Strain Softening in Rat Left Ventricular Myocardium

We investigated whether strain softening (or the Mullins effect) may explain the reduced left ventricular stiffness previously associated with the strain-history-dependent preconditioning phenomenon. Passive pressure–volume relations were measured in the isolated, arrested rat heart during LV balloon inflation and deflation cycles. With inflation to a new higher maximum pressure, the pressure–volume relation became less stiff, particularly in the low (diastolic) pressure range, without a significant change in unloaded ventricular volume. In five different loading protocols in which the maximum passive cycle pressure ranged from 10 to 120 mmHg, we measured increases at 10 mmHg in LV volume up to 350 percent of unloaded volume that depended significantly on the history (p < 0.05) and magnitude (p < 0.01) of maximum previous pressure. Although a quasi-linear viscoelastic model based on the pressure-relaxation response could produce a nonlinear pressure–volume relation with hysteresis, it was unable to show any significant change in ventricular stiffness with new maximum pressure. We incorporated a strain softening theory proposed by Johnson and Beatty (1992) into the model by modifying the elastic response with a volume-amplification factor that depended on the maximum previous pressure. This model more accurately reproduced the experimentally observed behavior. Thus, the preconditioning behavior of the myocardium is better explained by strain softening rather than viscoelasticity and may be due to damage to elastic components, rather than the effects of viscous tissue components.

Introduction

It is well known that the stress response in soft tissues depends on the history of strain (Fung, 1993). In resting cardiac muscle and other tissues, creep (Pinto and Patitucci, 1980), stress-relaxation (Fung, 1967), and preconditioning behavior (Viidik, 1968) have traditionally been recognized as viscoelastic properties, in which the stress depends upon the time history of deformation with a fading memory. For example, Pinto and Patitucci (1980) showed that the quasi-linear viscoelastic model (Fung, 1972) could accurately describe the stress in resting papillary muscle during rapid stretching.

Certain rubber materials demonstrate a different strain-history dependence known as strain softening or the Mullins effect. Mullins (1947) found that the stress–strain relation in vulcanized rubber depended on the maximum previous load experienced by the specimen. These and other rubber elastomers become permanently softened after the load reaches a new maximum for the first time. It has been suggested that strain softening may explain preconditioning behavior (Johnson and Beatty, 1993). Thus, some of the history dependence in soft tissues that has previously been attributed to viscoelasticity may actually be the result of strain softening.

The force-elongation relations in ligaments reported by Viidik (1968), for example, reveal a progressive loss of stiffness following stretch to successively higher maximum strains, but was described as stress-relaxation or plasticity. Although Fung (1993) suggested that the soft tissues are being structurally altered during repeated cyclic loading, no mechanism has been shown to be responsible for preconditioning. To date, the only established model of soft tissue strain history dependence that could be used to investigate preconditioning behavior is quasi-linear viscoelasticity (Fung, 1972).

We postulated that the preconditioning behavior of the left ventricular pressure–volume relation (Omens et al., 1993) and its specific history dependence may be better explained by strain softening (the Mullins effect) than viscoelasticity. Comparing analytical models based upon these theories may provide insight into alternative structural explanations for preconditioning, such as alterations in elastic structural components instead of tissue fluid movement.

