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Energy loss in the left ventricle obtained by vector flow mapping as a new quantitative measure of severity of aortic regurgitation: a combined experimental and clinical study

Marie Stugaard[1†], Hikaru Koriyama[1†], Keiko Katsuki[2], Kasumi Masuda[1], Toshihiko Asanuma[1], Yasuharu Takeda[2], Yasushi Sakata[2], Keiichi Itatani[3] and Satoshi Nakatani[1*]

[1]Osaka University Graduate School of Medicine, Suita, Japan; [2]Osaka University Hospital, Suita, Japan; and [3]Kitasato University School of Medicine, Sagamihara, Japan

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Aims In aortic regurgitation (AR), energy loss (EL) produced by inefficient turbulent flow may be a burden to the heart predicting decompensation. We attempted to quantify EL in AR induced in an acute dog model and in patients with chronic AR using novel echocardiographic method vector flow mapping (VFM).

Methods and results In 11 anaesthetized open-chest dogs, AR was induced by distorting the aortic valve with a pigtail catheter, in totally 20 cases. Regurgitant fraction was determined using pulsed Doppler echocardiography, $<30\%$ considered mild to moderate (Group 1, $n = 11$) and $\geq 30\%$ moderate to severe (Group 2, $n = 9$). The clinical study consisted of 22 patients with various degrees of AR; 11 mild to moderate (Group 1) and 11 moderate to severe (Group 2), and compared with 12 normals. VFM is based on continuity equation applied to colour Doppler and speckle tracking velocities, acquired from apical long-axis image. EL was calculated frame by frame, averaged from three beats. In the dog study, diastolic EL increased significantly with severity of AR (baseline vs. Group 1 vs. Group 2: 3.8 ± 1.6 vs. 13.0 ± 5.0 vs. 22.4 ± 14.0 [J/(m s)], ANOVA $P = 0.0001$). Similar to dogs, diastolic EL also increased in humans by the severity of AR (control vs. Group 1 vs. Group 2: 2.8 ± 1.5 vs. 14.3 ± 11.5 vs. 18.6 ± 2.3 [J/(m s)], ANOVA $P = 0.001$).

Conclusion VFM provides a promising method to quantify diastolic EL in AR. Diastolic EL increases in AR proportional to its severity. EL may be useful to determine the severity of disease from the aspect of cardiac load.

Introduction

Blood flow leaving the left atrium develops into a vortex within the left ventricle (LV), which moves towards apex and changes its course before ejection into aorta.[1] This pattern of flow has been reported to avoid collision of blood, thus preventing needless dissipation of energy.[2] In this way, energy efficiency is optimized in the healthy LV. However, when inefficient non-physiological flow occurs due to cardiovascular disease, vortex formation may change. For instance, in dilated cardiomyopathy, the vortex persists longer than that in normal ventricles.[3] Furthermore, following artificial valve replacement, the vortex rotates in the opposite direction to normal, causing increased energy dissipation.[4,5] It is, therefore, likely that such observations of blood flow will assist the evaluation of different conditions, and there is considerable interest in fresh attempts to quantitatively evaluate the blood flow within the LV.

Current methods used to evaluate blood flow within the LV are magnetic resonance imaging (MRI), echocardiography particle image velocimetry (echo-PIV), and vector flow mapping (VFM).[6,7] MRI allows observation of the flow in 3D without contrast media.[8]

* Corresponding author: Division of Functional Diagnostics, Osaka University Graduate School of Medicine, 1-7 Yamada-oka, Suita, Osaka 565-0871, Japan. Tel/fax: +81 6 6879 2561. Email: nakatani@sahs.med.osaka-u.ac.jp

† Marie Stugaard, MD and Hikaru Koriyama, MSc equally contributed to this study.

Furthermore, phase-contrast MRI allows computation of the energy of turbulence.[9] However, MRI requires a large-scale apparatus and long acquisition time for imaging, in addition to which the temporal resolution is low. Echo-PIV is an adaptation of the PIV technique, which is widely used for visualizing fluids. Echo-PIV allows computation of the flow velocity by tracking microbubbles that act as contrast medium.[5,10] Compared with MRI, echo-PIV has superior temporal resolution and allows more detailed observation of the flow. However, echo-PIV requires a contrast medium, and the range of velocities that can be measured is limited. VFM is a novel technique making use of recent developments in echocardiography, and it permits the display of velocity vectors of flow through colour Doppler imaging. Colour Doppler imaging itself cannot measure velocity in a direction perpendicular to the beam, but VFM, with the use of the continuity equation and speckle tracking echocardiography, permits computation of velocities perpendicular to the direction of the beam. The accuracy of velocity vectors computed by VFM has been verified by comparison with values computed from PIV.[11,12] At the same time as allowing computation of velocity vectors, VFM allows computation of the amount of energy dissipated by viscous friction. This energy loss (EL) is expected to become a new index of cardiac function.

