学位論文

Energy dynamics of the intraventricular vortex After mitral valve surgery

（僧帽弁術後左心室内渦流のエネルギー動態の検討）

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著者の宣言

本学位論文は、著者の責任において実験を遂行し、得られた真実の結果に基づいて正確に作成したものに相違ないことをここに宣言する。

要　旨

僧帽弁手術後の僧帽弁形態が心室内血流動態に影響を及ぼし、その事が遠隔期の心機能に影響する可能性があると考え今回の臨床研究を行った。
今回我々は Vector flow mapping(VFM)心臓超音波検査を僧帽弁手術後の患者に施行し、比較検討を行った。対象症例は機械弁置換術後の 11 症例、内 9 症例は非解剖学的な機械弁置換症例群であり、残り２症例は解剖学的な機械弁置換症例群、３症例は生体弁置換術群、４症例は僧帽弁形成術群であった。患者背景として手術時の患者年齢は 57.4±17.8 歳であり、VFM 心臓超音波検査の観察時期は術後 119.9±126.7 ヶ月であった。評価項目は Energy loss(EL)と Kinetic pressure(KP)、更にエネルギー効率比（EL／KP）とした。
心室内血流を VFM 心臓超音波で観察すると、異なる２方向の可視化された心室内渦流が観察された。一つの心室内渦流とは僧帽弁通過血流は、左室後壁に沿うように流入し心尖部を回り込み、その後心室中隔壁に沿い、最終的に左室流出路及び大動脈弁から流出される心室内渦流として観察される、つまりこの方向の心室内血流を「Clockwise な渦流」と定義する。それとは逆方向の心室内渦流を「Counterclockwise な渦流」と定義した。結果、解剖学的な位置で機械弁置換した 2 例と僧帽弁形成術施行した 4 例は Clockwise な渦流が観察され、非解剖学的な位置で機械弁置換した 9 例と生体弁置換した 3 例は Counterclockwise な渦流が観察された。なお非解剖学的な機械弁置換群の内、3 症例は収縮期早期に左室後壁の収縮タイミングが遅れる奇異性壁運動（非同期）を認め、遠隔期において心収縮力（EF; Ejection Fraction）の低下を認めていた。
この Clockwise な渦流群と Counterclockwise な渦流群を比較してみた。収縮期において EL と KP においては両群間に有意差は認めなかったが、エネルギー効率比（EL/KP）では Counterclockwise 群の方が Clockwise 群に比べて明らか高値を呈した。次に拡張期においては Clockwise 群において EL 及び KP 共に Counterclockwise 群に比べ高い数値を呈した
この事は拡張期において Clockwise の心室内渦流は Counterclockwise の心室内渦流に対してより高いエネルギー散乱を伴う大きなエネルギーを産生していると考えられるが、エネルギー効率比の値を両群間で比較してみると、拡張期において有意差は認めなかった。この結果より、僧帽弁手術後において心室内渦流の方向にも大きな関心を払うべきであると考えられた。心室内血流は心臓の構造や機能変化に影響を受けるために心臓手術に於いては効果的な心拍出を維持するための最適な心室内血流を考慮しなければならない。
本研究は僧帽弁手術後の心室内血流を観察・数量化した初めての試みであり、今研究を基礎に、VFM 心臓超音波検査を多くの僧帽弁術後症例に長期間観察し、EL と KP を測定する事は心機能と心臓手術のストラテジーの関連性を明確化すると考えられる。

目次

Energy Dynamics of the Intraventricular Vortex after Mitral Valve Surgery

Running Title: Echocardiography Flow Visualization Applied to Mitral Valve Surgery

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ABSTRACT

Background: Mitral valve morphology after mitral valve surgery affects postoperative intraventricular flow patterns and long-term cardiac performance. We visualized ventricular flow by echocardiography vector flow mapping (VFM) to reveal the impact of different mitral valve procedures.

Method: Eleven cases of mechanical mitral valve replacement (nine in the anti-anatomical and two in the anatomical position), three bioprosthetic mitral valve replacements, and four mitral valve repairs were evaluated. The mean age at the procedure was 57.4 ± 17.8 year, and the echocardiography VFM in the apical long-axis view was performed 119.9 ± 126.7 months later. Flow energy loss (EL), kinetic pressure (KP), and the flow energy efficiency ratio (EL/KP) were measured.

