Mechanical Properties of Human Pericardium
Differences in Viscoelastic Response When Compared with Canine Pericardium

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SUMMARY. Whereas most experiments on the mechanical function of the pericardium have been performed on dogs, very little is known about the applicability of those data to humans. To examine the tensile viscoelastic properties of fresh human pericardium, we have used the methods from our previous study of canine pericardium. Although the mechanical responses of canine and human pericardium were qualitatively similar, human pericardium displayed a significantly greater viscous character. Human pericardium was 7.3 times thicker than canine pericardium, but was more extensible in stress-strain tests, with lower stiffness at a given strain. The static (elastic) stiffness of human pericardium seems identical to that of canine pericardium; lower stiffness per unit thickness of the human tissue at predicted physiological stresses was almost exactly compensated by the greater wall thickness. This effect was also seen in data on fracture strength and stiffness. However, human pericardium displayed greater viscous responses than the canine tissue. This was seen in doubled cyclic hysteresis losses, and greater stress relaxation and creep. Our results suggest that experiments on the viscoelastic properties of canine pericardium may not be directly applicable to humans, especially where dynamic mechanical properties are most important: i.e., in studies of ventricular function and the time-course of pericardial effusions. (Circ Res 55: 475-481, 1985)

The canine pericardium has been the subject of considerable experimental activity over the last several years. As a result, ventricular diastolic properties are now acknowledged to be functions of both myocardial and pericardial mechanical properties. Almost all the relevant experiments have been conducted on anaesthetized dogs, either with the pericardium intact, with the pericardium opened, or, sometimes, with the pericardium resutured. Using these models, the pericardium has been shown to limit total ventricular volume acutely, enhance the interactions between left and right ventricular volumes, and affect the ventricular pressure-volume curves (Glantz et al., 1978; Tyberg et al., 1978; Mirsky et al., 1979; Ross, 1979; Shabetai et al., 1979; Stokland et al., 1980; Spadaro et al., 1981). Similar effects have also been observed in an isolated canine heart and pericardium preparation (Maruyama et al., 1982).

Although it seems reasonable to apply the results of canine experiments to our understanding of human pericardial function, we have as yet no clear foundation for doing so, and little is known about comparative differences. For example, when examining the effects of drugs on human ventricular diastole, Oldershaw et al. (1982) and others (Ludbrook et al., 1977; Mann et al., 1979) indicated that their pericardial results were not consistent with the results of experiments on canine pericardial function. Indeed, the gross appearance of human pericardium is substantially different from the canine tissue, being thick and opaque vs. thin and translucent, and Fingerote et al. (1980) have shown human pericardium to be less hydraulically permeable than canine pericardium.

In this study, we have examined the viscoelastic properties of isolated human pericardium using our previously published test regime for canine pericardium (Lee and Boughner, 1981).

Methods

Surgical samples of human pericardium were obtained from 10 patients (with apparently healthy pericardia) undergoing surgery for coronary artery bypass or valve replacement. In each case, the pericardium was routinely partially excised and left unclosed after surgery. The collection and use of the pericardium in this study was approved by the human experimentation committee of the Faculty of Medicine at the University of Western Ontario, and was covered under the surgical consent form signed by each patient upon admission. There were eight males and two females (age range, 26–73 years; mean, 53 years). Table 1 lists each patient's age, sex, diagnosis, and enlarged cardiac chambers prior to surgery. The tissue samples (measuring approximately 3 cm x 3 cm) were pinned to cork boards by the surgeons, and the anatomic location and orientation of each were indicated on an attached diagram. Each sample was immediately immersed in Hanks' physiological saline at room tempera-
ture. The location of the samples coincided with that of our previous study on canine pericardium (Lee and Boughner, 1981).

Human pericardium often had loosely adherent fat; it was removed prior to cutting. Vertical and horizontal (base-to-apex and circumferential) strips were cut as for the canine pericardium, and in the equivalent anatomic locations. A total of 18 vertical and 19 horizontal strips were tested at 37°C in Hanks' solution on an Instron Universal Testing Machine (model 1125). Nominally, strips 7 mm wide were mounted between sandpaper-lined brass grips to a gauge length of 10 mm.

