Initial Experience of Using Color Kinesis in the Diagnosis of Coronary Artery Disease

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Key Words
Color kinesis;
Coronary artery disease;
Digitization;
Echocardiography

Two-dimensional (2-D) echocardiography is widely used to evaluate global and regional left ventricular function. Quantitation of global systolic function can be done either by careful manual tracings of endocardial borders¹,² or by utilizing algorithms using ultrasonic backscatter which provides on-line

Background. Color kinesis (CK) is a recently developed echocardiographic technique. This report describes our initial effort in the validation of the use of CK for the diagnosis of coronary artery disease (CAD).

Methods. Two-dimensional (2-D) echocardiography and CK were studied in 30 normal subjects and 24 CAD patients. Coronary angiography was performed in the 24 patients. Significant (>70% luminal diameter stenosis) CAD was present in 18 patients (79%), all of whom had a history of myocardial infarction. Regional fractional area change in each segment was displayed as a stacked color histogram. The histograms derived from these 30 normal subjects were averaged to obtain the normal pattern of left ventricular contraction; the mean value ± 1 SD was considered the reference histogram. When the regional fractional area change deviated from this normal reference, this segment was considered as having regional wall motion abnormality. The detection of wall motion abnormalities by visual interpretation of 2-D echocardiography, reviewing the CK loop recording, and CK stacked histograms were compared. To assess the relationship of measurement of endocardial excursion of CK images, the width of the color band was measured at the mid point of each segment along a line perpendicular to the cardiac border. The endocardial excursion measured by two independent observers was compared using linear regression analysis and calculation of intraclass correlation coefficient.

Results. The sensitivity and specificity for detection of CAD were 77.8% and 66.6%, respectively, for CK loop reviewing, 83.3% and 66.7% for CK stacked histogram analysis, and 77.8% and 66.3% for 2-D echocardiography. The overall accuracies for CAD detection were 75% for CK loop reviewing, 79.2% for CK stacked his togram, and 79.2% for the 2-D echocardiography (not significant in all comparisons). The correlation of measurement of endocardial excursion from the CK images by two observers was good ($r = 0.85$, $p < 0.01$), and intraclass correlation coefficient was 0.99 ($p < 0.0001$).

Conclusions. Our data demonstrate that both the CK loop reviewing and stacked histograms were comparable to 2-D echocardiography for detecting CAD. [Chin Med J (Taipei) 2002;65:457-467]

Received: April 23, 2002. Accepted: July 18, 2002.
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quantification of left ventricular (LV) area, volume, and ejection fraction. To assess regional wall dynamics, one must rely on semiquantitative visual estimation or off-line quantitative methods. Quantification of regional wall motion using off-line system is time-consuming and impractical for clinical use.

To facilitate a more objective evaluation of LV endocardial motion, color kinesis (CK), a new technique based on acoustic quantification, has recently been developed and incorporated into a commercial ultrasound system (Agilent Technologies™ Andover, MA, USA). This technique compares backscatter values between successive acoustic frames and generates color overlays in which different colors are used to encode pixel transitions between blood and myocardial tissue. The end-systolic overlay provides an integrated display of the timing and magnitude of endocardial motion of the most recent heart beat in a single frame. The aims of this study were (1) to develop a method for automated quantitative analysis of LV endocardial motion during systole; and (2) to test the feasibility of this technique in detecting coronary artery disease (CAD).

**Methods**

**Study population**

The study population consisted of two groups. Group 1 initially consisted of 28 patients scheduled for cardiac catheterization study. Four patients were excluded because of poor echocardiographic images. Then, 24 patients with technically good quality echocardiographic recordings were enrolled. The coronary arteriography was studied within 2 weeks of echocardiography. There were 16 men and 8 women ranging in age from 45 to 76 years (mean 55). Echocardiographic image quality was considered to be adequate if > 80% of the endocardial border could be visualized in real time. Significant coronary stenosis was defined as > 70% angiographic reduction in the luminal diameter of any of the three coronary arteries or their primary branches, or > 50% reduction of the luminal diameter of the left main coronary artery.

Group 2 consisted of 30 healthy subjects (22 men and 8 women, age range 35-69 years, mean 52) who were with out chest pain, dyspnea, or evidence of myocardial ischemia or in farction on electrocardiogram or wall motion abnormalities over the two-dimensional echocardiograms.

CK technique defines endocardial motion by color coding for inward and outward motion. The CK software is incorporated into a commercially available ultrasound system (SONOS 2500, Agilent Technologies™, Andover, MA, USA.). Each pixel on a given value transition from blood to tissue and tissue to blood occurring during systole can be used to track endocardial inward excursion on a frame-by-frame basis. CK was performed in the parasternal long- and short-axis views and apical 4- and 2-chamber views. The images were stored on optical disks and analyzed subsequently with no knowledge of the clinical echocardiographic interpretation.

