Intraoperative mapping of the right atrial free wall during sinus rhythm: variety of activation patterns and incidence of postoperative atrial fibrillation

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Abstract

Objective: The atrial conduction properties associated with cardiac disease are speculated as the background of postoperative atrial fibrillation (POAF). We examined the atrial conduction patterns and conduction properties during sinus rhythm (SR) in patients that had undergone cardiac operations and evaluated the incidence of POAF in all patients. Methods: Fifty-two patients with stable SR who underwent cardiac surgery, with a diagnosis of valvular disease in 25, ischemic heart disease in 24, and others in 3, were enrolled in this study. The epicardial recordings were made using a mapping system with 60 unipolar electrodes placed on the right atrium (RA) intraoperatively. The activation patterns of the RA were assessed, and the longitudinal, transverse and oblique conduction velocity and max anisotropic ratio were also examined. Results: Sinus activation was initiated from various sites (single origin at the high-lateral RA in 40, mid-lateral RA in 4, low-lateral RA in 2, and multiple origins in 6 patients) and it demonstrated anisotropic conduction (1.8/0.6) with the longitudinal conduction being more rapid than transverse and oblique conduction. Fifteen patients demonstrated non-uniform activation patterns such as, a localized conduction delay in seven, functional conduction block in two and mosaic-activation pattern associated with multiple origins in six. A total of 21 patients (44%) developed POAF. A conduction delay and mosaic activation pattern was found significantly more often in patients with POAF than in patients who remained in sinus rhythm. Multivariate analysis revealed that non-uniform activation pattern (odds ratio = 8.71; 95% confidence interval [CI] = 1.74—43.67; \( p = 0.008 \)) and TR (odds ratio = 4.95; 95% CI = 1.14—21.37; \( p = 0.032 \)) were independently associated with the development of POAF. Although all patients had converted to SR at the time of discharge, the administration of antiarrhythmic drugs caused sinus bradycardia in two patients who demonstrated a mosaic activation pattern in RA. Conclusions: Cardiac surgery patients exhibited a variety of sinus activation patterns, which also provided an arrhythmogenic substrate for POAF. A better understanding of the sinus activation using an intraoperative mapping system may provide benefit in the clinical management of POAF.

Keywords: Sinus rhythm; Atrial mapping; Cardiac surgery

1. Introduction

Postoperative atrial fibrillation (POAF) is a common complication during the perioperative course of cardiac surgery, which affects the hospitalization duration and increases the health care cost. POAF occurs in approximately 10–65% of patients undergoing cardiac surgery [1]. Several pharmacologic and non-pharmacologic therapies including beta-blockers, amiodarone, and atrial pacing have been shown to successfully prevent POAF [2–4]. However, these strategies do not eliminate POAF in all patients, and they may also be unwarranted in patients deemed unlikely to experience POAF.

Preoperative and intraoperative factors such as advanced age, history of previous AF, chronic pulmonary disease, atrial myocardial ischemia, sudden beta-blocker withdrawal, excess circulating catecholamines, and prolonged aortic cross-clamping have been shown to be risk factors for POAF [5]. Recently, various electrophysiological studies have been performed to predict the occurrence of POAF and have demonstrated that patients who develop POAF have an intrinsic atrial electrical abnormality. A prolonged P-wave duration measured on the signal-averaged electrocardiogram is a reliable predictor of POAF [6]. This finding implies a lengthened atrial activation time and depressed atrial conduction. Heterogeneous propagation of sinus impulses is assumed to be the substrate for POAF.

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Recently, some animal studies have demonstrated that electrophysiological abnormalities such as conduction delays or conduction block of the atrial conduction are observed in structural heart disease [7—9]. These findings suggest that cardiac disease may provide an atrial substrate for initiating reentrant arrhythmias. Given these abnormalities, we hypothesized that patients with heart disease have a structural and functional heterogeneity of the atrium even during sinus rhythm (SR), which leads to POAF. The main purposes of our study were (1) to examine the activation patterns and conduction properties of the right atrium (RA) during SR by intraoperative mapping in patients with heart disease, and (2) to examine the occurrence of POAF in all patients.

