Non-Linear Pressure-Volume Relation in Left Ventricle

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SUMMARY

A thick-walled elastic cylinder contracting symmetrically is used as a model for the myocardium. The active force generated by the myocardium during systolic contraction is represented by body force (force/unit volume of myocardium). A mathematical formalism previously developed and based on large deformation analysis is used to derive a quadratic equation to represent the non-linear pressure volume (P-V) relation in the left ventricle in the Suga-Sagawa model. Experimental application of the results obtained confirms the consistency of the mathematical formalism developed to describe the P-V curve in the Suga-Sagawa model.

Additional Indexing Words:
Cardiac mechanics Left ventricular P-V relation Body force for the myocardium Non-linear P-V relation

In the first part of this study, an equation describing the pressure-volume (P-V) relation in the left ventricle was developed. The main feature of this equation is that the radial force/unit area developed by the myocardium on its inner surface during the systolic phase, which plays the role of an active or driving force during a normal ejecting contraction, is included in the mathematical formalism describing the P-V relation. The equation for the P-V relation in the left ventricle given in Shoucri was used to explain the linearity of experimental results obtained according to the Suga-Sagawa model. The purpose of the present study is to focus on the non-linear aspect of the P-V relation in the Suga-Sagawa model. Because of the lack of adequate experimental data for our purpose, we shall focus our attention to the quadratic approximation of the P-V curve in the Suga-Sagawa model and check the consistency of our formalism with the experimental data given by Little et al. The approach used in the present study can serve as a guide to derive higher order approximation to the P-V curve in the Suga-Sagawa model.

MATHEMATICAL FORMALISM

The assumptions are basically the same as those given in Shoucri. The myocardium is represented as an elastic thick-walled cylinder contracting sym-
metricaly without bending or twisting. As a result of the active state of the myocardium, the myocar-dium will develop a radial force \( D(r) \) (force/unit volume of the myocardium) during the systolic phase of a normal ejecting contraction (see Fig. 1). The corresponding radial force/unit area developed by the myocardium on its inner surface is given by \( \int_a^b Ddr = D_h \), with \( a = \) inner radius, \( b = \) outer radius, \( h = b - a = \) thickness of the myocardium, \( D \) is a value of \( D \) calculated by the mean value theorem. The equation describing the P-V relation in the left ventricle was derived as

\[
D_h - P = E(V_{ed} - V) 
\]

where 
\( D_h = \) radial force/unit area developed by the myocardium on its inner surface during the systolic phase of a normal ejecting contraction 
\( P = \) left ventricular cavity pressure 
\( V = \) left ventricular cavity volume 
\( V_{ed} = \) end-diastolic value of left ventricular cavity volume (when \( dV/dt = 0 \)).

The coefficient \( E \) in equation (1) is derived in Shoucri\(^9\) as

\[
E = \frac{W_s}{k} \left[ \frac{1}{V} - \frac{1}{V + V_w} + \frac{\ln\frac{V_{ed}}{V} - \ln\frac{V_{ed} + V_w}{V_{ed} - V}}{V_{ed} - V} \right] 
\]

where \( V_w = \pi(b^2 - a^2)l \) is the volume of the myocardium and \( k = dl/dl_{ed} \) is assumed independent of the spatial coordinates, \( l \) = length of the myocardium. \( W_s \) is calculated from the pseudo strain energy density function \( W \) in the way discussed in Shoucri\(^9\) (see also equation (4)). The study of the non-linearity of the P-V curve in the Suga-Sagawa model will be confined to the case of a quadratic approximation discussed by Little et al,\(^5\) where the P-V curve is approximated by a second degree curve.
The problem is consequently as follows:

a) how equation (2) can be approximated in a way to obtain from equation (1) a second degree polynomial in $V$ (or $(V_{ed} - V)$) to describe the $P$-$V$ curve in the Suga-Sagawa model;

b) how the second degree polynomial obtained from equations (1) and (2) can be split into two equations, one for $P$ and one for $\Delta h$, in such a way to recover a quadratic expression for $P$ similar to equation (3) that can be applied to the results experimentally determined by Little et al.\(^5\)

Since we want to approximate equation (1) by a quadratic polynomial in $V$, it is clear that $E$ in equation (1) should be linear in $V$. Consequently the first step is to determine a linear approximation for $E$ from equation (2).