Chronic aortic regurgitation (AR) results in enlargement of the LV and decrease in cardiac function because of volume overload over an extended period of time. Severity of AR is evaluated using conventional echocardiography.[13] Surgical treatment is desirable in cases of severe regurgitation before cardiac function declines, but there are cases of recurrent heart failure even after surgery where there was latent decrease in cardiac function or timing of surgery was delayed because of underestimation of the regurgitation. If the size of the load imposed on the LV by regurgitation could be quantitatively evaluated, it would be possible to take measures such as optimizing the timing of surgery even without any obvious decline in cardiac function. This would likely lead to improved treatment outcome.

When AR occurs, there is turbulence in the blood flow due to the regurgitant jet, and this probably results in an increased EL within the LV. However, there are few reports using EL as an index to evaluate AR,[14] and the details of this EL are not clearly known.

Therefore, the objective of this study was firstly to use the new technique of VFM to quantify EL within the LV during induction of AR in a dog model and further validate it clinically in patients with different grades of AR.

Methods

Dog model protocol

The dog study was approved and conducted in accordance with the rules of the animal experiments committee of Osaka University.

Eleven anaesthetized open-chest dogs (female, 9.0–15.6 kg) were included. Xylazine hydrochloride (0.5 mg/kg) was administered by intramuscular injection as preanaesthetic medication. The dogs were anaesthetized by pentobarbital sodium (25.9 mg/kg) administered via a peripheral vein. After induction of anaesthesia, the dogs were placed in supine position, and continuous intravenous infusion of lactated Ringer's solution was administered via a peripheral vein. Following tracheal intubation, the tube was connected to a Harvard respirator (SN-480-3, Shinano, Tokyo, Japan), and the dogs were ventilated with room air and oxygen. Electrocardiogram was continuously monitored. Anaesthesia was maintained through continuous infusion of pentobarbital sodium (6 mg/kg/h) and midazolam (0.18 mg/kg/h).

Aortic pressure was measured using a water-filled catheter introduced into the femoral artery. The chest was opened by cutting the ribs in sagittal direction, the heart was exposed by making a Y-shaped cut in the pericardium, and a pericardial cradle was created to hold the heart in place.

To create the AR model, a 6F pigtail catheter was inserted into the LV from the right common carotid artery, using echo imaging as a guide. Valvular disruption was caused by pulling the catheter to distort the aortic valve.

Subjects included were the dogs in which AR was confirmed by colour Doppler imaging and the severity of AR was evaluated by pulsed Doppler echocardiography for measuring regurgitant fraction (RF) using the following equations[15]:

Stroke volume

$$\text{SV} = \text{cross - sectional area} \times \text{velocity time integral (VTI)}$$

$$\text{SV}_{\text{LVOT}} = r^2 \times \pi \times \text{VTI}_{\text{LVOT}}$$

$$\text{SV}_{\text{MV}} = a^2 \times b^2 \times \pi \times \text{VTI}_{\text{MV}}$$

Regurgitant volume

$$\text{RV} = \text{SV}_{\text{LVOT}} - \text{SV}_{\text{MV}}$$

$$\text{RF} = \frac{\text{RV}}{\text{SV}_{\text{LVOT}}}$$

The diameter/radius (r) of the LV outflow tract (LVOT) at the aortic annulus was measured in parasternal long-axis view. As the mitral valve (MV) annulus is nearly elliptical in shape, measurements were done from apical four-chamber and two-chamber cross sections (a, b). VTI was measured by pulsed Doppler echocardiography at the level of the valves. Mean of three successive heartbeats was used. AR was classified into two groups: RF $<30\%$ considered mild to moderate, which is Group 1, and RF $\geq 30\%$ considered moderate to severe, which is Group 2.

Colour Doppler images were captured for VFM analysis simultaneously with heart rate, aortic systolic and diastolic pressures, and pulse pressure. Mean values were computed from three successive heartbeats.

Echocardiography

The ultrasound device was ProSound Alpha 10 (Hitachi Aloka Medical Ltd., Tokyo, Japan). Apical long-axis view was used for acquiring colour Doppler images using a UST-5296 probe through a water bag, at a transducer frequency of 5 MHz, depth of 8 cm, focal point of 5 cm, and frame rate of 29–57. Images were captured over five successive heartbeats, stored on the built-in hard disk, and analysed offline using VFM analysis software (DAS-RS1, Hitachi Aloka Medical Ltd.).

Image analysis

Vector flow mapping

The use of the continuity equation applied to colour Doppler and speckle tracking echocardiography in VFM allows velocity vectors of intraventricular blood flow to be determined. The principles of VFM are shown in *Figure 1*.

