原 著 (Original)

A Theoretical Analysis of Hemodynamics by Time Varying Elastance Model of Ventricle

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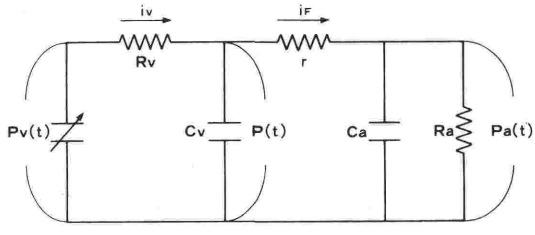
Although some disagreements[1,2] still exist about the reliability of load independency of the E(t) (the instantaneous pressure-volume ratio) of ventricle[3], we can never find any other superior physiological comprehensive model or concept of the ventricle to describe the dynamic properties of whole heart. As a result, we prefer to utilize this elastance model to characterize and analyze the total behavior of ventricle instead of mechanical concept for whole heart such as constant flow pump or pressure pump.

Nevertheless the ventricle was illustrated by the elastance model, we can not catch the total feature of interaction of ventricle-arterial system. Because no associated theoretical model had been proposed in which ventricle was expressed by the time varying elastance and arterial system was described by simple comprehensive model simultaneously.

In the present study we constructed a theoretical physiological model with time varying elastance as a heart and with Wind Kessel model as arterial system to describe the total behavior of cardiovascular system Present analysis was confined to 1) reconstruct physiological pressure curves, 2) quantitive analysis of effects of arterial system parameters on the maximum arterial and ventricular pressures, and 3) analyze the effects of diastolic arterial pressure on these pressures.

Methods

Fig. 1 shows the equivalent electrical circuit of present model. The ventricle is expressed by the modified elastance model[4]. The ventricle part is composed of 1. the contractile element which is the time varying elastance E(t). 2. the internal resistance Rv of viscous friction between cardiac muscles. 3. the passive serial elastance Cv. The arterial system is composed of fluid resistance Ra, the aortic compliance Ca



Pv(t) : Pressure generated by C. E
P (t) : Intraventricular pressure
Pa(t) : Aortic Pressure
Rv : myocardial Viscosity during systole
Cv : Compliance due to streching of the series elastic component of the myocardium
γ : Aortic Valve-resistance
Ca : Compliance of the arterial System
Ra : Total Peripheral Resistance

Fig. 1 Equivalent electrical circuit model of present study.

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and the aortic valvular resistance r. The system is expressed by following simultaneous differential-integral equations.

$$iF(t)=Pa(t)/Ra+Ca\cdot dPa(t)/dt \quad \cdots\cdots(1)$$

$$Pt(t)=iF(t)\cdot r+Pa(t) \quad \cdots\cdots(2)$$

$$iv(t)=iF(t)+Cv\cdot dPt(t)/dt \quad \cdots\cdots(3)$$

$$Pv(t)=iv(t)\cdot Rv+Pt(t) \quad \cdots\cdots(4)$$

$$Pv(t)=E(t)\cdot V(t) \quad \cdots\cdots(5)$$

$$V(t)=Vo-\int_0^t iv(\tau)\,d\tau \quad \cdots\cdots(6)$$

where $Pa(t)$ is the arterial pressure, $Pt(t)$ is the ventricular pressure degraded by the viscous resistance Rv, $Pv(t)$ is the pressure developed by the true contractile element $E(t)$. $iF(t)$ is the aortic flow rate. $iv(t)$ is the ventricular flow rate. $V(t)$ is the ventricular volume. Vo is the end diastolic volume. Equation (5) describes the linear property of the instantaneous pressure volume relation. Here we show briefly the mathematical procedure for solving above equations. By eliminating $P(t)$ from equation (2) and equation (4)

$$Pa(t)=Pv(t)-iv(t)\cdot Rv-iF(t)\cdot r \quad \cdots\cdots(7)$$

substituting equation (7) into equation (1) with utilizing equation (5)

$$iF(t)=[E(t)\cdot V(t)-iv(t)\cdot Rv-iF(t)\cdot r]/Ra+Ca\cdot d[E(t)\cdot V(t)-iv(t)\cdot Rv-iF(t)\cdot r]/dt \quad \cdots\cdots(8)$$

