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Effect of cardiac exposure by median sternotomy on atrial fibrillation cycle length

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Background Epicardial mapping is a powerful tool that has enabled us to gain insight into the electrical phenomena perpetuating atrial fibrillation and has guided the design of surgical and catheter-based therapeutic strategies. However, epicardial data are acquired during abnormal physiological conditions; the patients are anaesthetized, their chests opened, dislocating the heart and exposing it to air of room temperature, and the autonomic tone is modulated due to the surgery. The effect of intra-operative conditions on atrial electrophysiological properties have not been investigated before. Thus in the present study we assessed the atrial cycle length, shown to be an index of atrial refractoriness, and the ventricular rate before and during open-heart surgery in 10 patients with chronic atrial fibrillation and an underlying heart disease.

Methods and Results Using a newly introduced and validated ECG method known as frequency analysis of fibrillatory ECG (FAF-ECG), the atrial cycle length and the ventricular rate were determined just before surgery. After anaesthesia and median sternotomy, epicardial mapping of the entire right atrial free wall was performed. The mean ventricular rate as well as the dominant atrial fibrillation cycle length consistently increased, the former from 71 to 92 beats.min^{-1} (mean of all patients, $P<0{\cdot}05$) and the latter from 156 to 172 ms ($P<0{\cdot}05$).

Conclusions Atrial fibrillation cycle length, an index of atrial refractoriness, is increased as an effect of anaesthesia and heart exposure during open-heart surgery in patients with chronic atrial fibrillation, implying that atrial activation might be altered, which must be considered when interpreting data from epicardial conduction analysis.
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Key Words: Human, atrium, fibrillation, cycle length, open-heart surgery, anaesthesia.

Introduction

To improve our understanding of the mechanisms initiating and perpetuating complex arrhythmias such as atrial fibrillation, exploration of the electrical phenomena in the heart is essential. Such exploration can be accomplished by simultaneously recording the electrical activity at multiple sites within the atria, so-called 'mapping'. Open-heart surgery provides a unique opportunity to perform mapping of the epicardial surface of the heart. Epicardial atrial mapping has previously been performed in laboratory animals and in patients with Wolff-Parkinson-White syndrome with induced atrial fibrillation, and more recently also in patients with chronic atrial fibrillation[1–6]. These studies have provided valuable data on the activation sequence, the organization of the activation and the rate and propagation velocity of the activation waves involved in the fibrillatory process. This increased understanding of the nature of this complex arrhythmia has guided the design of intra-operative and more recently also catheter-based treatment strategies for atrial fibrillation[3,7–18]. However, the price to be paid for such epicardial data is the abnormal physiological conditions under which the data are acquired. The patients are under the influence of various anaesthetic agents and their chests are opened, thereby exposing the heart to air of room temperature. Whether, and if so how, these circumstances affect the electrophysiological properties of the atria, and thereby the electrical activity within the atria, is currently unknown. The purpose of this study was, therefore, to explore the influence of anaesthesia and heart exposure on the electrophysiological properties of the atria in patients with chronic atrial fibrillation. The atrial cycle length, previously shown to be a local index of atrial refractoriness during fibrillation[19–21], and the ventricular rate were measured both before and during the surgical procedure. Here, a new ECG method recently introduced and validated by us, known as frequency analysis of fibrillatory ECG (FAF-ECG), was used to estimate the right atrial fibrillation cycle length non-invasively before surgery[22]. Under intra-operative

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conditions, prior to cardiopulmonary bypass, epicardial mapping of the entire free wall of the right atrium was performed, thus providing data from which the atrial cycle length could be determined. The ventricular rate was also assessed before and during the surgical procedure. In another group of patients, without any cardiac arrhythmia, infra-red imaging of the epicardium was performed during open-heart surgery prior to cardiopulmonary bypass to explore the effect of heart exposure on the epicardial temperature.

