Isopotential Body Surface Maps and Their Relationship to Atrial Potentials in the Dog

By Terry D. King, Roger C. Barr, G. Scott Herman-Giddens, David E. Boaz, and Madison S. Spach

ABSTRACT

The origin of body surface P waves was evaluated in the intact dog by recording body surface isopotential maps and atrial epicardial potential maps. P waves were recorded from 150 points on the body surface, and 80 atrial unipolar electrograms were recorded by means of permanently implanted atrial electrodes during normal sinus rhythm and during atrial pacing. When the atrial pacing sites were changed, the associated shape changes in body surface P waves were highly dependent on the position of the recording sites. Throughout most of the P wave, multiple maxima were present on the body surface, and these were caused by widely separated right and left atrial excitation waves; however, the presence of several simultaneous atrial excitation waves could not be appreciated from the body surface maps when the atrial excitation waves were close to one another. In the last third of atrial excitation there were two maxima on the body surface, one due to atrial excitation waves and the other due to early atrial repolarization. In contrast to the more complicated patterns during excitation, during the P-R segment a single maximum and a single minimum were present on the body surface. The sequence of potential changes on both body surface and atrial epicardium during repolarization was similar to the sequence of excitation except that there was reversed polarity.

KEY WORDS

atrial excitation sequences atrial repolarization
atrial epicardial potentials atrial and body surface correlations
P waves unipolar electrograms atrial pacing

The interpretation of body surface P waves in terms of atrial electrical events remains somewhat vague. Recent studies in humans have used a variety of pacing sites to evaluate P wave changes for simulated ectopic rhythms (1). Moore et al. (2) found no change in P wave polarity in experimentally produced ectopic atrial rhythms and concluded that the lack of change was due to a specialized internodal conduction system. Clinically the configuration of P waves in some arrhythmias (3) is extremely difficult to interpret since, as yet, there is only a limited amount of published P wave information from many body surface points (4). No measurements have been published of the overall body surface events along with atrial electrical activity in the same animal.

For this study we used an experimental technique in the dog which allowed us to measure atrial potentials from the epicardial surface of both atria (5) and to relate atrial events directly to the body surface isopotential maps and P waves. To interpret body surface events, we particularly looked for the effects of three major features of atrial activity (5): (a) Multiple excitation waves, (b) atrial currents generated simultaneously by excitation and repolarization, and (c) on the epicardial surface the increased separation of the repolarization maximum and minimum to 3-5 cm, compared to 1 mm for depolarization.
The results show that although many atrial events were not detected on the body surface, all three of these features make distinctive contributions to the body surface potentials.

Methods

Eleven dogs weighing 20–30 kg were studied. Figure 1 shows the body surface format for the 150 recording points used to record the body surface data. Five leads were recorded simultaneously, along with an atrial epicardial lead for a time reference. Different sets of 5 points were sequentially recorded until all 150 points were covered. Analog-to-digital conversion and the data-processing methods used to construct body surface isopotential maps were adapted from those used for making body surface maps in children (7). In the final maps and in the P waves produced by the computer, the average potential over the surface was designated as zero volts; the average potential contour line is close to the zero contour line of Wilson's central terminal (7).

The most difficult problem we encountered was recording P waves with a low noise level. The problem was that the low voltages of the P waves on the body surface, particularly over the right lower chest and the back, were not much greater than the noise generated from time to time by muscle tremor, respiratory motion, and outside electrical interference. To facilitate recording the body surface data, a LINC-8 computer was used to display quickly each group of five P waves along with their time reference as soon as they were acquired. In this way, if excessive noise or other artifacts were present, the data could be rejected and another beat recorded. Since the recordings could be rapidly repeated until acceptable data were obtained, the problems involved in averaging multiple beats noted by Woolsey et al. (8) were avoided. These problems for us would have been (a) a considerably increased length of time for data recording, which would have reduced the number of different atrial excitation sequences that could have been recorded from a single animal and (b) a considerable increase in the complexity of the data-processing procedure, which we considered undesirable for an initial study designed to characterize the major features of the body surface potential distribution. Respiration was controlled with a Harvard respiration pump which allowed us to choose with ease those beats that occurred in the same phase of respiration. The noise level present in the final body surface maps was estimated to be ± 15 μV zero to peak.

