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Journal Title: Journal of Biomechanics
Volume: Volume 45, Number 8
Publisher: Elsevier: 12 months | 2012-05-11, Pages 1514-1516
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1016/j.jbiomech.2012.03.009
Permanent URL: https://pid.emory.edu/ark:/25593/sq60v

Final published version: http://dx.doi.org/10.1016/j.jbiomech.2012.03.009

NIH Public Access

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J Biomech. Author manuscript; available in PMC 2014 June 05.

Published in final edited form as:

J Biomech. 2012 May 11; 45(8): 1514–1516. doi:10.1016/j.jbiomech.2012.03.009.

In-vivo transducer to measure dynamic mitral annular forces

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Abstract

Limited knowledge exists regarding the forces which act on devices implanted to the heart's mitral valve. Developing a transducer to measure the peak force magnitudes, time rates of change, and relationship with left ventricular pressure will aid in device development. A novel force transducer was developed and implanted in the mitral valve annulus of an ovine subject. In the post-cardioplegic heart, septal-lateral and transverse forces were continuously measured for cardiac cycles reaching a peak left ventricular pressure of 90 mmHg. Each force was seen to increase from ventricular diastole and found to peak at mid-systole. The mean change in septal-lateral and transverse forces throughout the cardiac cycle was 4.4 ± 0.2 N and 1.9 ± 0.1 N respectively. During isovolumetric contraction, the septal-lateral and transverse forces were found to increase at peak rate of 143 ± 8 N/s and 34 ± 9 N/s, respectively. Combined, this study provides the first quantitative assessment of septal-lateral and transverse forces within the contractile mitral annulus. The developed transducer was successful in measuring these forces whose methods may be extended to future studies. Upon additional investigation, these data may contribute to the safer development and evaluation of devices aimed to repair or replace mitral valve function.

Keywords

Mitral valve; Ischemic mitral regurgitation; Force; Strain gage; Transducer

1. Introduction

Mitral valve (MV) disease is the most common valvular ailment among the US population (Roger and Go, 2011). Dysfunctions occurring from this disease can be functionally classified with clinical and surgeon specific factors influencing the decision to repair or replace the MV (Bonow and Carabello, 2006; Bolling and Li, 2010). The therapeutic success of these therapies varies and has motivated the development of technique specific

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Conflict of interest statement

None.

devices to improve patient outcomes (Fedak and McCarthy, 2008; Borger and Alam, 2006; Chiam and Ruiz, 2011).

To ensure the safety of these devices, International Standards Organization (ISO; Cardiovascular implants, 2005) 5840:2005 and Food and Drug Administration draft guidance recommend these devices to be tested under cyclic forces anticipated in vivo (Draft Guidance for Industry and FDA Staff, 2010). These tests can be used to evaluate structural durability and identify relevant modes of failure. Computational models have been used to supplement these tests whose simulated loading can aid in optimizing device structure and function (Aguel and Hillebrenner, 2011). While these tests significantly depend on prescribed device loading, limited knowledge exists for the cyclic forces acting on devices implanted in the mitral annulus.

In 1994, Hasenkam was the first to describe the forces generated by porcine myocardium on 29 mm Edwards-Duromedics mitral valves (Hasenkam and Nygaard, 1994). Results revealed a maximum in-plane force of 6–8 N to act 30° clockwise from the natural intercommissural line. Later in 2001, Shandas used 3D ultrasound to measure the deformation of St. Jude Medical Biocor® stented prosthetic mitral valves within two porcine subjects (Shandas and Mitchell, 2001). Measured ring deformations were used as boundary conditions within a finite element model to estimate the maximum septal-lateral forces to fall between 4.4 and 13.9 N. While groundbreaking, these studies were unable to identify a common direction of maximal radial force, quantitatively compare the magnitude of these forces with other radial directions, and describe the rate changes of these forces during device loading.