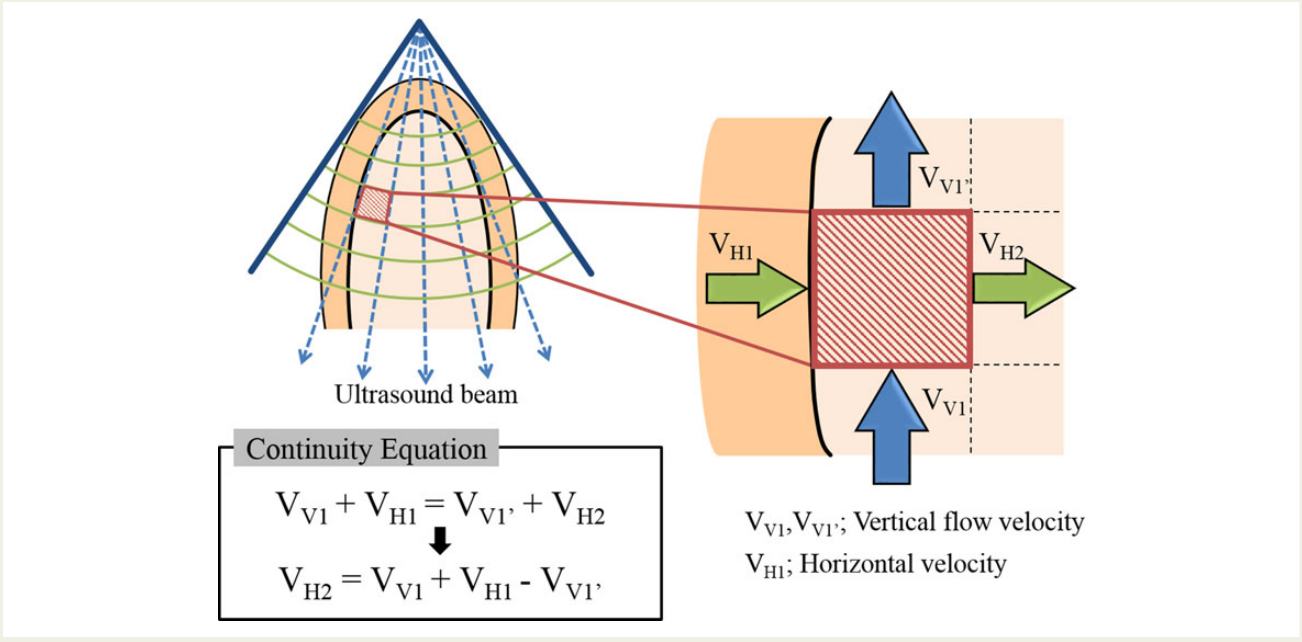

Figure 1 Principles of VFM. The LV is divided into a grid of small squares, and the continuity equation is applied to each square of the grid. According to the equation, influx of blood into a given square is equal to outflux from the square. Vertical velocities in the direction of the beam (V_{V1}, $V_{V1'}$) can be measured by the Doppler method, while horizontal velocities in the direction perpendicular to the beam (V_{H1}) can be measured as the wall velocity by speckle tracking. By substituting the values into the continuity equation, the remaining velocity (V_{H2}) can be computed. The velocity in the next square can be determined using the continuity equation in the same way, and the velocity in the direction perpendicular to the beam can be computed. Thus, velocity vectors of the flow within the LV can be determined.

VFM allows blood flow velocity to be used to determine EL due to viscous friction. EL is defined according to Eq. (1):

$$EL = \Sigma_{i,j} \int \frac{1}{2} \mu \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right)^2 dv$$

where μ is the coefficient of blood viscosity, u is the velocity vector component, and i and j are the coordinates of the 2D Cartesian coordinate system.

This parameter indicates energy dissipation due to blood viscosity in turbulent flow. The kernel of the integral displays the distribution of dissipated energy caused by inefficient flow, which is integrated with spatial increments dv. Eq. (1) expresses the total of squares of differences between neighbouring velocity vectors, and EL increases at points where size and direction of velocity vectors change.

The theoretical background for obtaining EL is included in Supplementary data online, *Text S1*.

Analysis of energy loss

The LV cavity in apical long-axis view was set as the region for analysis in this study. Dealiasing was manually carried out for those colour Doppler frames exhibiting aliasing. The endocardial border was manually traced at end-systole and then automatically determined throughout the remaining frames. The velocity of the wall was determined for each frame by speckle tracking echocardiography. The intraventricular flow velocity vectors were determined from wall velocities and colour Doppler velocity data. *Figure 2* shows the method for quantifying EL.

Human Study

To assess the clinical feasibility of grading AR severity by EL, 22 patients (mean age 67 $\pm$ 13 years, range 32–88, male:female ratio 12:10) with different grades of chronic AR ($n = 14$ with degenerative, $n = 3$ with congenital, and $n = 2$ with bicuspid aortic valve, in addition to $n = 3$ following aortic valve replacement) were consecutively enrolled at Osaka University Hospital over a period of 3 months. Exclusion criteria were mainly mitral regurgitation of moderate or higher grade, decompensated heart failure, and acute coronary syndrome.

For comparison, 12 healthy subjects (mean age 23 $\pm$ 1 years, range 22–25, male:female ratio 9:3) without any cardiac or other disease were included. These were recruited among students at Osaka University Graduate School of Medicine.