Methods

All animal studies were performed according to the NIH Guide for the Care and Use of Laboratory Animals. Animal use protocols were approved by the UCSD animal subjects committee. The surgical and experimental preparation follows that used by Omens et al. (1993). Briefly, 38 male Sprague-Dawley rats (370–530 g) were anesthetized with sodium pentobarbital (100 mg/kg) and ventilated with air. Following a median sternotomy, the aorta was clamped, and the heart was arrested via aortic injection of a hypothermic, hyperkalemic buffer solution containing (in g/l): 4.0 NaCl, 4.5 KCl, 3.0 NaHCO3, 0.2 MgCl2, 0.2 Na2SO4, 2.0 dextrose, 3.0 butanedione monoxime (BDM), and 10,000 Units/l of heparin. The heart was excised, rinsed, weighed, and the coronary circulation was flushed by retrograde perfusion with not more than 10 ml of arrest solution through an aortic cannula. During cardiac arrest and perfusion, care was taken to avoid ventricular dilation. The right ventricle was vented, and a drain tube inserted into the apex of the left ventricle (LV). A balloon, attached to a steel cannula, was inserted into the LV through the mitral annulus and secured with a purse string suture. The balloon, whose volume was sufficiently large that it would not develop significant pressure in the range of ventricular volumes, was inflated with water at approximately 1 ml/min by a volume infusion pump (KD Scientific Inc., Boston, MA). LV pressure was measured using a hydraulically coupled pressure transducer (Viggo-Spectramed, Oxnard, CA). LV pressure (P) and volume (V) were sampled at 10 Hz using an A/D data acquisition board (Strawberry Tree, Sunnyvale, CA). Throughout the duration of testing, the heart was periodically sprayed with arrest solution to prevent drying.
We used six different loading protocols to study the effects of strain history on the resting LV pressure–volume relation. In protocols A, B, C, D, and E (n = 25 hearts total), the LV was inflated at a constant rate to a maximum cycle pressure ($P_{max}$) and then deflated at the same rate to the unloaded volume (Fig. 1). This loading cycle was repeated at least three times for each $P_{max}$. In protocol A, the magnitude of $P_{max}$ was sequentially increased from 10 to 20, 30, 60, 90, and 120 mmHg. In protocol B, the sequence was changed only by including three extra cycles to $P_{max} = 60$ mmHg immediately after the cycles to $P_{max} = 10$ mmHg. Similarly, three extra cycles were included in protocol C to $P_{max} = 120$ mmHg. Protocol D was used to test the repeatability of the pressure–volume relation by using the same sequence of $P_{max}$ as in protocol A, but repeating each cycle six times instead of three. In protocol E, the stability of the pressure–volume relation over time was examined by loading the hearts three times to $P_{max} = 10$, followed by three cycles at $P_{max} = 60$ and 10 cycles at $P_{max} = 10$ mmHg. This latter sequence was repeated seven times.

Alterations in compliance were quantified by calculating the change in LV volume ($ΔV$) at a pressure of 10 mmHg between a reference cycle (#3, $P_{max} = 10$) and subsequent cycles for higher values of $P_{max}$. This difference was normalized by the resting volume $V_0$, the volume at zero pressure in cycle #3. $V_0$ was determined by adding the volume at the transition from negative to positive pressure during inflation to the volume of the balloon and LV cannula.

In five additional hearts, we examined the relaxation properties of the ventricle in response to step increases in volume. We measured the reduced pressure-relaxation function, $G(t)$, which we defined as $P(t)/P_0$, where $P_0$ is the peak pressure in response to a rapid (7 ml/min) step change in volume and $P(t)$ is the subsequent history of ventricular pressure. $G(t)$ was measured twice for 1000 seconds following step inflation to $P_0 = 60$ mmHg. The hearts remained unloaded for over 200 seconds between the two measures of $G(t)$ to minimize the influence of the first test on the second.

Statistical analysis of differences in ventricular volume with the effect of $P_{max}$ and between protocols A, B, and C was performed using two-way analysis of variance for repeated measures (SuperANOVA, Abacus Concepts, Berkeley, CA). Data from protocol D were analyzed by Student’s T-test. Post-hoc analysis was performed using Bonferroni correction for multiple comparisons. All data are reported as mean ± standard deviation except where noted. Results were considered significant if $p < 0.05$.

After measuring the relaxation function, we first used quasi-linear viscoelasticity (Fung, 1972) to describe the LV pressure history:

$$ P(t) = \int_{t_{-\infty}}^{t} G(t - \tau) \frac{\partial P^*(V(\tau))}{\partial V(\tau)} d\tau $$

where $V(t)$ is the current volume and $P^*(V)$ is the instantaneous elastic pressure–volume relation. $P^*(V)$ was fitted to data best representing the virgin (or non-preconditioned) material state (protocol C, cycle #4), using a least-squares method, to an exponential of the form

$$ P^*(V(t)) = \alpha (e^{P^*(V(t) - V_0)} - 1). $$

The pressure-relaxation function, $G(t)$, was also approximated by an exponential and fitted to the second experimental measurement of the pressure-relaxation function, since this better represents the state of LV after initial loading. The integration was performed numerically using a 10-point Gaussian quadrature routine (#D01AJF, Numerical Algorithms Group, Downers Grove, IL) in time steps of 50 ms.