Material

Ten patients, three females and seven males, with a history of chronic atrial fibrillation ranging from 5 months to 4 years, undergoing open-heart surgery for ischaemic and/or valvular disease, were included. Their ages ranged from 53 to 83 years with a mean age of 72 years. Their clinical characteristics are summarized in Table 1. In another four patients (mean age 68 years) undergoing open-heart surgery for ischaemic and/or valvular heart disease, infra-red imaging of the exposed epicardium was performed. The study was approved by the Ethics Committee of the Medical Faculty, Lund University, Sweden (approval number LU 184–90) and written informed consent was obtained from all patients before inclusion

Methods

Data acquisition in patients with chronic atrial fibrillation

Before the surgical procedure, a 12-lead surface ECG was measured digitally for 10 min during supine rest (1 kHz sampling rate, 16 bit A/D conversion, equipment supplied by Siemens-Elema AB, Solna, Sweden). Patients were then anaesthetized and the chest was opened using median sternotomy. The anaesthetic agents used in individual patients are given in Table 1. Prior to cardiopulmonary bypass, epicardial mapping of the right atrial free wall was performed. A total of nine recordings was made at 1 min intervals in each patient, using two different electrode arrays (Fig. 1). Both electrode arrays consisted of 56 electrodes, distributed in electrode array A to cover the entire free wall of the right atrium and in electrode array B in a circular fashion. The area covered by electrode array A was 23 cm^2 and that covered by electrode array B 11 cm^2. Three consecutive recordings were made with electrode array A and six consecutive recordings with electrode array B, in the latter case from two different positions (Fig. 2). Each recording consisted of 56 unipolar electrograms and three bipolar surface ECG leads (I–III), simultaneously acquired over 8 s. A Bard Cardiac Mapping System (1 kHz sampling rate, 12 bit A/D conversion and a frequency response of 0·05–300 Hz) was used to acquire the data, which were stored on removable disc media.

Data analysis in patients with chronic atrial fibrillation

The FAF-ECG method was applied to the 10 min pre-operative ECG recording in lead V_1. We have previously shown that this is the best lead for right atrial fibrillation cycle length reproduction[22]. As illustrated in Fig. 3, the FAF-ECG method suppresses the QRST complexes in the ECG and thereafter estimates the frequency spectrum of the residual ECG using Fast Fourier transformation. In the frequency spectrum, a frequency component is normally found in the interval 3–12 Hz, previously shown to represent a spatiotemporal mean of right atrial fibrillation cycle length. The peak frequency of this component is converted to a cycle and named dominant atrial cycle length, $DACL_{ECG}$, where the index shows the reference to the ECG. The FAF-ECG method and its validation are described in more detail elsewhere[22]. The $DACL_{ECG}$ as well as the mean ventricular rate were calculated for consecutive intervals of 8 s each, a total of 75 intervals in each pre-operative recording and patient.

The epicardial recordings were treated as follows: first, all electrograms were high-pass (cut-off frequency 2 Hz) and band-stop (stop-band 45–55 Hz) filtered to remove baseline fluctuations and 50 Hz noise, respectively. Thereafter, the steepest negative deflection of each local activation was taken as the local activation time in the electrograms. The atrial cycle length of an epicardial recordings, ACL_{EPI}, was taken as the peak cycle length of the histogram containing all local cycle lengths over the recording time (8 s) from all 56 electrodes, i.e. similar to the FAF-ECG method, an estimate of the dominant atrial cycle length. To preclude the influence of any systematic methodological differences on the comparison between the atrial cycle length before and during surgery, the FAF-ECG method was also applied to the 8 s electrograms in the epicardial recordings. Here, sums of the individual frequency spectra of each electrogram in a recording were calculated and the peak frequency of the component in the 3–12 Hz range was converted to a cycle length and named $DACL_{EPI}$, where the abbreviation DACL indicates that the FAF-ECG method was used and the index that the cycle length was assessed from the epicardial recordings. From the three surface ECG leads, the mean ventricular rate was calculated for each 8 s recording.