Conventional echocardiographic measurements were performed using ProSound a10 system (Hitachi Aloka Medical Ltd.), with a UST-52101 probe and a frequency of 1–5 MHz, with a frame rate of 17–43. For each parameter, mean of three successive heartbeats was calculated. Aetiology and severity of AR were evaluated using a combination of pulsed wave, continuous wave, and colour Doppler echocardiography according to current guidelines.[16,17] This was done partly in a qualitative way (colour flow regurgitant jet, continuous wave signal of regurgitant jet, flow reversal in descending aorta) and partly in a semi-quantitative way (vena contracta width, pressure half-time). AR patients were classified into two groups: mild to moderate as Group 1 and moderate to severe as Group 2. With VFM, velocity vectors of intraventricular blood flow and EL were similarly measured as in the dog model using apical long-axis image.

The human study was approved and conducted in accordance with the ethics committee of Osaka University Hospital and according to the Declaration of Helsinki, and informed consent was obtained from all subjects.

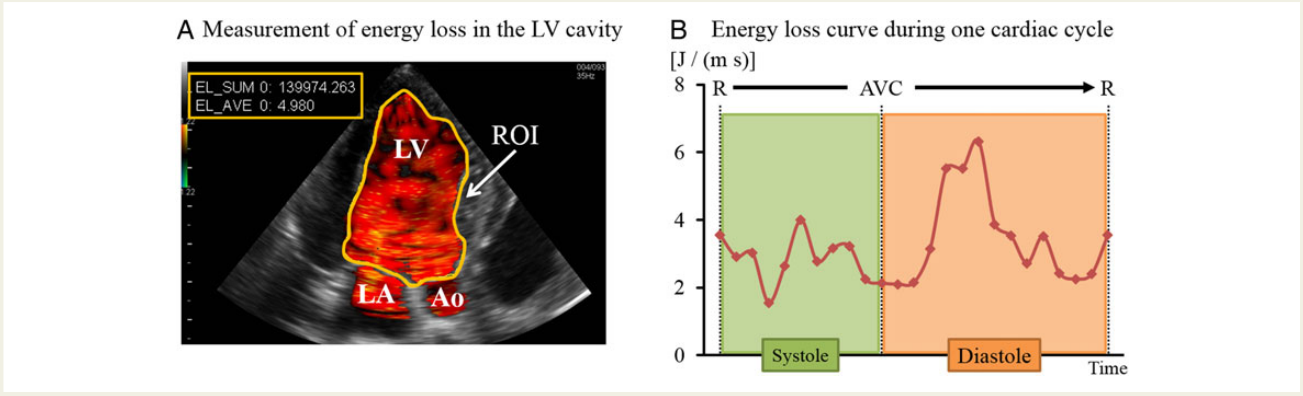

Figure 2 Measurement of EL in the LV cavity. EL is automatically calculated after selection of region of interest (ROI) (*A*). In the present study, ROI was established inside the endocardial border of the LV cavity. EL_SUM is the value of total EL, and EL_AVE is the value of averaged EL; the latter is calculated by dividing total EL by the number of pixels within the ROI. For the purpose of this study, averaged EL was calculated frame by frame from one R-wave to next (*B*) and presented as a mean of three successive cardiac cycles. Aortic valve closure (AVC) was used to separate systole from diastole. LA, left atrium; Ao, aorta.

Table 1 Haemodynamics in the dog model.

	Baseline ($n = 11$)	Group 1 ($n = 11$)	Group 2 ($n = 9$)
Heart rate (bpm)	125 ± 24	127 ± 24	135 ± 13
Aortic systolic pressure (mmHg)	147 ± 23	143 ± 18	126 ± 23
Aortic diastolic pressure (mmHg)	106 ± 14	90 ± 11	68 ± 15*
Pulse pressure (mmHg)	41 ± 12	53 ± 11	58 ± 8
LV end-diastolic volume (mL)	24 ± 9	28 ± 11	31 ± 7
LV end-systolic volume (mL)	11 ± 4	12 ± 6	14 ± 5
Ejection fraction (%)	53 ± 9	58 ± 7	53 ± 8
RV (mL)		2 ± 2	10 ± 3†
RF (%)		12 ± 10	43 ± 7†
Diastolic EL [J/(m s)]	3.8 ± 1.6	13.0 ± 5.0*	22.4 ± 14.0*,†

*$P < 0.05$ vs. baseline.
†$P < 0.05$ vs. Group 1.

Reproducibility

In 10 randomly selected subjects, intra-observer variation of diastolic EL was evaluated. Inter-observer variation was assessed by obtaining the same quantitative measurements using a blinded second observer.

Statistical analyses

All continuous variables were shown as mean ± standard deviation and range. For comparison of data, one-way ANOVA was performed, followed by multiple comparisons using the Bonferroni test. For correlation between parameters, univariate regression analysis was used. Reproducibility was assessed by Bland–Altman analysis. All statistical analyses were performed using SPSS software (SPSS, Chicago, IL, USA). Significance level was set at $P < 0.05$.

Results

Dog model

From the 11 anaesthetized open-chest dogs, a total of 20 cases of AR were induced; 11 were mild to moderate (Group 1) and 9 moderate to severe (Group 2). Haemodynamics is shown in *Table 1*. When moderate to severe AR was induced, aortic diastolic pressure was significantly reduced. Also, there was a tendency to decreased aortic systolic pressure and increased pulse pressure.

