Detection of aortic porcine valve dysfunction by maximum entropy spectral analysis


ABSTRACT A high-resolution method of spectral analysis, of the class generally called "maximum entropy method," was used in a study of aortic porcine valve closing sounds in 37 patients (ages 19 to 76). Spectra from 27 normal xenografts, implanted from 2 weeks to 61 months previously, were characterized by a dominant frequency peak, $F_1$, at $89 \pm 15$ Hz (mean ± SD), with a lower amplitude peak, $F_2$, at $154 \pm 25$ Hz. Eight of nine patients with aortic porcine valve dysfunction were proved surgically to have leaflet degeneration or infection and had either $F_1$ (139 ± 54 Hz) and/or $F_2$ (195 ± 74 Hz) significantly higher than normal ($p < .001$). In two patients with paravalvular leak but no leaflet abnormality, $F_1$ and $F_2$ were in the normal range. Estimation of $F_1$ and $F_2$ was highly reproducible and was unaffected by duration of implant up to 5 years. Spectral analysis of aortic porcine valve closing sounds by the maximum entropy method may be useful for detection of intrinsic xenograft dysfunction. *Circulation* 68, No. 1, 42-49, 1983.

THE USE OF glutaraldehyde-preserved porcine xenografts for heart valve replacement has become widely accepted over the past decade.1 However, in common with all prosthetic valve types, they remain subject to infection and thrombosis.2-5 In addition, studies of gross and histologic anatomy have shown that porcine leaflets often undergo progressive ultrastructural changes that result in increasing stiffening with time.6,7 Further degeneration may be accompanied by calcification and valve stenosis or valvular regurgitation from leaflet retraction or fracture.8-10

In patients who deteriorate clinically after heart valve replacement, it may be difficult to differentiate intrinsic valve dysfunction from left ventricular failure caused by myocardial disease and to identify valve infection when present. Although clinical evaluation will often establish the correct diagnosis, cardiac catheterization and angiography may be necessary in patients with suspected abnormal prosthetic valve function. These procedures are not without risk. Phonocardiographic, radiographic, radionuclide, and ultrasound techniques have been used to diagnose mechanical and bioprosthetic valve dysfunction.11-20 Recently, spectral analysis has been applied to valve sounds,21-25 including the closing sounds of aortic porcine xenografts.24 In one of these studies, relatively high frequency content was found in the frequency spectra derived from two aortic porcine valves with abnormal function, which had been in place for 5 and 7 years; these spectral alterations were the same as those obtained from normally functioning aortic porcine valves implanted for a similar period.24 However, this study was based on the fast Fourier transform (FFT) method of spectral analysis. FFT is inherently limited by the uncertainty principle, which states in this case that frequency resolution is directly proportional to the duration of the signal. With most phonocardiographic techniques, aortic porcine valve closing sounds are estimated to be 15 to 25 msec in duration, which thereby imposes a 40 to 70 Hz resolution limit on FFT-based spectral analysis.26 A radically different method of spectral analysis is the autoregressive method, one of several closely related methods that have been grouped under the general term "maximum entropy method" (MEM).26-28 The specific technique used in this study was the "covariance method."29 We will refer to data obtained with this method as the MEM estimate. This method is not limited in resolution by signal length and therefore may be particularly appro-
appropriate for analysis of signals of short duration, such as aortic porcine valve closing sounds.

We report here the results of a study of MEM spectral analysis of aortic porcine valve closing sounds to discriminate between normal and abnormal valve function.

Methods

Patients. Phonocardiograms were performed on 37 patients, ages 19 to 76 years, who had undergone aortic valve replacement with a porcine xenograft from 1 to 67 months previously (table 1). One patient (No. 27) had two separate aortic valve replacements and recordings from each valve were used. Of the 38 phonocardiograms available, 26 were from Hancock xenograft valves (sizes 19 to 29); 10 of these were modified by excision of the supportive muscle band. Twelve phonocardiograms were from Carpentier-Edwards xenografts (sizes 23 to 25).