The details of preparing the animals by surgically implanting 30 to 40 electrodes on the epicardial surface of each atrium have been described previously, along with the data acquisition and processing methods (5). The animals did well after surgery, appeared healthy, and were studied six weeks later. On the day of study, each dog was anesthetized with pentobarbital sodium, 30 mg/kg iv, and unipolar electrograms were recorded from each atrial site. The original analog data were digitized by the LINC-8 computer and later processed further by an IBM 360/75 computer. The final output, arranged in the format shown in Figure 1, consisted of atrial epicardial isopotential maps for intervals of 1 msec throughout the period of atrial excitation and repolarization into QRS. The same time...
BODY SURFACE MAPS FROM ATRIAL POTENTIALS

reference lead from a single atrial site was used for recording both heart and body surface data.

In each animal the body surface and atrial epicardial maps were first recorded during spontaneous sinus rhythm. The time required to record both the body surface and the heart data for a single sequence was 1 hour. Since changes in atrial rate affect both P and T waves, careful checks were made to ensure that during spontaneous beating the rate did not vary more than ± 6 beats/min from the initial rate of 140 to 160 beats/min. To ensure that no detectable changes in the excitation pattern of the atrium occurred throughout a recording sequence, a few selected atrial epicardial leads were recorded both before and after the entire sequence. Heart and body surface maps were also measured in each dog for a pacing site on the lower right atrium where the inferior vena cava joins the atrium near the coronary sinus and for a pacing site on the lower lateral left atrium; the pacing rate remained fixed between 160 and 180 beats/min throughout each sequence.

Woolsey, et al. (8) noted frequent and marked changes in the wave form shape of P waves in humans. Careful monitoring was carried out in our study to ensure that such changes did not occur during a single recording sequence, which included recording from both the heart and body surface leads. During spontaneous beating, we were unable to detect changes in the atrial excitation sequence or changes in the shape of the P waves recorded on the body surface for those intervals during which the heart rate did not vary more than 15 beats; however, with greater rate changes, there were alterations in both the excitation sequence and P waves. During the pacing sequences no such changes were noted over prolonged periods of time, presumably because the rate remained fixed.

After all data had been recorded, chest x-rays were obtained to confirm the position of the atrial electrodes and to establish the geometrical relationships between the recording points on the body surface and those on the atria.

Results

Comparison of the different sequences of atrial activation in the same animal increased the confidence with which changes in the body surface maps could be attributed to accompanying alterations in the atrial events, since any changes due to geometry could be excluded. For this reason, P waves, body surface maps, and atrial epicardial maps for the three pacemaker sites are shown for the same animal. The results shown for each sequence (normal sinus rhythm, pacing low right atrium, and pacing low left atrium) are characteristic of the results obtained in the other 10 dogs.

In the atrial maps, the line which separates the positive potential from the negative potential regions is taken to be the excitation wave during depolarization (5). In these maps, propagation of excitation waves is in a direction away from the negative area toward the positive one; in contrast, during repolarization the earlier areas to repolarize are positive with respect to the later areas.

NORMAL SINUS RHYTHM

With the onset of the P wave, the body surface distribution showed a lower chest maximum and right upper chest minimum (Fig. 2A, 11 msec). This body surface potential distribution was generated by an atrial excitation wave along the sulcus terminalis and upper venous atrium. The initial development of a maximum and minimum on the body surface occurred 4 to 8 msec after initial activity was detected in the sinus node area (5).

The magnitudes of the initial body surface maximum and minimum increased thereafter with little change in position; however, an additional isolated maximum suddenly developed on the right upper thorax (23 msec). The lower left chest maximum was accounted for by an excitation wave on the right atrial free wall near the AV groove and another one nearby propagating in the same direction in the superior left atrium at the base of the left atrial appendage. The isolated right upper thorax maximum was due to excitation of cardiac muscle in the superior vena cava.