2. Materials and methods

2.1. Patients

We studied 52 patients with stable SR who underwent cardiac surgery. The patients included 35 men and 17 women ranging in age from 34 to 81 years (mean 62 ± 11 SD). The preoperative diagnoses were as follows: ischemic heart disease in 24 patients, aortic valve disease in 15, mitral valve disease in 10, atrial septal defect in 2, and left atrial myxoma in 1. The clinical characteristics and surgical procedures performed are summarized in Table 1. All the mitral valve replacements and tumor extirpation were performed using superior a transeptal approach. There were 22 patients with minor tricuspid valve regurgitation (TR) graded on a scale of +1 or 2 on the basis of the gradiation of the TR severity according to the color Doppler flow criterion. None of these cases needed a concomitant surgical repair. A grade +3 TR was observed only in one patient, but due to complicating cancer, only a coronary revascularization by an OPCABG was performed. Patients having an episode of any arrhythmia or congestive heart failure within 1 month were excluded from the study. All patients gave informed consent to the study, which was approved by the hospital ethics committee.

2.2. Intraoperative mapping and analysis

The heart was exposed by a median sternotomy. Before the institution of cardiopulmonary bypass, epicardial recordings were made using a mapping system with 60 unipolar electrodes on the right atrial free wall during SR. The card-type electrode had 60 unipolar electrodes, 2 mm in diameter each, mounted in six rows of 10 on a flexible plastic rectangular sheet. Two sizes of card-type electrodes (small: 4 cm × 3 cm, large: 7 cm × 6 cm) were used selectively in accordance with the size of the RA. Each unipolar site contained a fine silver wire electrode separated by a distance of 3—5 mm. The unipolar data were recorded at a frequency response of 50—1000 Hz. A computer was used to store the digitalized unipolar data and display the waveforms. The card-type electrode was attached to the RA to record 60 local right atrial epicardial electrograms in 3 seconds. The recording area was on the lateral free wall, with the lateral rows of electrodes parallel to the superior—inferior vena cava line. The upper corner of the rectangular sheet was as close as possible to the RA-superior vena cava junction (sinus node lesion). When the small electrode card was used, the upper half and lower half of the RA were mapped differently. A computer program was used to determine the local activation times from unipolar tracings. The time of the local activation was defined as the peak negative derivative of the major deflection of the unipolar complex.

Activation maps with isochrones were drawn for three consecutive beats with a window of analysis of 120 ms each. The activation patterns of the RA were assessed, and the longitudinal, transverse, and oblique conduction velocities from the earliest activation site were also examined in the second beat. The conduction velocity of an activation wave was calculated as the propagated distance divided by the conduction time difference. Activation times of at least four consecutive electrode terminals along longitudinal and transverse lines were used to determine the conduction velocity. The conduction velocity in the oblique lines was determined by the activation time difference between the earliest activation site and local activation time of any electrode oriented at a 60° angle with respect to the transverse line (Fig. 1).

The anisotropic ratio was calculated as the maximal conduction velocity divided by the minimal conduction velocity among three directions. A conduction delay was defined as a local conduction velocity of ≤ 30 cm/s, associated with a bunching together of the isochrones. We also defined functional block as decremental conduction leading to a difference in the propagation or conduction properties or both.

2.3. Postoperative monitoring

All patients were monitored continuously by telemetry and Holter monitoring for 5 days after the operation and 12-
lead ECGs were obtained when necessary to confirm rhythm abnormalities. Thereafter they had daily electrocardiograms during the hospital stay. Atrial fibrillation was defined as any atrial activity that was either not discernible or completely unorganized, accompanied by an irregular ventricular rate. In this study, we included episodes of atrial fibrillation lasting longer than 1 hour.

2.4. Management of POAF

Digoxin was administered to the patients with atrial fibrillation and with ventricular response rates greater than 100 beats/min. If POAF persisted for more than 2 days after the administration of digoxin, oral pilsicainide was given at 50 mg three times a day.