Results: The cases with MVR in the anatomical position and with valve repair had normal vortex directionality ("Clockwise"; N = 6), whereas those with MVR in the anti-anatomical position and with a bioprosthetic mitral valve had the vortex in the opposite direction ("Counterclockwise"; N = 12). During diastole, vortex direction had no effect on EL ("Clockwise": 0.080±0.025 W/m; "Counterclockwise": 0.083 ± 0.048 W/m; P = 0.31) or KP ("Clockwise": 0.117 ± 0.021 N; "Counterclockwise": 0.099 ± 0.057 N; P = 0.023). However, during systole, the EL/KP ratio was significantly higher in the "Counterclockwise" vortex than that in the "Clockwise" vortex (1.056 ± 0.463 vs. 0.617 ± 0.158; P = 0.009).

Conclusions: MVP and MVR with a mechanical valve in the anatomical position preserve the physiological vortex, whereas MVR with a mechanical valve in the anti-anatomical position and a bioprosthetic mitral valve generate inefficient vortex flow patterns, resulting in potential increase in excessive cardiac workload.

Key words: Vector flow mapping (VFM), Mitral valve surgery, Flow energy loss

Abbreviations and Acronyms

CT: computed tomography

EL: energy loss

KP: kinetic pressure

LV: left ventricle

LVDd: Left ventricular diastolic dimension

LVDs: Left ventricular systolic dimension

LVEF: Left ventricular ejection fraction

MR: mitral regurgitation

MS: mitral stenosis

MVP: mitral valve plasty

MVR: mitral valve replacement

MRI: magnetic resonance imaging

PIV: particle imaging velocimetry

TTE Transthoracic echocardiography

VFM: vector flow mapping

Introduction

Flow visualization using echocardiography is making progress and can be widely applied for clinical issues including valvular heart disease[1,2,3,4], in which quantitative analysis is difficult with conventional imaging modalities[5,6]. Currently, the long-term function of the mitral valve and left ventricle after mitral valve procedures is considered to be essential in patient management, but the impact of different mitral valve procedures on this has not yet been clarified. Recent clinical evidence reveals that mitral valve plasty (MVP) may improve prognosis compared with artificial valve replacement. In artificial valve replacement, bioprosthetic valves tend to be preferred to mechanical ones currently. However, the physiological mechanism and theoretical rationale have not been clarified. In routine clinical practice, imaging for comprehensive analysis of left ventricular (LV) function is generally based on ventricular contractility, wall motion, and/or LV volume change. But this type of analysis is based on the geometrical features of the existing state of cardiac function. It cannot quantitatively evaluate cardiac workload and is not predictive of future cardiac function. VFM, by visualizing abnormal physiological vortexes in the cardiac cavity that allow calculation of kinetic stress and cardiac workload, potentially allows for predictive diagnosis of cardiac function. Blood flow visualization studies provide clues to reveal physiological and patho-physiological mechanisms by which abnormal turbulent flow increases cardiac workload and deteriorates ventricular functions[2,6]. We developed an echocardiography flow visualization system involving vector flow mapping[6,7]

(VFM), which not only shows the intraventricular flow vector but also estimates energetic parameters of hemodynamics including flow energy loss (EL) and flow kinetic pressure (KP).

In this study, we evaluated the long-term impact of different types of mitral valve procedures, comparing not only the vortex flow direction but also energetic flow efficiency based on the quantitative evaluation of flow EL and KP inside the left ventricle. We also observed the long-term impact on LV wall motion.

Methods

Patients

Seventeen patients were enrolled after mitral valve surgery. At the time of surgery, they were 57.4 ± 17.8 years of age, and the mean interval between surgery and echocardiography was 119.9 ± 126.7 months. Nine patients underwent mitral valve replacement (MVR) with a mechanical valve placed in an anti-anatomical position, in which the leaflets were aligned side-by-side. Two patients underwent MVR with a mechanical valve in an anatomical position, like normal anterior and posterior position. Three patients underwent MVR with a bioprosthetic mitral valve, and four underwent mitral valve plasty (MVP) with a mitral annular ring. Preoperative diagnosis was as follows: two patients had mitral valve stenosis (MS), ten had mitral regurgitation (MR), and five had MS with MR. Nine patients had chronic atrial fibrillation before mitral valve surgery.