Colour Doppler images, VFM vector images, and EL images at baseline and with moderate AR are shown in *Figure 3A* and *B*. In baseline VFM vector images, a vortex was observed in the anterior mitral leaflet region, while during AR induction, the flow entering from the left atrium collided with the AR jet and disturbed blood flow could be observed; furthermore, there was no vortex near the MV.

An example of time phase changes in EL during AR is shown in *Figure 4*. EL showed an increase in relation to the degree of severity of AR in both systole and diastole. Mean EL during diastole is shown in *Figure 5*. Mean EL during diastole increased significantly with greater AR severity {baseline vs. Group 1 vs. Group 2: 3.8 ± 1.6 vs. 13.0 ± 5.0 vs. 22.4 ± 14.0 [J/(m s)], overall ANOVA $P = 0.0001$}. Diastolic EL showed a significant positive correlation with RF, $r = 0.46$ and $P = 0.041$.

Human study

Eleven patients had mild to moderate AR (Group 1) and 11 moderate to severe (Group 2). Haemodynamics is shown in *Table 2*. There was a significant increase in both LV end-diastolic and end-systolic volumes in Group 2 compared with controls. Ejection fraction tended to decrease, but mean values in AR were still normal.

Compatible with the dog results, high EL was clearly demonstrated along with the AR jet (*Figure 6*). Diastolic EL was significantly higher in AR compared with normals {16.5 ± 11.8 vs. 2.8 ± 1.5 [J/(m s)], $P = 0.0001$} and increased by the severity of AR