In the strain softening analysis, we adapted the one-dimensional model of Johnson and Beatty (1993) for the Mullins effect in rubber. We assumed that the volume change at time $t$ can be linearly scaled from the volume change for the fully softened state as

$$ (V(t) - V_0)|_{P=0} = \phi(P_{max})(V(t) - V_0)|_{P=0} $$

where $\phi(P_{max})$ is the volume amplification factor and $P_{th}$ refers to the largest maximum pressure in the protocol. This factor is directly analogous to the strain amplification factor defined by Johnson and Beatty (1993) and has a range of $0 < \phi(P_{max}) \leq 1.0$. Thus, the instantaneous elastic response in Eq. (1) was modified to represent the exponential fit to the pressure–volume relation of the last cycle in each protocol and took the form:

$$ P^*(V(t)) = \alpha (e^{P^*(V(t) - V_0)/\phi(P_{max})} - 1). $$

Following Johnson and Beatty (1993), we also assumed that the softening may be sufficiently described using $\phi$ as a piecewise, rather than continuous, function of $P_{max}$. The pressure–volume relations of both models were compared after prescribing the loading protocols A, B, and C.

Results

LV pressure–volume relations for three consecutive loading cycles in a typical heart from protocol A (Fig. 2) showed a distinct loss of stiffness for the loading cycle (#8) that immediately followed the first cycle (#7) to a new maximum pressure. The ascending limbs of the third pressure–volume relation for each new value of $P_{max}$ become successively less steep with increasing $P_{max}$ in protocol A (Fig. 3(A)). In protocol B (Fig. 3(B)), there was a substantial change in curve shape from cycle
Fig. 2  Left ventricular pressure–volume relations for three cycles for a typical rat heart in protocol A. The volume includes that of the balloon and cannula inside the left ventricle. Note the distinct softening of the ascending limb for cycle #6 after the heart had experienced a new maximum pressure in cycle #7.

#3 ($P_{\text{max}} = 10$) to #6 ($P_{\text{max}} = 60$), but no change after cycle #6 until $P_{\text{max}}$ exceeded 60 mmHg in cycle #15. In protocol C (Fig. 3(C)) an even larger change was seen between cycles #3 and #6, but no changes were evident after the early cycles to the

Table 1  Summary of animals used and experiment duration for each experimental loading protocol

<table>
<thead>
<tr>
<th>Protocol</th>
<th>n</th>
<th>Body Mass (g±SD)</th>
<th>Heart Mass (g±SD)</th>
<th>Exp. Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5</td>
<td>40±15</td>
<td>1.2±0.15</td>
<td>30</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>41±15</td>
<td>1.5±0.15</td>
<td>35</td>
</tr>
<tr>
<td>C</td>
<td>5</td>
<td>40±15</td>
<td>1.4±0.11</td>
<td>35</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>38±15</td>
<td>1.35±0.15</td>
<td>45</td>
</tr>
<tr>
<td>E</td>
<td>3</td>
<td>38±15</td>
<td>1.29±0.06</td>
<td>85</td>
</tr>
<tr>
<td>G(t)</td>
<td>3</td>
<td>37±15</td>
<td>1.29±0.08</td>
<td>40</td>
</tr>
</tbody>
</table>

highest maximum pressure of 120 mmHg. The characteristics of the animals used in all six protocols are summarized in Table 1. Four animals were excluded because of leaks in the system, one because the balloon became wedged against the papillary muscles, and one because of improper volume calibration.

The normalized volume change, $\Delta V/V_o$, depended on the maximum pressure or volume previously experienced by the LV (Fig. 4). This load history varies with each protocol. In protocol A, LV volume increased consistently with increasing $P_{\text{max}}$. Volume changes in protocol B, while initially greater than those in protocol A for low maximum cycle pressure, remained constant until $P_{\text{max}}$ exceeded 60 mmHg. Protocol C produced the largest initial volume change but produced no subsequent changes with $P_{\text{max}}$. Two-way analysis of variance, the differences in mean $\Delta V/V_o$ within $P_{\text{max}}$ and between protocols were significant ($p < 0.01$) and $p < 0.05$, respectively. Post-hoc analysis with Bonferroni correction yielded significant differences between protocols A and B and between A and C ($p < 0.01$) at $P_{\text{max}} = 20$ and 30 mmHg. The values of $\Delta V/V_o$ at each maximum pressure for cycles #3 and #6 in protocol D (Fig. 5(A)) were not significantly different ($p > 0.88$). The change in $\Delta V/V_o$ during protocol E (Fig. 5(B)) did not begin to reverse for at least 30 minutes.