All mechanical valves used were bileaflets. They included St. Jude Medical (St. Jude Medical, St. Paul, MN, USA) in nine patients, Carbo-Medics (CarboMedics Inc., TX, USA) in four, and an Omni-carbon mitral valve (Medical Inc., Inver Grove Heights, Minn.) in one. All three bioprosthetic mitral valves were mitral Carpentier-Edwards PERIMOUNT pericardial bioprosthesis (Edwards Lifesciences LCC, Irvine, CA). A Carpentier-Edwards Physio Ring (Edwards Lifesciences LCC) was used in all cases of MVP. Concomitant surgical procedures included tricuspid annuloplasty in six patients and a maze procedure with cryoablation in three patients. Four patients, including the three patients after the maze procedure, had chronic atrial fibrillation even after surgery. After mitral valve surgery, all patients were evaluated by echocardiography during follow-up. Some of the patients with mitral valve replacement using a mechanical valve had minor peri- or paravalvular leakage without mechanical valve dysfunction. Patients with mitral valve replacement using a bioprothetic valve and mitral valve plasty had trivial mitral valve regurgitation.

The ethics committee of our institution approved this study, and written informed consent was obtained from each patient.

Data acquisition

Transthoracic echocardiographic (TTE) was performed in the left lateral decubitus position. Commercially available ultrasonic equipment (Prosound F75; Hitachi-Aloka Medical, Tokyo, Japan), with a 2.00 MHz phased array cardiac transducer, was used for the examination. We measured the LV diastolic and systolic dimensions (LVDd/Ds), left ventricular ejection fraction (LVEF) with Teichholz's method, and the transmitral flow (E/A wave). The VFM data were obtained by color Doppler imaging in the apical long-axis view. The maximum velocity range of the color Doppler (Nykist limit) was set at 60–80 cm/sec, and the color baseline was kept at 0 cm/sec. The frame rate of color Doppler flow images was maintained at 23–30 frames/sec. To maintain flow data quality in left ventricular apex, ample coupling gel was applied between the transducer and the thoracic surface during the echocardiography. In all cases, we acquired left ventricular real-time two-dimensional grayscale and color Doppler flow images in standard apical three chamber views during a few continuous cardiac cycles and stored them in DICOM file format. All stored dynamic color Doppler flow images were transferred to a VFM workstation (DAS-RS1, Aloka Co, Japan) for off line analysis. All images were captured in an apical long axis view and analyzed with the anteroseptal side on right side of the view. Thus, a vortex formed from the posterior to the septal wall (normal direction) becomes "Clockwise," whereas a vortex formed from septal to posterior wall becomes "Counterclockwise" (Figure 1), as previously described[6]. In addition to diastolic vortex direction, VMF analysis provided the systolic and diastolic flow energy loss (EL, W/m) inside the LV, and the kinetic pressure (KP, N) inside the LV.

Flow energy loss (EL) was defined with the following equation.

$$\mathrm{EL} = \int_{LV\ chamber} \sum_{i,j=x,y} \frac{1}{2}\mu \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right)^2 dA$$

, where μ indicated viscosity of the blood (0.004 Pa s) , and *A* was the area increment of the integral.

Kinetic energy (KE) of the transmitral flow was defined with the following equation.

$$\mathrm{KE} = \int \frac{1}{2}\rho\ |\vec{u}|^2\ \vec{u} \cdot d\vec{l}$$

, where ρ indicated blood density (1060 kg/m^3) and integral was line integral on the mitral annulus.

Even though the intraventricular flow EL was caused by turbulent flow, the dissipated energy itself was generated by ventricular wall motion. Therefore, the ratio of EL to the energy generated by ventricular muscle work is essential to assess ventricular performance[6)]. However, ventricular muscle work itself is difficult to access noninvasively. Therefore, we calculated flow energy efficiency ratio, defined as EL/KP inside the LV, to estimate flow energy efficiency.

