Increased Regional Systolic Myocardial Stiffness of the Left Ventricle during Coronary Artery Occlusion in a Dog: Analysis of the Finite Element Model

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HONDA, H., TANI, J., MIYAZAKI, T., KOIWA, Y., TAKISHIMA T. and SHIRATO, K. Increased Regional Systolic Myocardial Stiffness of the Left Ventricle during Coronary Artery Occlusion in a Dog: Analysis of the Finite Element Model. Tohoku J. Exp. Med., 1995, 177 (2), 125-137 —— (1) We measured the instantaneous systolic transfer function of an isolated canine left ventricle (LV) before and after the ligation of the left anterior descending coronary artery (LAD). The instantaneous transfer function before the ligation of the LAD showed a resonance curve whose peak frequency was 30 to 70 Hz. On the other hand, the transfer function 40 min after the ligation of the LAD showed a divided peak in the resonance curve. (2) We constructed a finite element model of a thick-walled spherical shell with a non-uniform structure. In this model, the myocardial elasticity and viscosity of the ischemic region are different from those of non-ischemic regions. One can calculate the theoretical transfer function using modal analysis and also estimate the elasticity and the viscous coefficient of both non-ischemic and ischemic myocardium by fitting the theoretical transfer function to the experimental one. (3) The estimated elasticity of the ischemic myocardium was three to five times larger than that of the non-ischemic myocardium. The estimated viscous coefficient of the ischemic myocardium was about half that of the non-ischemic myocardium. These results showed that ischemia alters the viscoelastic properties of the myocardium during systole as well as during diastole. —— left ventricle; viscoelastic properties; transfer function; finite element method

There is ample experimental evidence that diastolic myocardial stiffness is increased during ischemia. However, examinations of alterations in systolic myocardial stiffness have seldom been attempted because of technical difficulties. Tani et al. (1993) reported a method for evaluating systolic myocardial stiffness and the viscous coefficient. Their method used the finite element model and analyzed the instantaneous transfer function of the left ventricle (LV). Here, the
transfer function indicates the ratio of the induced vibration of LV to the external input vibration applied to the LV epicardium. The method proposed by Tani et al. assumed that LV has a uniform structure, and was, therefore, not applicable to the left ventricle with regional ischemia.

We reported in another study that regional ischemia induces a division of the resonance peak of the instantaneous transfer function (Hashiguchi et al. 1988). The experimental setup is displayed in Fig. 1. The means of obtaining the instantaneous transfer function has been detailed elsewhere (Koiwa et al. 1986).

Fig. 2 is a schematic illustration of changes in the instantaneous transfer function when regional ischemia is induced in LV myocardium. The transfer function without regional ischemia had a single peak. On the other hand, the transfer function with regional ischemia had a double peak. The area between the two curves (hatched region in the figure) had a positive correlation with the infarct size (Hashiguchi et al. 1988).

![Fig. 1. Schematic illustration of experimental setup.](image-url)
The purpose of the present study is to interpret this division of the resonance peak. The proposed model in this study enables us to estimate the elasticity of both ischemic and non-ischemic myocardium, and to prove that the systolic elasticity of the ischemic myocardium was larger than that of the non-ischemic myocardium.

**METHODS**

**Analytical model**

We used a thick-walled spherical shell model to analyze the transfer function of LV. We divided the spherical shell into finite elements as shown in Fig. 3. Each element included a material point indicated by an open circle, elasticity connecting each material point and viscosity located in series to elasticity. The mesh structure of the present model was much simpler than that used in our previous study (Tani et al. 1993). The outer and inner radius of the sphere was assumed to be 3.0 and 1.8 cm, respectively (approximation of the isolated heart), and the density to be 1.04 g/cm³. The elasticity and viscosity of the ischemic myocardium (dotted region in Fig. 4; the area and the position are approximate
The left end point, indicated by "input", was forcefully vibrated sinusoidally and we calculated the vibration induced in the right end point, indicated by "output", using the technique of modal analysis, the details of which are described in the Appendix. The theoretical transfer function is a ratio of the output vibration to input vibration.