**Linear Approximation for $E$**

The coefficient $W_s/k$ in equation (2) is the value of $(1/k) (\partial W/\partial I) (dr_{ed}/dR)^2$ determined by the mean value theorem, where $W$ is the pseudo strain energy density function describing the biomechanical properties of the incompressible fluid surrounding the muscular fibers and $I$ is the strain invariant as explained in Shoucri.\(^9\) From equation (19) of Shoucri,\(^9\) we reproduce the following integral

\[ 2 \int_{\lambda_a}^{\lambda_b} \frac{\partial W}{\partial I} \left( \frac{dr_{ed}}{dR} \right)^2 \left( 1 + \frac{1}{\lambda^2 k} \right) d\lambda \]

\[ = \frac{2W_s}{k} \int_{\lambda_a}^{\lambda_b} \left( 1 + \frac{1}{\lambda^2 k} \right) d\lambda \]

\[ = E(V_{ed} - V) \quad (4) \]

where $E$ is given by equation (2). Details of the calculation are given in Shoucri,\(^9\)

\[ \lambda_a = a/a_{ed}, \quad \lambda_b = b/b_{ed}, \quad \lambda = r/r_{ed}, \] where $r$ is the radial distance in cylindrical coordinates, $\partial W/\partial I$ has a near linear form as a function of the strain invariant $I$ as shown in Fig. 1 of Humphrey and Yin\(^3\) for a passive myocardium, and we assume the relation to hold also for the myocardium in the active state since it applies to the incompressible fluid surrounding the muscular fibers. We do not know the quantity $dr_{ed}/dR$, $(r_{ed} =$ radial distance at end-diastole, $R =$ radial distance in the stress-free configuration), since the stress-free configuration is not well defined. However, as we shall see, the exact expression of $dr_{ed}/dR$ is not needed for our calculation.

From Shoucri,\(^9\) we have

\[ I = (1 + 2\epsilon_r) + (1 + 2\epsilon_\theta) + (1 + 2\epsilon_z) \]

\[ = \left( \frac{dr}{dR} \right)^2 + \left( \frac{rd\theta}{Rd\theta} \right)^2 + K^2 \quad (5) \]

where $K = dz/dZ$ is the longitudinal compression ratio and is assumed to be independent of the spatial coordinates, $(r, \theta, z)$ refer to the cylindrical coordinates in the deformed configuration, $(R, \theta, Z)$ refer to the cylindrical coordinates in the stress-free configuration. $\epsilon_r, \epsilon_\theta, \epsilon_z$ are a measure of the Lagrangian strain in the three principal directions $(r, \theta, z)$. The incompressibility condition is given by
The left ventricular cavity volume is \( V = \pi r^2 l \). The variation in \( K \) when \( V \) varies is usually small because of the small variation of the longitudinal dimension of the myocardium. If we assume that the stress free configuration remains practically unchanged and that \( d\theta/d\Theta \) can be approximated by a constant (see Chuong and Fung), then equation (6) can be used to express equation (5) in the form

\[
I \approx \frac{C_1}{V} + C_2 V + C_3
\]

where \( C_1, C_2, C_3 \) are constants along a \( P-V \) curve in the Suga-Sagawa model. We have

\[
\frac{1}{V} = \frac{1}{V_{ed}} - \frac{1}{V_{ed} - V} \approx \frac{1}{V_{ed}} + \frac{V_{ed} - V}{V_{ed}^2}.
\]

Since we can approximate \( 1/V \) by a linear relation in \( (V_{ed} - V) \) and since the relation between \( \partial W/\partial I \) and \( I \) can be approximated by a near linear relation (Fig. 1 of Humphrey and Yin), one can consequently write

\[
\frac{W_s}{k} \approx C_4 + C_5 (V_{ed} - V)
\]

where \( C_4 \) and \( C_5 \) will depend on \( V_{ed} \) and are constant along a given \( P-V \) curve of the Suga-Sagawa model. In addition, we have the following approximation

\[
\frac{1}{V} + \frac{1}{V + V_w} \approx \frac{1}{V_{ed}} + \frac{1}{V_{ed} + V_w} + \left( \frac{1}{V_{ed}^2} - \frac{1}{(V_{ed} + V_w)^2} \right)(V_{ed} - V).
\]

