Conduction left-to-right and right-to-left across the crista terminalis

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Matsuo, Kunihiro, Kikuya Uno, Celeen M. Khrestian, and Albert L. Waldo. Conduction left-to-right and right-to-left across the crista terminalis. Am J Physiol Heart Circ Physiol 280: H1683–H1691, 2001.—A line of block between the vena cava and the crista terminalis (CT) region is important for atrial flutter (AFL), but whether it is fixed or functional is controversial. To test the hypothesis that conduction across the CT normally occurs, but when block occurs in this region it is functional, we analyzed atrial activation during right and left atrial pacing (cycle lengths of 500–130 ms), AFL, and atrial fibrillation in 15 dogs with sterile pericarditis and 7 normal dogs. Electrograms from 396 right, left, and septal atrial sites were simultaneously recorded. Activation across the CT occurred during atrial pacing, AFL, and atrial fibrillation. Activation wave fronts from the right to the left atrium and vice versa traveled over several routes, including Bachmann’s bundle and inferior to the inferior vena cava, as well as across the CT. In these models, there is no fixed conduction block across the CT, and when block in the CT region occurs, as during AFL, it is functional.

The usual atrial flutter reentrant circuit in the right atrium has been well characterized (5–7, 22, 23, 27, 29). During atrial flutter in both animal models and patients, it is clear that a line of block, which seems critically important for the development and maintenance of atrial flutter, is present between the superior and inferior vena cava (5, 6, 35). This line of block is generally thought to be in the region of the crista terminalis. Recent studies (20, 21) in patients have suggested that this line of block is, in fact, in the crista terminalis and also that the block is fixed rather than functional. Most recently, a study (28) in patients that analyzed the effects of premature beats indicated that when such block occurred, it was functional. The present study in canine hearts was performed to study conduction across the crista terminalis under a variety of rhythms (during threshold pacing from selected atrial sites at a series of rapid rates, during induced atrial fibrillation, and during induced atrial flutter) to test the hypothesis that conduction across the crista terminalis normally occurs, but that when block does occur in this region, as during atrial flutter, it is functional.

METHODS

We studied activation patterns simultaneously in both atria including the atrial septum using simultaneous multisite mapping techniques in 22 adult mongrel dogs weighing 19–25 kg. Seven normal dogs were studied acutely. Fifteen dogs were studied 2 days after surgical creation of sterile pericarditis (25). All studies were performed in accordance with guidelines specified by our Institutional Animal Care and Use Committee, the American Heart Association Policy on Research Animal Use, the United States Public Health Service Policy on Use of Laboratory Animals, and the “Guiding Principles in the Care and Use of Animals” of the American Physiological Society.

Creation of the Sterile Pericarditis Model

The canine sterile pericarditis model was created as previously described (25). At the time of surgery, pairs of multifilament stainless steel wire electrodes (interelectrode distance 3–5 mm) were sutured on the right atrial appendage, Bachmann’s bundle, and the posterior-inferior left atrium close to the proximal portion of the coronary sinus in all dogs. Also, another pair was sutured on the right ventricular apex to be used for pacing, principally after radiofrequency His bundle ablation to create complete atroventricular block as part of studies in the open-chest state (24). At the completion of surgery, the dogs were given antibiotics and analgesics and then were allowed to recover. Postoperative care included administration of antibiotics and analgesics.

Studies in the Open-Chest State

For all mapping studies, acutely for the normal dogs and on the second postoperative day for pericarditis dogs, an open-chest study was performed using standard techniques (15, 24). After His bundle ablation, with the use of the previously placed ventricular electrodes, ventricular pacing was initiated at a rate of 100 beats/min using a Medtronic 5375 external demand pulse generator (Medtronic; Minneapolis, MN). During the periods of simultaneous multisite mapping, ventricular pacing was performed at 60 beats/min to decrease still further the temporal superimposition of atrial and ventricular events. The heart was then exposed using standard surgical techniques. The body temperature of the dogs was kept within the normal physiological range...

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CRISTA TERMINALIS CONDUCTION

throughout the study by using a heating pad and a warm saline infusion.