In equation (8), about the integration of $iv(t)$, we set

$$\int_0^t iv(\tau)\cdot d\tau=Iv(t).\quad \text{then}-dV(t)/dt=d\int_0^t iv(\tau)\,d\tau/dt=dIv(t)/dt \quad \cdots\cdots(9)$$

Converting from the differential operator to the difference and changing from continuous time system to the discrete time system

$dIv(t)/dt=\lim_{dt\to 0}[Iv(t+dt)-Iv(t)]/dt$ (anterograde difference) or $\lim_{dt\to 0}[Iv(t)-Iv(t-dt)]/dt$ (retrograde difference), it can be approximated as

$dIv(t)/dt=[Iv(k\cdot dt)-Iv(k-1)dt]/dt$, since $Iv(k\cdot dt)$ is an integral and can be approximated by Simpson's trapezoidal law for numerical integration

$$Iv(k\cdot dt)=[(Iv(0)=Iv(k\cdot dt)]/2+\sum_{m=1}^{k-1} Iv(m)]dt \quad \cdots\cdots(10)$$

and

$$Iv((k-1)dt)=[(Iv(0)+Iv((k-1)dt))/2+\sum_{m=1}^{k-2} Iv(m)]dt \quad \cdots\cdots(11)$$

Similarly with respect to the differential of $iF(t)$ and $iv(t)$, they are approximated as

$$diF(t)/dt=[iF(k\cdot dt)-iF((k-1)dt)]/dt \quad \cdots\cdots(12)$$

$$div(t)/dt=[iv(k\cdot dt)-iv((k-1)dt)]/dt \quad \cdots\cdots(13)$$

Putting $V(t)=vo-(iv(0)/2+\sum_{m-1}^{k-3} iv(m))dt$

Then we obtained

$iF(k)=C1\cdot iF(k-1)+C2\cdot iv(k)+C3\cdot iv(k-1)+C4\cdot iv(k-2)+C5\cdot V$ for $k>3$. Same procedure is used to obtain $iv(k)$. From equation (4) $Pt(t)=Pv(t)-iv(t)\cdot Pv(t)$, substituting this expression into equation (3)

$iv(t)=iF(t)+Cv\cdot[dE(t)/dt\cdot V+E\cdot((iv(k-1)+iv(k-2))/(1-2)]]-Cv\cdot Rv\cdot div(t)/dt$, then using equation (9) and equation (13)

$$iv(k)=C6\cdot iv(k-1)+C7\cdot iv(k-2)+C8\cdot iF(k-1)+C9\cdot V \quad \cdots\cdots(14)$$

for $k>3$.

So we could redue a linear simultaneous algebraic equations. Same mathematical procedure was used to obtain $iF(1)$, $iF(2)$ and $iv(1)$ and $iv(2)$.

The initial condition for these equations.

We require only $iv(0)$ bacause of equation (14). In equation (3), $iF(0)=0$ at immediately beggining of ejection. Then

$iv(0)=Cv\cdot dP(t)/dt\ (t=0)$. From equation (2), $Pa(t)=P(t)-r\cdot iF(t)$. Substituting this equation into equation (1) and utilizing $iF(0)=0$. Putting $P(0)=A$ (the end diastolic arterial pressure)

$iF(t)=P(t)/Ra-iF(t)\cdot r/Ra+Ca\cdot dP(t)/dt-Ca\cdot r\cdot diF(t)/dt$. Then

$dP(t)/dt(t=0)=r\cdot diF(t)/dt(t=0)-A/$

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$(Ra \cdot Ca)$. Consequently

$$iv(0) = Cv \cdot [r \cdot diF(t)/dt - A/(Ra \cdot Ca)] \quad (t=0)$$

We calculated the iv(0) by iterating technique until the absolute of difference between calculated diF(t)/dt (t=0) and assumed diF(t)/dt (t=0) reaches below 0.05. According to Yamakoshi[5] and Takaya[12], the standard values of Ra and Ca are set to be Ra=6 mmHgsec/m*l*, Ca=0.1 m*l*/mmHg, while r, Rv, Cv and Vo are set to be r=0.1 mmHgsec/m*l*. Rv=0.65 mmHgsec/m*l*. Cv=0.45 m*l*/mmHg. Vo=20 m*l* respectively. We utilized the experimental data of instantaneous pressure volume ratio E(t) as input (numerical values).