Each strip was preconditioned by cyclic loading at an extension rate of 10 mm/min between 0 load and a maximum load of 40 or 500 g. The initial load-extension curves and subsequent curves were recorded until a stable, repeatable curve was obtained. The initial and final curves were examined to determine the effect of preconditioning and of maximum load. After preconditioning, each tissue strip was tested for: (1) stress relaxation (decrease in stress at constant strain) from loads of 20 and 40 g, or from loads of 250 and 500 g, depending on the maximum preconditioning load, or (2) creep (increase in strain under constant load) under the same loads. The order of application of the two loads was reversed for each subsequent sample. Some samples were tested for strain rate response at extension rates from 5–500 mm/min. Finally, each sample was extended at 10 mm/min until fracture.

Actual gauge length and mean strip width of each strip were determined by macro-photography during testing, and thickness was obtained using a Starrett nonrotating thickness gauge. Load-elongation curves were digitized and converted to true stress vs. strain data, as per our previous study. Stress relaxation data were converted to percent stress remaining expressed as \( \sigma(t)/\sigma_0 \), the ratio of the stress at time \( t \) divided by the stress at the beginning of relaxation. Creep data were converted to percent elongation, expressed as \( \Delta L(t)/L_{\text{eq}} \), the ratio of extension during creep to the initial length after the creep load was applied. Four parameters were calculated from the fracture data: (1) tissue modulus, the slope of the linear portion of the stress-strain curve at high stress, (2) ultimate tensile strength (UTS), the ratio of the applied force at fracture to the original cross-sectional area of the strip; (3) resilience, the energy per unit volume required to fracture the strip (and by definition the area under the stress-strain curve to fracture), and (4) strain at fracture.

All data are presented as the mean ± SEM. Differences with species (canine/human comparisons) or with species and load were examined with a one- or two-way analysis of variance.

### Analysis

In our previous paper, we used the analysis of stress in a thin-walled membrane (termed Laplace's law by physiologists) to calculate the appropriate mass-loads in a test strip which would be equivalent to pericardial end-diastolic stress (Lee and Boughner, 1981). This calculation requires estimates of transmural pressure, and principle radii of curvature. We may consider an extreme range of ventricular end-diastolic pressures as lying between a normal range of 4–12 mm Hg (0.5–1.6 kN/m²) (Hurst et al., 1978) and an upper limit of perhaps 30 mm Hg (3.9 kN/m²) during acute pericardial effusion (Shabetai, 1981). What fraction of this pressure is present as intra-pericardial pressure? The only available guide in this matter is the work of Holt et al. (1968) who measured ventricular and intrapericardial end-diastolic pressure in open-chested dogs. We have used their work and normal pleural pressure to calculate pericardial transmural pressure (and here we make the perhaps incorrect assumption of applicability of the canine data to humans). For radii of curvature, we have assumed the pericardium in the area of interest to be a portion of a 5-cm (radius) sphere (compared to an assumption of a 4-cm sphere for the dog). These values simulate the curvature of the anterior pericardium, compensating somewhat for the relative sizes of the hearts of humans and dogs. We note that the radius of curvature of the anterior surface of the heart is greater in the base-to-apex (vertical) direction than in the circumferential (horizontal) direction. However, since the shapes of the hearts in the dog and human are quite similar, the use of two principle radii of curvature would simply shift...
the predicted pericardial stress levels by the same percentage, and leave the arguments which follow unaffected. (For example, using a second radius of curvature 100% larger and at 90° to the first would increase the predicted stresses in both human and canine pericardium by 30%) Therefore, for clarity of presentation, we will use the simple spherical model.