Since \( \ln (1+y) \approx y - (y^2)/2 \) for \( y < 1 \),

\[
\ln \frac{V_{ed} + V_w}{V} - \ln \frac{V_{ed} + V_w}{V_{ed} + V_w} \approx (V_{ed} - V) \left( \frac{1}{V_{ed}} - \frac{1}{V_{ed} + V_w} \right) \times \left[ 1 + \frac{V_{ed} - V}{2} \left( \frac{1}{V_{ed}} + \frac{1}{V_{ed} + V_w} \right) \right].
\]

From equations (2), (8), (9) and (10), we can write

\[
E \approx [C_4 + C_5 (V_{ed} - V)] \left( \frac{1}{V_{ed}} - \frac{1}{V_{ed} + V_w} \right) \left[ 2 + \frac{3}{2} (V_{ed} - V) \left( \frac{1}{V_{ed}} + \frac{1}{V_{ed} + V_w} \right) \right],
\]

or

\[
E \approx \alpha_1 + \alpha_2 (V_{ed} - V) + \alpha_3 (V_{ed} - V)^2.
\]

The quantity \( \alpha_3 \) involves the factor \( (1/V_{ed}^2) - (1/(V_{ed} + V_w)^2) \) and is negligible compared to \( \alpha_1 \) and \( \alpha_2 \). Consequently,

\[
E \approx \alpha_1 + \alpha_2 (V_{ed} - V)
\]

which, combined with equation (1), gives a quadratic approximation of the \( P-V \)
Fig. 2. Approximate representation of equation (14) near end-systole when $E$ reaches its maximal value $E_{\text{max}} = (\alpha_1)_m + (\alpha_2)_m (V_{\text{ed}} - V_m)$ (the suffix $m$ when $E = E_{\text{max}}$ has been dropped in the text for convenience). The left ventricular cavity pressure is supposed to be constant and equal to $P_m$. The dotted lines represent the slope of the P-V curve at the two extreme positions determined by $V_m$ and $V_{\text{ed}}$. Note the change $\Delta(Ph)_m$ corresponding to $\Delta V_{\text{ed}}$ according to the Frank-Starling mechanism.

\[
\Delta h - P \approx [\alpha_1 + \alpha_2 (V_{\text{ed}} - V)](V_{\text{ed}} - V) \tag{14}
\]

$\alpha_1$ and $\alpha_2$ will depend on $V_{\text{ed}}$ but are constant along a given P-V curve of the Suga-Sagawa model. The representation of equation (14) near end-systole (when $E$ reaches its maximum value $E_{\text{max}}$) is shown in Fig. 2. The suffixes $m$ and max in Fig. 2 have been eliminated in the remainder of this paper to simplify the notation.

The splitting of equation (14)

Equation (3) can be written in the form

\[
P = [A(V - V_i) + B + 2AV_i](V - V_i) \tag{15}
\]

on the basis of the relation

\[
AV_i^2 + BV_i + C = 0 \tag{16}
\]

where $V_i$ is the intercept of the P-V curve with the volume axis. Equation (3) can also be written in the form

\[
P = [A(V_{\text{ed}} - V) - (B + 2AV_{\text{ed}})](V_{\text{ed}} - V) + AV_{\text{ed}}^2 + BV_{\text{ed}} + C. \tag{17}
\]

By writing the isovolumic pressure $P_{\text{ed}}$ as

\[
P_{\text{ed}} = AV_{\text{ed}}^2 + BV_{\text{ed}} + C \tag{18}
\]

we get

\[
P_{\text{ed}} - P = [B + 2AV_{\text{ed}} - A(V_{\text{ed}} - V)](V_{\text{ed}} - V). \tag{19}
\]