Statistical analysis

Continuous variables were presented as means ± standard deviations. Between-group differences were tested for significance using the unpaired Student *t*-test. Statistical significance was defined as $P < 0.05$.

Results

Previous studies revealed that after MVR with a mechanical valve, transmitral flow is directed to, and collides with, the anteroseptal wall and then turns toward the apical and posterolateral wall, defining a "Counterclockwise" vortex. The direction of travel is in the opposite direction of the normal "Clockwise" vortex, in the left ventricle (LV)[5]. In this study, a "Clockwise" vortex was observed during diastole in the MVR patients with a mechanical valve placed in the anatomical position and in all MVP patients. In contrast, a "Counterclockwise" vortex was observed in the patients with a mechanical valve placed in an anti-anatomical position and in patients with a trileaflet bioprothetic valve. During diastolic phase in those groups, transmitral flow collided with the anteroseptal wall, turned to the apex and sequentially to the posterolateral wall. In patients with a bioprothetic mitral valve, the main vortex was formed in the mid-portion of the LV and was "Counterclockwise," but because of the flexible soft leaflets, the vortex often slipped, and a smaller size vortex in the opposite direction was observed in the apical portion of the LV. In three patients with the mechanical valve in the anti-anatomical position, dyssynchronic posterior wall motion in the early systolic phase was detected, resulting in reduced EF.

Differences in flow dynamics between the “Clockwise” and “Counterclockwise” vortices were identified by VFM. During systole, comparing clockwise vortex with counter-clockwise vortex, flow EL (“Clockwise”: 0.037 ± 0.034 W/m, “Counterclockwise”: 0.064 ± 0.064 W/m, P = 0.250) and KP (“Clockwise” 0.056 ± 0.036 N, “Counterclockwise” 0.060 ± 0.045 N; $P = 0.832$) were not significantly different. The flow energy efficiency ratio EL/KP, the ratio was significantly higher in cases with a “Counterclockwise” vortex (“Clockwise”: 1.056 ± 0.463, “Counterclockwise”: 0.617 ± 0.158) than in those with a “Clockwise” vortex flow (P = 0.009) (Figure 2). During diastole, clockwise vortexes had higher energy loss (“Clockwise”: 0.157 ± 0.045 W/m, “Counterclockwise”: 0.109 ± 0.045 W/m, P = 0.042) and kinetic pressure (“Clockwise” 0.220 ± 0.030 N, “Counterclockwise” 0.152 ± 0.085 N; $P = 0.023$) than “Counterclockwise” vortexes. During diastole, “Clockwise” vortexes generated larger energy with higher energy dissipation than “Counterclockwise” vortexes. The flow energy efficiency ratio EL/KP in “Clockwise” and “Counterclockwise” vortexes during diastole were not significantly different (“Clockwise”: 0.711 ± 0.168, “Counterclockwise”: 0.831 ± 0.330, P = 0.309).

Discussion

Especially in heart valve disease, we are still confronting discrepancies between the patients' symptoms and examination parameters related to the cardiac functions obtained from imaging studies. Comprehensive assessments of LV function based on the geometric changes, including speckle tracking or ventricular volume measurements, are essential tools in the clinical practice of valvular heart disease, but they describe the current state of cardiac functions and do not always indicate the prognosis. Interest in the analysis of intraventricular flow has been developing recently[1,6)]. Ventricular flow analysis has important incremental value over conventional cardiovascular imaging modalities including echocardiography, magnetic resonance imaging (MRI)[2,6)], and computational flow study with computed tomography (CT). Several novel modalities have been reported for intraventricular flow analysis including echocardiography, and magnetic resonance imaging (MRI). One of the most desired applications of these study is the evaluation of flow after cardiac surgery[5,8)].