Using this method, we find normal end-diastolic stress for human pericardium to be in the range of 19–57 kN/m² and the maximum stress of interest to be 140 kN/m². (Compare these with a normal range of 110–320 kN/m² and a maximum of 830 kN/m² for dogs.) The differences in values are largely due to the difference in thickness between human and canine tissue. The average thickness of human pericardium was 7.3 times that for our canine samples. The lower wall stress resulting from greater wall thickness greatly overshadows any effects from the spherical model assumptions above. Thus, human pericardium must experience a lower physiological tensile stress at end-diastole than does its canine counterpart. This is an important point to note when examining stress-strain results.

The stress range of interest can be translated into appropriate strip loads for uniaxial testing. The normal load range for human pericardium would be 13–41 g and the maximum load 70 g. For our testing, we used maximum loads of 40 g and 500 g to encompass both the physiological and extreme load ranges.

Results

The average thickness of the human pericardial strips was 1.02 ± 0.08 mm, the mean gauge length of the cut strips was 9.7 ± 0.1 mm, and the mean cross-sectional area was 7.65 ± 0.66 mm². The maximum applied loads of 40 and 500 g therefore produced maximum strip tensile stresses of 51 and 640 kN/m².

Preconditioning

The preconditioning responses of human pericardium were much like those of the canine tissue (Lee and Boughner, 1981). The stress-strain curve again shifted toward higher strain values during cyclic loading and changed shape. There was no evidence of plasticity (permanent deformation). Vertical strips achieved a stable stress-strain response after 25–33 cycles, horizontal strips after 30–39 cycles.

Raising the maximum preconditioning load from 40–500 g produced a slight shift in the stress-strain response. This shift was less than 1.5% of the strain value at any stress level. No plasticity resulted.

Cyclic hysteresis (percent loss of loading energy to heat during one loading cycle) was independent of preconditioning load, falling from a mean of 35.1 ± 5.4% on initial extension to a mean of 17.1 ± 2.9% after preconditioning.

Stress-Strain Response

Figure 1 shows the mean stress-strain curves for vertical strips of human pericardium to a maximum stress of 400 kN/m². At a normal end-diastolic level of 43 kN/m² (9 mm Hg), the resulting strain was 11%. The low stiffness (slope) at low strains gave way to a steep linear portion of the curve at high stress (not shown). This final stiffness was termed the tissue modulus (see Fracture, below).

Stress Relaxation and Creep

Figure 2 shows stress relaxation results for vertical strips of human pericardium plotted against log₁₀(t) for periods up to 1000 seconds. No asymptotic limit to relaxation was observed. In addition there was no indication of a limit to creep extension (Fig. 3). Both stress relaxation and creep data were independent of initial load. Whereas both experiments produced shifts in the stress-strain curve (see Lee and Boughner, 1981), neither produced any permanent (plastic) deformation.
FIGURE 3. Creep of preconditioned vertical strips of human and canine pericardium, n = 6 (human) and 7 (canine). All differences significant with P < 0.05. Mean ± se. %Creep is calculated as the ratio creep extension ΔL to initial (loaded) length L₀.

Effect of Strain Rate and Strip Orientation

The stress-strain curves for human pericardium were independent of strain rate from 5%/min to 500%/min. Hysteresis was also independent of strain rate, in each case.

Strip orientation did not significantly affect any mechanical data from human pericardium.

Fracture

The fracture of human pericardium was qualitatively similar to that of canine pericardium, with a steep linear stress-strain response prior to limited plastic deformation and strip tearing (Lee and Boughner, 1981). Table 2 shows the results for tissue modulus, ultimate tensile strength (UTS), and resilience, as well as those for strain at fracture. As can be seen from Figure 4, there was a reasonably strong linear regression between tissue modulus and UTS, the regression being significant with P < 0.001, r = 0.90.