This study population was selected over a 12 month period from routine postoperative follow-up visits, from patients admitted to the hospital with suspected abnormalities of valve function, and from patients in the early recovery period after aortic porcine valve replacement. All patients had diastolic blood pressures within the normal range. This population was divided into three groups. Group 1 consisted of 27 patients (patients 1 to 26 and patient 27, study 2) with normal valve function as assessed by the clinical history, physical examination, and laboratory investigations, including serial electrocardiograms (ECGs) and chest x-rays. In two of these subjects, left heart catheterization and angiography indicated normal aortic porcine valve function. In 10 of these 27 patients examined by M mode and two-dimensional echocardiography, no abnormalities of the valve prostheses were shown. To obtain recordings from valves that had undergone only minimal ultrastructural changes of normal aging, 22 patients in this group were studied within the first 6 months after their aortic valve replacement. Four patients had undergone aortic valve replacement from 6 months to 5 years previously, and one patient had an aortic valve replacement more than 5 years before the study.

Group 2 consisted of two patients (patient 27, study 1, and patient 28) who had aortic porcine paravalvar leak with normal leaflet anatomy. In patient 27 the presence of paravalvular leak was confirmed at valve surgery. In patient 28, a supravalvar aortogram demonstrated a paravalvular regurgitant jet of moderate severity, with normal aortic prosthetic valve leaflet motion. The finding of anatomically normal valve leaflet was supported in each patient by M mode and two-dimensional echocardiography. The two patients in this group had undergone valve replacement 23 and 20 months before the study.

Group 3 consisted of nine patients with abnormal prosthetic valve function. Clinical findings and laboratory investigations, including serial ECGs and chest x-rays, were consistent with prosthetic valve dysfunction. Seven of the nine patients had M mode and two-dimensional echocardiography, and all nine patients underwent left heart catheterization and aortography. The valve leaflet abnormality was ultimately confirmed by surgery in eight patients. Four patients had intrinsic valve dysfunction with leaflet thickening and various degrees of calcification. All four had fracture of one cusp, with significant valvar regurgitation. Three patients had active bacterial endocarditis with vegetations, two having in addition significant valve regurgitation. Two patients had healed endocarditis with valve scarring and lesser degrees of regurgitation. Three patients in group 3 were studied within 6 months after valve replacement. Four patients had undergone aortic valve replacements from 6 months to 5 years previously, and two patients had aortic valve replacement 5 years or longer before the study.

Phonocardiograms. Phonocardiograms were taken with the patient lying supine at 45 degrees. Recordings were made from the left sternal border. To identify each component of the second heart sound and its variation with respiration, a standard

<table>
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<th>Patient No.</th>
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<th>Cardiac rhythm</th>
<th>Ao root size (mm)</th>
<th>HT (%)</th>
<th>Type</th>
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<td>42</td>
<td>33</td>
<td>Hm</td>
<td>23</td>
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| Group 2     |     |     |                |                  |       |      |      |                   |
| 27 (1)      | 62  | F   | SR             | 42               | 31    | H    | 23   | 20 mo             |
| 28          | 35  | M   | SR             | 45               | 36    | H    | N/A  | 23 mo             |

| Group 3     |     |     |                |                  |       |      |      |                   |
| 29          | 29  | M   | SR             | 32               | 37    | C/E  | 29   | 4 mo              |
| 30          | 63  | M   | SR             | 33               | N/A   | C/E  | 25   | 5 mo              |
| 31          | 65  | M   | AF             | 43               | 35    | C/E  | N/A  | 48 mo             |
| 32          | 25  | M   | SR             | 29               | 35    | H    | 23   | 67 mo             |
| 33          | 59  | F   | SR             | 36               | 34    | H    | 23   | 50 mo             |
| 34          | 39  | M   | SR             | 39               | 34    | H    | N/A  | 17 mo             |
| 35          | 49  | M   | SR             | 35               | 28    | H    | 23   | 63 mo             |
| 36          | 62  | M   | SR             | 39               | 33    | H    | 25   | 3 mo              |
| 37          | 47  | M   | SR             | 31               | 34    | Hm   | 25   | 8 mo              |

SR = sinus rhythm; AF = atrial fibrillation; Ao = aorta; HT = hematocrit; C/E = Carpentier-Edwards; H = Hancock; Hm = Hancock modified; N/A = not available.