Results

I) Reconstruction of ventricular and arterial pressure curves. (Fig. 2)

The ventricular pressure Pt(t) and arterial pressure Pa(t) increase rapidly at the beggining of the ejection. They produce clear peaks then decrease. Each curve changes with system variables. The times in parenthesis indicate the time to peak pressure. The continuous curve in each figure expresses the numerical values of E(t) used as input. With increases in Ra and Rv, the time to peak pressures are prolonged while they are not affected by changes in Ca.

II) Quantitive analysis of the maximum ventricular pressure max Pt(t) and the maximum arterial pressure max Pa(t).

1) The effects of Ra.

The max Pt(t) and max Pa(t) increase with Ra. A rapid change occur at $1<Ra<3$

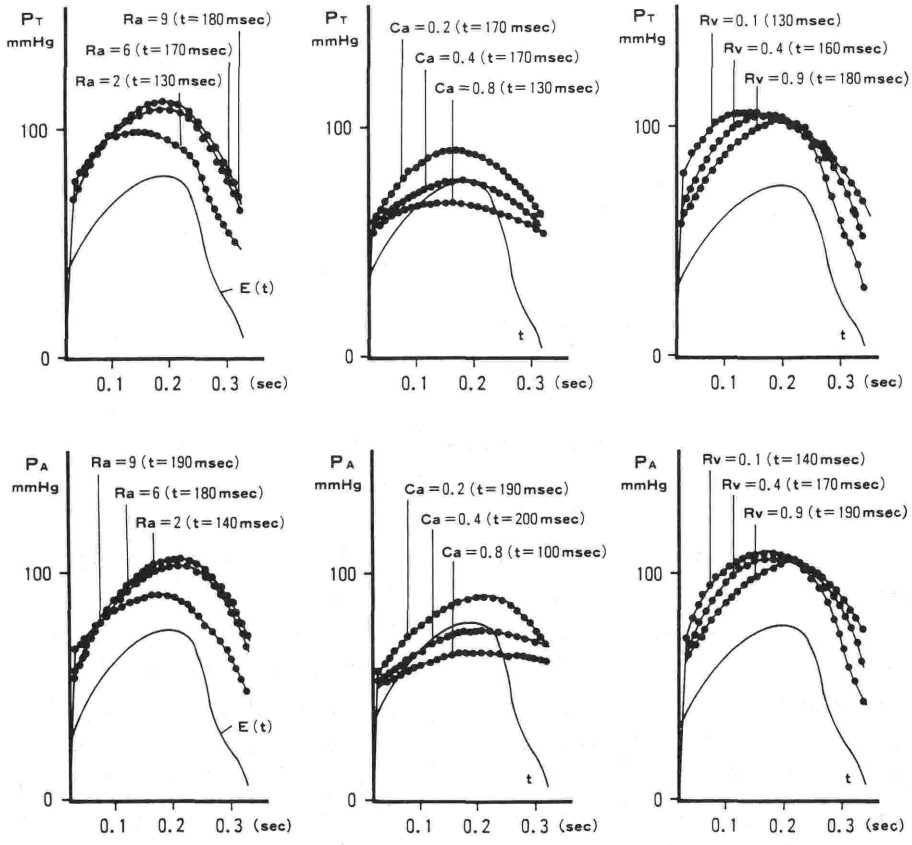

Fig. 2 Calculated ventricular (upper column) and arterial pressure curves (lower column) with changes in system parameters (Ra, Ca, Rv).