Mapping Studies During Pacing from Selected Sites and During Induction of Stable Atrial Flutter or Atrial Fibrillation

Five seconds of overdrive atrial pacing of sinus rhythm was performed from two to three selected sites during sinus rhythm in each study at selected cycle lengths from 500 to 130 ms (500, 462, 428, 375, 333, 300, 280, 250, 200, 180, 150, and 130 ms). When the spontaneous sinus cycle length was shorter than 500 ms, we started pacing at the first of the above cycle lengths, which was shorter than sinus cycle length. The selected atrial pacing sites were the following: 1) the posterior-inferior left atrium (site i) (n = 18 dogs; acute = 5, pericarditis = 13); 2) an epicardial aspect of the crista terminalis region (site ii) (n = 6 dogs; acute = 1, pericarditis = 5); and 3) the right atrial free wall (site iii) (n = 17 dogs; acute = 4, pericarditis = 13; Fig. 1). These sites were chosen to examine the left-to-right and right-to-left activation across the crista terminalis during overdrive pacing of sinus rhythm. To pace while recording from the entire electrode array, two pairs of thin (0.2-mm diameter) nickel-cadmium wire electrodes bared of insulation at the distal end (3 mm) were placed using the plunge-wire technique (no. 26 needle) at an epicardial aspect of the crista terminalis region (site ii) or the right atrial free wall (site iii). We used the previously placed stainless steel wire electrodes when the pacing was performed from site i.

In the sterile pericarditis dogs, if neither atrial fibrillation nor atrial flutter was induced by this pacing protocol, we decreased the pacing cycle length until either was induced. If neither atrial fibrillation nor atrial flutter was induced by pacing from these three sites, we also paced from the pair of stainless wire electrodes previously sutured on the Bachmann’s bundle area. Only atrial fibrillation or atrial flutter episodes lasting longer than 5 min were analyzed. All pacing was performed using stimuli at just diastolic threshold delivered by a Bloom electrophysiology programmable stimulator (Fischer Imaging; Denver, CO) with a pulse width of 1.8 ms.

Simultaneous Multisite Mapping

Our multiplexing system can record continuously for 60 min (15). For studies of the sequence of right and left atrial activation, an electrode array containing 372 unipolar electrodes arranged in 186 bipolar pairs was used as previously described (15). There were 95 pairs for the right atrium and 91 pairs for the left atrium; the latter included 14 pairs placed separately on Bachmann’s bundle (Fig. 2). The electrode array for the Bachmann’s bundle area was positioned first; it was inserted behind the right atrial appendage between the superior vena cava and aortic root and advanced to the left atrial appendage. The entire electrode array was placed around the atra and secured with a Velcro belt. In 12 cases, the interatrial septum was also mapped simultaneously with a single 24-pole electrode catheter with an interelectrode distance of 1 mm in seven dogs or a basket catheter (EP Technologies) with 64 electrodes (the basket catheter had 8 flexible splines, and each spline had 8 electrodes) in five dogs. When we used the 24-pole electrode catheter, as previously described (15), the electrode catheter was inserted into the right external jugular vein and advanced to the right atrial septum through the superior vena cava. The distal tip of the electrode catheter was placed in the orifice of the coronary sinus for stability, so that we only recorded from 22 of 24 electrodes. The location of the distal tip of the electrode was confirmed by manual palpation (15). The electrode catheter was then torqued against the septum and sutured in place at the insertion site in the external jugular vein. When we used a 64-pole basket catheter, the basket catheter was inserted into the right femoral vein and advanced to the right atrial septum through the inferior vena cava under fluoroscopic guidance. The distal tip of the basket catheter was placed in the superior vena cava where the latter entered the right atrium. We then recorded from the three splines (24 electrodes) of the basket catheter that were in contact with the atrial septum.

During these studies, electrocardiogram (ECG) lead II was recorded simultaneously along with electrograms from the right atrial free wall (190 electrodes), the left atrial free wall (154 electrodes), Bachmann’s bundle (28 electrodes), and the atrial septum (22–24 electrodes) so that we were able to record from a total of 372–396 electrodes simultaneously along with ECG lead II. Also during these studies, surface ECG lead II and bipolar electrograms obtained from the previously placed atrial epicardial electrodes were both monitored on a VR-16 Electronics-for-Medicine oscilloscope and recorded simultaneously on a Honeywell 101 FM tape recorder for later playback and analysis. For these recordings, the ECG was recorded between a bandpass of 0.1–250 Hz.
and the bipolar electrograms were recorded between a band pass of 30–500 Hz.