*Manufacturers designation in millimeters (internal orifice diameter of the sewing ring).
phonocardiogram was made with a Siemens Elema-Schonander microphone (Model EMT 25 C) together with simultaneous recording of ECGs (lead II), carotid pulse, and respiratory trac-
tings. These were recorded on an Elema-Schonander four-channel strip chart recorder (Model EM34) with paper speeds of 25
to 500 mm/sec.

Recordings were made during 10 to 15 cardiac cycles with the patient in “held” expiration. The recording system (figure 1)
used a Hewlett Packard microphone (Model 21050B). The output
of the microphone was filtered and amplified by a preampli-
ifier with adjustable band-pass filters (Princeton Applied Re-
search Model 113) set to a flat frequency response from 30 Hz to
1 kHz and a 6 dB per octave roll-off beyond these frequencies.
The signals were then passed through a preemphasis filter, which
accentuated the higher frequencies and allowed their recording
in the presence of the higher amplitude low-frequency
components. The preemphasis filter had a 6 dB per octave rise
from 20 Hz to 3 kHz. The filtered signals were finally recorded
onto an audio tape system with a two-channel reel-to-reel re-
corder (Teac Model A2300-SX). The total system frequency
response curve was linear, with a rise of 6 dB per octave,
between 30 Hz and 1 kHz (figure 2).

When replayed for subsequent analysis, the output of the tape
recorder was passed through a second band-pass filter (Rock-
land Model 751A) set at 30 and 1500 Hz, with 60 dB per octave
roll-off beyond these frequencies. After analog-to-digital con-
version at a sampling rate of 3000 Hz, the digitized phonocar-
diogram from the aortic porcine valve was displayed on a Tek-
tronix 4010 graphics terminal. Closing sounds recorded with the
microphone at the second left sternal border during held expira-
tion usually provided the best signal-to-noise ratio and satisfac-
tory separation of aortic (A2) from pulmonic (P2) components.
If not, phonocardiograms recorded from the fourth left sternal
border were used. To obtain an ideal spectral estimate, A2
should be clearly separated from P2 as well as from any noise,
murmur, or friction rub. In practice, this was not always pos-
able, and in two cases the signal was judged to be unsuitable for

Spectral analysis. The aortic closing sound was analyzed by
two methods, the FFT and the MEM. With FFT, the signal is
expressed in terms of a series of fixed complex exponentials.
With covariance MEM,28,29 the signal is modeled as a linear
combination of a small number of exponential terms and the
best exponentials are calculated for each signal. Equivalently,
an autoregressive model is derived to represent the signal. The
coefficients of the autoregressive model for the MEM estimate
were calculated by the covariance method of linear predic-
tion.27,28 The model order was restricted to less than one-third
the data length, so that large spurious spectral peaks would not
be generated.28 In practice, this was accomplished by beginning
the analysis with a model order equal to one-third the data length
and reducing model order until three successive model orders
showed stable F1 and F2 localization (ordinarily only three to
four model order numbers). Both methods of analysis were
implemented as programs run on a Data General Nova 4 mini-
computer. The frequency spectra obtained for each prosthetic
heart valve contained two or more frequency peaks, the two
highest of which were used for the statistical analysis. F1
was defined as the location of the frequency peak that had the
highest amplitude and F2 as the location of the peak with the second
highest amplitude.