Dotted region indicates regional ischemia whose elasticity \((E_2)\) differs from non-ischemic elasticity \((E_1)\). The viscous coefficient is also different in these two regions.

to the experimental results) were assumed to be different from those of the non-ischemic myocardium (non-dotted region). Vibrating sinusoidally the left end point in Fig. 3 or Fig. 4 (indicated by "input"), we calculated the vibration induced in the right end point (indicated by "output"), and then obtained the
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Theoretical transfer function (the ratio of output vibration to input vibration; the details of the calculation are given in the appendix of this paper). Changing the elasticity and the viscous coefficient of the model, we selected the theoretical transfer function best fitted to the experimental results. The procedure of curve fitting was detailed elsewhere (Tani et al. 1993). The elasticity and the viscous coefficient which offered the best fit were considered to be the elasticity and the viscous coefficient of the myocardium (Fig. 5). To examine the validity of our method to estimate elasticity by curve fitting of the theoretical transfer function to the experimental one, we applied this method to a spherical shell made of silicone rubber (Bondo Silicone Kohwa; Konishi Inc., Osaka). The outer and inner radius of the silicone spherical shell was 3.65 and 2.5 cm, respectively, and the density was 1.04 g/cm³. The elasticity of the silicone rubber measured by stretch test was $1.10 \times 10^6$ Pa. Then we applied this method to non-ischemic and ischemic heart.

**RESULTS**

**Myocardial elasticity and viscous coefficient**

The calculated elasticity obtained by the uniform silicone shell, $1.20 \times 10^6$ Pa, was approximately identical to that obtained by the stretch test, $1.10 \times 10^6$ Pa.

Fig. 6 shows the relationship between left ventricular pressure (LVP) and the myocardial elasticity ($E$), that between LVP and the viscous coefficient ($\alpha$) under non-ischemic condition during contraction. In the present study, all data were taken while LVP was increasing. The elasticity was approximately in proportion to LVP, and the viscous coefficient increased slightly with an increase of LVP, both of which were approximately the same as those in our previous report (Tani et al. 1993) the mesh structure of which was more minute than that of the present study.

Fig. 7 shows an example of the transfer function when LVP was 25 mmHg under ischemic condition.

Fig. 8 shows the relationships between LVP and the elasticity, and those between LVP and the viscous coefficient under ischemic condition. The elastic-
The relationship between systolic left ventricular pressure (LVP) and myocardial elasticity ($E$) and viscous coefficient ($\alpha$) of the left ventricle without regional ischemia.

An example of the transfer function of left ventricle with regional ischemia at LVP being 15 mmHg. $\phi$ (deg): the phase difference between input and output vibration. $|G|$: the absolute value of the transfer function. Open circles indicate the experimental data and the solid line indicates the calculated transfer function with best fitting.

The stiffness of the ischemic myocardium ($E'$) was three to five times as large as that of the non-ischemic myocardium ($E$). The viscous coefficient of the non-ischemic myocardium ($\alpha$) was approximately twice as large as that of the ischemic myocardium ($\alpha'$).
DISCUSSION

The effect of the shape of the analytical model

In the present study, we assumed that the left ventricle is a spherical shell. We examined whether ellipsoidal deformation had an effect on resonance frequency using an ellipsoidal silicone shell. When the axis ratio (long axis/short axis) increased from 1.0 (=sphere) to 2.0, the peak frequency also increased by about 30%. This leads to the speculation that there is an error of 30% at maximum in the calculated elasticity caused by the difference in the shape of the analytical model because the actual axis ratio of the isolated LV was between 1.0 and 2.0.