**Color kinesis data acquisition**

Digitized end-systolic left ventricular color-encoded images were stored on an optical disk. It was retrieved and then displayed in the monitor. Figure 1 depicts the methods of segmentation of the conventional 2-D echocardiograms. On the left upper panel, the parasternal long-axis view was divided into 4 segments. Four points were defined manually. The junction of interventricular septum and anterior aortic root was point C. The junction of LV posterior wall and posterior mitral valve was point D. Points A and B were on the inner border of the left ventricle ap proximately at the level where papillary muscle arose. The mid dle point of line AB (point E) and the middle point of line CD (point F) were connected. A perpendicular line across the middle point of EF (point X) could divide the LV cavity into 4 segments.

In the short-axis view (Fig. 1, right upper panel), the segment originated from the left ventricular end-systolic cavity centroid de fined by its $\overline{x}_{1,2}$ coordinates as follows:

$$\overline{x}_{12} = (\overline{x}_1, \overline{x}_2) = \left( \frac{\int_s x \, dx \, dx_2}{\int_s dx \, dx_2}, \frac{\int_s x \, dx_1 \, dx_2}{\int_s dx_1 \, dx_2} \right),$$
where \((\chi_1, \chi_2)\) is the coordinate of a point \(\chi_{12}\) in \(S\), and \(\bar{\chi}_1\) and \(\bar{\chi}_2\) are the means of the two coordinates, and \(S\) is the end-systolic left ventricular cavity area. The zero line was defined by the centroid, and a manually determinedatomic landmark represented by the junction between the right ventricular posterior wall endocardium and interventricular septum (point C). The left ventricle was divided into 60° wedge-shaped segments from the zero line (CX).

In the apical four-chamber view, the roots of both mitral valves (points A, B) were connected. The perpendicular line from the distal apical endocardium (point P) to the middle point of line AB (point O) separated the LV cavity into 2 sections. Line PO was divided into 3 equal sections, at points X and Y. Two horizontal lines perpendicu lar to line PO from points X and Y could further divide the LV into 6 segments. In order to decrease the effect of mitral valve on the CK images, the area inside the \(\Delta YAB\) was not taken into account (Fig. 1, left lower panel). Similarly, the apical 2-chamber view could also be divided into 6 segments using procedures similar to those for apical 4-chamber view (Fig. 1, right lower panel).

CK analyzes regional backscatter in each acoustic frame in real time and classifies each pixel as either blood or myocardial tissue. Pixel transitions from tissue to blood during diastole are detected and color-encoded. The first systolic frame is red color, followed by shades of orange, yellow, green, and light blue, resulting in a color overlay that is superimposed on the 2-D echocardiographic image. The color overlays are updated on a frame-by-frame basis by adding one color at a time (30 frames/s) (Fig. 2). Thus, a single systolic frame provides an integrated display of the timing and magnitude of endocardial wall motion.

In each segment, pixels of each color and pixels marked as blood were counted. The number of pixels of each color represents the incremental area change that occurred during the time frame corresponding to that specific color (33-ms period). The end-diastolic area of each in di vidual segment is represented by the total pixel count, i.e., all colored pixels and those marked as blood. Normalization of the incremental area change by the end-diastolic area of the corresponding segment results in a regional fractional area change (in percent of end-diastolic area of that specific segment). Incremental fractional area changes in all segments were displayed as a stacked color histogram in which each time frame is represented by a specific color identical to that used in CK images. The mean value \(\pm 1\ SD\) of 30 normal control subjects was obtained and saved for further comparative analysis.

**Detection of regional wall motion abnormalities**

Regional fractional area changes in all segments were displayed as stacked color histograms in which each time frame is represented by a specific color identical to that used in color kinesis images. Histograms obtained from these 30 normal subjects were averaged to obtain the normal pattern of left ventricular systolic endocardial excursion. These averaged histograms were then used to evaluate the intersegmental variability of systolic endocardial excursion and as a normal reference for comparison with those obtained from patients with suspected regional wall motion abnormalities.

In di vidual histograms obtained from these 24 pa-

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**Fig. 1.** Methods of segmentation of different cross sections. The myocardium of parasternal long-axis view was divided into 4 segments (left upper panel). The other 3 sections were each divided into 6 segments (see text for detail).
Patients with regional wall motion abnormalities diagnosed with 2-D echocardiography were compared with the averaged reference histograms obtained from normal subjects. To facilitate objective detection of regional wall motion abnormalities, individual histograms were superimposed on the normal reference, defined as 1 SD around the mean of the normal control group. CAD was diagnosed when the regional fractional area change in at least one segment deviated from this normal reference, i.e., there was any evidence of regional wall motion abnormalities.