Infra-red imaging

Using a focal plane array infra-red camera (Inframetrics ThermaCAM SC 1000, Inframetrics, Inc., Billerca, MA, USA), infra-red images were obtained of the exposed epicardial surface of the heart. At the time of image acquisition, the temperature in the patient's urinary bladder, here considered to be identical to the temperature of the blood, was noted. From the infra-red images,

Table 1 Patient characteristics

Patient	Sex (M/F)	Age (years)	Basal heart disease	Duration of CAF	LA size (mm)	RA size	Anaesthetic agents
1	F	75	MI	7 month	67	enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, nitrous oxide
2	M	79	AS	>1 year	47	enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, ketamine, isoflurane, nitrous oxide
3	M	73	IHD	4 years	55	enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, isoflurane, nitrous oxide
4	M	83	AS	1 year	55	slightly enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, propofol, nitrous oxide
5	F	70	MI, IHD	8 month	47	slightly enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, isoflurane, nitrous oxide
6	M	81	IHD	>1 year	41	normal	fentanyl, midazolam, pancuronium bromide, isoflurane, nitrous oxide
7	F	77	MI	5 month	53	slightly enlarged	fentanyl, midazolam, suxamethonium chloride, vecuronium bromide, isoflurane, nitrous oxide
8	M	77	MI, AS	2 years	59	markedly enlarged	fentanyl, midazolam, suxamethonium chloride, vecuronium bromide, isoflurane, nitrous oxide
9	M	53	MI	2 years	65	normal	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, propofol, nitrous oxide
10	M	55		6 month	45	slightly enlarged	fentanyl, midazolam, pancuronium bromide, suxamethonium chloride, propofol, nitrous oxide
Mean		72		16 month	53		

CAF=chronic atrial fibrillation; LA=left atrium; RA=right atrium; MI=mitral valve insufficiency; AS=aortic valve stenosis; IHD=ischaemic heart disease. The LA size was determined by transthoracic echocardiography whereas the RA size was visually estimated during surgery.

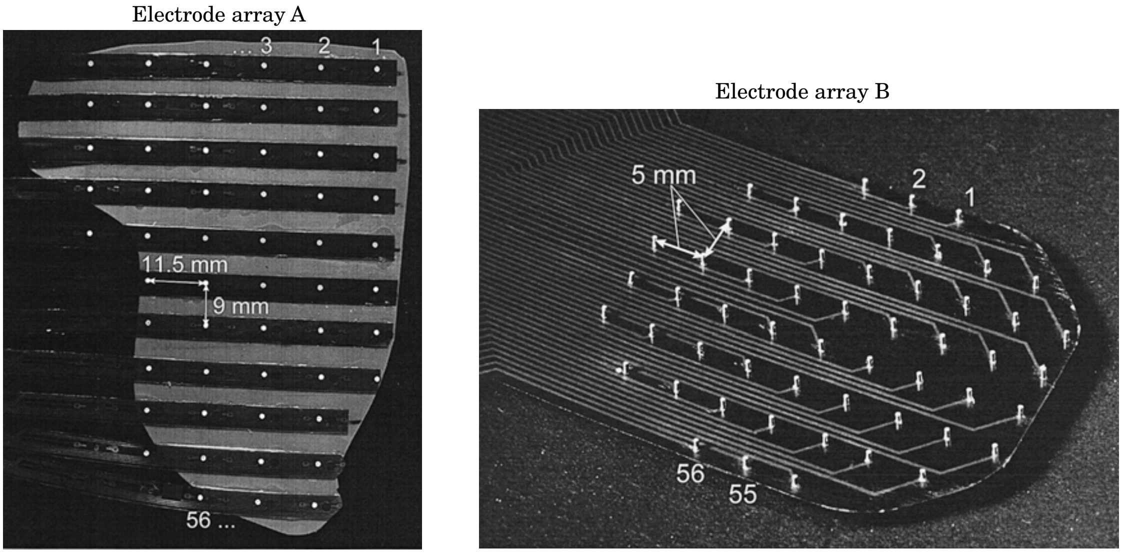

Figure 1 **The two electrode arrays used to acquire epicardial data, shown from the electrode side. Electrode array A (left panel) was designed to cover almost the entire epicardial free wall of a normal-sized right atrium, the distance between the electrodes being 11·5 and 9 mm, respectively, in different directions. The electrodes of electrode array B (right panel) were arranged in a circular fashion with a distance between the electrodes of 5 mm in both directions. The contact area of each electrode was 0·8 mm^2 and 0·2 mm^2 in electrode array A and B, respectively. Both electrode arrays were flexible to allow firm contact of all electrodes with the epicardial surface.**