The isolated right chest maximum disappeared as rapidly as it had appeared; thereafter another maximum developed over the right lower thorax while that on the left persisted (36 msec). This map is similar to the one published by Taccardi for the dog (4). These surface changes between 23 msec and 36 msec were due to completion of excitation of cardiac muscle in the superior vena cava and to the development of the two widely separated excitation waves, one in the lower

Circulation Research, Vol. XXX, April 1972
Normal sinus rhythm. For this and subsequent sequences, the time-aligned events on the body surface and on the atrium are shown for various instants throughout atrial activation and repolarization. For each instant, the format for data presentation is that shown in Figure 1; the body surface potential distribution is shown above the atrial potential distribution. At the bottom of each panel are right and left atrial unipolar electrograms with a vertical bar identifying the time instant throughout atrial depolarization and repolarization. In the body surface maps (top) the line separating the area of horizontal hatching from the clear area is the average potential line (zero volts). The horizontal hatching indicates positive potentials, the more dense horizontal lines denoting more positive potentials. The clear and stippled areas indicate negative potentials, the more dense stippling denoting more negativity. For the maps shown during atrial depolarization (11 msec–70 msec) the increments between contour lines in the body surface maps is 50 μV. The values of the maxima (+) and minima (−) shown in the body surface maps varied from ±50 μV to ±300 μV. During atrial repolarization (97 msec–103 msec) the increment between contour lines in the body surface maps is 30 μV. In the atrial
right atrium and the other in the upper left atrium. At 54 msec, the two maxima persisted on the lower thorax with a minimum on the upper. The associated atrial events were much more complex at 54 msec than suggested by the body surface map. Although excitation waves were still present in the lower right atrium and lateral left atrium, two new excitation waves due to activation via the atrial septum (5) had been initiated in the central atrium inferiorly, and there was another excitation wave in the left atrial appendage. Finally, in addition to these many excitation waves, there were repolarization maxima over the right atrium.

During the last part of the P wave, the lower left chest maximum persisted although the one on the right chest disappeared (Fig. 2B, 70 msec). Additionally, positive potentials extended anteriorly over a broad area to the right upper chest. The epicardial map showed that the lower right atrial excitation waves had disappeared, causing the disappearance of the right lower chest maximum; colliding excitation waves in the lower left atrium continued to produce the maximum on the lower left chest. The repolarization maximum in the right atrium was the reason for the positive potentials on the right upper chest.

During the P-R segment, the maximum on the lower left chest disappeared while another maximum developed on the right upper chest (97 msec). The associated epicardial map showed disappearance of all excitation waves, and the repolarizing atria had a right atrial maximum and a left atrial minimum—these were separated by an enormously greater distance than were depolarization maxima and minima.

Suddenly, at 103 msec, ventricular excitation began and produced a rapidly increasing anterior chest maximum and posterior-inferior minimum. These were superimposed on the atrial repolarization maximum and minimum on the upper thorax. The atrial epicardial map remained unchanged over the right atrium, but an intense minimum developed rapidly over the inferior left atrium, indicating that early ventricular excitation currents affect the left atrium for several milliseconds before affecting the right atrium.

To gain insight into the cause of the polarities and varied shapes of the body surface scalar tracings, a Calcomp plotter was used to draw P waves for all of the 150 original body surface recording sites (Fig. 3). Over the lower thorax the P waves were uniphasically positive, and over the upper thorax they were uniphasically negative. The transition from upright to negative P waves occurred within a narrow band along row E of Figure 3.

P waves within the narrow region on the mid-anterior chest were M-shaped. The following events produced these M-shaped P waves. The initial positive deflection was due to the initial anterior chest maximum from right atrial excitation (Fig. 2A, 11 msec). The subsequent negative dip was from the central anterior chest minimum due to the widely separated right and left atrial excitation waves (36 msec). The final positive deflection was caused by the extension of positive potentials from the lower left chest maximum, which was generated primarily by excitation of the lateral and inferior left atrium (54 and 70 msec).

P waves recorded on the right upper chest near position H-5 had an early transiently positive deflection that interrupted the otherwise negative curve. The body surface and atrial epicardial maps showed that this deflection was caused by excitation of cardiac muscle in the superior vena cava.