Note the similarity between equation (19) and equation (14). To recover equations (15) and (18) from equation (19), we split equation (19) into two equations

\[
P_{\text{ed}} = [B + 2AV_{\text{ed}} - A(V_{\text{ed}} - V)](V_{\text{ed}} - V_i) - \beta(V_{\text{ed}} - V_i)(V - V_i) \tag{20}
\]

\[
P = [B + 2AV_{\text{ed}} - A(V_{\text{ed}} - V)](V - V_i) - \beta(V_{\text{ed}} - V_i)(V - V_i). \tag{21}
\]
By noting that $A(V_{ed} - V) = A(V_{ed} - V_e) - A(V - V_e)$ and by comparing equation (21) with equation (15), we see that

$$-A(V_{ed} - V_e) + B + 2AV_{ed} - \beta(V_{ed} - V_e) = B + 2AV_e$$  

which implies that $\beta = A$.

The same approach can be used with equation (14):

$$Dh = [\alpha_1 + \alpha_2(V_{ed} - V)](V_{ed} - V_e) - \beta(V_{ed} - V_e)(V - V_e)$$  

$$P = [\alpha_1 + \alpha_2(V_{ed} - V)](V - V_e) - \beta(V_{ed} - V_e)(V - V_e).$$  

Note the similarity between equations (23) and (20), as well as the similarity between equations (24) and (21). A direct comparison of the coefficients of these equations shows that $\beta = A = -\alpha_2$ and $\alpha_1 = B + 2AV_{ed}$, hence $B = \alpha_1 + 2\alpha_2 V_{ed}$, $C = -(\alpha_1 + 2\alpha_2 V_{ed} - \alpha_2 V_e)$. By substituting $\beta = -\alpha_2$ in equation (23) and (24), we obtain

$$Dh = [\alpha_1 + \alpha_2(V_{ed} - V_e)](V_{ed} - V_e)$$  

$$P = [-\alpha_2(V - V_e) + \alpha_1 + 2\alpha_2(V_{ed} - V_e)](V - V_e).$$

Equation (26) is equivalent to equation (15) and is similar to equation (2) of Kass et al.4) Equation (25) shows that in a quasi-static approximation, $Dh$ is constant along a $P$-$V$ curve. $Dh$ is also equal to the isovolumic pressure $P_{ed}$, obtained from equation (26) by substituting $V = V_{ed}$; thus $P \rightarrow Dh = P_{ed}$ when $V \rightarrow V_{ed}$. Note that $Dh$ is also the radial force/unit area developed in an ejecting contraction to maintain the quasi-static equilibrium of the cylindrical cavity according to equation (1). Hence it appears that within the quasi-static approximation and for the same inotropic state of the cardiac muscle, the force developed by an isotonic, auxotonic or isovolumic contraction is mainly determined by the initial stretch of the muscle.

The slope of the $P$-$V$ curve

As shown by Burkhoff et al,1) the slope $E_s$ of the $P$-$V$ curve can be obtained by differentiating equation (3)

$$E_s = \frac{dP}{dV} = 2AV + B$$  

or by differentiating equation (26)

$$E_s = \alpha_1 + 2\alpha_2(V_{ed} - V).$$  

$E_s$ will vary between a maximum value at $V = V_e$

$$E_{s\ max} = \alpha_1 + 2\alpha_2(V_{ed} - V_e)$$  

and a minimum value at $V = V_{ed}$

$$E_{s \ min} = \alpha_1.$$

The mean value $E_i$ is defined as follows:

$$E_i = \frac{E_{s \ max} + E_{s \ min}}{2} = \alpha_1 + \alpha_2(V_{ed} - V_e)$$
E₁ will be used to estimate the slope of the linear approximation of the P-V relation (Eₑₑ in the work of Little et al⁵).  

**Experimental Application**

Verification of the results given in the present study has been based on the work of Little et al.⁵ where a quadratic equation similar to equation (3) was fit to different sets of experimentally measured points of P-V curves obtained near end-systole. The different sets of A, B and C values determined by least square fitting are given in Table III of Little et al.⁵ (As already mentioned, we shall drop for simplicity the suffix m used to indicate the different variables when E=Eₑₑₑₑ). However, the value of the end-diastolic volume Vₑₑ is not given in Little et al.⁵ is needed for our calculations. This volume Vₑₑ was calculated as follows:

1) Calculate

\[
E₁ = \frac{1}{2} \left( \frac{dP}{dV} \bigg|_{V=V_{\text{f}}} + \frac{dP}{dV} \bigg|_{V=V_{\text{ed}}} \right).
\]

We assume that the average value E₁ of the slopes at the two extreme volumes (Vₑₑₑₑ and Vₑₑ) is approximately the slope of the linear P-V relation (Eₑₑₑₑ in Table III of Little et al⁵). Since

\[
E₁ = A(V_{\text{f}} + V_{\text{ed}}) + B = \alpha_1 + \alpha_2(V_{\text{ed}} - V_{\text{f}})
\]

we deduce that

\[
V_{\text{ed}} = \frac{E₁ - B}{A} - V_{\text{f}}.
\]

where Vₑₑ is indicated as V₀,ₑₑ in the notation of Little et al.⁵ By means of equation (31), Vₑₑ can be calculated from Table III of Little et al.⁵

2) From equation (26), applied at P=100 mmHg, and the corresponding volume Vₑₑₑₑ in Table III of Little et al.⁵ we have

\[
V_{\text{ed}} = \left( -\frac{1}{A} \right) \left( \frac{100}{V_{100} - V_{\text{f}}} - E₁ \right) + V_{100}.
\]

The values of the variables in the right-hand side of equations (31) and (32) are taken from Table III of Little et al.⁵ The results for Vₑₑ are given in Table I. The two equations (31) and (32) give comparable values for Vₑₑ.

The next step is the calculation of Dₑₑ.

1) When V=Vₑₑ (isovolumic contraction), the isovolumic pressure (P)ₑₑ was calculated from the results of Little et al.⁵ such that

\[
(P)ₑₑ = AVₑₑₑₑ² + BVₑₑₑₑ + C.
\]

Next, (P)ₑₑ is compared with (see equation (25))

\[
\bar{D}ₑₑ = [\alpha_1 + \alpha_2(V_{\text{ed}} - V_{\text{f}})](V_{\text{ed}} - V_{\text{f}}).
\]

The coefficient \(\alpha_1 + \alpha_2(V_{\text{ed}} - V_{\text{f}}) = A + BV_{\text{ed}}\), where A, B and Vₑₑ are taken from Table III of Little et al.⁵ Values of Vₑₑ are listed in Table I. The
Table I. Calculation of End-Diastolic Volume $V_{ed}$

<table>
<thead>
<tr>
<th>Case</th>
<th>A</th>
<th>B</th>
<th>$V_i$ ml</th>
<th>$E_i$ mmHg/ml</th>
<th>$V_{100}$ ml</th>
<th>$V_{ed}$ ml equation (31)</th>
<th>$V_{ed}$ ml equation (32)</th>
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<tbody>
<tr>
<td>1</td>
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<td>25.6</td>
<td>7.9</td>
<td>8.8</td>
<td>14.3</td>
<td>27.8</td>
<td>28.8</td>
</tr>
<tr>
<td>2</td>
<td>-1.59</td>
<td>45.9</td>
<td>6.0</td>
<td>12.0</td>
<td>11.6</td>
<td>15.3</td>
<td>15.3</td>
</tr>
<tr>
<td>3</td>
<td>-0.52</td>
<td>27.2</td>
<td>13.3</td>
<td>9.9</td>
<td>18.8</td>
<td>22.9</td>
<td>23.3</td>
</tr>
<tr>
<td>4</td>
<td>-0.03</td>
<td>6.2</td>
<td>37.1</td>
<td>2.7</td>
<td>66.9</td>
<td>79.6</td>
<td>88.8</td>
</tr>
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<td>10.0</td>
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<td>47.1</td>
</tr>
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<td>6.7</td>
<td>6.3</td>
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<td>20.9</td>
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<td>20.7</td>
<td>8.3</td>
<td>29.0</td>
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<td>34.9</td>
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</table>

$A$, $B$ = coefficients of the quadratic expression of the P-V curve; $V_i$ = intercept of the P-V curve with the volume axis; $E_i$ = slope of the linear P-V line; $V_{100}$ = left ventricular cavity volume when $P=100$ mmHg. Values of $A$, $B$, $E_i$, $V_{ed}$, $V_{100}$ are taken from Table III of Little et al.\(^5\)