Several echocardiography flow visualization methods have been reported. Kim HB et al[9)]. describes an echo particle imaging velocimetry (PIV) method based on speckle pattern tracking injected contrast medium in ventricular blood. This method has been applied in patients after mitral valve surgery[5)]. However, recent validation revealed that high velocity vectors of over 50 cm/sec have insufficient accuracy[10)]. On the other hand, VFM is a color Doppler-based flow visualization method. It was first reported by Ohtsuki et al[11], and subsequently modified by Garcia D[12] et al and Itatani K et al[7]. Currently, VFM enables evaluation of hemodynamic parameters such as flow EL, vorticity, and wall shear stress[7]. EL and KP can be measured in each pixel on each frame, and their integrals inside the LV chamber can be given frame by frame. We can thus independently estimate flow efficiency during systole and diastole. In recent reports of intraventricular flow patterns, vortex formation is dominant during diastole, and it was shown to be affected by age and gender[12] or myocardial disease[13,14]. Several quantitative parameters for describing vortex properties have been reported, including vortex location, morphology, vortex formation time (VFT)[15], and kinetic energy (KE). Parameters related to the flow energy would be associated with the prognosis of ventricular performance[16].

The goal of treating heart valve disease is not to simply stop regurgitation or to reduce the pressure gradient, but to preserve ventricular function by reducing the ventricular workload caused by ineffective diseased blood flow. This study sheds light on the intraventricular vortex and the intraventricular EL, which are key factors, in addition to valvular regurgitation or the pressure gradient, affecting prognosis after mitral valve surgery. Mitral valve surgery has been modified several times in recent decades, and flow patterns after heart valve surgery are receiving much attention. Normal transmitral flow is known to cause a vortex ring along the mitral valve[14]. A vortex develops along the anterior leaflets and propagates towards the apex under the large anterior leaflets[6] (Figure 3).

In contrast, artificial mitral valve structures differ from the original anatomy, and their symmetrical leaflets cause straightforward flow normal to the plane formed by the mitral annulus. Only the anatomical position of the bileaflet mechanical valve replacement has the potential to generate physiological vortex directions. Flexible soft trileaflet bioprosthetic valve seem to cause multiple separated vortexes in the LV chamber, whereas hard mechanical valves cause a single large vortex. In previous reports, only geometrical features of the vortexes that form have been reported. In a basic experimental study using optical PIV, Akutsu et al compared phantom chamber flow obtained with anatomical and anti-anatomical positions of mechanical valves[17]. Because the structure and motion of the phantom was quite different from that of the actual human heart chamber, the vortex flow pattern was far different from the in-vivo observations[18] Faludi et al demonstrated left ventricular vortex flow patterns after the mitral surgery with Echo-PIV[5]. Their results with regard to the direction of the vortex observed after mitral valve surgery were quite similar to ours. The similarity of the two studies ensures that these results are the actual vortex patterns inside the cardiac chamber. However, energetic efficiency has not been analyzed in these previous studies; consequently, the visualized flow pattern could not be related to ventricular function or postoperative prognosis.

We studied flow EL[6,8], not only the loss itself, but also its proportion relative to the energy generated by the ventricle[6], is essential to evaluate flow efficiency. The energetics of the “Clockwise” and

"Counterclockwise" vortexes were different, not only in the vortex dominant in the diastolic phase, but also in the systolic phase, when the vortex itself is almost disappears[15)]. In systole, the direction of "Counterclockwise" vortex caused flow collision or cross-linking between the inertial vortex and outflow, resulting in increase in EL/KP. In three patients with large 'Counterclockwise' vortexes, we found posterolateral wall motion delay during early systole with reduced EF (Figure 4), and the delay in the posterolateral wall could be caused by the flow collisions during early systole. Although we detected these cases with large 'Counterclockwise' vortex and wall motion delay during early systole with reduced EF, we could not determine the relationship between energy loss and LV ejection fraction in this study.

Limitations and future studies

There were several limitations in the present study. First, the number of cases evaluated was small, especially mechanical valves with an anti-anatomical position. Second, in echocardiography VFM is estimated from 2-dimentional distribution. In mitral valve disease, complicated three-dimensional flow occurs, and we could not validate all of them in the two-dimensional flow assumption. Third, we could not evaluate the amount of kinetic energy of total cardiac performance. Kinetic energy generated by the ventricle is not easy to measure; therefore, in this study, we only measured total KP inside the LV chamber. But the dimension of the parameter is not equal to the EL, we could not calculate energy efficiency itself. Fourth, the VFM evaluations in cases of atrial fibrillation were not always reproducible. Fifth, the follow-up of MVP patients was relatively short compared with that in patients with MVR.