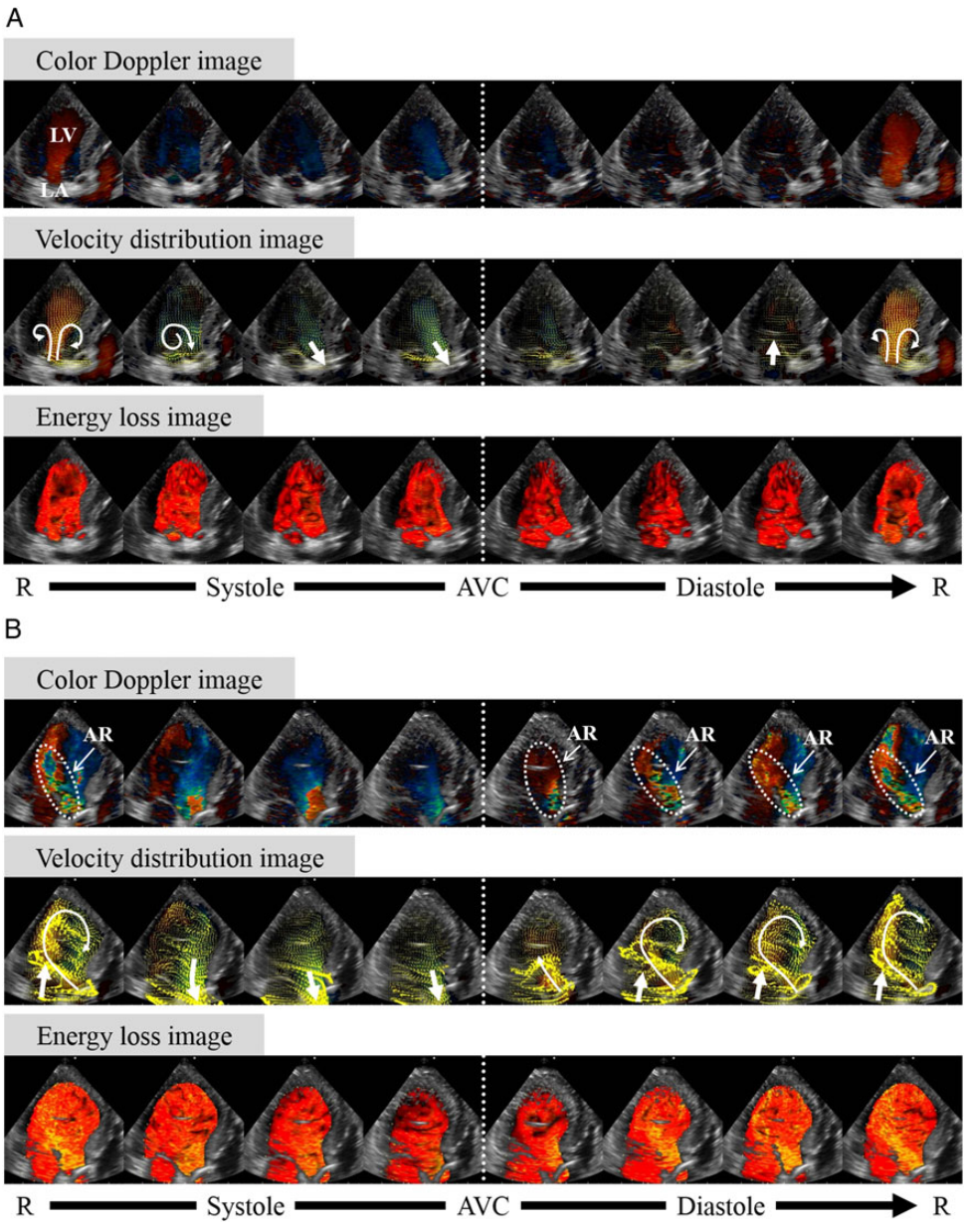

Figure 3 Colour Doppler, velocity vector, and EL images before and after inducing AR. (*A*) Before inducing AR (baseline), velocity vector images showed formation of a large intraventricular vortex in the anterior mitral leaflet side and a small one in the posterior mitral leaflet side. (*B*) After inducing AR (moderate case), velocity vector images showed that flow from the left atrium collided with the AR jet and turbulent flow occurred at that site. In the EL images, the region of AR jet is displayed in yellow, indicating high EL. AVC, aortic valve closure.

{Group 1: 14.3 ± 11.5, Group 2: 18.6 ± 12.3 [J/(m s)], overall ANOVA $P = 0.001$} (*Figure 6*).

Video clips from one control subject and one patient with moderate AR are included in Supplementary data online, *Videos S1* and *S2*, respectively.

Reproducibility

Bland–Altman plots are shown in *Figure 7*. The intraclass correlation coefficient (ICC) was 0.91 for intra-observer measurements (95% confidence interval 0.63–0.98, $P = 0.001$). For inter-observer measurements, ICC was 0.87 (95% confidence interval 0.49–0.97, $P = 0.002$).

Discussion

AR of different grades was induced in an experimental acute dog model, and EL in the LV was quantitatively evaluated using VFM. EL was clearly highest in the region of the LV corresponding to the turbulence produced by the AR jet. Diastolic EL increased significantly with increased severity of AR.

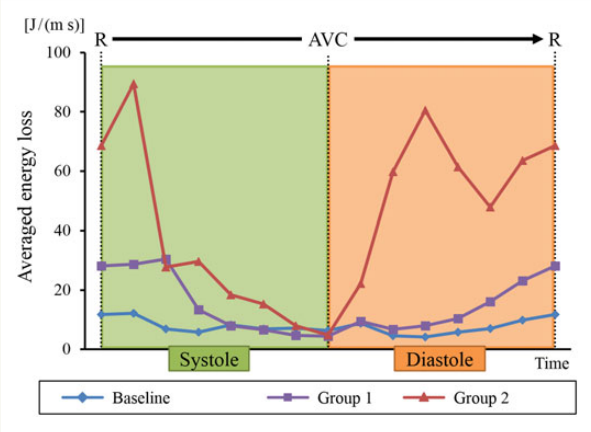

Figure 4 EL throughout the cardiac cycle in the dog model. Averaged EL during systole and diastole increased in AR. The peak in systole seen in the moderate case (Group 2) reflects AR flow during isovolumic contraction. AVC, aortic valve closure.

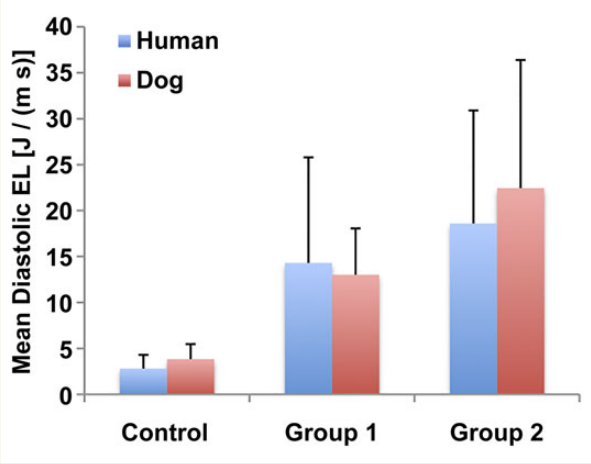

Figure 5 Mean EL in the LV cavity during diastole. Mean EL during diastole increased significantly according to AR severity both in dogs and humans (overall ANOVA $P = 0.0001$ and 0.001, respectively).

Furthermore, we attempted to reproduce a similar pattern and evaluate the usefulness of EL in the clinical setting in an unselected group of patients with chronic AR of different grades. In accordance with the dog study, we found increased diastolic EL with the severity of AR.

Changes in energy loss during AR

EL is calculated from the square of the difference of adjacent velocity vectors [Eq. (1)]. Therefore, EL increases if the size or direction of adjacent velocity vectors changes.[12] In the present study, EL during AR increased with the severity of AR, probably because the size and direction of the intraventricular velocity vectors changed as a result of the turbulence caused by the AR jet. EL determined by VFM may contribute to the evaluation of the severity of AR.

Table 2 Haemodynamics in the human study.