Determining these endpoints will contribute to the safer development of novel designs that repair or replace MV function. Such data will provide a more accurate description of the force magnitudes and rates required for uniaxial and biaxial fatigue testing. Moreover, these forces may be valuable in setting more accurate boundary conditions within finite element models. To this end, we describe the development and first use of a novel transducer to dynamically measure in-plane radial forces resulting from mitral annular contraction within a healthy ovine model.

2. Methods

2.1. Mitral annular force transducer

A strain gage transducer was developed to measure in-plane radial forces resulting from mitral annular contraction. Similar to the native annular shape, the transducer's spring element possessed a D-shaped profile whose size was constrained to ovine annular dimensions measured previously (Gorman and Gorman, 2003; Fig. 1). This element consisted of two measurement arms oriented in the septal-lateral and transverse directions of the mitral annulus with lateral suture passages for transducer-annular anchoring.

Combining finite element analysis (SolidWorks, Waltham, MA) with forces previously measured (Hasenkam and Nygaard, 1994; Shandas and Mitchell, 2001) the design of the spring element was optimized for force measurement. Cross-sections chosen for strain gage adhesion were designed with a slight curvature to improve strain gage signal-to-noise ratios and reduce strain gradients. The central-bridge area was also designed to minimize transmitral flow obstruction, increase the moment inertia to resist shear or torsion, and minimize the transmission of forces between each measurement arm. Based on these analyses, the spring element was fabricated from MicroFine Green Resin using sterolithography (Fineline Prototyping, Raleigh, NC).

Resistance strain gages (EA-031DE-350, Vishay Micro-Measurements, Malvern, PA) in a quarter-bridge configuration were attached to the spring element and environmentally protected using standard techniques (Window, 1989). The electrical outputs of these gages during transducer deformation were correlated to known forces within a well-defined calibration apparatus (Fig. 2). The apparatus had the ability to impose septal-lateral and transverse forces either independently or in concert. Based on previous studies, each transducer was calibrated from 0 to 8.4 N (in 1.2 N increments) while submerged in a 37 °C water bath to mimic the physiologic temperature of the ovine subjects.

The transducer was loaded in the aforementioned range for 10 consecutive runs. A linear relationship between voltage and calibrated force was observed with a correlation of R^2=0.99. After calibration, the relative difference between measured and true values was less than 2%. Testing of the device found peak loading (8.4 N) along one measurement arm to minimally influence the perpendicular arm, resulting in measured forces less than 0.1 N. Out-of-plane deformation using forces previously reported also minimally influenced force measurements with results less than 0.1 N (Jensen and Jensen, 2008). The frequency response of strain gage transducers has been previously published by our group and shown to exceed the requirements for intracardiac measurement (Nielsen and Soerensen, 2004; Nichols and O'Rourke, 2007).

2.2. Experimental protocol

The animal used in this work received care in compliance with the protocols approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania in accordance with the guidelines for humane care (National Institutes of Health Publication 85-23, revised 1996).

The ovine subject (42 kg) was intubated, anesthetized, and ventilated with isofluorane (1.5% to 2%) and oxygen. After establishment of Cardiopulmonary Bypass (CPB), epicardial echocardiography was completed. The transducer was zeroed and implanted as completed with mitral annuloplasty (Fig. 3). After implantation, the forces due to device-annular sizing were measured. Following separation from CPB, a pressure transducer (SPR-3505; Millar Instruments, Houston, TX) was passed percutaneously into the left ventricle through the femoral artery to monitor left ventricular pressure (LVP). Upon establishing baseline hemodynamics, forces resulting from annular contraction were measured within the post-cardioplegic heart.

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2.3. Data acquisition and analysis

Mitral annular forces and LVP were continuously acquired using a compact Data Acquisition System (cDAQ 9174), strain gage bridge module (NI 9237), and analog voltage module (NI 9215; National Instruments, Austin, TX) at 1613 Hz. Forces and LVP were monitored and recorded using a custom-built program within the LabVIEW version 9.0 software (National Instruments, Austin, TX). Recorded data were processed offline using a custom Matlab program (Mathworks, Natick, MA). This data was analyzed for the change in each force from ventricular diastole to systole, the rate change of force with time *dF/dt* during isovolumetric contraction, peak LVP, and the rate change of left ventricular pressure with time during isovolumetric contraction *d(LVP)/dt*. These quantities were averaged over 5 consecutive cardiac cycles and reported as a mean ±1 standard deviation.

