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The clinical value of ultrasonic tissue characterization in the management of heart transplant patients

E. Lieback, M. Nawrocki, R. Meyer, J. Bellach, H. Warnecke, and T. Cohnert

Germany Heart Institute, Berlin, FRG

Abstract. The purpose of this study was to evaluate the rejection process by ultrasonic tissue characterization. Serial 2D echocardiographic images were obtained within 24 h prior to an endomyocardial biopsy. The end-diastolic echoframes were digitized into a computer matrix. A region of interest was placed into the anteroseptal segment of each scan. Image texture was analysed by four major groups of texture analysis (first-order histogram, co-occurrence matrix, run-length statistic, power spectrum). In 23 patients, 408 biopsies were taken after each examination, so that correlation between the ultrasonic tissue measurements and the histological state of the tissue could be determined. When rejection occurred, heterogeneity, brightness and contrast of texture increased. Of 117 texture parameters originally claculated, three parameters (inverse difference moment, run-length non-uniformity, ring sums of power spectrum) that characterized rejection were determined by means of discriminance analysis. Compared with biopsy findings, echocardiographic sensitivity for moderate rejection was 93.3% and specifity 83.6%. Our study indicates that acute rejection is associated with changes in echocardiographic texture. Serial echocardiographic texture analysis can reliably identify heart transplant rejection.

Key words: Heart transplantation – Rejection – Echocardiography – Tissue characterization

To date echocardiographic diagnosis of rejection has mainly been concerned with the analysis of functional, particularly diastolic, parameters of the heart [1]. We wanted to prove with our study whether morphological, i.e. structural, changes of the myocardium caused by rejection, can be discovered by analysing the grey-level distribution (texture analysis) of echocardiograms. This echocardiographic tissue characterization procedes in the reproducible connection which exists between the structure of tissue and its acoustic properties [2]. The digital processing of echocardiographic images with texture analysis is one possibility to detect acoustic properties of tissue. Echocardiographic texture is defined as spatial distribution of echo amplitudes or grey levels.

Offprint requests to: Evelin Lieback, Germany Heart Institute, Augustenburger Platz 1, 1000 Berlin 65, FRG

Methods

The study group comprised 23 heart transplant recipients. The mean follow-up period was 16.8 ± 9.8 months. A total of 408 endocardiographic examinations were compared with the results of endomyocardial biopsies. The echocardiographic examinations were strictly standardized.

The end-diastolic echocardiographic images were digitized in a $512 \times 512 \times 6$ bit matrix of the image-processing system. In each echocardiogram a region of interest with a standard size of 25×25 pixels was placed in the anteroseptical segment of the left ventricle. In this region of interest the texture parameterization was done. Four main groups of texture analysis [3, 4] were used: (1) first order histogram; (2) co-occurrence matrix; (3) run length analysis; (4) power spectrum.

At each examination 117 texture parameters were calculated and set in relation to the histological results of the biopsies. Then we tried to prove which set of texture parameters were necessary and sufficient to distinguish between the histological conditions of the myocardium after heart transplantation, and we tried to prove as well whether rejection can be discovered by analysing the ultrasound image texture. Step by step we reduced all available parameters using the Friedmann tests and Fischer's analysis of discriminance.

Results

Figures 1 and 2 show the grey-level distribution in the region of interest of a selected patient in a phase without rejection and at the time of rejection. Already visually you can notice a significant difference in grey-level distribution. Additionally, texture analysis can quantify this visual difference.

The reduction of the 117 texture parameters using Friedmann tests and Fischer's analysis of discriminance led us to the result that three texture parameters describe

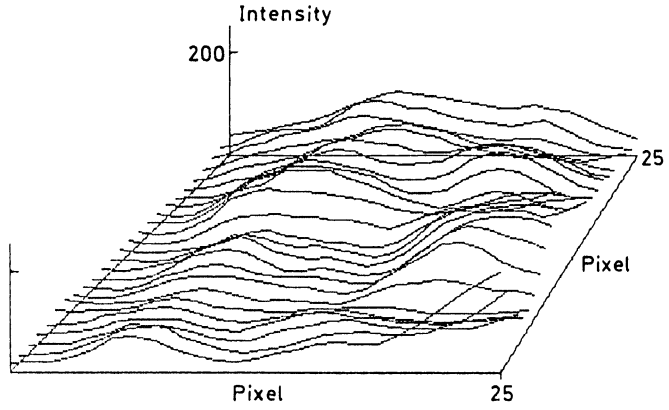

Fig. 1. Pixel map of the region of interest of a patient in a phase without rejection