---

epicardial maps the solid line surrounding the horizontal hatching represents the 0.2-mv equipotential line. The dotted line surrounding the stippled areas represents the -0.2-mv isopotential line. The areas of the atrium with no hatching or stippling are those where the voltage was less than ±0.2 mv. The voltages at the locations of the maxima and minima, marked by plus and minus signs respectively, varied from ±0.5 mv to ±4.8 mv.
P waves for normal sinus rhythm. P waves are shown for each of the 150 recording sites. The vertical line through each P wave denotes the same instant of time. The straight horizontal line which connects one P wave to the next on each of the 10 rows is the base-line level. The sudden return to the base line at the end of each P wave, like that at 1-3, represents the end of the tracing of one P wave and the onset of the base line for the next. Note that the P waves near point D-11 are initially negative. The first body surface map shown in Figure 2 (11 msec) does not show a corresponding minimum at this position since the 11-msec instant occurred further into the initial rise of the P wave. The base line (zero volts) for measuring the voltages throughout each P wave was selected at a time approximately 50 msec before the onset of the P wave. Tracings such as shown above for D-11 show a small negative dip after the time of base-line selection.

LOW RIGHT ATRIAL PACING

The P wave began with an upper right chest maximum and inferior chest minimum (Fig. 4A, 14 msec), a pattern which was the reverse of the one at the start of normal sinus rhythm. While only a single maximum and minimum were on the chest surface, two excitation waves were present in the lower right atrium—one propagating superiorly and another laterally toward the left atrium. Thereafter, the initial body surface maximum and minimum increased in intensity, and a second maximum developed on the left side of the thorax (38 msec). Associated with the presence of these two separate maxima were the two distinct atrial excitation waves which had become widely separated. Both body surface and atrial epicardial maps at this time were mirror-image forms of those which occurred at 36 msec during normal sinus rhythm.

Subsequently, the intensity of the left chest maximum increased while that of the central chest minimum decreased (45 msec); the maximum on the right chest had disappeared. The atrial map showed continued propagation of the left and right atrial excitation waves. In addition, an isolated area of excitation commenced on the superior left atrium between the two atrial appendages. This early onset of excitation superiorly can be accounted for by conduction via the atrial septum (5, 9).

After this, the left chest maximum shifted more to the center, with extension of the surrounding positive potentials inferiorly (58 msec). Although there was a single maximum on the body surface, multiple excitation waves were present in the upper atria. Excitation...
waves were present in the proximal superior vena cava, in the base of the right atrial appendage, in the base of the left atrial appendage, and in the lateral wall of the left atrium. By 70 msec (Fig. 4B), the body surface map had changed considerably, with a rapid decrease in the area of positive potentials on the left anterior chest while the maximum moved to the right upper thorax.

There was also a decrease in the magnitude of the minimum as it shifted on the lower thorax from the right to the left side. The epicardial map showed that excitation waves had disappeared everywhere except in the superior vena cava and both atrial appendages.

During the terminal P wave, the body surface map became more complex—the upper thoracic maximum persisted while a...
second area of positive potentials developed inferiorly (93 msec). The atrial events producing these surface changes were the disappearance of excitation in the superior vena cava while excitation waves continued in the atrial appendages. In addition, a repolarization maximum was present over the lower atrium.

During the P-R segment (108 and 111 msec), the upper chest excitation maximum disappeared while the inferiorly positioned repolarization maximum increased in magnitude and moved superiorly on the anterior chest. On the atria, the positive potentials of repolarization spread over the inferior atrium and progressed superiorly while repolarization minima occurred on the upper right atrium and the lateral left atrium.

Figure 5 shows the P waves recorded at each point on the body surface. In general, the deflections were opposite in polarity to those of normal sinus rhythm. However, in certain regions on the mid-thorax there was practically no change in P wave shape, e.g., position E-6 (cf. Fig. 3). The change from upright to inverted P waves occurred within a narrow band near row E, as was found during normal sinus rhythm.

The upright P waves on the right upper chest contained three separate peaks. To determine if any of these peaks could be related specifically to the excitation wave in the superior vena cava, simultaneous recordings were made from electrodes on the superior vena cava and from the body surface on the right upper thorax (Fig. 6). During normal sinus rhythm (A) the intrinsic deflections of the superior vena cava wave forms occurred coincident with the transiently positive deflection of the body surface tracing. When the inferior right atrium was paced near the coronary sinus (B), the intrinsic deflections of the superior vena cava wave forms shifted to coincide with the second peak of the upright P wave. Furthermore, comparisons of the upright P waves of Figure 5 with the body surface and atrial epicardial maps (Fig. 4) showed that the first peak was due to excitation waves in the right atrium and the third peak to excitation of the right and left atrial appendages.