Conclusion

Analysis of EL and EL/KP after Mitral valve surgery by echocardiogram is useful tools to evaluate the efficiency of postoperative cardiac function. In this study, we demonstrated two different directions of vortex, a Clockwise direction like the physiological vortex and a Counterclockwise direction. In diastole, we did not find a significant change ($P = 0.31$) in either EL or KP with the direction of intra-ventricular vortex flow. In systole, the loss ratio in the Counterclockwise vortex flow was significantly higher than that of clockwise vortex flow (P = 0.0091). Our results show that it would be of great practical importance to pay attention to the direction of the vortex in the ventricular chamber after mitral valve surgery.

Intraventricular flow is altered by structural and functional changes in the heart. Therefore, optimizing intraventricular blood flow to preserve efficient cardiac output is essential in cardiovascular surgery. This study is the first attempt to characterize and quantify the vortex flow of intraventricular chamber in patients after mitral valve surgery. Based on this study, future long-term follow-up and a large-scale retrospective study evaluating EL and Kinetic energy using echocardiography VFM after mitral valve surgery are mandatory to clarify the relationships between cardiac function and surgical strategy.

Conflict of interest

Dr. Keiichi Itatani was an endowed chair of Kitasato University, financially supported by Hitachi-Aloka Medical Co., Ltd. (Oct 2012–Jun 2015). He is an endowed chair of Kyoto Prefectural University of Medicine, financially supported by Medtronic Japan Inc. (Apr 2016-present). He has a stock option of Cardio Flow Design Inc. The other authors have no conflicts of interest.

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Figure legends

Figure 1:

Intraventricular vortex flow pattern after various types of the mitral valve surgery.

A: color Dopplar and Flow Vector, B: Energy Loss and Streamline.

Figure 2:

The comparison between counter-clockwise intraventricular vortex and clockwise intraventricular vortex in EL and KP during systole and diastole.

Figure 3:

The intraventricular vortex pattern and energetic parameters in MVR with anatomical position. Upper stand; color Dopplar and flow vector. Lower stand; flow streamline and vorticity.

Figure 4:

The intraventricular vortex pattern and energetic parameters in case of reduced cardiac function after the MVR with anti-anatomical position: Upper stand: color Dopplar and flow vector, Lower stand: flow streamline.

Figure 1;