	Control ($n = 12$)	Group 1 ($n = 11$)	Group 2 ($n = 11$)
Heart rate (bpm)	63 ± 8	60 ± 10	59 ± 10
Systolic blood pressure (mmHg)		134 ± 13	129 ± 19
Diastolic blood pressure (mmHg)		72 ± 12	68 ± 10
LV end-diastolic volume (mL)	99 ± 13	137 ± 43	169 ± 57*
LV end-systolic volume (mL)	32 ± 8	52 ± 33	76 ± 51*
Ejection fraction (%)	68 ± 5	60 ± 14	60 ± 14
E wave velocity (cm/s)	84 ± 12	65 ± 16	71 ± 25
A wave velocity (cm/s)	46 ± 11	81 ± 29*	62 ± 26
E/A	1.9 ± 0.6	0.9 ± 0.2*	1.4 ± 0.6
E/E′	5.8 ± 0.9	10.7 ± 4.2*	8.4 ± 2.7
Diastolic EL [J/(m s)]	2.8 ± 1.5	14.3 ± 11.5*	18.6 ± 12.3*

*$P < 0.05$ vs. control.

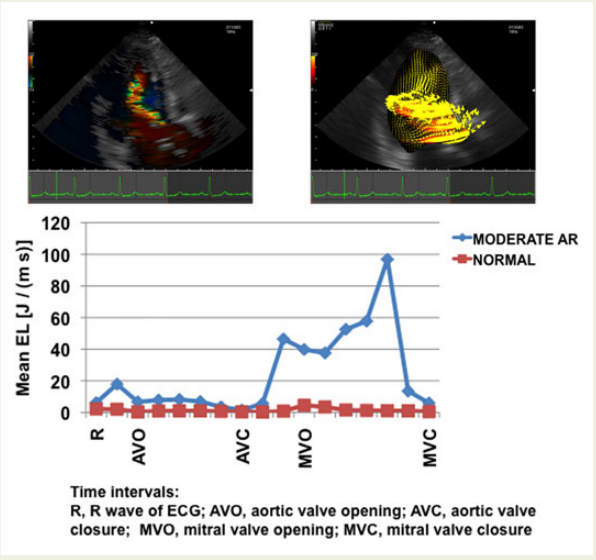

Figure 6 EL throughout the cardiac cycle in humans. High EL was clearly demonstrated along with the AR jet (moderate case) in yellow in diastole (upper left—original flow image, upper right—EL image with overlaying velocity vectors). EL in normals (one representative subject in red) was mostly constant in the cardiac cycle, while that in AR (one moderate case in blue) increased in diastole with two peaks corresponding to early and late filling (lower).

The significance of evaluating AR severity through energy loss

Echocardiography is currently the key examination in diagnosis and evaluation of the severity of AR. It is also important for evaluation of the mechanisms of regurgitation and the valve anatomy.[16,17]

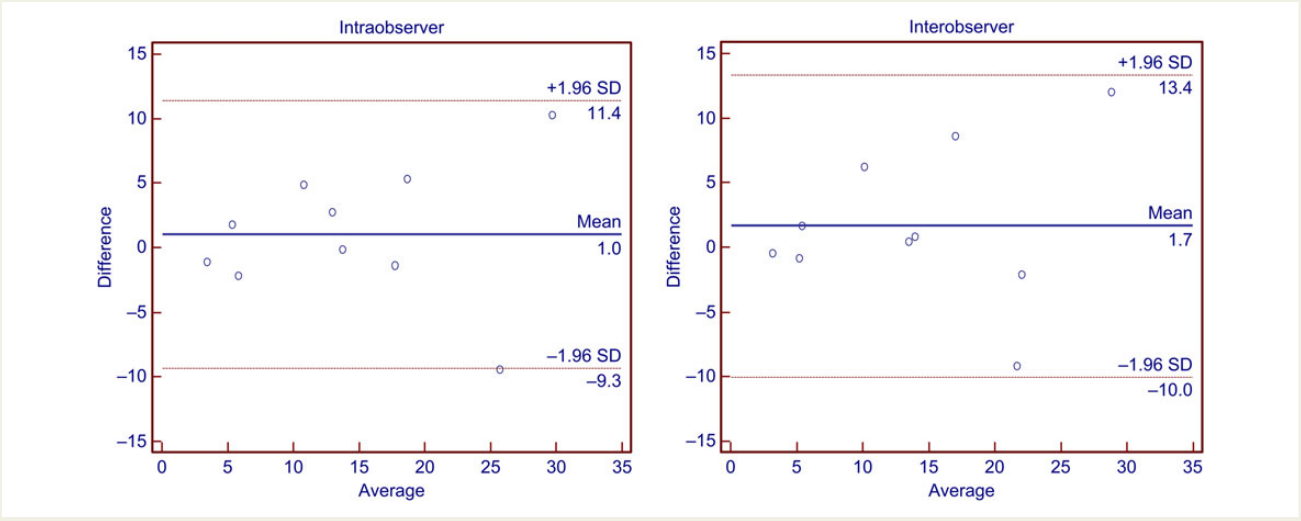

Figure 7 Bland–Altman plots of intra- (left) and inter-observer (right) variability of diastolic EL. Average values of measurements are plotted against difference of measurements. The arithmetic mean (continuous line) and 95% limits of agreement (equal to ± 1.96 SD; dotted lines) are determined.