Statistical methods. To detect differences in the location of
F1 and F2 between each group, stepwise discriminant analy-
sis was employed. A multiple regression31 was performed to exam-
ine further the effects on F1 and F2 of the patient’s age and sex,
microphone location (second left sternal border vs fourth left

![Diagram](http://circ.ahajournals.org/)

**FIGURE 1.** Block diagram of the recording system used for the spectral analysis. The phonocardiogram (A), recorded with a
Hewlett Packard microphone, was passed through a band-pass filter (B) with a 6 dB per octave roll-off beyond 30 Hz and 1 kHz.
The filtered signal was passed through a preemphasis filter (C), which had a 6 dB per octave rise from 20 Hz to 3 kHz and was
recorded in analogue format simultaneously with lead II of the ECG onto a two-channel reel-to-reel tape recorder (D). The output
of the tape recorder was then passed through an antialiasing filter (E) with 60 dB per octave roll-off beyond corner frequencies at
30 Hz and 1.5 kHz and converted from analogue-to-digital (A/D) format by sampling at 3000 Hz. F. Segment of the final output
of the system, the second heart sound (S2), expanded in time and amplitude. SEM = systolic ejection murmur; S1 = first heart

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FIGURE 2. Frequency response curve of the recording system. Solid line, total system frequency response, which includes the antialiasing filter set to have 60 dB per octave roll-off at 30 Hz and 1.5 kHz. Dotted line, system frequency response before antialiasing filtering. Note that the total system has a frequency response linear between 30 and 1.0 kHz.

sternal border), cardiac rhythm, aortic root size as measured by echocardiography, hematocrit (if available within 24 hr of the study), type and size of valve prosthesis, classification of valve function, and the time after valve implantation (table 1). A linear discriminant analysis was used to derive the sensitivity and specificity of the predictors of normal or abnormal valve function.

A reproducibility study on 20 of the 37 patients was performed by two observers, each without knowledge of the patients' classification into one of the three groups. Twelve to 14 aortic closure sounds, previously recorded on tape and used for the original spectral analyses, were identified for each patient. Six to eight A2 recordings were selected, time windows were placed, and analysis was repeated independently. The resulting MEM spectra from this second analysis of 20 patients were then compared with the frequency spectra obtained from the first independent analysis.

Results

Technically satisfactory phonocardiograms were obtained from the second left intercostal space in 32 valves (table 2). In the phonocardiograms from the remaining six valves, the signal-to-noise ratio at this location appeared insufficient for analysis, and the fourth left intercostal space was used.

When all the results were reviewed, the MEM spectral estimate was confirmed in its ability to resolve frequency peaks that were lost by the FFT method. An example is provided in figure 4, which shows that peaks not resolved by FFT were clearly separated by MEM. In all patients, peak resolution was better with MEM, and F1 and F2 were more easily defined. In addition, peak selection with the FFT was often made difficult by artifactual "side-lobing," which is inherent in this method27 but not present in the spectra derived by the MEM. Therefore the latter method was used to derive F1 and F2 for the multivariate analyses.

The MEM frequency spectra from patients in both normal and abnormal groups (table 2) contained two or more major peaks in the range of 68 to 317 Hz (figure 4). In group 1, F1 was 89 ± 15 Hz (mean ± SD), range 68 to 138 Hz and F2 154 ± 25 Hz (range 109 to 197 Hz). In this group, F2 was always higher in frequency than F1 but was at lower amplitude, 7 ± 4 dB below (range 1 to 16 dB) the major peak F1. Peaks of smaller amplitude appeared at higher frequencies but were generally 15 to 20 dB below F1 and were not used in this analysis.

In group 2, the two patients with normal aortic porcine leaflet anatomy but paravalvar regurgitation had frequency spectra that were indistinguishable from those of patients in the normal group. In patient 27, F1 was 91 Hz and F2 197 Hz; 12 dB separated the two peaks. The frequency spectrum derived from this phonocardiographic recording (study 1) was similar to that obtained after replacement of this valve for paravalvar leak (study 2). In patient 28, F1 was 85 Hz and F2 was 6 dB lower at 165 Hz.