Discussion

The mechanical behavior of human pericardium was at least qualitatively similar to that of canine pericardium, as examined in our previous paper (Lee and Boughner, 1981). Each tissue displayed a family of stress-strain responses. During cyclic loading to a selected strain, both loading energy and hysteresis losses fell similarly in each tissue until a stable post-preconditioning response was obtained. Again, the stress-strain curve for human pericardium could be shifted by stress relaxation and creep experiments and recover during renewed cyclic loading. Thus, the accommodation and recovery mechanisms demonstrated in canine pericardium were present in both types of tissue; no plasticity was associated with accommodation, only shifts in the stress-strain response.

In view of the large amount of experimentation performed on canine pericardium, it is important to recognize the differences in mechanical function between canine and human pericardia. Foremost is the difference in thickness between the two tissues. Human pericardium was 7.3 times thicker (on average) in our experiments, than canine pericardium. From the analysis section, it is clear that this must result in a much lower end-diastolic stress in human pericardium: 43 kN/m² compared to 250 kN/m² in the dog under 9 mm Hg end-diastolic pressure. Thus, from Figure 1, we see that the human pericardium operates much nearer the “elbow” in the stress-strain curve than does the canine pericardium. As a result, if the lower part of the stress-strain curve is dominated by the properties of matrix and elastin fibers, we should expect a more viscous character to the mechanics of the human tissue in the physiological range of stress.

It is possible to separate the viscous and elastic components of the experimental mechanical re-

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Units of MN/m². n = 9 (human) and 10 (canine). Mean ± se.
* Difference significant with P < 0.01.
sponses by comparing the "viscoelastic" responses from hysteresis, stress relaxation, and creep experiments with those from "elastic" low-stress-rate stress-strain experiments. Hysteresis loss to heat in human pericardium was some 17.5 ± 2.9% compared with only 7.9 ± 0.8% in the dog (significant with P < 0.01). This greater viscoelastic response is supported by the data in Figures 2 and 3. Human pericardium showed significantly greater stress relaxation and creep at all stress levels examined, even those well above the physiological range. In the "elastic" stress-strain experiments, we can compare the "elastic" stiffnesses of the human and canine pericardia at physiological end-diastolic stresses. (These are simply the slopes of the stress-strain curves at the appropriate stress levels.) The elastic stiffness of canine pericardium is 6.9 times that of human pericardium; however, this stiffness must be corrected for wall thickness in each case (a factor of 7.3). When this is done, the human and canine pericardia have almost exactly the same elastic component to their responses (the difference is not significant).

From these results, we conclude that human and canine pericardia offer nearly the same elastic opposition to diastolic filling. However, human pericardium must supply a much greater viscous opposition to filling. We have already pointed out how the greater tissue thickness of human pericardium must reduce the maximum wall stress and allow a greater viscous contribution from the matrix material. However, this is not sufficient to explain the greater stress relaxation and creep responses in human tissue even at high stress levels. An interesting hypothesis is suggested by our fracture data.

The lower elastic stiffness of the human material was also reflected in fracture data where the stiffness of the human tissue before fracture (tissue modulus) was much lower than that for dogs. The ultimate tensile strength of human tissue was lower than that for dogs, in exact inverse proportion to the wall thickness. Most interesting, however, is the shared linear relationship of the two tissues in the scatter plots of Figure 4. These data suggest that the two tissues share a common type of structural support in fracture, perhaps due to a similar collagen fiber structure. However, the human tissue has a proportionally overall reduction in strength and stiffness with wall thickness. The most likely explanation is that the human tissue has a lower effective volume fraction of fiber compared to the canine tissue, and that this reduction is inversely proportional to the thickness of the tissue. If the volume fraction of fiber is lower, then the volume fraction of matrix must be greater, contributing to the greater viscous component of mechanical behavior in the human pericardium.

Existing studies of pericardial histology in dogs and humans (Wallraff, 1937; Nelemans, 1940; Elias and Boyd, 1960; Kluge and Hovig, 1967; Ishihara et al., 1980) have not examined the volume or weight fraction of collagen in these tissues. Although this hypothesis could be addressed biochemically by assaying for collagen, such a study is beyond the scope of this paper.