LOW LEFT ATRIAL PACING

Figure 7A shows that initially there were an anterior right chest maximum and a posterior
Simultaneous superior vena cava electrograms and P waves on the right upper thorax. The unipolar electrograms from the superior vena cava (points 1 and 2) are shown at the top and the P wave recorded at point 3 on the thorax is shown at the bottom of the panels. A: Normal sinus rhythm. B: Pacing the inferior right atrium. See text for further discussion.

left chest minimum (18 msec). An imaginary line connecting the maximum and minimum was more nearly horizontal than was a similar line in the initial maps of the two previous sequences. At this time there were two excitation waves in the left atrium, both progressing rightward.

The single body surface maximum and minimum increased in intensity (36 msec). Two excitation waves were still present, one on the upper and the other on the lower left atrium. At 44 msec the positive potential area extended to the superior and inferior limits of the map in the mid-chest region. Although still only one maximum and minimum were present on the body surface map, now there were three excitation waves in the atrium. The two previous upper and lower left atrial excitation waves had moved to the right atrium, and now a third was present in the left atrial appendage.

A rapid change in the body surface distribution occurred at 48 msec, with disappearance of the positive potentials over the lower anterior chest while the upper maximum persisted. This was associated with completion of excitation of the inferior portion of the right atrium followed by the excitation waves progressing superiorly. Meanwhile, the upper atrial excitation wave had propagated to the base of the right atrial appendix and was oriented to the right and inferiorly, while, additionally, excitation of the left atrial appendage continued.

During the latter part of the P wave, there were positive potentials over the upper chest and negative potentials over the lower chest (Fig. 7B, 62 msec). Associated atrial events were the upper and lower right atrial excitation waves propagating toward one another and a new excitation wave invading the proximal superior vena cava. In addition to all of the excitation waves, positive potentials of repolarization were present on the left atrium.

The end of the P wave was associated with a right chest maximum, which was decreasing in magnitude (69 msec); an additional development was the extension of positive potentials over the left lower chest. At this time, there were colliding excitation waves in the right atrial free wall, and excitation continued in the superior vena cava. The repolarization maximum on the left atrium had become more prominent and produced the positive potentials on the lower left chest.

During the P-R segment, the right chest excitation maximum had disappeared (83 msec); the early repolarization pattern was similar to the initial excitation pattern with the polarities reversed. On the atrium there were left atrial positive potentials and right atrial negative potentials. As repolarization continued (115 msec), positive potentials spread over the entire lower chest; the epicardial map showed that the positive repolarization potentials now extended over the entire left atrium to the right atrium.

The body surface P waves for low left atrial pacing are shown in Figure 8. Over the lower left thorax the wave forms were quite similar to those found when the lower right atrium was paced but opposite in polarity to those for normal sinus rhythm. On the other hand, P waves on the middle and upper left thorax appeared quite similar to those for normal sinus rhythm, e.g., position F-13. Although on the inferior torso the P waves were quite similar during low left and low right atrial
Low left atrial pacing. The format for the body surface and atrial epicardial maps is the same as for Figure 2. The increment between contour lines in the body surface maps is 50 µV during atrial depolarization (18 msec–69 msec) and the increment during atrial repolarization (83 msec–115 msec) is 30 µV. The range of voltage values for the maxima (+) in the atrial epicardial maps was 0.6 to 2.8 mV and the range for the minima (−) was −0.9 to −5.0 mV. In the atrial electrograms shown below, the initial spike represents the stimulus artifact.

Discussion

EXPERIMENTAL TECHNIQUES

To determine the genesis of body surface potentials from the heart, we considered it imperative to measure the potentials of both in the same intact animal. Otherwise, there is no way to account for such changes as variations in atrial repolarization due to opening the chest. Additionally, rate changes often occur between the time of body surface recordings and the time of measurements with the chest open.

To check for changes produced by the surgery, a control body surface map was made.
for each animal prior to operation; these compared quite favorably with those obtained on the day of the study. Postmortem examination indicated that the wires from the atrial epicardium to the neck of the dog, although they became encased in fibrous tissue, occupied little space and caused no significant alteration of intrathoracic structures, e.g., there were no fluid accumulations. Atelectasis was minimal. When present, it was localized to the apex of the lungs.