2.5. Statistical analysis

All continuous variables are expressed as the mean ± SD. Categorical variables are presented as n (%). Differences in the average of the mean conduction velocity in the respective direction was tested by the Wilcoxon’s signed rank test. Univariate comparisons between patients developing/not developing atrial fibrillation were made by the $\chi^2$ test for categorical data, and by the Mann–Whitney test for continuous data. A multivariate logistic regression analysis was performed using the preoperative characteristics and conduction properties of the patients as independent covariates and the occurrence of postoperative atrial fibrillation as a dependent variable, by selecting a forward-stepping selection method with maximum likelihood estimates and default criteria. A p-value less than 0.05 was considered significant. All the statistical procedures were performed by the SPSS 11.5 statistical package (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. The activation pattern and conduction properties of the right atrium

Initiation of sinus activation was distributed widely along the line between the superior vena cava (SVC) and inferior vena cava (IVC). Among 52 patients, 40 exhibited an impulse originating in the high-lateral RA (sinus node region) and propagating radially toward the atrioventricular groove antero-inferiorly (Fig. 2A). A distinct origin was observed at the mid-lateral RA in four patients and in the low-lateral RA (beside the IVC) in two patients (Fig. 2B and C). In the other six patients, more than two origins existed in the lateral RA simultaneously. The major propagation direction was determined by a single initiation site. The activation from the mid-lateral RA spread anteriorly towards the AV groove, and the activation from the low lateral RA (beside the IVC) spread superiorly toward the RA appendage.

The conduction velocity was examined only in those activation maps presenting an activation pattern with a single initiation site. Sinus activation originating in the lower RA was excluded from the study. The mean conduction velocity from the earliest activation site was 125 ± 53 cm/s.
in the longitudinal direction, 97 ± 45 cm/s in the transverse direction, and 82 ± 19 cm/s in oblique direction. The mean anisotropic conduction ratio was 1.8 ± 0.6. The longitudinal conduction was significantly more rapid than that in the transverse (p < 0.001) and oblique directions (p < 0.001).

The atrial activation patterns in the isochronal maps were visually uniform in 37 of 52 patients. In the remaining 15 patients, the activation map displayed a non-uniform activation pattern in every atrial beat. Crowding of isochrones, which corresponded to a conduction delay, was observed in seven patients. Fig. 3A shows an example of a conduction delay in which the transverse conduction velocity is remarkably delayed, compared to the longitudinal conduction velocity. The site and direction of the conduction delay was different in each patient.

Functional conduction block was observed in only two patients. A definite conduction block line was located in the high RA in both patients (Fig. 3B). Another six patients demonstrated a plural initiation of the atrial activation. The wavefront from each initiation collided in the free wall, resulting in a confused, mosaic activation pattern (Fig. 4). The underlying cardiac disease included in each activation pattern is shown in Fig. 5. No relationship was observed between the type of non-uniform activation pattern and cardiac disease.

### 3.2. Incidence of POAF

A total of 21 patients developed POAF, with an overall incidence of 44%. In the majority of these patients, POAF occurred on postoperative Day 2, and 15 (75%) patients developed POAF within 3 days after the operation. Atrial premature contractions (APCs) occurred before the onset of the POAF in five patients. One patient initially had atrial tachycardia, which lead to POAF thereafter. The mean AF duration was 1.9 ± 1.7 (1—7) days. Nineteen (81%) of 21 patients were given digoxin to achieve rate control; 8 did not revert to SR and required additional oral pilsicainide. All patients had converted to SR at the time of discharge. Two cases needed temporary pacing due to sinus node dysfunction lasting a few days.

### 3.3. Clinical characteristics and conduction properties in the POAF patients

Table 2 lists the preoperative clinical characteristics and conduction properties of the patients classified by the maintenance of SR or development of POAF. The patients with POAF were older than those who remained in SR (59 ± 11 vs 67 ± 8, p = 0.009). No significant differences in the underlying disease were noted, apart from an expected excessive number of TR in patients who had developed POAF (14 [66%]...
There were significantly more patients who had a previous history of paroxysmal atrial fibrillation (PAF) (3 [14%] vs 0, \( p = 0.03 \)) or antiarrhythmic drug treatment (5 [23%] vs 1 [3%], \( p = 0.02 \)) in the POAF group than in the group who remained in SR.

With regard to the conduction properties, there were no observed significant differences between the groups in the directional conduction velocity and anisotropic conduction ratio; however, more patients in the group that developed POAF had some abnormality of the activation, i.e., a non-uniform activation pattern (13 [61%] vs 3 [9%], \( p < 0.001 \)).