the absolute temperature of the epicardial surface was determined with an accuracy of 1°C and with a spatial resolution between adjacent areas of 0·1°C. The lowest temperature of the exposed right atrial free wall epicardium was determined as was the maximum temperature difference within an area of approximately 3 cm^2 at the right atrial free wall. Areas with visual presence of epicardial fat were excluded from the analysis.

Statistical analysis

To test whether there were any significant differences in individual patients in mean ventricular rate and dominant right atrial cycle length, respectively, during surgery compared with before surgery, t-tests were used. Input data were chosen as the values from the 75 consecutive 8 s intervals before surgery and the three consecutive 8 s intervals (recordings) during surgery. A *P* value less than 0·05 was considered significant. Paired t-tests were also used to compare the mean values of all the patients before and during surgery.

Results

The results from the 10 patients with chronic atrial fibrillation are summarized in Table 2. Another two patients were excluded from the study, one due to incomplete recordings and another to a poor signal-to-noise ratio in the epicardial recordings caused by marked fibrosis of the atrial epicardium. In nine of the 10 patients, the mean ventricular rate over 8 s was higher during surgery than before, the difference being significant in seven of the patients. In contrast, the dominant right atrial cycle length was in general longer, i.e. the right atrial rate was lower, during surgery than before surgery, although the difference was only significant in half of the patients (Fig. 4). Regarding the mean value of the whole group of patients, both the mean ventricular rate and the dominant right atrial cycle length were significantly prolonged during surgery compared with before. The spatial differences between the posterior part of the right atrial free wall and the right atrial appendage, given as the ranges of the cycle lengths in these two areas, showed a spatial and/or temporal variation ranging from 0 to 35 ms. The two different methods used to determine the dominant cycle length in the epicardial recordings (peak of the cycle length histogram and the FAF-ECG method) gave very consistent results with the same statistical significance.

From the infra-red images, it was obvious that the temperature at some of the exposed areas of the right atrial free wall epicardium was lower than the blood temperature. The maximum difference between blood temperature and the temperature of the right atrial free wall epicardium varied between 2 and 5°C in different patients, whereas the maximum temperature difference within a 3 cm^2 area at the right atrial free wall varied between 1 and 1·5 °C. The lowest epicardial temperature was consistently found close to the apex of the right atrial appendage. One of the infra-red images of an exposed heart is shown in Fig. 5.