3. Results

Prior to implantation, echocardiography revealed the subject's mitral annulus to exhibit end-diastolic septal-lateral and transverse diameters of 25.3 and 31.5 mm respectively. After successful implantation, the flaccid annulus exerted forces of 2.3 N and −1.0 N in the septal-lateral and transverse directions respectively. These data indicate that the transducer oversized the septal-lateral annular dimension while undersizing the transverse. During force acquisition, the mean heart rate and LVP were 86 beats/min and 90/9 mmHg/mmHg (systolic/diastolic).

Throughout each cycle, compressive forces were seen to increase from ventricular diastole and peak at mid-systole. Five consecutive representative cardiac cycles of the change in septallateral and transverse forces with LVP are plotted in Fig. 4. From diastole, a small elevation in force was seen during the atrial kick shown to be more prominent in the transverse direction. This elevation was followed by a sharp rise in force during isovolumetric contraction, reaching a peak at mid-systole.

The mean change in septal-lateral and transverse forces throughout the cardiac cycles was 4.4±0.2 N and 1.9±0.1 N respectively (Table 1). During isovolumetric contraction, the mean peak *d(LVP)/dt* was 1757±96 mmHg/s while the mean peak *dF/dt* in the septal-lateral and transverse directions were 143±8 N/s and 34±9 N/s respectively. 3D echocardiography images were acquired and the transducer was found to remain fixed in the annular plane with no apparent twisting or shearing during annular contraction. Upon the study's completion, the heart was explanted and transducer found to remain firmly secured to the mitral annulus within negligible thrombus formation.

4. Discussion

This study was successful in the development of a novel transducer to measure dynamic radial forces resulting from mitral annular contraction. This study was the first to quantify the rate change of these forces during isovolumetric contraction which upon further investigation may have strong implications for accelerated axial and biaxial fatigue tests. These measurements are not without limitations. These forces are reported relative to a well-defined calibration apparatus and may not fully represent device implantation. Absolute forces experienced by the device after CPB were difficult to quantify due to observed variations in the diastolic forces from combined changes in annular contractility, temperature effects, and signal offsets caused by inadvertent tugging of the transducer's wires. For these reasons, the change in force throughout the cardiac cycle is reported. These forces are limited to a healthy ovine model and may not represent those in varying mitral etiologies. Future studies will evaluate these forces in a normal and chronic ischemic mitral regurgitation ovine model to evaluate directional and disease differences in force profiles. Determining these endpoints will contribute to the safer development of devices for advancing future techniques in MV surgery.

Acknowledgments

This study was supported by a research grant awarded from the Food and Drug Administration (FDA1061718) and by grants from the National Heart, Lung and Blood Institute of the National Institutes of Health, Bethesda, MD (HL63954 and HL73021). Dr. Robert Gorman and Dr. Joseph Gorman were supported by individual Established Investigator Awards from the American Heart Association, Dallas, TX. We acknowledge the contributions to and development of the data acquisition platform provided by members of the Cardiovascular Research Unit in Århus, Denmark.

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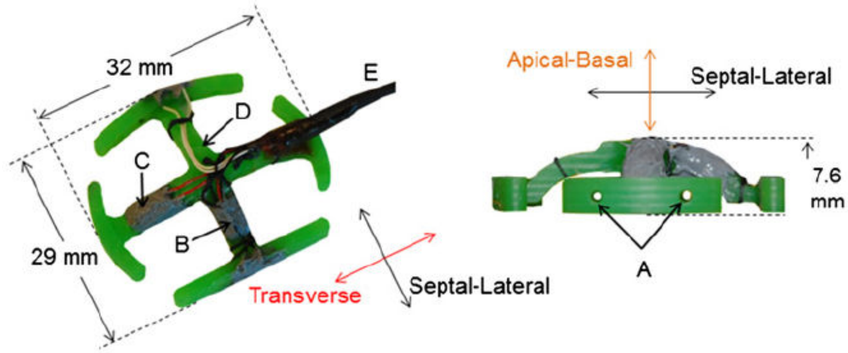