A non-uniform activation pattern was observed in five of eight patients requiring antiarrhythmic drug treatment postoperatively (two conduction delays, one conduction block, and two mosaic activation patterns). The two patients demonstrating a mosaic activation pattern developed incompetent sinus node function after the administration of antiarrhythmic drugs. The three patients free from conduction abnormalities each had a prior history of antiarrhythmic drug treatment for PAF.

### 3.4. Predictor of POAF

A multivariate logistic regression analysis was performed to identify the independent predictors for the POAF. The results demonstrated that the non-uniform activation pattern and TR were significant independent predictors for the POAF. When the presence of the aging of patients was combined with these predictors, a much better likelihood of the occurrence of a POAF was obtained (Table 3).

### 4. Discussion

#### 4.1. Abnormal sinus initiation

Since Keith and Flack [10] reported that the sinus node, located at the junction of the superior vena cava and the RA, is the activation origin for the RA, developments in cardiac
electrophysiology have shown that there are cases demonstrating various early activation sites during sinus activation. According to a mapping study by Boineau et al. [11], a subsidiary origin known as the pacemaker complex was observed along the long axis of the crista terminalis, extending from the SVC-RA junction to the IVC-RA junction. The pacemaker shifts its location from one area to another abruptly with autonomic changes, and such areas are occasionally widely separated. This fact suggests that there is a limited preferential exit from the sinus node to the myocardial fibers, and the determination as to which is used is modulated by the distribution of adrenergic and muscarinic cholinergic receptors [12]. Consequently, when an early excitation site unlike a typical sinus node site is observed at the mid- or lower RA, it may also be affected by temporary autonomic changes accompanying surgical invasion.

We found that multiple ectopic origins were present simultaneously on the free wall of the right atrium in six patients. A similar finding was that, outside of the effects induced by the autonomic change, such origins were also observed during escape rhythms, and when activation broke through to the free wall from the areas most separated from the pacemaker complex, the septum or left atrium, multiple activations arose [11]. However, the excitation patterns on the right atrial free wall were comparatively uniform in each case, which does not explain the mosaic patterns presented in all of the cases that we mapped. A recent electroanatomic mapping study in sinus node disease patients found that the pacemaker complex was shifted caudally; sinus activation from this location was accompanied by a conduction delay or block in the area of the crista terminalis; and longitudinal, non-uniform, circuitous conduction occurred on the atrial free wall [13]. These conditions are not regarded as particular to patients with symptomatic sinus node disease and are also thought to occur in patients with heart failure [14]. Our findings also suggest a high possibility that functional remodeling of the atrial myocardium occurred from the sinus node to the crista terminalis. In actuality, postoperative sinus node dysfunction was observed in two patients demonstrating mosaic patterns.

4.2. Structural changes and conduction properties

It is generally accepted that the preferential spread of conduction along the atrial muscle bundles and the orientation of the muscle fibers result in rapid and uniform activation in the normal atrium, although the architecture of the atrium is highly non-uniform. In our study, sinus activation demonstrated anisotropic conduction, in which the longitudinal conduction velocity was higher than the transverse and oblique conduction velocities, even if the activation pattern was quite uniform macroscopically. One explanation for this finding is that the conduction velocity was rapid in the crista terminalis, which is the most developed muscle fiber bundle in the RA. This finding also concurs with the report by Spach et al. [15] in which the found that the conduction velocity was higher longitudinally than transversely in myocardial fibers.

The spread of conduction from a cardiac origin is restrained by naturally occurring barriers and orifices. The crista terminalis is well known as an anatomic region demonstrating marked anisotropy of conduction because of directional differences in gap junction distribution and functional block during atrial flutter [16,17]. A recent rabbit heart study revealed that atrial pressures affect the architecture of the myocardium, resulting in slowed conduction and increased intra-arterial conduction block [7]. On the basis of experimental evidence indicating that a thinner layer was stretched more than a thickened layer [18], the authors theorized that conduction disturbances may also occur in thin areas between large trabeculae. Anatomically, one or two upper pectinate muscles were very large and extended to the RA [19]. In our experiment, functional block observed in the high RA suggested that this is an area extremely prone to localized conduction block caused by acute atrial dilation.