The mesh structure of the model

The calculated elasticity of the uniform silicone spherical shell, $1.20 \times 10^6$ Pa, was approximately identical to that obtained by the stretch test, $1.10 \times 10^6$ Pa. The relationship between LVP and the elasticity or viscous coefficient of the non-ischemic myocardium was approximately the same as that of our previous study (Tani et al. 1993). The model in this study has larger meshes than those in our previous study. The number of mass points in the present model was one-fourth of that in our previous model. The mesh structure in the model was much simpler than that of the previous model. These results proved that the difference in mesh structure had affected little on the estimation of the myocardial viscoelasticity, and that the model in this study provided the approximate elasticity of the uniform spherical shell.
Elasticity of the ischemic myocardium

The systolic myocardial elasticity and the viscous coefficient in the ischemic region were calculated in only one case in this study. We have reported, however, that regional ischemia always divided the single peak of the transfer function in the same manner 40 min after the induction of regional ischemia (Hashiguchi et al. 1988). Therefore, we speculated that the myocardial elasticity of the ischemic region would be higher than that of the non-ischemic region forty minutes later.

The result of the present study, in which an increase of local elasticity divided the peak of the transfer function, suggests that the cause of the double peak of the cardiac transfer function lies in the alteration of the myocardial viscoelastic properties. Many researchers reported that diastolic regional stiffness of the ischemic myocardium increased (Hess et al. 1980; McPherson et al. 1987; Sys and Brutsaert 1989; Ross 1989). Edwards et al. suggested that a sevenfold increase in passive loading would be sufficient to produce the acute elongation of the ischemic myocardium (Edwards et al. 1981), which is roughly consistent with the result in this study. That is, the stiffness of the ischemic myocardium was five times as large as that of non-ischemic myocardium when LV pressure was less than 10 mmHg (approximately at end-diastole).

There is only one report by Templeton et al. the results of which were inconsistent with those of the present study. They reported that the systolic ventricular elastic stiffness (not myocardial elasticity but a kind of chamber stiffness coefficient) did not change, and that the ventricular viscous stiffness (not myocardial viscosity but a kind of chamber viscous coefficient) increased during ischemia (Templeton et al. 1975). Their results differed from those which showed that the diastolic myocardium with regional ischemia was stiffer than that without regional ischemia. Although we have not found a clear reason for this discrepancy, we speculate that the major reason might come from the difference in the definition of elastic and viscous stiffness and/or a difference in the experimental conditions (size, duration of ischemia, etc.).

The present study showed that systolic as well as diastolic regional stiffness of the ischemic myocardium increased. The possible mechanisms involved in the increase in ischemic diastolic myocardial stiffness are the persistent attachment of the crossbridges, tissue edema, and other factors (Amano et al. 1987). Similar mechanisms might also be involved in the elevation of the systolic regional myocardial stiffness.

Elasticity of the ischemic myocardium and left ventricular pressure

The present study showed that the stiffness of the ischemic myocardium increased little with an increase of LVP. A study on experimental myocardial infarction has shown that ischemic segments of the myocardium do not regain the ability to shorten, even after 3 weeks (Theroux et al. 1977). In the ischemic
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region, there would be no change in myocardial stiffness due to “active cross-bridges” between diastole and systole. However, the viable myocardium should pull the infarcted region, which would increase the stiffness of the ischemic myocardium due to the passive muscle element. Thus, the stiffness of the ischemic myocardium might actually increase slightly with an increase of LVP as suggested in this study.

The results of the present study showed the usefulness of estimating viscoelastic properties of the ischemic myocardium by analyzing the global transfer function of LV.

References


APPENDIX

Theoretical transfer function of a spherical shell with an ischemic region.

Basic model

The equation of motion of a system with viscous damping for forced oscillation is expressed as

\[ [M] \{ \ddot{X} \} + [C] \{ \dot{X} \} + [K] \{ X \} = \{ F \} \]  \hspace{1cm} (1)

where \([M]\), mass matrix; \([C]\), viscous matrix; \([K]\), stiffness matrix; \(\{ X \}\), displacement vector; \(\{ F \}\), vector of external force.