Since atrial currents are smaller than those from the ventricle, any noise present in the body surface recordings is more detrimental to the interpretation of P waves than QRS. Because of this, we have shown only surface potential patterns that were considerably above the noise level and that were reproducible from dog to dog. If the noise in the final surface data could be reduced substantially, it might be possible to see considerably more complicated potential distributions.

INTERPRETATION OF BODY SURFACE POTENTIALS

Possibly the most salient finding of this study was that the presence of several simultaneous atrial excitation waves could not be appreciated from the body surface when multiple atrial excitation waves were positioned close to one another; however, when two or more excitation waves were located far apart, more than one body surface maximum usually was present. Perhaps this is not surprising since it is well established that as the distance of the measuring points from the location of the electrical sources becomes large in comparison to the distance separating the electrical sources, the recorded potential distribution will become increasingly simplified, finally having only a single maximum and minimum (10). Examples of this phenomenon for two dipoles have been shown recently by DeAmbroggi and Taccardi (11).

On the body surface, changes in configuration of P waves due to changes in the pacing site were highly dependent on the recording site. Since there are no definitive data showing atrial excitation and repolarization sequences for naturally occurring "coronary sinus" or "left atrial" rhythms, we are unable to specify the relationship between our sequences and what may occur in these spontaneous abnormal rhythms. The P waves remained uniphasic with negative polarity on the left upper chest for excitation sequences due to normal sinus
rhythm and to low left atrial pacing (sites of origin of excitation which are located at diametrically opposed atrial positions). However, P waves over the low thorax were of different shapes, and the surface maps had even greater differences. The polarity of P waves was particularly sensitive to small vertical shifts of the recording site on the mid-chest, an area commonly used for precordial lead positions in dog experiments.

Waldo et al. (12) recently studied the effects of incisions and of variation in artificial pacemaker sites on the P wave polarity and morphology by recording leads II, III, and aVF in open-chest dogs. They concluded that the polarity, morphology, and duration of the P wave were a poor indicator of the site of origin of atrial activation, a conclusion similar to that of Moore et al. (2). Our results suggest caution in making interpretations concerning atrial events from a limited number of body surface leads. For example, under the conditions of our experiments we have found easily detectable changes in the body surface maps due to 1-2 cm shifts of the artificial pacemaker site along Bachmann's bundle, along the lateral wall of the left atrium, and along the free wall of the right atrium. However, in many of the 150 leads no P wave polarity changes occurred nor were there major P wave morphology changes.

P waves over the mid-precordium and upper right chest commonly had multiple notches and peaks. These peaks, when compared to the body surface maps, were found to be related to either (a) an overall change in the surface distributions associated with movement of distant maxima or minima, or (b) the appearance or disappearance of a new maximum at the local recording site. Most of the peaks were due to changes in the overall pattern; e.g., the M-shaped P waves over the mid-precordium during normal sinus rhythm. The one exception was a peak recorded on the right upper chest; this was due to excitation of cardiac muscle in the superior vena cava (Fig. 6).

Often excitation waves were present in both atria at the same time. This result emphasizes that analysis of P waves cannot be divided into consecutive periods or right and left atrial activation since they overlap throughout most of the P wave.

During the latter third of atrial excitation, both the body surface and atrial epicardium showed the effects of currents due to excitation waves and due to early repolarization. During the P-R segment, the epicardial potentials had a much simpler distribution than during excitation—there was usually a single region of positive potentials and one of negative potentials with the maximum and minimum separated by a distance of as much as 5 cm. This difference between excitation and repolarization in the epicardial potentials was reflected by a similar difference in the body surface maps. During the P-R segment the body surface maps never contained more than a single maximum and minimum, and there were low potential gradients between the two. The body surface repolarization maximum and minimum and their accompanying areas of positive and negative potentials shifted in a manner consistent with the shifting areas of positive and negative potentials on the atrium as repolarization progressed. Just as the different sequences of atrial excitation produced distinctive body surface patterns, the differences in the atrial repolarization patterns were equally distinctive.

References

Circulation Research. Vol. XXX. April 1972
Isopotential Body Surface Maps and Their Relationship to Atrial Potentials in the Dog
TERRY D. KING, ROGER C. BARR, G. SCOTT Herman-Giddens, DAVID E. BOAZ and
MADISON S. SPACH

Circ Res. 1972;30:393-405
doi: 10.1161/01.RES.30.4.393

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1972 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circres.ahajournals.org/content/30/4/393

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/