Our observations indicate that, whereas the elastic component of pericardial opposition to diastolic filling is the same in dogs and humans, the viscous component in the human tissue is very much greater. This implies that canine studies of the pericardial contribution to the viscoelastic properties of the ventricle in diastole may not be applicable to the human. We must emphasize that the actual strain rates during diastole may be as high as 17,000%/min, some 30 times our maximum strain rate. [This figure is taken from the epicardial photogrammetry data of Ingels et al. (1971), assuming that the pericardium must expand as quickly as the epicardium.] Therefore, we may actually be underestimating the importance of the increased viscous response in the human tissue. Further, the differences in viscous response as seen in stress relaxation and creep experiments suggest that the response to rapidly and slowly accumulating effusions may also be quite different in the two species.

The higher maximum operating strains observed in human pericardial strips compared to those of dogs may also be a function of lower fiber volume fraction. This would allow greater collapse of fiber weave in the direction of stress during loading and a greater maximum strain. Biaxial testing and an in vivo study of canine and human pericardium would be required to quantify the actual maximum (and minimum) strains during function and the changes in strain which occur during the cardiac cycle.

The observed isotropy of human pericardium can be well explained by the crossed-fibrillar structure of the material noted in the histological studies above. Since the pericardium is subject to very little flexure during function, a system of three fiber directions of 60° to each other would provide a reasonable degree of planar isotropy with minimum thickness and fiber cost. The interweaving of several layers in each direction could provide increased resistance to shear and give a continuous structure with sufficient coherence to allow preconditioning of an isolated strip. If this were not the case, a strip with an aspect ratio of 1.4 (as in our experiments) tested at a 30° angle between fiber directions would have only 19% of the fibers from any one layer gripped by both grips. This would probably not be enough to sustain cyclic loads in a strip experiment. We note, however, that tests in two strip directions are not adequate to confirm planar isotropy totally. For instance, in our paper on canine pericardium, we found some difference in tensile strength with strip direction. However, our test results give no reason to suspect gross differences in fiber structure between canine and human pericardium.

In reviewing these data, it must be considered that we have compared the pericardia of mature mongrel
dogs with those from a human population with a mean age of 53 years. Two objections come to mind. First of all, what differences exist in the mechanical properties of pericardia from mature to elderly individuals? Holt (1970) points out that the waviness of pericardial collagen (in humans) is absent at birth, increases to a maximum in the young adult, and disappears again in old age. The increase in waviness at adolescence correlates with the appearance of elastin in the sac; the amount reaches a maximum in the young adult and remains constant until death. In our study, the human sample is weighted to older individuals, i.e., to lower elastin content and reduced collagen waviness. This does not explain the species differences, however. Instead, it should lead to an earlier rise in elastic stress on extension of human tissue (counter to our results) and an overall more elastic character. Further, we found no systematic differences in responses when the 26- and 34-year-old individuals are compared with the 67- and 73-year-old individuals.

Second, in the absence of evidence for pericardial disease, would enlarged cardiac chambers affect mechanical data? Only patients 2 and 4 had significantly enlarged chambers. If the size accommodation is due to viscoelastic creep, the principal effect would be to reduce the relaxation properties observed in the in vitro samples (the collagen network being already more collapsed). This would imply that the data from these two patients actually masked some of the greater creep and stress relaxation effects seen in the data on human pericardium. If actual growth of the sac occurred, we would expect no change in properties. We must conclude that these concerns do not invalidate the species differences observed.

This study indicates that the mechanical properties of canine and human pericardium differ in their viscous responses, and that these differences should be considered when applying the results of canine studies to the human situation. In situations where the rate of pericardial expansion is important, the human pericardium must be seen as being more important in determining ventricular mechanics than is that in the dog. Therefore, those experimental results which include the viscous component of pericardial properties should be closely examined for species peculiarities; e.g., studies on the dynamic properties of the ventricles and studies on the ability of the pericardium to accommodate slowly and rapidly developing effusions. On a more fundamental level, it may be appropriate to consider why, in species with similar cardiovascular function, such differences in structure and function should exist.

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