The elementary stiffness matrix, \([Ke]\) is calculated as

\[
[Ke] = \int_{-1}^{1} \int_{-1}^{1} [B]^T [D] [B] \det[J] d\xi d\eta d\zeta
\]  \hspace{1cm} (2)

Here displacement-strain matrix \([B]\) is expressed by the following equation;

\[
[B] = \begin{bmatrix}
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\
0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1
\end{bmatrix}
\]

\([J]\) is a Jacobian matrix and is expressed as

\[
[J] = \begin{bmatrix}
\partial \{ N \} / \partial \xi \\
\partial \{ N \} / \partial \eta \\
\partial \{ N \} / \partial \zeta
\end{bmatrix} = \begin{bmatrix}
\{ X_n \} \{ Y_n \} \{ Z_n \}\end{bmatrix}
\]  \hspace{1cm} (4)

\(\{ X_n \}\), \(\{ Y_n \}\) and \(\{ Z_n \}\) represent the coordinates of the nodal points of the elements. \(\{ N_i \}\) is a shape function and expressed as follows;

\[
N_1 = (1 - \xi) (1 - \eta) (1 - \zeta) (-1 - \xi - \eta) / 8
\]
\[
N_2 = (1 + \xi) (1 - \eta) (1 - \zeta) (-1 + \xi - \eta) / 8
\]
\[
N_3 = (1 + \xi) (1 + \eta) (1 - \zeta) (-1 + \xi + \eta) / 8
\]
\[
N_4 = (1 - \xi) (1 + \eta) (1 - \zeta) (-1 - \xi + \eta) / 8
\]
\[
N_5 = (1 - \xi^2) (1 - \eta) (1 - \zeta) / 4
\]
\[
N_6 = (1 + \xi) (1 - \eta^2) (1 - \zeta) / 4
\]
\[
N_7 = (1 - \xi^2) (1 + \eta) (1 - \zeta) / 4
\]
\[
N_8 = (1 - \xi) (1 - \eta^2) (1 - \zeta) / 4
\]
\[
N_9 = (1 - \xi) (1 - \eta) (1 + \zeta) (-1 - \xi - \eta) / 8
\]
\[
N_{10} = (1 + \xi) (1 - \eta) (1 + \zeta) (-1 + \xi - \eta) / 8
\]
\[
N_{11} = (1 + \xi) (1 + \eta) (1 + \zeta) (-1 + \xi + \eta) / 8
\]
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\[
N_{12} = (1 - \xi) (1 + \eta) (1 + \xi) (-1 - \xi + \eta)/8 \\
N_{13} = (1 - \xi^2) (1 - \eta) (1 + \xi)/4 \\
N_{14} = (1 + \xi) (1 - \eta^2) (1 + \xi)/4 \\
N_{15} = (1 - \xi^2) (1 + \eta) (1 + \xi)/4 \\
N_{16} = (1 - \xi) (1 - \eta^2) (1 + \xi)/4
\]  

\{N_i\} is a vector which is obtained from partially differentiating \{N_i\} by \xi, \eta and \xi, and arranging lengthwise. Stress-strain matrix \([D]\) is expressed by

\[
[D] = \frac{E(1-v)}{(1+v)(1-2v)} \times
\begin{bmatrix}
1 & v/(1-v) & 0 & 0 & 0 \\
v/(1-v) & 1 & v/(1-v) & 0 & 0 \\
v/(1-v) & v/(1-v) & 1 & 0 & 0 \\
0 & 0 & 0 & (1-2v)/(1-v) & 0 \\
0 & 0 & 0 & 0 & (1-2v)/(1-v)
\end{bmatrix}
\]  

Here, \(E\) represents longitudinal elasticity (in the case of regional ischemia, \(E\) represents elasticity of the non-ischemic myocardium and \(E'\) represents that of the ischemic myocardium), \(v\) represents a Poisson's ratio. The myocardium was assumed to be incompressible and Poisson's ratio to be 0.49. Element mass matrix \([Me]\) can be obtained from the following equation;

\[
[Me] = \rho \int_{-1}^{1} \int_{-1}^{1} \int_{-1}^{1} \{N\} \{N\}^T \text{det}[J] d\xi d\eta d\xi
\]  