FIGURE 3. A. Digitalized time display of ECG (lead II) and phonocardiogram of one cardiac cycle illustrating S2. B. Digitized time display of phonocardiogram after expansion in time and amplitude, illustrating the portion of S2 with window placed to include the aortic porcine valve closing sound (A2) and to exclude the pulmonary component (P2).
TABLE 2

Results

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2L = second left sternal border; 4L = fourth left sternal border.

The frequency spectra derived from patients in group 3 had, in every case, higher frequency content than those from groups 1 and 2. F1 was 139 ± 54 Hz (range 85 to 244 Hz) and F2 was 195 ± 74 Hz (range 106 to 317 Hz); each was significantly different from those of groups 1 and 2 at p < .001. Two patterns of abnormal frequency spectra were observed (figure 5). In four of the nine patients the dominant peak F1 was at a higher location than F1 of groups 1 and 2 (190 ± 33 Hz, range 156 to 244 Hz; p < .001), with the second highest amplitude peak at a lower frequency (122 ± 22 Hz, range 106 to 160 Hz) at 7 ± 6 dB below the major peak (range 1 to 16 dB). In five patients the frequency of F1 was normal (99 ± 15 Hz, range 88 to 126 Hz), while F2 was at an abnormally high location (252 ± 44 Hz, range 203 to 317 Hz) that was significant at p < .001 and 2 ± 1 dB down from the major peak (range 1 to 3 dB). When F1 and F2 were considered together, the sensitivity in predicting valve function (determined by comparison with cardiac catheterization or surgical data) was 100% and specificity was 93% by linear discriminant analysis.

In addition to the higher location of F1 or F2, prominent third and fourth peaks above 300 Hz were common in patients of group 3. Although both group 3 patterns were clearly different from those derived from patients in groups 1 and 2, neither was associated with a particular anatomic abnormality of the leaflet. The locations of F1 and F2 and the frequency spectra of closing sounds from Carpentier-Edwards, Hancock, or modified Hancock xenografts were similar. There was no correlation between the location of frequency peaks and xenograft size. In subjects with normally and abnormally functioning valves, the location of the dominant frequency peak of valves implanted 10 days to 6 months before study was not statistically different from that of valves implanted 16 months to 5 years or greater than 5 years before study. There was no effect in these patients of age, sex, cardiac rhythm, hematocrit, or aortic root size.

The MEM spectra exhibited a high degree of reproducibility. The two independent observers agreed on the classification of valve function as normal or abnormal in all but one (patient 37) of the 20 patients analyzed (table 3). In this patient the amplitude of the second and third peaks were almost identical. Thus the difference in classification was caused by minor amplitude differences between the two studies.

Discussion

We have shown that high-resolution spectral analysis of aortic porcine valve closing sounds facilitates the diagnosis of intrinsic valve dysfunction caused by leaflet degeneration or infection.

Other methods used for the investigation of porcine valve dysfunction include fluoroscopy, radionuclide gated blood-pool scanning, echocardiography, and Doppler techniques. Exaggerated rocking of the sewing ring by fluoroscopic techniques may provide indirect evidence for paravalvar regurgitation.14 Similarly, the regurgitant fraction in patients with paraprosthetic or valvular leak can be estimated by radionuclide
peak location was also unaffected by the duration of valve implantation within group 3. However, as porcine valves approach 5 years of age, leaflet distortion and calcification without clinically abnormal function may be present. Therefore, although peak frequency location was unaffected by the duration of implantation within all groups of our study, one should use caution in diagnosing abnormal valve function when abnormal frequency spectra from valves older than 5 years are obtained. Of the other clinical variables tested for their influence on frequency content, there was no difference observed between valves of different types and sizes and no effect of age, sex, cardiac rhythm, hematocrit, or aortic root size.