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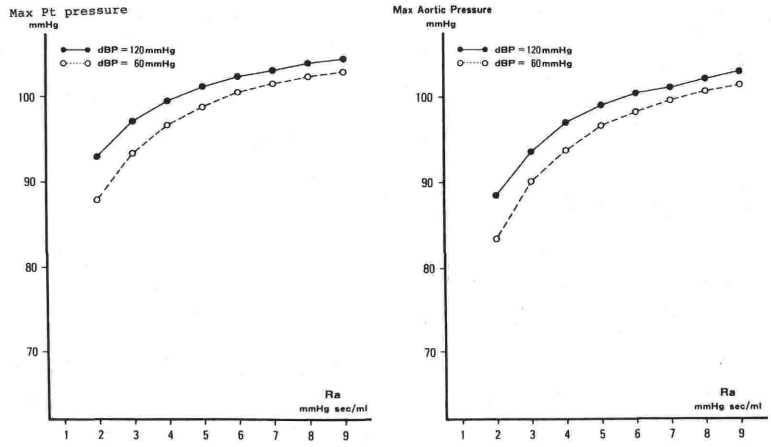

Fig. 3 right: the maximum arterial pressure as a function of Ra with parametric change in diastolic arterial pressure. left: the maximum vetricular pressure as a function of Ra with parametric change in diastolic arterial pressure.

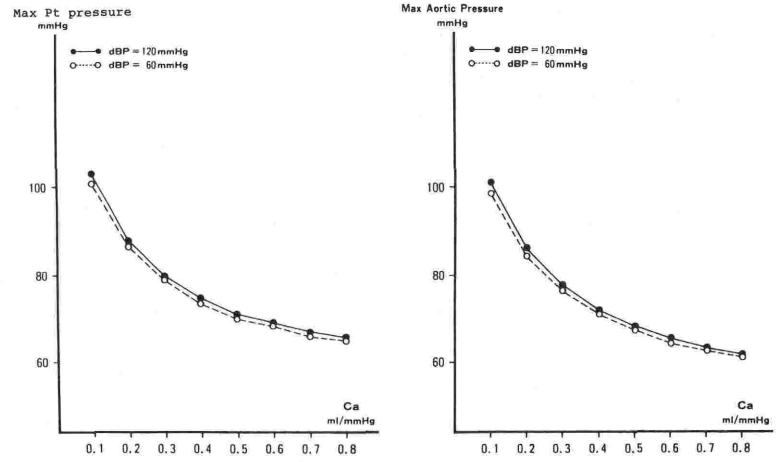

Fig. 4 right: the maximum arterial pressure as a function of Ca with parametric change in diastolic arterial pressure. left: the maximum ventricular pressure as a function of Ca with parametric change in diastolic arterial pressure.

mmHgsec/m*l* while they increase a little at Ra>7 mmHgsec/m*l*. The effect of difference in diastolic pressure on these pressures is clear at smaller Ra than at larger Ra.

2) The effects of Ca.

The max Pt(t) and max Pa(t) decrease with Ca. Rrapid changes occur at 0.1, Ca<0.3 m*l*/mmHg while at Ca>0.5 m*l*/mmHg, those changes are small. The effect of the difference in diastolic pressure on these pressures is small and is independent from changes in Ca.

3) The effects of the r.

The max Pa(t) decreases continuously with r at all ranges of r. On the other hand, the max Pt(t) decreases at lesser degree than the max Pa(t). The max Pt(t) decreases only a little at r>0.5 mmHgsec/m*l*. The effect of the difference in diastolic arterial pressure on these pressures is independent from changes in r.

4) the effects of Rv.

