The Stiffness of Normal and Abnormal Mitral Valves

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Background: Although it is well known that valvular lesions show changes in stiffness, this fact has not been studied objectively or quantitatively.

Methods: Using a tactile sensor, stiffness of the mitral valve was measured at 11 autopsies and 19 surgically excised specimens. The relationships between stiffness and histological state were investigated in 394 points of resected specimens.

Results: In normal mitral valves, the anterior leaflet was significantly stiffer than the posterior leaflet in all zones. The rough zone had the least stiffness in both leaflets. Mitral stenotic valves were significantly stiffer than normal in all zones, the rough zone had the greatest stiffness. The grade of fibrosis ($r=0.862$), hyalinosis ($r=0.783$), and calcification ($r=0.464$) had positive correlation with the stiffness, respectively. An $S$ score that was composed of these three factors had strong positive correlation ($r=0.935$). The regression equation was: stiffness = $2.882 + 2.304 \times S$ score ($r^2=0.88$). With cut-off values of 8 g/cm for severe fibrosis, 10 for focal hyalinosis, 13 for diffuse hyalinosis, 15 for mild calcification and 18 for massive calcification, these changes were accurately (>90%) detected. The grade of myxoid change had mild negative correlation with the stiffness ($r=-0.507$).

Conclusion: The actual value of stiffness of normal and abnormal mitral valves and the relationships between stiffness and histological changes were obtained. A tactile sensor promptly and accurately shows stiffness of the heart valve indicating its histological state. It can be a useful device for cardiovascular surgery. (Ann Thorac Cardiovasc Surg 2007; 13: 178–184)

Key words: mitral valve, stiffness, tactile sensor

Introduction

Valvular heart diseases have been, and will continue to be, important heart diseases. Valvular lesions cause changes in stiffness. Such changes are thought to correlate with the histological state, but this fact has not been studied objectively. First, the actual values of the stiffness of the normal heart valves remain unknown. The human finger can not evaluate stiffness objectively nor distinguish several adjacent points of differing stiffness. In this study, the stiffness of normal and abnormal mitral valve were measured using a tactile sensor, which can measure the stiffness of objects reliably just by a touch. It was investigated whether the stiffness measured by a tactile sensor represented histological changes and its grades.

Materials and Methods

Tactile sensor
A catheter-type tactile sensor with a small round tip, 2 mm in diameter, was used in this study. It has a piezoelectric transducer (PZT) and a vibration detector made of ceramic at its tip. The principles of the sensor are based on the fact that each material has its own resonance.
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The frequency which depends on its stiffness. When PZT vibrating at its resonance frequency touches an object, a shift in the frequency occurs. The value of the shift (Δf) depends on the stiffness of the object. The vibration detector picks up the shift and sends a signal to the frequency counter (Advantest, Tokyo, Japan). This procedure is processed by a computer, and the Δf is recorded (Fig. 1).

As the objects were non-linear living valves, the relationship between the Δf and the stiffness was calibrated employing pellets of gelatin made from porcine and bovine skin. The stiffness of nonlinear material like gelatin is determined as the compressing weight divided by the depth of indentation made in it, i.e. g/cm. Using a viscoelastance measurement machine (Axiom, Fukushima, Japan), sensor probe was put on a gelatin with known loads, and the depth of indentation and the Δf were simultaneously measured (counter-weight and depression method). Both well correlated with each other. The calibration formula for our tactile sensor was as follows:

\[
\text{Stiffness [g/cm]} = 10^{(\Delta f [\text{Hz}] + 4,834.946)/3,742.415} \quad (r=0.994)
\]

Measurement of mitral valve stiffness

The influence of temperature on Δf was evaluated in several points of the excised valves by changing the temperature from 37°C to 5°C. Δf showed no change at any point (data not shown). Therefore, all measurements were done at room temperature, and to prevent drying on cotton gauze soaked in saline.

Normal valves: Stiffness was measured in autopsied specimens obtained from 11 patients (8 male and 3 female, 67.3±6.6 years of age) who had died of cancer 7.4±3.9 h after death. Both the anterior leaflet (AML) and the posterior leaflet (PML) were partitioned into three zones, i.e. rough zone (RZ), clear zone (CZ), and basal zone (BZ). Points of measurement were about 3 mm apart from each other, and their number was from 8 to 12 in each zone of each case. In all cases, the mitral valves were diagnosed as essentially normal macroscopically and microscopically.

Diseased valves: The stiffness of 19 AML excised during prosthetic valve replacement [degenerative mitral regurgitation (MR) 7, rheumatic mitral stenosis (MS) with or without regurgitation 12] was measured every 3 mm apart. The partitioning described above was also used and the number of measured point was the same. Transverse subdivisions into three equal lengths was expediently used for distinction of RZ, CZ, and BZ in rheumatic MS valves, because the margins of each zone were unclear. Contour-line graphs of stiffness were drawn.

Histological change and stiffness: The relationship between histological change and the stiffness was investigated at 394 points in 19 excised mitral valves. Prior to formalin fixation, valves were subdivided into compartments of about 3×3 mm using a scalpel, and Δf of each compartment was measured. After that, valves were sectioned along the subdivision line, and each compartment was histologically evaluated without knowing the results of Df measurement. Hematoxylin–Eosin, Azan–Mallory, and Elastica–van Giesson stain was performed for each
Normal valves
In all 3 zones, the stiffness of AML was significantly greater than that of PML (p<0.05 in RZ, p<0.01 in CZ and BZ). In both leaflets, the stiffness was greatest in BZ, and least in RZ. The differences between each of the zones were statistically significant (p<0.01). In this study population, age and gender did not show significant correlation with the stiffness in any zone.