Abnormal valve function with anatomically abnormal leaflet was characterized in each case by spectra with higher frequency content. This was manifest by a higher than normal location of F₁ within the range of approximately 150 to 250 Hz or a higher than normal secondary peak F₂ in the range of about 200 to 400 Hz. Neither of these abnormal spectral patterns was associated with specific valve abnormality. In some patients of group 3, prominent third and fourth peaks occurred above 300 Hz. These peaks were also observed in several patients (not included in this analysis) with normal valve function who were studied in the early postoperative period but who had pericardial rubs superimposed on aortic closing sounds. By appropriate window placement, A₂ could usually be separated from noncoincident, relatively high-frequency peri-

**FIGURE 4.** Frequency power spectra of a normal porcine aortic valve closure sound analyzed with FFT and MEM. Note that the broad peak (F = 106) defined by FFT is better resolved by MEM and that it is a composite of two peaks, F₁ = 94 and F₂ = 144. This superior peak resolution exhibited by MEM was seen in each of the 38 phonocardiograms analyzed.
cardiac rubs, aortic regurgitant murmurs, or artifactual sounds. This was greatly simplified in our study by the use of a time- and amplitude-expanded display of the phonocardiogram.

Other investigators have examined the spectral content of closing sounds from normal and stenotic native aortic valves as well as from porcine heterografts in the aortic and mitral position. 24, 25 Our range of frequency peak location from normally functioning aortic porcine valves is higher than that previously reported. 24 This difference in frequency peak location for normal valves may be accounted for by our phonocardiographic and spectral analysis technique. First, frequency content is dependent on the way the sound is recorded and can be modified according to the filtering functions used. We used a system that attenuated frequencies between 30 Hz and 1.5 kHz at 6 dB per octave and that virtually excluded frequencies outside that range (figure 2). Since high-amplitude low-frequency sounds otherwise mask the higher frequency components, this system permitted accurate recording of higher frequencies within the range of interest. Second, the expanded display of the second heart sound generally facilitated isolation of the aortic porcine closure sound from the pulmonary closure sound, which is a lower frequency sound (figure 3). Furthermore, we have confirmed preliminary studies 26 which have suggested that an FFT-based analysis of the phonocardiogram is inappropriate for the analysis of short-duration sounds because the method has a resolution limit dis-

![Diagram](http://circ.ahajournals.org/)

**FIGURE 5.** MEM frequency power spectra of aortic porcine valve closing sounds. A, Normal valve leaflet function (group 1) with three major peaks, F₁, F₂, and F₃. For the purposes of this analysis, only F₁ and F₂ were considered. B and C represent two patterns found with abnormal valve function (group 3). B, Highest amplitude peak (F₁) at 200 Hz, outside the normal range found in patients of group 1. F₂, the second highest amplitude peak, is at 112 Hz. C, F₁ is within the normal range while F₂ is located at 306 Hz, outside the normal range.

<table>
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<tr>
<th>Patient No.</th>
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*Patients 29 and 35, despite differences in selection of F₂ location between observers, were classified by both observers as abnormal.  
*Patient 37 was classified differently by observers A and B, based on differences in locating F₂.
rectly determined by the signal length. In addition, sidelobing, an artifact inherent in the FFT analysis, can mask low-amplitude secondary peaks. The covariance method used in this analysis does not have these limitations of resolution and peak definition. Thus both recording and analysis techniques may account for the relatively high-frequency peaks found in our normal subjects and for the ability to differentiate normal from abnormal closure sounds in this study.

The method of spectral analysis used in this study was time consuming and must be considered experimental. Furthermore, the study was prospective in the sense that the data were acquired and analyzed before the patient was identified as having normal or abnormal prosthetic valve function. However, it was retrospective in the sense that the data so generated were used as a training set for definition of diagnostic criteria. We have recently developed a program that permits semiautomated sampling and analysis of valve sounds and that achieves a highly significant economy of time. This program makes practicable a prospective clinical study of a larger group of patients to test the validity of the criteria derived from the present study as well as to determine the cost-effectiveness of spectral analysis in the diagnosis of porcine valve dysfunction.

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