Left ventricular digitized color-encoded images were evaluated by reviewing the stored loops obtained from these 24 patients with suspected CAD. Endocardial tracking was considered adequate when visually assessed systolic excursion matched the color-encoded images. The left ventricle was divided into 16 segments, as recommended in the American Society of Echocardiography guidelines. The CAD was diagnosed if there was any evidence of absence of color hue at any segment during the reviewing of the stored images. 2-D echocardiograms were also recorded on videotapes; the wall motion abnormalities of all patients were analyzed subsequently. CAD was diagnosed if hypokinesis, akinesis or dyskinesis was found at any segment.

To evaluate the feasibility of automated detection of regional wall motion abnormalities with segmental analysis of CK data, 2-D echocardiographic images obtained from these 24 patients were interpreted by an independent observer. This observer did not have knowledge of the coronary angiographic data.

**Quantitative analysis of endocardial excursion**

To test the inter-observer reproducibility of measurement of the thickness of the color band representing endocardial excursion, we screened 20 of our study...
Statistical analysis

To assess the correlation of measurement of endocardial excursion of the CK images between two independent observers, two statistical measures including the simple linear regression and the intraclass coefficient of correlation (R) were studied. R is a simple and accurate estimate of the reliability of a measurement. To calculate R, we first estimated the overall variability of the measurement as the sum of two components, $s_e^2$ and $s_T^2$. $s_e$ is the standard error of the estimate of the reliability of a measurement, and $s_T$ is the standard error of the estimate of the reliability of a measurement. $s_T$ was calculated as $(BMS-WMS)/K_o$. The $R$ was then calculated as follows: $R = s_T^2 / (s_T^2 + s_e^2)$.\(^{18}\)

The sensitivity, specificity, positive and negative predictive value, and accuracy of CK in predicting the presence of significant CAD were defined as follows: sensitivity = [true positives (TP)] / [true positives + false negatives (FN)]; specificity = [true negatives (TN)] / [true negatives + false positives (FP)]; positive predictive value = $TP/(TP+FP)$; negative predictive value = $TN/(TN+FN)$; accuracy = $(TP+TN)/(TP+TN+FP+FN)$. The differences of sensitivity, specificity, positive or negative predictive value and accuracy between different groups were studied using Chi-squared test. A $p$ value < 0.05 was considered to be statistically significant.

Results

Figure 3 shows an example of comparison of CK images and stacked histograms between normal subjects and patients with CAD. The images depict the parasternal long- and short-axis views (left upper and right upper panels) and the apical 4- and 2-chamber views (left lower and right lower panels). These 4 panels are images from different cases. The his to grams obtained with segmental analysis of the end-systolic color-encoded images are shown below the corresponding view, and displayed as a stacked his to gram. These his to grams reflect the incremental regional fractional area change (RFAC) in percent of regional end-diastolic area (% REDA). The shade area (with ver ti cal lines) was the data of mean SD of the regional fractional area change of 30 control subjects. The small arrows point to the segments that did not reach the normal control area, which indicates the presence of significant CAD were defined as follows: $s_e^2$ was calculated as $(BMS-WMS)/K_o$. The $R$ was then calculated as follows: $R = s_T^2 / (s_T^2 + s_e^2)$.\(^{18}\)

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tracked endocardial motion adequately in 20 segments. Thus, to tally 364 of 384 (94.7%) left ventricular segments were successfully tracked. For the angiographic investigations, 4 cases had normal angiographic coronary findings and 2 had insignificant coronary artery lesions. Significant CAD was present in 18 patients, all of whom had history of myocardial infarction. Real time 2-D echocardiography found that 64 segments were hypokinetic and 10 segments were akinetic. Re view of the stored CK loop images found that 68 segments were hypokinetic and 8 segments were akinetic. All abnormal wall motion segments did not reach the normal area of contraction by CK stacked his to gram.