Data Acquisition and Analysis

As indicated above, for all studies, atrial electrograms from all electrode sites in both atria and the interatrial septum along with a marker channel and ECG lead II were recorded during overdrive pacing of sinus rhythm and during induced stable atrial fibrillation or atrial flutter. Data recording and processing were performed as we have previously described (15, 16, 24, 32).

Multisite mapping: data acquisition. Data were recorded and processed with two cardiac mapping systems (that is, one for the right atrium and another for the left atrium, Bachmann’s bundle, and the atrial septum) designed at Case Western Reserve University (Cleveland, OH) and described previously (15, 16, 24, 32). All signals were individually amplified, filtered between a bandwidth of 1 and 500 Hz, sampled at 1,000 Hz, and digitized with a 12-bit analog-to-digital converter. The data were then transferred to a Pentium class computer with 16 megabytes of memory via optoisolators. The system had all processing units designed to operate in parallel and was capable of storing and archiving 60 min of continuous data from all electrodes. Data were archived on a hard drive in their raw format and then edited and transferred to a network server (Dell Pentium II) for analysis.

During periods of mapping, the start key of the computer keyboard of each system was simultaneously enabled to start recording. For time alignment of the two mapping systems, a common marker channel was used through which a marker was introduced manually at deliberate intervals throughout the study. Markers were then numbered consecutively to permit temporal lining up of the data for analysis.

Multisite mapping: data analysis. Data were analyzed as previously described (15, 16, 24, 32). Analysis was based on sequential time windows. For each episode of atrial flutter and fibrillation, at least 1.2 s of data were analyzed, and the activation sequences were depicted by activation maps. Analysis of data consisted of selecting activation times and computation of an isochronous map with a maximum resolution of 2 ms. Data in both their raw unipolar format and computer-processed bipolar format (obtained by subtracting raw unipolar data from a bipolar pair) were available to assist in the selection of activation times. Data were filtered in software with a low cutoff frequency (high-pass filter) of 10 Hz before analysis to avoid baseline drift of the electrograms. A time-reference signal was selected from one of the electrode sites or a pacing stimulus, as appropriate, and was used to depict zero activation time. The electrograms recorded at each site during the time window were displayed on a graphics screen, and selection of activation time was done manually with a cursor. The moment of activation at each site was taken as the peak of the first rapid deflection in a predominant monophasic recording or as the time of the intrinsic deflection in a predominantly biphasic recording. The activation time at sites at which multiple-component electrograms were recorded was assigned to the major deflection (highest amplitude for bipolar electrograms or fastest downstroke for unipolar electrograms). Care was taken first to identify all components that were due to ventricular activation by using the QRS complex in the ECG as a marker. If there were two discrete deflections for one atrial ECG complex in the ECG (i.e., a so-called double potential), the activation time at these sites was assigned to the deflection with the highest amplitude for bipolar electrograms or the more rapid deflection for unipolar electrograms.

RESULTS

Activation Across the Crista Terminalis During Overdrive Pacing of Sinus Rhythm

Figure 3A shows four different representative examples of patterns of left-to-right activation across the crista terminalis in four different sterile pericarditis dogs during overdrive pacing of sinus rhythm from the posterior-inferior left atrium at a cycle length of 300 ms. These representative examples (the data were similar for all normal and pericarditis dogs) show a variation of a basic theme: namely, that left-to-right conduction occurs across the crista terminalis. Atrial septal activation is indicated in the drawing in which the roof of the right atrium has been removed. The asterisk in Fig. 3A at the Bachmann’s bundle indicates epicardial breakthrough from the septum. In the example illustrated in Fig. 3A, top left, the right atrial free wall was predominantly activated by a wave front that came from between the pulmonary veins and the inferior vena cava. Note also the wave front that travels inferior to the inferior vena cava and participates in activation of the right atrium. In the example illustrated in Fig 3A, top right, the right atrial free wall was also activated by these two wave fronts in a somewhat different but basically similar manner. In the example illustrated in Fig 3A, bottom left, the wave front that activated the right atrium came predominantly from the wave front that traveled inferior to the inferior vena cava. Note that a wave front also came from the region between the pulmonary veins and the inferior vena cava. In the example illustrated in Fig. 3A, bottom right, because of slow conduction of the wave front traveling inferior to the inferior vena cava, the right atrium was activated only by the wave front that came from between the pulmonary veins and the inferior vena cava.