Fig. 1.
Developed mitral annular force transducer with measurement directions and features identified: (A) suture passages for transducer-annulus anchoring, (B) strain gage to measure septal-lateral force, (C) strain gage to measure transverse force, (D) transducer spring element, and (E) exit wire harness.

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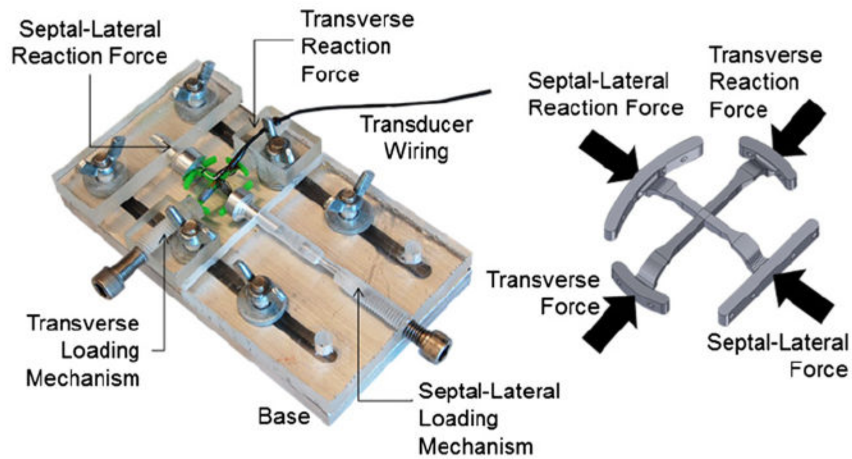

Fig. 2.
Left: Calibration apparatus; right: schematic of applied forces during calibration.