The measured volume-amplification factor (Fig. 6(A)) also depended on the maximum previous load and approached a distinct asymptote for each $P_{\text{max}}$. We therefore quantified $\phi(P_{\text{max}})$ as the largest measured value for each $P_{\text{max}}$. As seen in Fig. 6(B), there was a distinct trend for $\phi(P_{\text{max}})$ to monotonically increase in all three loading protocols.

The mean pressure-relaxation behavior (Fig. 7) shows rapid decay within 50 seconds, followed by a much slower decline. The second step-increase in volume produced a different relaxation function from the first. In both tests, however, G(t) appeared to approach an asymptotic value after 1000 seconds.

Table 2 summarizes the functions and parameter estimates used for the elastic response and pressure-relaxation response.

Fig. 3 Pressure–volume relations for a typical heart in protocols A, B, and C. Only the preconditioned ascending limb for each unique maximum pressure is shown. (A) With each maximum pressure in protocol A, the pressure–volume relation becomes less stiff. (B) The pressure–volume relations in protocol B for maximum pressures of 20 and 30 mmHg fall on the same curve as that of the early maximum pressure of 60 mmHg. The relations become less stiff after the maximum pressure exceeded 60 mmHg. (C) Similarly, all the pressure–volume relations following the early inflation to 120 mmHg lie on the same curve. Note that the volume at zero pressure changed very little.

Fig. 4 Mean volume change (±S.E.M.) as a function of maximum cycle pressure for protocols A, B, and C. Two-way ANOVA revealed significant differences between protocols ($p < 0.05$) and within maximum pressure ($p < 0.01$). All volume changes equal zero at $P_{\text{max}} = 10$ by definition (see text). At 120 mmHg, the relative volume changes in all hearts were equivalent.
Fig. 5 (A) Mean volume change (± S.E.M.) as a function of maximum cycle pressure for protocol A. Repeating the loading cycle four or more times has little effect on relative volume changes. No significant differences exist between cycles #3 and #6. (B) Volume changes as functions of time for three hearts in protocol E. For all three hearts, the volume changes did not decline below the initial value until at least 30 minutes.

$P'(V)$ in the viscoelastic analysis was fitted to the inflation limb from the mean of five pressure-volume relations for cycle #4 ($P_{max} = 120$ mmHg) in protocol C, while $P'(V)$ for the strain softening model was fit to the mean of cycle #18 in protocol A. Due to relaxation during the finite time required to perform this experimental loading, however, these fitted estimates are not the true instantaneous elastic response $P'(V)$. We corrected for this by scaling $\alpha$ in Eqs. (2) and (4) with a constant of 1.19. This value was the slope of the regression that fitted the pressure computed from Eq. (1) using the initial estimate of $P'(V)$ without any relaxation versus the experimental (relaxed) pressure.

There were marked differences between the results of the two model analyses (Fig. 8). When we prescribed the loading history of cycles #6–8 in protocol A, the pressure-volume relations in the strain softening model (Fig. 8 (B)) more closely approximated the experimentally observed behavior (Fig. 2). In cycle #7 the descending limb became more compliant following loading to the new maximum pressure, whereas the shape of the curves in the viscoelastic model did not change after cycle #7. Hysteresis in the strain softening analysis also decreased after the first inflation to the new maximum pressure. The area enclosed within the pressure-volume loop declined by 0.32 mmHg·ml from cycle #7 to #8. In the protocol A experiments, hysteresis also consistently fell from cycle #7 to #8 by a mean of 0.17 ± 0.15 mmHg·ml ($p < 0.05$). In contrast, the hysteresis of the viscoelastic analysis model did not change.

The difference between the models was also present when the entire loading history of experimental protocols A, B, and C was prescribed in both analyses. Pressure-volume relations obtained from the viscoelastic model overlapped one another and did not change significantly with maximum pressure (Figs. 9 (A–C)). Those of the strain softening model (Fig. 10 (A–C)) did exhibit a dependence on the history of maximum previous pressure that was similar to that of the experiments (Fig. 3).

Discussion

In an isolated, arrested rat heart preparation, we measured the passive left ventricular pressure-volume relation during a variety of load histories. The consistent changes in the pressure-

Fig. 6 (A) Experimentally measured volume-amplification factor versus pressure for a typical animal from protocol A. With increasing maximum cycle pressure, $\phi(P_{max})$ asymptotically approaches a higher value with pressure. (B) Mean (± S.D.) of $\phi(P_{max})$ versus maximum cycle pressure for all three loading protocols. For all protocols, $\phi(P_{max}) = 1.0$ at $P_{max} = 120$ mmHg by definition.