Table II. Comparison of $(P)_{ed}$ with $Dh$ (isovolumic contraction)

<table>
<thead>
<tr>
<th>Case</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>$V_{ed}$ ml</th>
<th>$V_i$ ml</th>
<th>$(P)_{ed}$ mmHg</th>
<th>$Dh$ mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-0.47</td>
<td>25.6</td>
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<td>175</td>
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<td>-217.4</td>
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<td>112</td>
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<tr>
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<td>113</td>
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<td>174</td>
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<td>20.7</td>
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<td>121</td>
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</table>

$A$, $B$, $C$ = coefficients of the quadratic expression of the P-V curve; $V_{ed}$ = end-diastolic volume (Table I); $V_i$ = intercept of P-V curve with volume axis. Values of $A$, $B$, $C$, and $V_i$ are taken from Table III of Little et al.\(^5\)

results for $(P)_{ed}$ on $Dh$ are given in Table II. The estimates of these parameters are comparable.

2) When $P=100$ mmHg and $V=V_{100}$, $Dh$ can be calculated from the work of Little et al.\(^5\) by using the formulas

\[
Dh = [a_1 + a_2(V_{ed} - V_i)](V_{ed} - V_i) \quad (34a)
\]

\[
Dh = P + [a_1 + a_2(V_{ed} - V_i)](V_{ed} - V) \quad (34b)
\]

\[
Dh = P + \frac{P}{V_i - V}(V_{ed} - V) \quad (34c)
\]

Note that equation (34a) is equation (25). Equation (34b) is an alternative form of equation (1) in the non-linear case when we assume a quadratic approximation with $E$ given by equation (13). Equation (34c) assumes a linear approximation. The results are shown in Table III. The results of equations (34a) and (34b) compare well; results from equation (34c) are of greater magnitude.
Table III. Calculation of the Radial Force/Unit Area ($D_h$) at $V = V_{100}$

<table>
<thead>
<tr>
<th>Case</th>
<th>$A$</th>
<th>$V_{eq}$ ml</th>
<th>$V_{100}$ ml</th>
<th>$V_s$ ml</th>
<th>($D_h$) equation (34a) mmHg</th>
<th>($D_h$) equation (34b) mmHg</th>
<th>($D_h$) equation (34c) mmHg</th>
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<td>11.6</td>
<td>6.0</td>
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<td>6</td>
<td>-1.09</td>
<td>22.3</td>
<td>19.5</td>
<td>6.7</td>
<td>98</td>
<td>79</td>
<td>122</td>
</tr>
<tr>
<td>7</td>
<td>-0.63</td>
<td>35.3</td>
<td>29.0</td>
<td>20.7</td>
<td>121</td>
<td>119</td>
<td>176</td>
</tr>
</tbody>
</table>

The meaning of the variables as in Tables I and II, $V_{100}$ = left ventricular cavity volume when $P = 100$ mmHg as given in Table III of Little et al.5)

CONCLUSION

In previous studies,7)-9) a linear approximation of an equation of the P-V curve in the Suga-Sagawa model was derived and applied to experimental results to explain the linear appearance of the P-V curve. In the present study, the same mathematical formalism is used to derive a quadratic approximation of the P-V curve in the Suga-Sagawa model. The results obtained in the present study confirm the results obtained with the linear model that the radial force/unit area $D_h$ developed by the myocardium on its inner surface is constant along a P-V curve of the Suga-Sagawa model and is given by the isovolumic pressure $P_{ed}$ (see equations (33a) and (33b)). In other words the P-V curve in the Suga-Sagawa model is obtained as if a balloon is blown up against a constant $D_h$. Both the results of the present study and the theoretical discussion in Shoucri9) indicate that the P-V curve is essentially non-linear. The value of $D_h$ as obtained from a linear model tends to be slightly higher than the value obtained from the non-linear model (Table III). $D_h$ reaches its maximum value near end-systole (defined as the value $V = V_{eq}$ when $dV/dt = 0$) and for the same inotropic state of the muscle appears to be mainly determined by the initial stretch of the muscle (initial value of $V_{eq}$) for either isotonic, auxotonic or isovolumic contractions (inertia forces neglected).

REFERENCES

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