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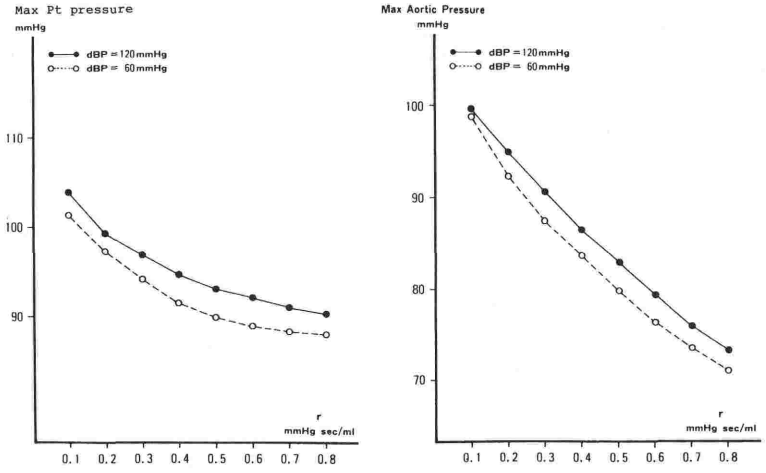

Fig. 5 right: the maximum arterial pressure as a function of r with parametric change in diastolic arterial pressure. left: the maximum ventricular pressure as a function of r with parametric change in diastolic arterial pressure.

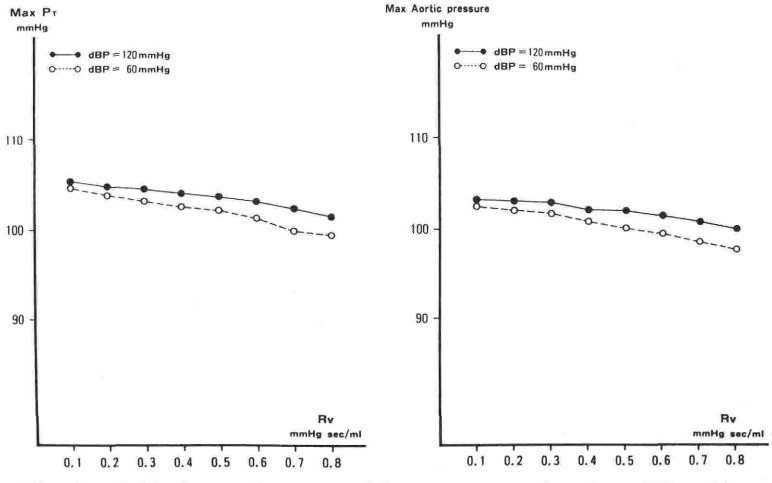

Fig. 6 right: the maximum arterial pressure as a function of Rv with parametric change in diastolic arterial pressure. left: the maximum ventricular pressure as a function of Rv with parametric change in diastolic arterial pressure.

The max Pt(t) and the max Pa(t) decrease a little with Rv. The effect of difference in diastolic pressure on these pressures is small but it increases with Rv.

Discussion

1) The E(t) (instantaneous pressure volume ratio) as a contractile element.

Several kinds of models or concepts had been proposed to illustrate the mechanical dynamical properties of the whole heart[6,7,8]. They, however, did not refer about the time dependent feature of beating heart. Suga and Sagawa[3] proposed an elastance model (time varying elastance) to express the total contractile nature of whole heart. Further it was verified experimental that it is insensitive to the changes in afterload, preload and the heart

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rate[3].

Later they modified[4] their elastance model to describe the pressure deficit during ejection period. The factors that contributed to this pressure deficit are 1) Uncoupling effect of shortening of cardiac muscle, 2) viscoelastic properties (creep and stress relaxation) of cardiac muscle, and 3) instantaneous and gradual length dependent changes in myofilamental calcium affinity, transsarcolemal kinetics of calcium[9].

Suga et al.[4] overcome these insufficiency of prototype model by incorporating the viscous internal resistance Rv and passive elastance Cv. The Cv, in skeleton muscle, corresponds to the S-2 portion of the cross bridge of cardiac muscle[10]. The Cv was measured as the passive elastance during isotonic contraction after acute release of cardiac muscle. Covel et al.[11] measured the Cv by quick volume release method which impose unphysiological loading of impulsive volume change. On the other hand Takaya[12] used a parametric method which is a physiological technique and they calculated the value of Cv to be $0.012-0.093$ ml/mmHg. These small values corresponds, but not perfectly, to the coefficient reported by Suga et al.[4] to express the factors of pressure deficit other than viscous resistant factors.

