronous with valve closure. The flow and pressure signals are processed through 100 Hz low-pass analogue filters whereas POVA is unfiltered to preserve maximum frequency response (~0-337 KHz).

Synchronized hydrodynamic oscillations emerge post valve closure due to the pooled reactive compliances of the test valve and holder. These damped oscillations are observed in the unadjusted volume flow rate signals (dashed grey) and are ascribed to the combined movement of test valve components (i.e., leaflets plus stent) within the elastic silicone rubber holder. Oscillations evident for all valves and sites have similar periodicity ~20 ms (50 Hz).

Statistical analysis For each experiment, we acquired 10 consecutive cycles and report average velocity measurements and cycle-to-cycle variations of 10 negative peak flow velocities recorded using Confidence Limits (CL). Summary of the valve flow velocity test datasets utilize EXCEL**** (****: Microsoft, Redmond, WA, USA) data analysis tool labeled descriptive statistics with options Analysis ToolPak and Solver Add-in. In Figures 3-5, mean negative peak flow velocities and CL=95% indicated by CL bars adjacent to the flow velocity waveforms show the predicted uncertainty.

Experimental valve design

The BV3D rapid prototype valve design shown in Figures 2A and 2B show a working model that resulted from several designs trialed. Consideration of competing factors produced 56 laboratory constructed prototype valves with data from

experiments producing empiric optimization through interaction of leaflet profile, pivot location and surface characteristics. These led to the rapid printed prototype model BV3D with advantageous forward and especially closing flow dynamics. In this work, Leonardo provided immediate feedback on the impact of even subtle geometric changes on valve dynamic behavior.

RESULTS

Aortic vs. mitral dynamics When fluid in motion is abruptly halted or changes its direction (momentum change) water hammer is observed. This unwanted transient motion closely associates with valve closure timing, property of valve mountings and has been previously reported in vitro. Figures 3-5 illustrate snapshots of shock water-hammer dynamics with mean flow velocities reaching -29.0 m/s for the On-X mitral and -65.2 m/s for the On-X aortic valve and is absent for the Lapeyre-Triflo-F6, prototype BV3D, mock-TAVI, and Edwards-Perimount control valves. The mock-TAVI valve was untested in the mitral site.

For the On-X, SJM, and LT valves in the mitral site, a brief fractional reopening is evident in POVA post initial valve closure. In Figure 4, negative peak transvalve pressure spikes range over comparable levels in the mitral site (-75 to -90 mmHg). However, in the aortic position (Figure 3) pressure spikes encompass a wider range (-40 to -95 mmHg).

Signature shock water hammer dynamics for aortic and mitral valves are evident for POVA, transvalve pressures, volume flow rates, and derived valve flow velocity waveforms. We found that shock water hammer dynamics can be mitigated by valve designs optimized for soft valve closure which reduces retrograde valve flow velocity in the early closing phase as observed for the BV3D and EP valves.

DISCUSSION

Over the past 60 years, heart valve design and performance evolved to provide improved durability and hemodynamic function. While preferences for mechanical vs. bioprosthetic valves fluctuated widely, the advent of transcatheter delivered devices and their less invasive insertion methodology, the balance shifted progressively in favor of bioprostheses. Although initially restricted to use in the elderly or patients designated too fragile for conventional surgical implantation, use is now extended to younger and lower risk candidates. Younger patient cohorts receiving bioprosthetic heart valves have longer life expectancies (>20 years) and thus a higher likelihood of re-intervention. The shift in favor of BHVs may prove to be premature as more (or lack of) long-term data is in hand. A recent surgical AVR study by in patients aged 50 to 69 years, found long-term survival was better in those who received mechanical compared to Perimount bioprosthetic valves and suggested a substantial survival advantage be recognized in patients with mechanical valves [15]. To respond to an incidence of technical failure in contemporary transcatheter valves and perhaps in anticipation of increasing frequency of degenerated valves in younger patients, a variety of transcatheter “rescue” devices are offered. Inserted within a degenerated or malfunctioning primary valve or a previously implanted rescue device, the predicted durability of rescue devices is speculative.

CONCLUSION

This work exposes the central relationship between thrombogenicity and predicted high velocity flows and shear forces at valve closure. As practical application of our findings, specific valve geometric features were identified that led to prototype designs with potential for further development. The application of unique technology, rapid prototyping and ranking of flow velocity patterns near valve closure optimized experimental valve geometry for reduced thrombus potential compared with control valves. We compared the hydrodynamics and kinematics of prosthetic heart valves at valve closure to control valves. The in vitro results suggest that the potential for blood clots caused by high velocity flows and shear forces can be reduced by focusing on specific valve geometric features, leading to the development of improved clinical devices. The study however raises the question of whether optimum mechanical valve performance requires similar, identical or lower valve closing flow velocities compared to contemporary clinical bioprostheses. The work opens an experimentally assisted pathway for developing new, durable and less thrombogenic devices and the prototype model BV3D serves as evidence that focused laboratory efforts can yield promising results. Additionally, the study indicates that valve flow velocity differentials and associated shear are significant activators of thrombogenicity for the On-X valve, emphasizing the importance of valve closure behavior in reducing thrombus potential and improving clinical devices, despite the challenges in introducing new prosthetic heart valves to the market. The Holy Grail goal of a mechanical valve independent of chronic anticoagulation still beckons.