Fig. 7 Mean reduced pressure-relaxation function $G(t)$ (± S.D.) for three hearts as measured for 1000 seconds. By definition, $G(t) = 1.0$ for both tests. $G(t)$ approached a lower value for the first test than the second.
Table 2. Functions and parameter values for quasi-linear viscoelastic model (Eq. (1)). Parameters were determined by least-squares fits to experimental data. C is the volume loading rate used in experiments.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Function</th>
</tr>
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<tbody>
<tr>
<td>Viscoelastic</td>
<td>( g(\theta) )</td>
</tr>
<tr>
<td>( P'(V_0) )</td>
<td>1.46</td>
</tr>
<tr>
<td>Strain Softening</td>
<td>( a_2 )</td>
</tr>
<tr>
<td>( C_t )</td>
<td>1.67 x 10^6 M/s</td>
</tr>
<tr>
<td>( G_0 )</td>
<td>2.035 GPa</td>
</tr>
</tbody>
</table>

\[ G_0 = A_0 \omega^m + A_2 \omega^{m2} + \frac{1}{1-A_1-A_2} \omega^{m3} + G_1 \]

\[ A_0 = 0.109; A_2 = 0.126; G_1 = 0.610 \]

\[ C_t = 1.41 \times 10^{-6} \text{ m}^2/\text{s} \]

The volume relation with the history of maximum previous pressure support our hypothesis that left ventricular stiffness decreases as the maximum previous load increases. This altered compliancance was most evident at the low pressure range. The LV pressure-relaxation response was not sufficient to explain these history-dependent effects in a quasi-linear viscoelastic model of the pressure-volume relaxation. When we incorporated a simple description of the observed strain softening in the model, however, we could reproduce the large hysteresis during cycles to new maximum load and the subsequent increase in LV compliance. Therefore, we conclude that the preconditioning behavior of the resting myocardium is due to strain softening (Mullins effect) and is relatively independent of the time history of the load for at least 30 minutes.

The trends in volume change with \( P_{\text{max}} \) suggest that permanent strain softening may exist in the passive LV and is strongly dependent upon the magnitude of maximal loading (protocol A). Protocols B and C showed that softening is also dependent upon the sequence of load. Following the early cycles of \( P_{\text{max}} = 60 \) in protocol B, the degree of softening remained constant until \( P_{\text{max}} = 90 \), after which the LV experienced a new maximum load and began to soften again (Fig. 3(B)). After the early inflation to \( P_{\text{max}} = 120 \), the hearts in protocol C had fully softened (Fig. 3(C)). Once all hearts in A, B, and C had experienced 120 mmHg, their volume change was equivalent (Fig. 4). The assumption that the third cycle accurately reflects the repeatable state of the pressure-volume relation is validated by the small changes in \( \Delta V/V_0 \) between the third and sixth cycle for each \( P_{\text{max}} \) in protocol D (Fig. 5(A)). While these changes are not negligible, they were too small to account for our results.

Sources of error in the experimental results may include the accuracy of measuring the pressure-volume relations with a balloon-infusion technique. Leaks in the system were minimized through careful observation and stringent exclusion criterion. The apparent viscoelastic properties of the experimental system, such as flow resistance and compliance in the tubing and pressure transducer, were modeled as lumped parameter elements of springs and dashpots. The calculated time constants (~1 x 10^-6 s) and equivalent capacitance (5.22 x 10^-9 m/s kPa) for the system were orders of magnitude smaller than those measured for the resting heart and considered negligible.

Other potential factors that may influence our measurement of changes in ventricular compliance include infusset rate and the use of BDM in our cardioplegic buffer solution. We found...
and Beatty (1993), that no incremental softening occurred during the loading to a new maximum pressure. Calculation of $\phi(P_{\text{max}})$ in cycle #4 relative to #5 for protocol C, however, did show a continuous variation as $P_{\text{max}} = P$ between 10 and 120 mmHg. Since preconditioning appears to be a consequence of instantaneous changes in myocardial elasticity, a better model of softening may result from using $\phi$ as a continuous function of $P_{\text{max}}$.