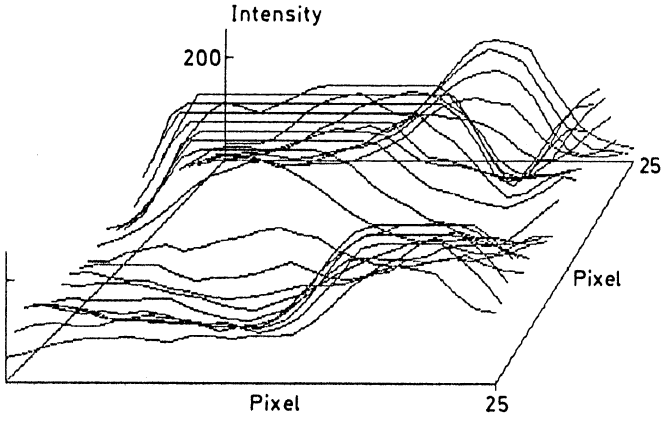

Fig. 2. Pixel map of the region of interest of the same patient at time of rejection

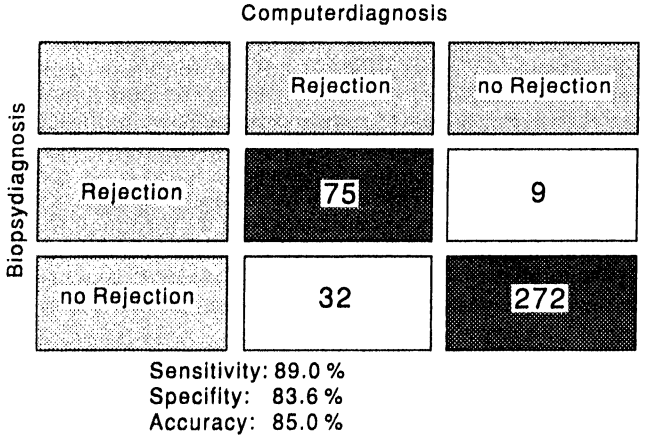

Fig. 3. Computer classification 'rejection' and 'no rejection'

the echocardiographic texture of the myocardium after heart transplantation. These three parameters are: inverse difference moment DX = 2 unjudged, run length non-uniformation vertical and power spectrum sector sum 0–30°.

Figure 3 shows the computer classification of 'rejection' or 'no rejection' using these three texture parameters. The sensitivity of the computer classification compared with biopsy diagnosis was 89% and the specificity 83.6%.

Discussion

We assume that, although there is no direct relationship between image texture and structure of tissue during rejection, with rejection the connected processes of cell infiltration, myocytolysis, interstitial oedemas and perfusion changes can lead to changes in the acoustic properties of the myocardium and therefore, also, to changes in the echocardiographic texture.

In a few cases the results of biopsies were different from those of the texture analysis. Because of artefacts of echocardiographic examination, the results of texture analysis can be wrong positive or wrong negative. Wrong positive texture analysis can also occur when there are other toxic effects on the myocardium (i.e. toxic noxes or myocarditis). On the other hand the biopsies can be wrong negative, because of the so called 'sampling error'. The echocardiographic examination area is many times larger than the histological one. The echocardiographic region of interest with the 25 × 25 image points is equivalent to a myocardial area of about 8 × 8 mm, in comparison with the nm area of histological myocardial samples.

We found limitations which lower the diagnostic value of this method also in the technical/method area. It was not always possible to analyse the 2D echocardiogram quantitatively, although there were no strong adiposities or lung emphysema in heart transplant recipients. It depends mainly on the technical representation of cardial structures and the connected digital image analysis whether a reliable diagnosis of rejection with the texture analysis of echocardiographic images can be done. Early postoperatively, the diagnostic security can be improved with additional examinations by noninvasive processes, for example intramyocardial ECG.

Summary and conclusion

Summarizing our research results, we come to the following conclusions:

1. You can infer the structure of the myocardium using the analysis of grey-level distribution (texture analysis) of echocardiograms.
2. The results of texture analysis correlate with the histomorphological results after heart transplantation.

This opens new possibilities for non-invasive diagnosis of rejection after heart transplantation.

Therefore, postoperatively, transplant recipients should be checked echocardiographically in short time intervals. If texture parameters point to suspicion of rejection, a control biopsy should be taken. The number of necessary biopsies can be decreased by this method. This is recommended particularly in the first 12 postoperative months after transplantation.

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