Here we mentioned the necessity of incorporation of Rv and Cv, however, the essential elastance concept was same with their original one.

2) Ra

According to the experiment of isolated canine left ventricle connected to the servo controlled afterload system[13], the systolic ventricular pressure increased and the time to peak pressure was prolonged with Ra ($1.5<Ra<6.0$ mmHgsec/ml). The curves of calculated pressures in the present study are similar with their experimental results. The time to peak pressure was prolonged from 130 msec to 170 msec at $2<Ra<6$ mmHgsec/ml in the present study which also are compatible with their experimental data. Quantitively, the behavior of the maximum ventricular pressure and the arterial pressure as a function of Ra in the present study were also compatible with their experiment.

3) Ca

Sunagawa et al.[13] reported that the systolic pressure decreased and the time to peak pressure was shortened with Ca at $0.2<Ca<0.8$ ml/mmHg. In the present results, both of the maximum ventricular pressure and arterial pressure showed similar pattern with their experiments at corresponding range of Ca. Further more, the time to the peak pressure also showed quite similar pattern (170 msec at $Ca=0.2$ to 130 msec at $Ca=0.8$) with their experimental results. Then, at least with these ranges of Ca, calculated results are compatible with biological phenomenas and the elastance model can describe the effects of Ca.

4) r

Sunagawa et al.[13] changed the characteristic impedance Rc at high frequency range at $0.1<Rc<0.4$ mmHgsec/ml. In the present study, r is compatible with Rc. In their experimental data, the ventricular systolic pressure increased with Rc. Conversely in present work, the maximum ventricular and arterial pressure decreased with r. This difference can be explained that when the aortic valvular resistance was increased, a reactive compensatory mechanism of ventricle soon operates in cardiovascular system. Then the ventricular pressure increase up to overcome the increased aortic valvular resistance. However in the present theory, we did not incorporate such adaptive compensatory mechanisms into ventricular elastance model since 1) originally the elastance concept can be applicable only to the physiological state. 2) it is not our purpose to expand the properties of model beyond pathophysiological state. The pressure decrease with r in the present study should be the non compensated state of heart

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without secondary adaptive change in ventricular function. Therefore the present results are not inconsistent with physiological phenomenon.

5) Rv

Templeton et al.[14] reported the increase of the viscous resistance of ventricle at ischemic state. As in Fig. 2, the maximum ventricular and arterial pressure decreased with Rv and the time to peak pressure were clearly prolonged. These results can in some part illustrate the reduced ventricular function which also can be interpreted as the state of ischemic change. Although it is difficult to have the perfect comparison with servo controlled experiment, a reasonable speculation about functional significance of the Rv is possible. In summary, the following conclusions were obtained.

1) A theoretical study was performed to describe the total behavior of cardiovascular system. The ventricle was expressed by the modified time varying elastance model and the arterial system by Wind Kessel model. The model was illustrated by an equivalent electrical circuit and expressed by linear simultaneous differential integral equations which were solved by numerical technique.

2) Realistic and physiological pressure curves could be drawn and the maximum pressures decreased with Ra, Rv, and r while it increased with Ca.

3) The present model can describe the total behavior of normal physiological cardiovascular system without adaptive nor compensatory changes in ventricular function.

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心室の可変弾性体モデルによる血行力学の理論的研究

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菅らの可変弾性体モデルによる心臓の力学的表現と動脈系をウィンドケッセルモデルで表現し体循環の統合的解析を理論的に行なった．心臓は可変コンデンサを基本的収縮要素とし圧欠損を近似する目的で内部抵抗と直列受動的弾性を含めた．ウィンドケッセルモデルは血流抵抗，コンプライアンス，弁抵抗とした．これらを電気的等価回答で表わし連立線形微分，積分方程式を数値的に解いた．

再現された血圧波形は生理的であった．最大動脈血圧，心内圧は血流抵抗の増加で増大し大動脈コンプライアンス，弁抵抗，心室内抵抗の増加で減少した．大動脈拡張期血圧の変化もよく反映された．本モデルは心臓を含む体循環を全体として表現することができる．

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