The quasi-linear formulation has been used extensively in biomechanics literature as a concise, efficient method to describe the viscoelastic properties of soft tissues. Pinto and Patricci (1980) showed that it could effectively model the stress-strain relation in papillary muscle. Huyngh and others (1991) also used it in a three-dimensional poroelastic finite element model of the passive ventricle. They employed the continuous spectral-relaxation function $G(t)$ with 10 Maxwell elements, but their model required a 1000-fold increase in one relaxation parameter to give reasonable description of passive stiffness and hysteresis. Thus, they concluded that myocardium may not be quasilinear viscoelastic, but did not suggest an alternative theory.

We found that the LV relaxation response, $G(t)$, also depends on the history of maximum previous pressure (Fig. 7). This, however, cannot account for softening of the pressure-volume relations, since the ventricle relaxed less in the second test. Additionally, the time constants (Table 2) for relaxation were also well below the measured duration of the softening effect. It is possible that the calculated time constants of the relaxation response are affected by the inability of our experimental system to change the LV volume instantly. This dependency may account for some of the discrepancy in the hysteresis between the experimental data and the model analysis. For example, the mean experimental hysteresis in cycle #7 was 1.46 versus 0.64 mmHg/ml for the strain softening model. These observations suggest that a more general, nonlinear viscoelastic model should include the relation between $G(t)$ and maximum previous deformation.

Although the measured changes in ventricular stiffness occur over a range of diastolic volumes not typically seen in normal function, dilatation and high diastolic pressures are common in cardiac failure (Millner et al., 1991). Furthermore, the decrease in stiffness appears to be greatest in the range of low (0–15 mmHg) LV pressure for all values of $P_{\text{max}}$ (Figs. (A–C)), which has important ramifications for diastolic function via the Frank-Starling mechanism. Thus, abnormally high wall stresses may lead to a reduction in myocardial stiffness, such as in the onset of acute ischemia. Systolic pressure generated by viable myocardium during early ischemia subjects the noncontracting region to passive overstressing and may reduce its diastolic stiffness (Forrester et al., 1972; Pirzada et al., 1976). Ischemia-induced changes in passive stiffness have also been described in viscoelastic terms such as diastolic creep (Glower et al., 1987; Downing et al., 1992) or stress-relaxation (Forrester et al., 1972). Strain softening may account for the changes in myocardial stiffness associated with acute ischemia better than previous explanations based upon viscoelasticity.

The preconditioning behavior of myocardium and other soft tissues has been widely reported, but, to our knowledge, no statistical correlation has yet been made between decreased tissue stiffness and the specific time history of maximal loading in the context of strain softening. Vildik (1968) published results of rat hind-limb tendon subjected to increasing maximal stretches and showed plastic rightward shifts in the load-elongation curves without stiffness changes. He also demonstrated for the anterior cruciate ligament that the stiffness at low loads did decrease for repeated loading at the same force, but attributed it to load relaxation.

In load model, Johnson and Beatty (1993) approximated the irreversible softening process by scaling the strain with an amplification factor that changed only when the previous load-
ing reached a new maximum value. In this work, we incorporated a volume amplification term that depended on $P_{max}$ into a quasi-linear viscoelastic analysis and only alters the elastic response of the ventricle. This implies that the strain softening (preconditioning) is more likely a maximum load-dependent change in the elastic structural components in the myocardium, rather than a time-dependent effect of viscous components such as interstitial or vascular fluid.

In this study, we did not attempt to elucidate the exact elastic structures responsible for the experimental observations of strain softening in the heart. Since the endomyocardial collagen matrix may contribute to LV geometry at low loads (MacKenna et al., 1994), stretch-dependent damage to this endomyocardial collagen may explain strain softening. Caulfield and Berg (1979) and Weber (1989) have shown that altered myocardial mechanical properties may be attributed to changes in collagen matrix. Alternatively, the work of Granzier and Irving (1995) and Wang et al. (1993) suggest that myofilament or cytoskeletal disruption may be involved. Granzier and Irving (1995) showed for rat cardiac muscle that the myofilament titin, which links myosin filaments to the Z-line, is largely responsible for passive tension development for low sarcomere lengths (1.9 – 2.1 μm). Wang et al. (1993) observed a decrease of passive stiffness in rabbit psoas muscle fibers following passive stretch that exceeded the yield-point of titin in skeletal muscle. They postulated that the reduced fiber stiffness may arise from a stretch-dependent detachment of the titin from the myosin filament, which results in a net increase in slack length of the extensible filaments without a change in their inherent stiffness. Determination of regional strain and histological analysis of the alterations in cellular and extracellular structures may elucidate the specific mechanism underlying strain softening.

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References