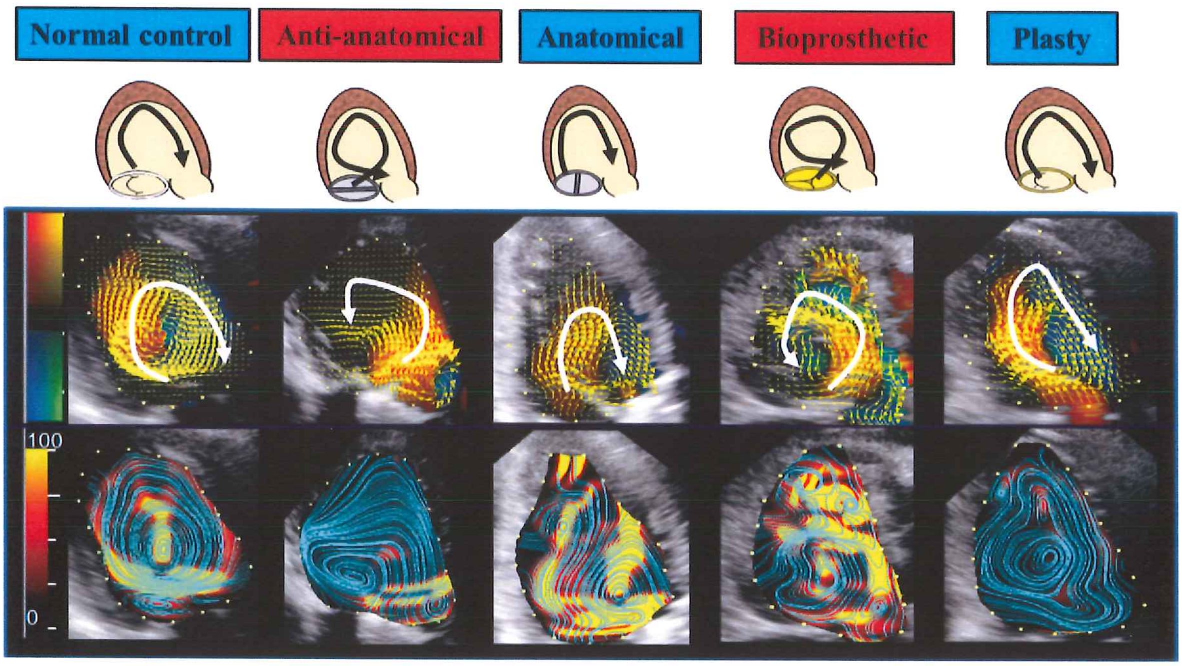
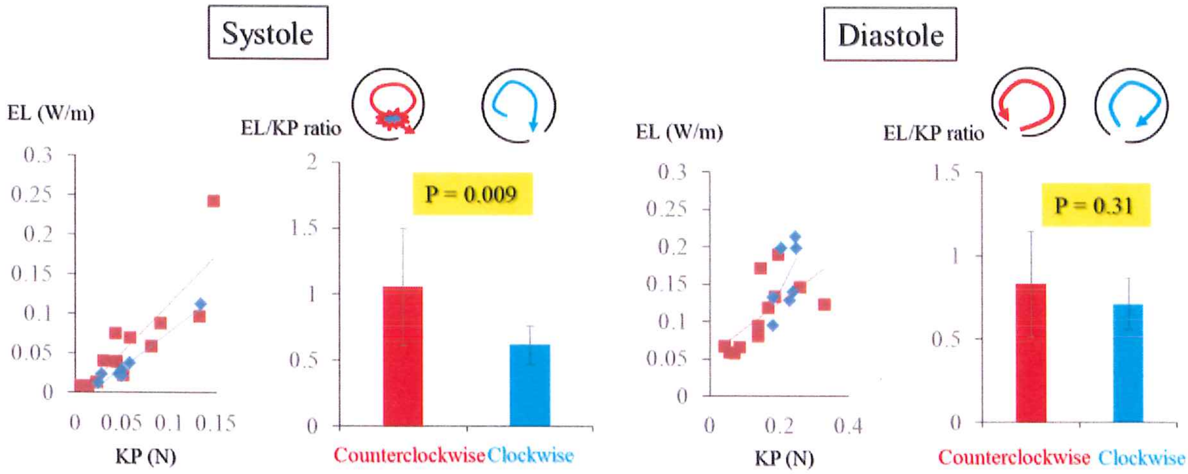

Normal control
Anti-anatomical
Anatomical
Bioprosthetic
Plasty
100
0

Figure 2;



Systole
Diastole
EL (W/m)
0.3
0.25
0.2
0.15
0.1
0.05
0
0 0.05 0.1 0.15
KP (N)
EL/KP ratio
2
1.5
1
0.5
0
P = 0.009
Counterclockwise
Clockwise
EL (W/m)
0.3
0.25
0.2
0.15
0.1
0.05
0
0 0.2 0.4
KP (N)
EL/KP ratio
1.5
1
0.5
0
P = 0.31
Counterclockwise
Clockwise

Figure 3;