Surgical intervention is indicated in symptomatic patients with severe AR and in asymptomatic cases if there is deterioration in cardiac function, and it should further be considered in severe LV dilatation even if ejection fraction is normal.[16,17] Thus, objective, quantitative evaluation of AR is desirable. RV, RF, and effective regurgitant orifice area (ERO) are used for quantitative evaluation, and these are measured by volumetric methods or by the proximal isovelocity surface area (PISA) method. However, volumetric methods cannot be used if there is turbulence due to the AR jet deviating mitral inflow or if there is mitral regurgitation. Using PISA to compute ERO is possible whether or not there is mitral regurgitation, and PISA is less sensitive to loading conditions. However, in many cases, accurate evaluation of PISA is not easy, and it is currently not often used in clinical routine.

Furthermore, cases of poor prognosis are sometimes found among patients who have undergone surgical intervention.[18] This is probably the result of delay in surgery because of underestimation of regurgitation or latent deterioration of cardiac function. As can be seen from the formula for determining EL by VFM, it is affected by change not only in the size of the velocity vectors but also in their direction. Therefore, for a given RV, EL and load on the LV may vary according to the direction of the AR jet. If the EL could be used as a method to quantitatively evaluate the load exerted on the LV[14,19] and thereby the severity of AR, it may be possible to early identify cases in which reduced cardiac function is likely to occur and take measures such as accurately determine the timing of surgery.

The aforementioned considerations suggest that the evaluation of AR severity using EL may have additional significance that is lacking in conventional indices and would allow for precise decision-making regarding treatment strategy in various clinical settings.

LV function and energy loss

In the dog study, no obvious enlargement of the LV was observed; however, in the human study, the size of the LV increased significantly in moderate to severe AR. This difference is most likely due to the fact that the dog study was an acute model, while in the humans, AR had become chronic and thus there was time for LV dilatation to occur, although there were no cases included with decompensated heart failure. Abnormal flow has been reported in dilated cardiomyopathy with enlarged LV,[3] in heart failure,[20] and in patients with acute ST elevated myocardial infarction at different stages of LV systolic dysfunction.[21] If the flow in the LV changes, there are also likely to be changes in EL.[14] Further research is needed to investigate the extent to which the size of the LV and decompensation affect EL.

Normalization of energy loss

In the present study, EL during diastole was actually observed in ventricles with no AR jet. This is probably a reflection of mild turbulence occurring even in the normal LV. When the severity of AR is evaluated, the computed EL needs to be normalized. Specifically, determining what proportion of the workload performed by the heart is accounted for by EL will allow the load of the LV to be evaluated. The workload of the LV can be determined from LV pressure–volume loops. Future work is needed to determine the optimal method of normalization.

Vortex in the LV before and after AR induction

In the present study, formation of specific vortices was seen before AR induction during diastole. The occurrence of vortex during diastole has previously been reported, so that the present study is consistent with prior reports.[1,22] The vortex has several roles, among which is to efficiently transport blood flow by preventing needless energy dissipation.[2,7] In the present study, we focussed on this role by using EL, while simultaneously observing normal vortex formation being impeded by the AR jet. If the physiological cardiac function is disrupted, the vortex loses its proper shape and the expenditure of

energy is increased. More detailed investigation of how a vortex is related to blood flow patterns or EL is needed.

Limitations

The AR jet is a 3D entity, and evaluation in 3D would be desirable to ensure accurate determination of the severity of AR. At present, however, VFM has not been converted to 3D. By VFM, velocity vectors are computed using the continuity equation on colour Doppler images, and loss of temporal resolution would be a problem if this was carried out in 3D. Further development of the software is needed to resolve this issue.

In the present study, manual correction for aliasing was performed on frames with aliasing of the colour Doppler velocity data. As double or higher aliasing cannot be corrected by VFM, aliasing needs to be prevented when acquiring image data by adjusting the velocity range where it occurs. However, there are limits to the velocity range, and if the velocity of blood flow exceeds the limit, the calculated velocity may be underestimated in relation to the actual velocity.

In the case of an AR jet, there will be turbulent flow and high velocities in particular around the tip of the aortic cusps, while flow velocity decreases towards apex. In this case, VFM will underestimate the high velocities, while measurements inside the LV cavity will be correct. We used averaged EL, calculated by dividing total EL by the number of pixels within the ROI, to try to compensate at least partly for this problem. Furthermore, in the VFM software, the differential process at a given point is influenced by the adjacent velocity. Further resolution to correct for aliasing is needed; however, this will decrease frame rate, at present there is a balance between reasonable frame rate and spatial resolution.

In the human study, a relatively small number of subjects were included, and also, there was heterogeneity regarding the cause of the AR. However, we do not believe that this represents a major limitation, as we could reproduce similar results as in the dog model.

Controls were young students, not age- and sex-matched.
Comparison with gold standard such as MRI was not available.

Conclusions

VFM provides a new promising method to quantify diastolic EL in AR, both in an experimental acute model and in a clinical setting of chronic AR. Diastolic EL increases in AR proportional to its severity. Quantification by use of EL may be useful to determine the severity of disease from the aspect of cardiac load.

Prospective studies are needed to evaluate the usefulness of EL as a prognostic marker of AR.

Supplementary data

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

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Conflict of interest: none declared.

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