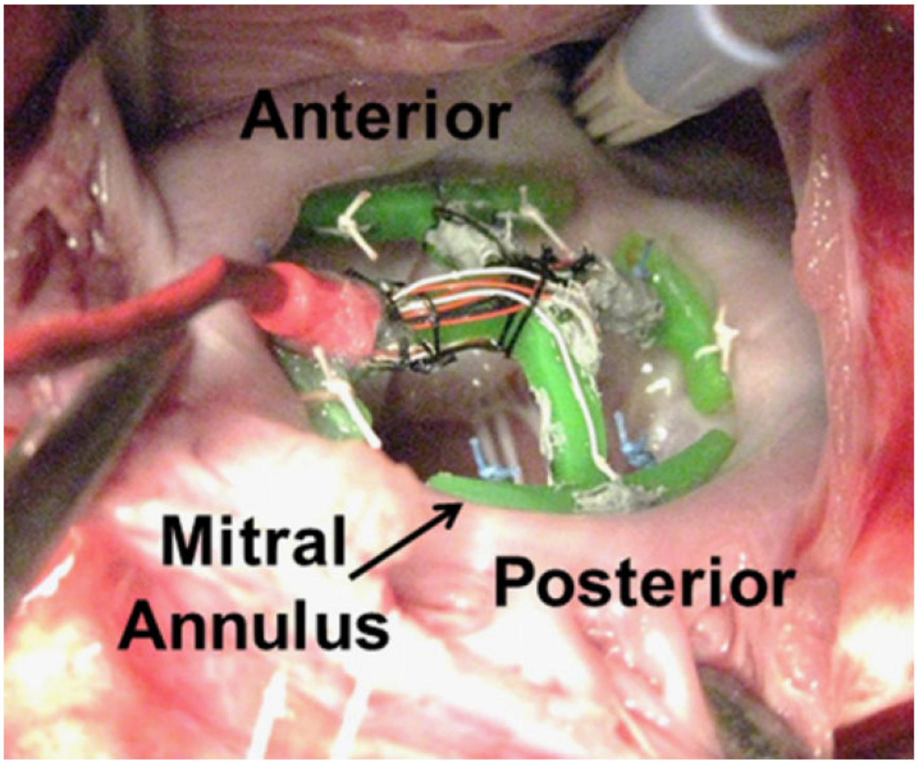

Fig. 3.
Transducer shown anchored within the mitral annulus aligned with the septal-lateral and transverse directions of the native mitral annulus.

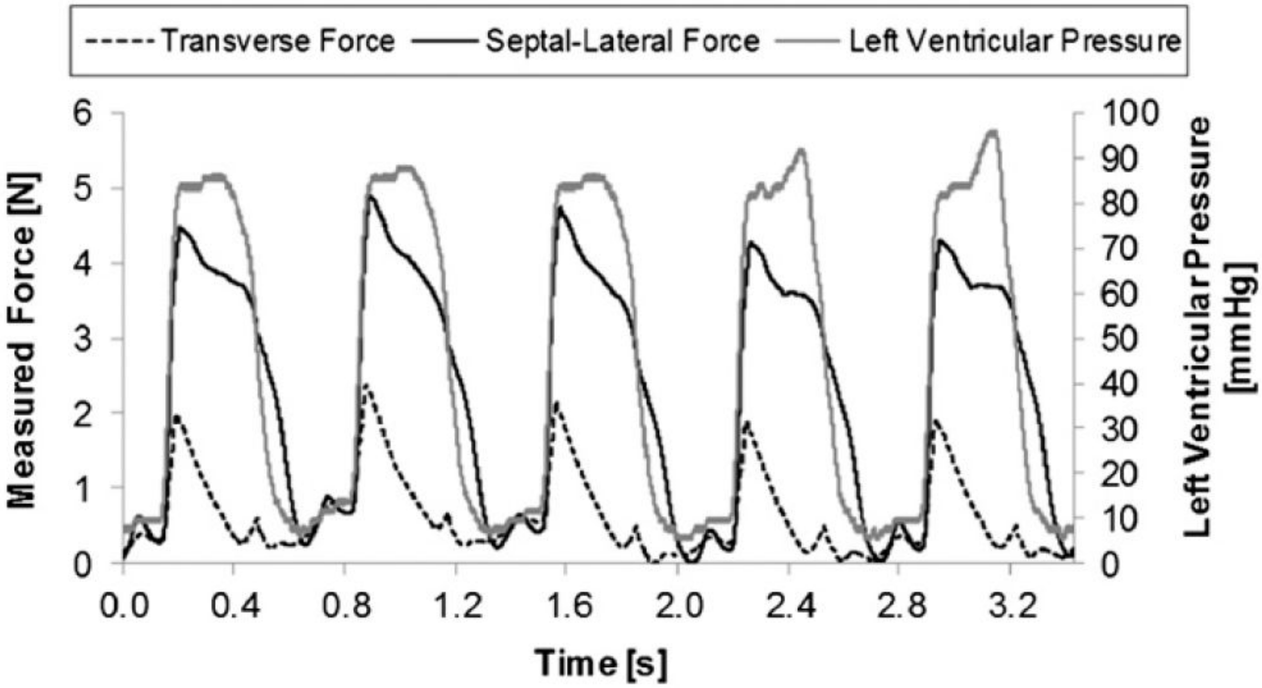

Fig. 4.

Five consecutive cardiac cycles of septal-lateral and transverse forces resulting from mitral annular contraction plotted against time and left ventricular pressure.

Table 1

Force profiles for the ovine subject at baseline hemodynamics.

		Change in force throughout the cardiac cycle [N]	Time rate of change during isovolumetric contraction [N/s]
Measurement direction	Septal-lateral	4.4 ± 0.2	143 ± 8
	Transverse	1.9 ± 0.1	34 ± 9