Regional systolic wall motion abnormalities were identified by CK in 14 of 18 patients with CAD. Of the 6 patients with normal or insignificant coronary artery stenosis who had normal wall motion, 2 had false positive CK findings. The detection rates of CAD by different methods can be referred to Table 1. The sensitivity

Fig. 3. Comparison of color kinesis (CK) images and stacked histograms between control subjects and patients with coronary artery disease. The images depict the parasternal long- and short-axis views (left upper and right upper panels) and the apical 4- and 2-chamber views (left lower and right panels). The histograms obtained from the segmental analysis of the end-systolic color-encoded images are shown below the corresponding CK images. These histograms reflect the incremental regional fractional area change in percent of regional end-diastolic area. The shaded area (vertical lines) is the data derived from the mean value ± 1 SD of the regional fractional area change of control subjects. The small arrows point to the segments that do not reach the normal control area, which indicates the presence of segmental hypokinesis. RFAC = regional fractional area change, REDA = regional end-diastolic area (see text for detail).
and specificity for detection of CAD were 77.8% and 66.6% for loop review ing, 83.3% and 66.7% for CK stacked his to gram anal y sis, and 77.8% and 83.3% for 2-D echocardiography, re spectively. The pos i tive and negative predictive values for detecting CAD were 87.5% and 50% for CK loop review ing, 88.2% and 57.1% for CK stacked his to gram anal y sis and 93.3% and 55.6% for two-dimensional echocardiography, re spectively. The over all ac cu racy for CAD de tec tion was 75% for CK loop review ing, 79.2% for CK stacked his to gram anal y sis, and 79.2% for 2-D echocardiography (Ta ble 2). It seems that both the CK loop review ing and stacked his to gram anal y sis were compara-
ble to the two- dimensional echocardiography in de tecting the CAD (not sig nif i cant in all com par i sons).

For study of the interobserver reproducibility and re li abil ity, 440 seg ments were ini tially an a ly zed; but 30 (6.8%) seg ments were ex cluded from quan ti ta tive anal y sis be cause of inap pro pri ate track ing of the endocardial bor der by CK. Af ter ex clu sion, 410 seg ments were stud i ed. The cor re lation of mea sure ment of endocardial excursion from the CK images by 2-ob servers was very good, with a equa tion of $y = 0.99x + 0.66$ and had a cor re lation co ef fi cient of 0.85 ($p < 0.01$) (Fig. 4). Ta ble 3 pres ents the re sults of mea-

Table 1. Detection of coronary artery disease by three different methods

<table>
<thead>
<tr>
<th></th>
<th>CK loop reviewing</th>
<th>CK stacked histogram</th>
<th>2DE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=24)</td>
<td>(n=24)</td>
<td>(n=24)</td>
</tr>
<tr>
<td>CAD</td>
<td>Abn N</td>
<td>Abn N</td>
<td>Abn N</td>
</tr>
<tr>
<td>Positive</td>
<td>14 4</td>
<td>15 3</td>
<td>14 4</td>
</tr>
<tr>
<td>Negative</td>
<td>2 4</td>
<td>2 4</td>
<td>1 5</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease, CK = Color Kinesis, 2DE = two-dimensional echocardiography, Abn = abnormal wall motion, N = normal segmental wall motion.

Table 2. Comparison of different methods for detecting the coronary artery disease

<table>
<thead>
<tr>
<th></th>
<th>CK loop reviewing</th>
<th>CK stacked histogram</th>
<th>2DE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>77.8</td>
<td>83.3</td>
<td>77.8</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>66.6</td>
<td>66.7</td>
<td>83.3</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>87.5</td>
<td>88.2</td>
<td>93.3</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>50</td>
<td>57.1</td>
<td>55.6</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>75</td>
<td>79.2</td>
<td>79.2</td>
</tr>
</tbody>
</table>

CK = Color Kinesis; 2DE = two-dimensional echocardiography; NPV = negative prediction value; PPV = positive predictive value. P = no significant difference of any variable between different groups.

Table 3. Results of measurements of endocardial excursion by two observers (n = 410)

<table>
<thead>
<tr>
<th></th>
<th>Endocardial excursion (mm)</th>
<th>95% CI for a single measurement</th>
<th>r</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SE</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td>Observer I</td>
<td>7.389</td>
<td>0.108</td>
<td>± 0.216</td>
<td>0.998</td>
</tr>
<tr>
<td>Observer II</td>
<td>6.977</td>
<td>0.111</td>
<td>± 0.222</td>
<td></td>
</tr>
</tbody>
</table>

CI = confidence interval; R = intraclass coefficient of correlation; SE = standard error.
pressed as the mean and standard error, the 95% confidence interval for the error-free value of single measurement, the intraclass correlation coefficient (R) and its statistical significance level. R was equal to 0.99 ($p < 0.0001$), which indicates a perfect reliability of measurement of the endocardial excursion of CK images.