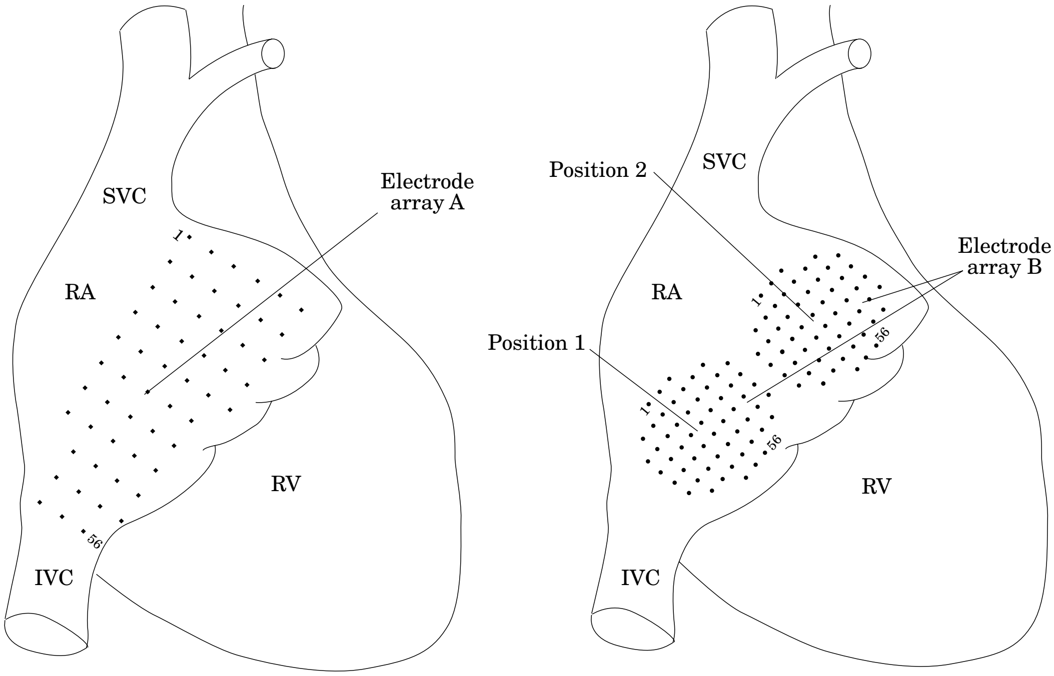

Figure 2 **The recording positions at the epicardial right atrial free wall. Three consecutive recordings were made with electrode array A, positioned as shown in the left panel. Six consecutive recordings were made with electrode array B from two different positions according to the right panel. The distance between the borders of the areas covered by position 1 and 2 was approximately 1 cm (SVC=superior vena cava, IVC=inferior vena cava, RA=right atrium, RV=right ventricle).**

Discussion

In this study, we have shown that in patients with chronic atrial fibrillation, the right atrial cycle length and the ventricular rate are markedly modulated during anaesthesia and heart exposure compared to the resting conscious state immediately before surgery.

The right atrial cycle length before surgery was assessed using a new ECG method, providing an estimate of the dominant right atrial cycle length. As only the dominant atrial cycle length and no other statistics, e.g. the median cycle length, was available in the pre-operative situation, we chose also to estimate these statistics from the intra-operative data to allow direct comparison. When analysing the intra-operative data, two different methods were used to estimate the dominant right atrial cycle length. One method estimated the local activation times and then calculated a histogram containing spatial, temporal and local fibrillation cycle lengths; the frequency analysis method, as used for the pre-operative data, but now applied to the epicardial electrograms was also used. As these two methods applied intra-operatively gave very consistent results, it is strongly suggested that the differences between electrophysiological properties before and during operation are due to true changes in the physiological conditions.

As the median atrial cycle length has been assessed in previous mapping studies of human atrial fibrillation, comparison with these data is not fully relevant[4,6]. Assuming a normal distribution of the atrial fibrillation cycle length, the mean, the median and the dominant cycle length are all identical. However, previous data indicate that this is not always the case with the atrial cycle length during fibrillation[4,6].

A striking result in the present study is that the ventricular rate consistently increased while the atrial rate decreased as a result of the anaesthesia and the heart exposure. The increase in ventricular rate is probably due to a change in sympathetic tone, while the depression of the atrial rate was probably due to an increase in atrial refractoriness; it has previously been shown that these two latter variables strongly correlate during fibrillation[19–21].

Factors that, in turn, may affect atrial refractoriness include changes in the tone of the autonomic nervous system, administration of anaesthetic agents, stretching or compression of parts of the myocardium due to the opening of the chest and cooling of (parts of) the myocardium due to exposure to air of room temperature. We know that an increase in sympathetic tone causes not only an increase in ventricular rate but also a shortening of the atrial fibrillatory cycle length[23]. That the atrial fibrillatory rate decreased intra-operatively, suggests that other factors may dominate the change in sympathetic tone in the atria.