Diseased valves
Rheumatic MS valves showed significantly greater stiffness than normal valves and MR valves in all three zones (p<0.01). The stiffness of each zone was significantly different (p<0.01). It was greatest in RZ and least in BZ. This relationship was contrary to that of normal valves.

The stiffness of each zone of degenerative MR valves did not differ significantly. As compared with normal valves, it was significantly greater in RZ (p<0.01) and significantly less in CZ and BZ (p<0.01).
Fibrosis, hyalinosis, and calcification were integrated to devise one parameter named “S score,” which was graded from (–) to (7+). a: (–) no fibrosis, no hyalinosis, no calcification (±) trivial increase of collagen without thickening, no hyalinosis, no calcification. b: (+) mild fibrous thickening, no hyalinosis, no calcification. c: (2+) moderate fibrous thickening, no hyalinosis, no calcification. d: (3+) severe fibrous thickening, no hyalinosis, no calcification. e: (4+) any grade of fibrosis, focal hyalinosis, no calcification. f: (5+) any grade of fibrosis, diffuse hyalinosis, no calcification. g: (6+) any grade of fibrosis, any grade of hyalinosis, mild focal calcification. h: (7+) any grade of fibrosis, any grade of hyalinosis, dense calcification.

Fig. 2. The category of S score.
Histological change and the stiffness

Univariate analysis showed that the grade of fibrosis, hyalinosis and calcification had significant positive correlation, and the grade of myxoid change had a significant negative correlation with the stiffness (Table 3). The mean stiffness values for each grade of these factors were significantly different. The grade of elastosis and angiogenesis and the existence of atrial muscle were not significantly correlated with the stiffness. Multiple stepwise regression analysis revealed that the grade of fibrosis, hyalinosis and calcification were the determinants of the stiffness. The regression equation was:

$\text{Stiffness} = 3.174 + 2.060 \times \text{fibrosis} + 2.634 \times \text{hyalinosis} + 2.625 \times \text{calcification}$

($r^2 = 0.869$).

When $S$ score was adopted, the regression equation was:

$\text{Stiffness} = 2.882 + 2.304 \times S$ score ($r^2 = 0.88$).

The grade of fibrosis, hyalinosis, calcification, and myxoid change caused significant intergroup differences. These histological changes had significant correlation with the stiffness values. **, $p < 0.01$ among groups; $r$, correlation coefficient.

Discussion

Histological examination has been the only method to evaluate the heart valve tissue objectively, but it requires time and causes irreversible damage to the objects. By using a tactile sensor, stiffness of the normal and diseased valves, and the differences among zones or conditions were investigated in this study. To the best of our knowledge, this is the first attempt to evaluate the heart valve.
objectively, promptly, and without any substantial effect to the objects. These features are indispensable for the method of evaluation that is applicable during cardiovascular surgery.

In the normal mitral valves, the stiffness was least in RZ in both leaflets, probably because the pars spongiosa is rich in RZ. This result also coincides with results of a study using acoustic microscopy.6) In both rheumatic and degenerative valves, RZ showed the greatest change in stiffness and was proved to be the main locus of affection.

The close relationship between the stiffness and histological condition, the regression equation, and fair stiffness values that indicate the histological states of the valve were revealed. The tactile sensor thus permits displaying the stiffness and grading the histological state of target areas promptly and accurately just by a touch.

This can be valuable because there will be some situations in which heart valves must be evaluated objectively in cardiovascular surgery such as in operations that spare the native valve. The quality of the valve, as well as morphology and function, is very important in such operations, because spared valves are not always normal and some initially successful cases require reoperation.7,8) In some cases, focal pathological changes in the valve, especially sclerotic change, preclude successful valvuloplasty.9,10) Stiffness may have great importance for early and late results of valvuloplasty for stenotic valves. The tactile sensor can contribute to successful valvuloplasty operations by providing objective information on the valve. Another experimental study revealed that the tactile sensor was useful for the evaluation of effects of ultrasonic debridement of sclerotic valvular lesions.

Another application is in minimally invasive valvular surgery. Surgeons may touch the valve very lightly or not at all. Tactility is very important in valvular surgery and will have to be substituted by devices, especially when minimal or remote access technique is used.11,12)

The tactile sensor can thus be clinically useful for evaluation of the histological condition of the heart valve in various settings.

**Limitation of the study**

Our tactile sensor is very sensitive to firm materials. When the measured object is quite inhomogenous and very firm tissue is in front, the value of \( \Delta f \) is highly dependent on that part, and soft parts behind it are missed. Therefore, \( \Delta f \) of very thick and possibly inhomogenous objects can be inaccurate.

Because PML is usually preserved during mitral valve replacement in our institution, the stiffness of abnormal PML could not be obtained. Only leaflets were investigated in the present study, but chordae are also very important for successful valvuloplasty. The objective evalu-
ation of chordae should be attempted by further study. The stiffness of the normal mitral valve was measured in only aged persons, and the number of specimens were small. The influences of age and gender on the stiffness need to be determined in a large study population including younger people.

**Conclusion**

The stiffness of normal and diseased mitral valves was revealed using a tactile sensor. The stiffness accurately reflects histopathological changes of the valve. The tactile sensor can be a valuable device in the field of cardiac surgery.

**References**