**Discussion**

In this investigation, we have shown the ability of CK to detect on-line regional wall motion abnormalities and its sensitivity and specificity in patients with CAD. In our experience, it was possible to acquire adequate CK images in 84% of patients, with better interobserver concordance than in 2-D echocardiography. Similar to acoustic quantification and other ultrasound-based techniques, the ability of CK for adequate tracking of the endocardial border is dependent on the quality of the 2-D images. With repeated data acquisitions and analyses, the reproducibility of CK proved to be similar to other methodologies based on manual tracing of the endocardial border. 19,20 Endocardial tracking was achieved in all left ventricular segments, except for a reduced ability to track boundaries in the apical lateral wall because of anisotropy of the myocardium in these zones. 21,22

Off-line quantitative studies have shown heterogeneity of left ventricular systolic function in patients with CAD; 23,24 however, these quantitative methods are impractical for routine clinical use. CK has the advantage of being usable on-line, without time-consuming manual tracing of endocardial boundaries. In addition, a single end-systolic color image contains the entire picture of spatial and temporal contraction and can be digitally stored and retrieved.

The potential of this technique to improve the qualitative and quantitative assessment of wall motion abnormalities has been recently described. 28-30 In agreement with the results of the present study, we have performed analyses of data in standard echocardiographic views and found that evaluation of color-encoded images allowed detection of decreased amplitude of endocardial motion in abnormal contracting segments.

This study assessed the reliability of measurement of endocardial excursion by CK images. As indicated by the R, the interobserver measurement was reliable ($r = 0.998, p < 0.0001$). The measurement of endocardial excursion between two observers was highly correlated ($r = 0.85, p < 0.01$). We felt that the endocardial border of the stop frame CK image was very clear, which caused the measurement to be highly reproducible and reliable.

**Sensitivity**

Abnormalities of wall motion and thickening are known markers for myocardial ischemia and in farction. 30-35 Experimental studies support the concept of a threshold phenomenon, 32 that is, the infarct must extend beyond the subendocardial layer for a contraction abnormality to be detectable by echocardiography. 2-D echocardiography is a sensitive technique for detecting regional contraction abnormalities associated with myocardial infarction when the infarction region is large and transmural (> 18% of left ventricular mass), but it is insensitive to small, subendocardial infarcts. Adoption of strict echocardiographic criteria for contraction abnormalities (not considering abnormal hypokinesia because even normal myocardium may show only minimal regional contraction) may contribute to the poor sensitivity of echocardiography in detecting small infarcts. Less strict criteria tend to change the sensitivity, but at the expense of specificity.

In our population, the presence of regional systolic wall motion abnormalities by CK had a sensitivity and specificity of 88 and 77%, respectively, and an overall accuracy of 86% in identifying the presence of CAD. The slight increase in sensitivity in comparison with 2-D echocardiography may have resulted from the ease of CK in detecting hypokinetic segments.
Limitations

Some methodological limitations are inherent in the automatic border detection technology. The threshold for the boundary determination is directly influenced by operator-defined gain settings. Also, a potential limitation is the need for an echocardiographic image with adequate endocardial definition, a problem that is similar to those reported in transthoracic quantitative echocardiographic studies and not unique to this CK system. Further more, CK is affected by cardiac translation and rotation, as is the case for other quantitative methods utilizing endocardial excursion. The current algorithm does not include correction for translational or rotational motion even if, for rest echocardiograms, translation is not an important confounding factor in the interpretation of wall motion abnormalities. The number of normal subjects in this study is not enough to establish the range of normal data, which would require acquisition and analysis of data from large numbers of normal subjects. This study reports our initial experience using CK; future study is needed to obtain the mean ± 2 SD in large samples of normal population. Moreover, CK allows evaluation of endocardial excursion rather than of wall thickening. This limitation has to be taken into account in patients with abnormal septal motion (left bundle-branch block, pericardial dis ease, ventricular pacing, and diastolic flattening due to right ventricular volume overload). Finally, the accuracy of the algorithm is due to the presence of high or low heart rates, and this limitation could be minimized by use of higher-frame-rate imaging in a situation with an extended color scale.

In conclusion, CK is a promising new technique that allows qualitative and quantitative evaluation of regional wall motion in normal subjects, provided that the endocardial boundaries are adequately defined. In the present study, CK demonstrates the sensitivity and specificity for the detection of CAD, which is comparable to those of 2-D echocardiography. Further improvements in CK imaging and quantitative software are needed for future clinical studies.

Acknowledgments

This study was supported in part by Kaohsiung Veterans General Hospital, Taipei, R.O.C., Grant No. VGHKS 87-66 and Veterans General Hospital, Tsin-Hua, Yang-Ming Research Program, Grant No. VTY88-P3-25.

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