Figure 3B shows the patterns of left-to-right activation during overdrive pacing of sinus rhythm from the same pacing site in each dog shown in Fig. 3A but now at a cycle length of 180 or 150 ms. Figure 3B, bottom right (dog 372), shows an activation pattern during pacing at 180 ms because atrial fibrillation was induced when we paced at 150 ms. Although there are some changes in conduction time noted by relative crowding of isochrones, conduction across the region of the crista terminalis is little changed compared with pacing at the 300-ms cycle length. Thus the relative dominance of two wave fronts (one from the region between the pulmonary veins and the inferior vena cava, and the other that traveled inferior to the inferior vena cava) were not affected by the pacing cycle lengths in each dog.

Figure 3C is a representative example of electrograms recorded from selected atrial sites during overdrive pacing of sinus rhythm. In the example shown, electrograms were recorded during overdrive pacing from the posterior-inferior left atrium in the example

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illustrated in the Fig. 3A, top left. The locations of the recording sites (a–e) are shown in the Fig. 3A, top left. These sites were chosen to illustrate the relative right atrial activation sequence in relation to the location of the crista terminalis and the region of the inferior vena cava. Note that activation of site a occurs before site e, so that right atrial free wall activation results from fusion of two wave fronts. Note also that no complex
electrograms (e.g., fractionated electrograms or double potentials) were recorded in association with conduction across the crista terminalis in this representative example. Such electrograms were rarely recorded in these studies.

In Fig. 4, we summarize all the observed left-to-right atrial activation patterns across the crista terminalis while pacing from the posterior-inferior left atrium. Left atrial-to-right atrial activation across the crista terminalis was always seen, but there were some variations. Numbers equal the number of pericarditis or normal dogs with that activation pattern. Abbreviations and symbols are the same as in Figs. 1 and 3. PV, pulmonary vein. *Epicardial breakthrough from the septum to Bachmann’s bundle.

In Fig. 5, we show representative examples of activation maps from one sterile pericarditis dog during right atrial pacing from two right atrial sites (sites ii and iii) at two cycle lengths (300 and 150 ms). In these examples, there is conduction across the crista terminalis from right-to-left at both pacing cycle lengths. These observations were consistent in all studies. In these two examples, as in all other instances, neither pacing cycle length nor pacing site (site ii or iii) made any substantive difference in the nature of right-to-left atrial conduction across the crista terminalis. Although there are some changes in conduction time (noted by relative crowding of isochrones), conduction across the region of the crista terminalis during pacing at 150 ms is little changed compared with pacing at the 300-ms cycle length.

Figure 6, A and B, diagrammatically shows the variations in right-to-left atrial activation across the crista terminalis observed in the 17 dogs studied. The thickness of the arrows shows the relative dominance of the activation wave front. Figure 6A shows variations in conduction in relation to the superior vena cava and Bachmann’s bundle during right atrial free wall pacing. Note that activation proceeds across the crista terminalis from the right atrium to the left atrium in 16 dogs. However, in one dog with pericarditis, because of slow epicardial conduction from the pacing site, activation breakthrough in the midportion of Bachmann’s bundle via atrial septal activation (shown by asterisk) proceeded activation across the crista terminalis. Figure 6B indicates right-to-left atrial activation across the crista terminalis in relation to the inferior vena cava during right atrial free wall pacing. There were some variations in conduction. In 16 of these 17 dogs, right-to-left atrial conduction across the crista terminalis was noted. In one dog, right-to-left atrial activation relative to the inferior vena cava occurred inferior to the latter structure. In 6 of these 17 dogs, we performed a pace mapping study from two different right atrial sites (sites ii and iii) in each dog.
pacing from these two different sites, the relative dominance of the two wave fronts did not change, although conduction times from the two different pacing sites to the right superior pulmonary vein were different (from site ii, 10 ms, vs. from site iii, 20 ms) (Fig. 5). The relative dominance of two wave fronts was not affected by pacing cycle length (Fig. 5, top right and bottom right).