Recent studies investigating pathologies representing AF precursor conditions have provided some understanding of regional structural and functional changes of the atrial myocardium. Experiments using canine models of MR or CHF found that chronic atrial dilation increases interstitial fibrosis and fiber separation with chronic inflammation, resulting in a regional conduction delay or conduction block [8,9]. Locations of interstitial fibrosis extended over the entire atrial region, but the occurrence of this phenomenon along comparatively healthy muscle fibers suggested that the location of conduction disturbances depends on individual anatomic configurations of the atrial muscle bundles. In our experiment, we observed various regional conduction delays which differ in seven individuals. The fact that structural heart disease was present in five of those individuals, including those with TR, also suggests the possibility of atrial remodeling caused by chronic atrial stretching.

In contrast, our study also demonstrated that ischemic heart disease without any structural disease may include an atrial conduction disturbance. A canine study also observed slowing of conduction due to atrial ischemia [20]. This electrophysiological and histological examination confirmed that a severe conduction delay arose at sites of extensive ischemia-induced necrosis, resulting in a non-uniform activation pattern.

4.3. Arrhythmogenic substrate and management of POAF

Unlike chronic atrial fibrillation, POAF involves reentry resulting from increased dispersion of the atrial refractoriness [21]. Atrial ischemic injury resulting from aortic cross-clamping during cardioplegic arrest has been suggested as a factor in this dispersion. According to a recent report, an animal study investigating atrial inflammation after atriotomies and pericardiotomies found that such inflammation was associated with atrial conduction abnormalities and POAF [22]. However, the results of our study show that 66% of patients who develop POAF had preexisting conduction abnormalities in the RA. In reality, patients with either a conduction delay or a mosaic activation pattern have a significantly higher incidence of POAF. This finding suggests that, irrespective of surgical invasion, cardiac surgery patients have intrinsic conduction abnormalities in the RA.
providing a basis for unidirectional conduction slowing or block and initiation and maintenance of atrial reentrant arrhythmias, a notion substantiated by prior reports that atrial fibrillation could be induced in 94% of patients experiencing POAF preoperatively [23].

The main objectives in treating POAF include ventricular rate control, conversion and maintenance of SR, and prevention of thromboembolic events. Unlike any other atrial tachyarrhythmias observed clinically, POAF is more likely to convert to SR spontaneously, and 25–80% of patients convert within 24 h [1]. This is the reason that acute ventricular control is given priority over rhythm control in the management of POAF. However, regardless of the occurrence of POAF, the presence of an established arrhythmogenic substrate suggests that active administration of an antiarrhythmic agent is more useful than rate control.

In our study, TR and a non-uniform activation pattern in the RA were predictors of POAF. This finding suggests all the more that an arrhythmogenic substrate in the RA is the target of the POAF treatment. At the same time, it is also possible that patients demonstrating a mosaic pattern of sinus activation experience a reduction in the sinus node function. Caution over the occurrence of bradycardia must always be exercised when administering negative chronotropic agents to such patients. We also observed occurrence of POAF in three patients with a history of PAF preoperatively but without predictors. Ectopic beats originating from the pulmonary veins are well known as the mechanism of PAF. Our finding suggests a possibility that preoperative treatment for PAF effectively suppresses the irritable atrial foci that may provide a substrate for POAF. On this basis, we believe that the use of intraoperative mapping findings to investigate the POAF risk in individual patients may also allow for a selective prophylactic therapy.

5. Limitations

With the 60-channel mapping system that we used, differences in the size of the RA in individual cases and the inability to cover the whole atrium prevented measurement of the atrial conduction time. A prolonged P-wave duration, the purported substrate for reentrant arrhythmias, arises not only from a delayed atrial activation propagation accompanying a non-uniform activation, but depends also on the distance from the sinus origin to the lateral wall of the left atrium, and on the conduction velocity. The former factor is affected by mitral valve disease or other such expansions of left atrial diameter [24], and one case relating to the latter factor included an inter-atrial conduction delay in a patient with PAF [25]. Understanding these conditions requires simultaneous mapping of both atria using a mapping system with more channels.

6. Conclusion

Cardiac surgery patients exhibited a variety of sinus activation patterns which also provided an arrhythmogenic substrate for POAF. The use of an intraoperative mapping system to better understand the sinus activation may be beneficial in the clinical management of POAF.

Acknowledgements

We acknowledge the excellent technical assistance of Makoto Taguchi. We also thank Jhon Martin for preparation of the manuscript.

References