REFERENCES

1) Brownlee RT, Scotten L. The in vitro assessment of left ventricular flow patterns on the closure of a new mitral valve "bioprosthesis". Trans Am Soc Artif Intern Organs. 1976;22:341-346.
2) Scotten LN, Walker DK. New laboratory technique measures projected dynamic area of prosthetic heart valves. J Heart Valve Dis. 2004;13(1):120-133.
3) Scotten LN, Siegel R. Importance of shear in prosthetic valve closure dynamics. J Heart Valve Dis. 2011;20(6):664-672.
4) Scotten LN, Siegel R. Are anticoagulant independent mechanical valves within reach—fast prototype fabrication and in vitro testing of innovative bi-leaflet valve models. Ann Transl Med. 2015;3(14):197.
5) Chaux A, Gray RJ, Stupka JC, Emken MR, Scotten LN, Siegel R. Anticoagulant independent mechanical heart valves: Viable now or still a distant holy grail. Ann Transl Med. 2016;4(24):525-531.
6) Lee JH, Rygg AD, Kolahdouz EM, Rossi S, Retta SM, Duraiswamy N, et al. Fluid-Structure Interaction models of bioprosthetic heart valve dynamics in an experimental pulse duplicator. Ann Biomed Eng. 2020;48(5):1475-1490.
7) Carpenter AJ. Commentary: A surgeon's view of engineer's data. JTCVS Open. 2020;6:84.
8) Obrist D, Carrel TP. Commentary: Leaflet fluttering of bioprosthetic valve–Does it matter?. JTCVS Open. 2021;6:82-83.
9) Sheriff J, Wang P, Zhang P, Zhang Z, Deng Y, Bluestein D. In vitro measurements of shear-mediated platelet adhesion kinematics as analyzed through machine learning. Ann Biomed Eng. 2021;49(12):3452-3464.
10) Scotten LN, Siegel R, Blundon DJ, Deutsch MA, Martin TR, Dutton JW, et al. Canary in the cardiac-valve coal mine: Flow velocity and inferred shear during prosthetic valve closure–predictors of blood damage and clotting. bioRxiv. 2022.
11) Kovarovic BJ, Rotman OM, Parikh PB, Slepian MJ, Bluestein D. Mild paravalvular leak may pose an increased thrombogenic risk in Transcatheter Aortic Valve Replacement (TAVR) patients-insights from patient specific in vitro and in silico studies. Bioengineering. 2023;10(2):188.
12) Lee JH, Scotten LN, Hunt R, Caranasos TG, Vavalle JP, Griffith BE. Bioprosthetic aortic valve diameter and thickness are directly related to leaflet fluttering: Results from a combined experimental and computational modeling study. JTCVS Open. 2021;6:60-81.
13) Deutsch MA, Scotten LN, Siegel R, Lange R, Bleiziffer S. Leaflet thrombosis and clinical events after TAVR: Are paravalvular leaks a crucial trigger. EuroIntervention. 2018;14(6):716-717.
14) Herbertson LH, Deutsch S, Manning KB. Near valve flows and potential blood damage during closure of a bileaflet mechanical heart valve. J Biomech Eng. 2011:133(9):094507.
15) Lu R, Dismorr M, Glaser N, Sartipy U. Aortic valve replacement with mechanical valves vs. perimount bioprostheses in 50-to 69-year-old patients. JACC: Adv. 2023;2(4):100359.
16) Tseng EE. When valve-in-valve implantation is not sufficient: Bioprosthetic Russian dolls. J Thorac Cardiovasc Surg. 2016;152(2):624-625.
17) Zilla P, Brink J, Human P, Bezuidenhout D. Prosthetic heart valves: Catering for the few. Biomaterials. 2008;29(4):385-406.
18) Woldendorp K, Indja B, Bannon PG, Fanning JP, Plunkett BT, Grieve SM. Silent brain infarcts and early cognitive outcomes after transcatheter aortic valve implantation: A systematic review and meta-analysis. Eur Heart J. 2021;42(10):1004-1015.
19) Ding J, Chen Z, Niu S, Zhang J, Mondal NK, Griffith BP, et al. Quantification of shearâ□□induced platelet activation: High shear stresses for short exposure time. Artif Organs. 2015;39(7):576-583.
20) Kolahdouz EM, Bhalla AP, Craven BA, Griffith BE. An immersed interface method for discrete surfaces. J Comput Phys. 2020;400:108854.