One can obtain mass matrix \([M]\) by adding all element mass matrices. Damping was assumed to be proportional viscous damping, and the damping matrix \([C]\) was given by the following equation;

\[
[C] = \alpha [M]
\]  

The magnitude of damping force is in proportion to the velocity of each point and can be estimated by the coefficient \(\alpha\). In case of regional ischemia, we indicated the viscous coefficient in non-ischemic region by \(\alpha\) and in ischemic region by \(\alpha'\).

**Calculation of theoretical transfer function**

In order to solve the equation (1), we considered a non-damping system of the following characteristic equation (9). The values of \(\omega_1, \omega_2, \ldots \omega_n\), are the eigenvalues and \(\{\Psi_1, \Psi_2, \ldots \Psi_n\}\) are the eigenvectors of the equation (9).

\[
\text{det}[-\omega^2 [M] + [K]] = 0
\]  

Here, \(n\) indicates the degree of freedom. Modal reduced mass, \(m_s\), modal reduced stiffness, \(k_s\), and modal reduced damping, \(c_s\), are assumed to be expressed as
The transfer function, \( \frac{\text{displacement at point } i}{\text{external force at point } j} \), at frequency \( \omega \), is expressed as

\[
g = \frac{X_i}{F_j} = \sum_{r=1}^{n} \frac{\psi_{ir} \psi_{jr}}{-\omega^2 m_r + j\omega C_r + k_r}
\]

The transfer function comparable to the experimental result is expressed as

\[
G = \frac{X_i}{F_j} = \frac{\sum_{r=1}^{n} \psi_{ir} \psi_{jr}}{-\omega^2 m_r + j\omega C_r + k_r}
\]

Curve fit technique

We used the same method as previously reported (Tani et al., 1993) to obtain the value of elasticity and viscosity to minimize the difference between experimental transfer function and theoretical transfer function. The unknown factors \( E, \alpha \) or \( E, E', \alpha, \alpha' \) are indicated by \( r_j(j=1, \ldots, n) \). One can obtain \( \{\Delta r\} \) by arranging lengthwise the increments of \( r_j(\Delta r_j) \). Here, \( n \) indicates the number of the unknown factors. The vector for error \( \{T\} \) is expressed by

\[
\{T\} = [H]\{\Delta r\}
\]

Here, \( \{T\} \) is a row vector with \( 2m \) rows, and its components are expressed as

\[
T_i = Re \, G_{e}(\omega_i, r_0) - Re \, G(\omega_i, r_0)
\]

\[
T_{i+m} = Im \, G_{e}(\omega_i, r_0) - Im \, G(\omega_i, r_0)
\]

\( \{H\} \) is matrix with \( 2m \) rows and \( n \) columns, and its component are expressed as

\[
H_{i,j} = Re \frac{\partial G(\omega_i, r_0)}{\partial r_j}
\]

\[
H_{i+m,j} = Im \frac{\partial G(\omega_i, r_0)}{\partial r_i}
\]

\( \{r_0\} \) is a vector which can be obtained by arranging the initial value of \( r_j \).

We define the function for error, \( \lambda \), as follows:

\[
\lambda = \{T\}^T[W]\{T\}
\]

\( [W] \) is a diagonal matrix with \( 2m \) rows and \( 2n \) columns, and expressed as

\[
[W] = \begin{bmatrix}
W & 0 \\
0 & W
\end{bmatrix}
\]
We can obtain the solution, \( \{\Delta r\} \), of the equation (13) using the least square method expressed as follows:

\[
\Delta r = \left[ [H]^T [W][H] \right]^{-1} \left[ [H]^T [W] \{T\} \right]
\]  

(18)