**Activation Across the Crista Terminalis During Atrial Flutter or Atrial Fibrillation**

Figure 7 shows a representative example of an atrial activation map during one cycle (168 ms) of sustained atrial flutter due to a figure-eight (double loop) shape reentry (solid arrow) in a dog with sterile pericarditis. In this example, as our laboratory has recently shown (34), induced sustained atrial flutter is associated with two reentrant circuits, which share a common pathway in the right atrial free wall. These two circuits share a common pathway in the anterior right atrial free wall. This representative example well illustrates that a daughter wave from the reentrant circuit in the right atrial free wall crosses the crista terminalis from right to left (indicated by ⭐). Our findings in the atrial flutter examples in this study confirmed the data of Uno et al. (34), showing right-to-left atrial activation across the crista terminalis in all examples of figure-eight atrial flutter and in examples of single-loop reentry atrial flutter (similar to typical or reverse typical atrial flutter in patients) where the line of block between the vena cavae was not complete (i.e., conduction occurred at least at one end of the line of block).

Figure 8 shows a representative activation map of six 90-ms windows during atrial fibrillation. For the entire duration of the episode, a stable reentrant circuit with a regular cycle length of 96–98 ms was present in the left atrium. This reentrant circuit drove the atria, but the right atrium and a small portion of the left atrium could not follow the very short reentrant circuit “drive” cycle length in a 1:1 manner, resulting in fibrillatory conduction (18). These points are even more clearly demonstrated in Fig. 9, in which left atrial sites a–d (identified in window 1 of Fig. 8) occur at the drive cycle length, as do right atrial sites e and f but not sites g and h (sites e–h are also identified in window 1 of Fig. 8). Thus, as shown in Fig. 9, a small portion of the intercaval region was activated in a 1:1 fashion by the stable reentrant circuit of short cycle length. But as shown during window 3 of Fig. 8, functional block lines developed in the region of the crista terminalis. Therefore, the wave front that came from region (a circuit similar to that of reverse typical atrial flutter in patients). The other circuit travels around the functional line of block in the right atrial free wall. These two circuits share a common pathway in the anterior right atrial free wall. This representative example well illustrates that a daughter wave from the reentrant circuit in the right atrial free wall crosses the crista terminalis from right to left (indicated by ⭐). Open asterisk, entrance of the wave front from the epicardium to the atrial septum. Solid arrows, the reentrant circuit; gray arrows, daughter wave fronts. Other abbreviations and symbols are as shown in Figs. 1, 3, and 4. *Epicardial breakthrough from the septum to Bachmann’s bundle.
the stable reentrant circuit of short cycle length could not activate the right atrial free wall during this window. However, as clearly evident in windows 1 and 2 of Fig. 8, daughter waves from the left atrial reentrant circuit crossed the crista terminalis from left to right. Note also in window 4 of Fig. 8 that a wave front crossed the crista terminalis from right to left. In all examples of atrial fibrillation, due to this mechanism, left-to-right atrial activation was always seen.

DISCUSSION

In this study, we present data that demonstrate that there is no fixed conduction block along the crista terminalis in either direction (right-to-left atrium or left-to-right atrium) during 1) atrial pacing in either the normal canine atria or in the canine sterile pericarditis model, or 2) induced atrial flutter or induced atrial fibrillation in the canine sterile pericarditis model. During induced atrial fibrillation, conduction block lines sometimes appeared in the region of the crista terminalis, but such block was only temporary because it was functional. The data from the atrial flutter studies are especially noteworthy in this regard, because the presence of block between the vena cava is
particularly important for the development and maintenance of atrial flutter (35). In fact, in most animal models of atrial flutter, block must be created between the vena cavae to induce atrial flutter. This was first recognized by Rosenbleuth and Garcia-Ramos (26), who created a crush lesion between the vena cavae. This model has subsequently been used (2) or modified by others (12, 38). In another model, Rosenbleuth and Garcia-Ramos (26) painted the sulcus terminalis with cocaine to obtain block, which was transient, but which permitted a period of stable atrial flutter until the cocaine-induced block wore off. The point is that, in the normal canine atria, block between the vena cavae was not normally present and had to be created. Otherwise, induction of atrial flutter in the normal canine atria was a rare event, as first emphasized by Lewis et al. (17).