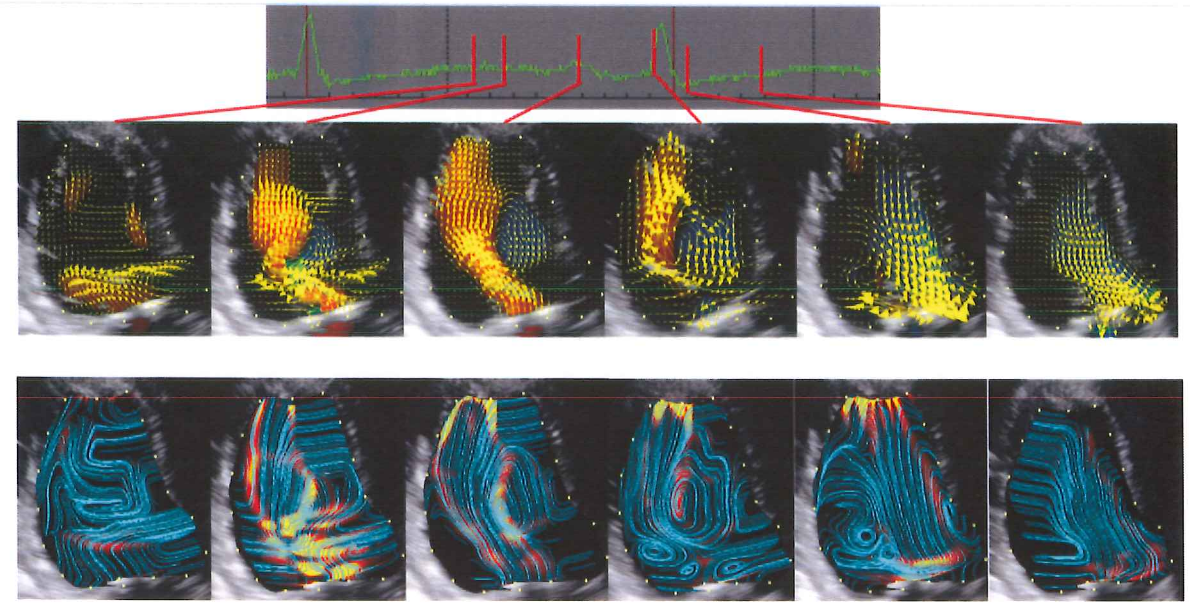
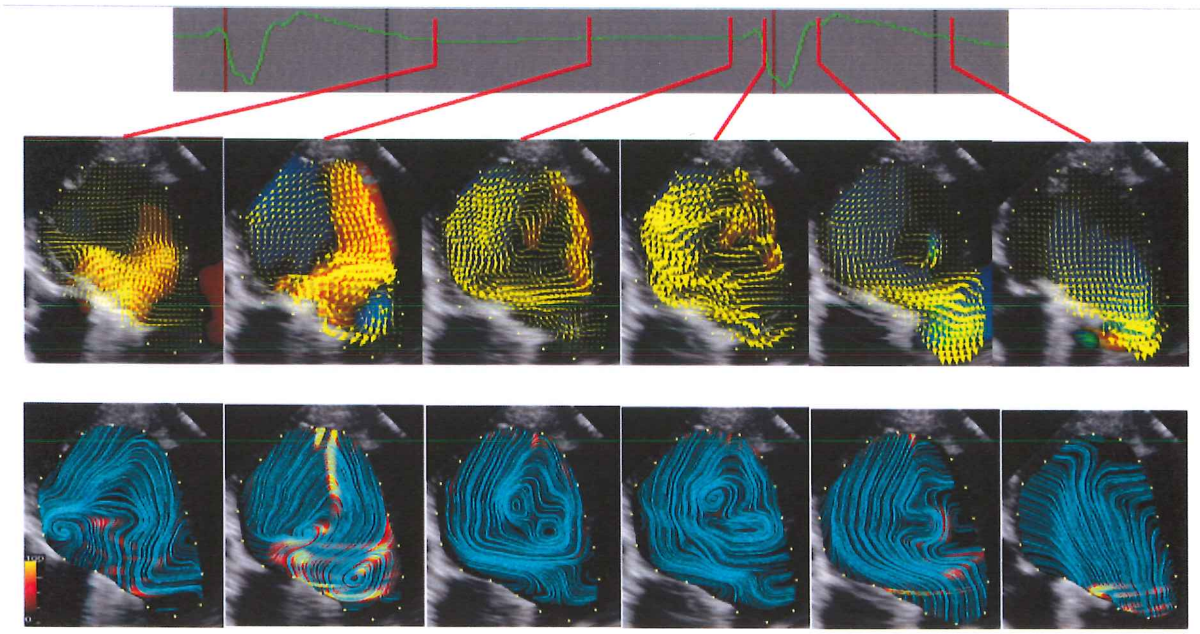


Figure 4;



Acknowledgments

This study was already presented in Mitral Conclave, AATS in April 2015 at New York, USA. This is the first findings regarding the intraventricular flow efficiency caused by the vortex flow pattern after the mitral valve surgery. We believe that this study would help cardiovascular surgeons to find the optimal mitral valve surgical procedures in their clinical practice.

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なし

（Ⅳ）症例・臨床治験・その他

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