Related Studies in Humans

It seems clear from observations in humans that an area of block in the lateral right atrium between the vena cavae is present during classical atrial flutter (5–7, 10, 11, 20, 21, 29). Cosio et al. (5–10) in studies of both typical and reverse typical atrial flutter were the first to report double potentials (which virtually always denote conduction block; see Ref. 31) recorded along the lateral right atrium in the region of the crista terminalis and suggested the block was functional. However, subsequent studies by Olgin et al. (20, 21) indicated that the crista terminalis was the anatomic structure where the line of block between the vena cavae occurred during atrial flutter in humans. Olgin et al. (20, 21) further suggested that this line of block in the crista terminalis was fixed. They also speculated that structural abnormalities of the crista terminalis on a microscopic level were the primary abnormalities in patients with atrial flutter, which, they suggested, may explain the occurrence of atrial flutter even in patients with grossly normal atria (20, 21).

Subsequently, Shah et al. (29) suggested that the area of the line of block in atrial flutter corresponds broadly to the expected position of the crista terminalis, although the irregular outline and scattered distribution of double potentials indicated the area of block to be beyond this discrete anatomic structure. Interestingly, the latter is also true in some animal models of atrial flutter (3, 19, 30, 34) and a recently reported catheter electrode mapping study (14) of atypical atrial flutter in patients. Also recently, Arenal et al. (1) suggested that in patients with typical atrial flutter, rate-dependent block across the crista terminalis may occur, and Schumacher et al. (28) showed in patients that functional block in the crista terminalis can be elicited by introduction of premature beats with a short coupling interval. In addition, a retrospective analysis of data from a study (4) in patients describing a method for intraoperative atrial activation mapping can be interpreted as consistent with activation bidirectionally across the crista terminalis. Most recently, Friedman et al. (13) in a mapping study of atrial flutter in patients found the posterior line of block not to be in the crista terminalis but rather in the posteromedial right atrium in the region of the sinus venosa.

Additional Relevant Studies

Previous studies (30, 33) in the canine sterile pericarditis atrial flutter model demonstrate that during atrial flutter, a line of functional block develops in the region between the vena cava during a preceding transitional rhythm of atrial fibrillation. Furthermore, we (36) have shown that the spontaneous onset of atrial flutter in patients after open-heart surgery is preceded by a transitional rhythm of atrial fibrillation. These observations are consistent with the observations first reported by Watson and Josephson (37), that typical atrial flutter induced in patients during electrophysiological study generally starts after an initial period of atrial fibrillation. We (30, 35, 36) previously suggested that a transitional rhythm is usually necessary for the development of typical atrial flutter in patients because it is during the transitional rhythm that the requisites for initiation of typical atrial flutter, particularly a line of block between the vena cava, develop. The important point is that there is no complete fixed anatomic reentrant circuit waiting to be engaged by a premature atrial beat or beats. Rather, it is during the transitional rhythm that the functional requisites for the atrial flutter reentrant circuit develop. The present study lends further support to this concept by demonstrating conduction across the crista terminalis in both directions under a variety of conditions.

Summary and Conclusions

With the use of high-resolution mapping, we showed in the normal canine atria and in the canine sterile pericarditis model that there is no fixed conduction block across the crista terminalis. Therefore, when block in the region of the crista terminalis occurs in this model, as during atrial flutter, it is functional. We further extrapolate from these data and the weight of evidence in other studies in animal models and patients to suggest that during atrial flutter in patients, block in the region of the crista terminalis, which is critical for the establishment of stable atrial flutter, is very likely functional. Furthermore, the block may not be in the crista terminalis itself.

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