The influence of various anaesthetic agents on the electrophysiological properties of the myocardium is sparsely reported in the literature, and only occasionally has the combination of two or more agents been

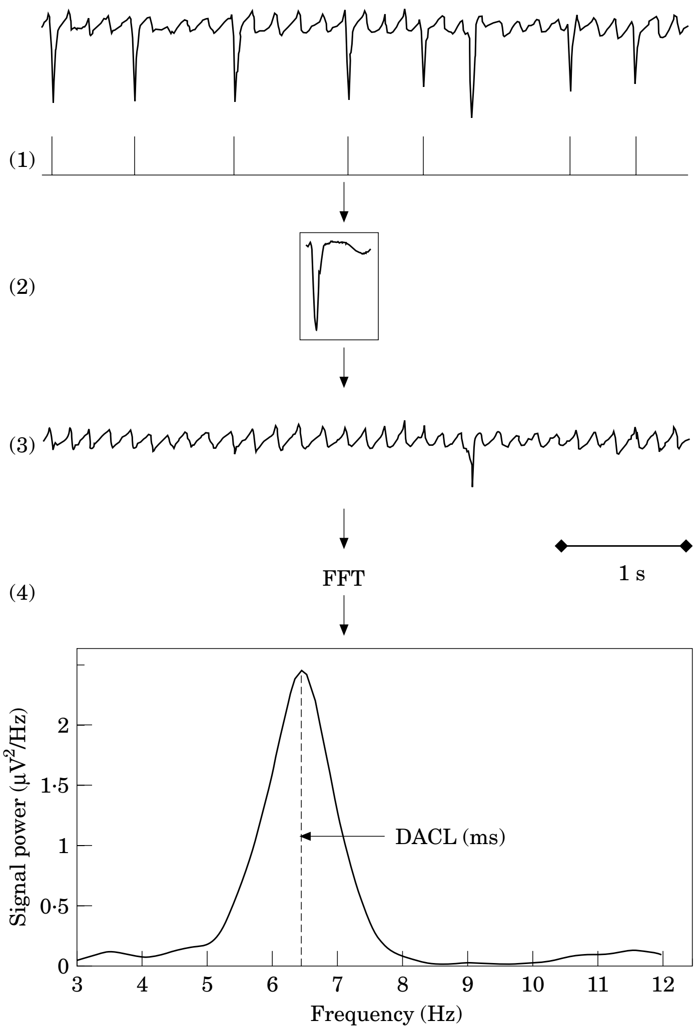

Figure 3 **The different steps of the FAF-ECG method. (1) Classification of QRST morphology and alignment of beats were conducted using a cross-correlation procedure. (2) An average of the time-aligned QRST complexes was calculated and (3) subtracted from the identified QRST complexes. Finally (4), the frequency distribution of the residual ECG was estimated using fast Fourier transformation (FFT), where the dominant frequency component in the 3–12 Hz range was identified and the peak frequency was converted to a cycle length and named DACL.**

investigated[24–29]. The available data show that some of the agents used increase atrial refractoriness, some decrease it and in many no significant effect has been documented.

The effect of stretching and/or compression of the atrial myocardium on the atrial refractory period is somewhat contradictionary in the literature. While one study has shown that acute dilatation of the dog atria prolonged the atrial refractory period and also increased the dispersion of refractoriness due to heterogeneous stretching of the atrial myocardium[30], another study showed that increased pressure in the isolated rabbit heart shortened the atrial refractory period[31].

The influence of temperature on refractoriness and conduction velocity was earlier investigated in isolated strips of rabbit atrium. Here it was found that the atrial refractoriness was prolonged and the conduction velocity decreased when the temperature was lowered[32]. The change in temperature from 37 to 27°C resulted in an almost linear change in both refractoriness and conduction velocity. The results from the infra-red imaging in this study revealed that the temperature in some areas of the epicardium decreases up to 5°C during heart exposure which, assuming a linear relationship between temperature and refractoriness and also between refractoriness and cycle length, would give a prolongation of the cycle length of the

Table 2. The mean ventricular rate and the dominant right atrial cycle length under preoperative and intra-operative conditions, respectively

Patient	Pre-operative				Intra-operative						
						ACL_{EPI} (ms)				$DACL_{EPI}$
	Mean HR (beats.min^{-1})		$DACL_{ECG}$ (ms)		Mean HR (beats.min^{-1})	Entire RAFW		Posterior RAFW	RAA	Entire RAFW
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Mean ± SD	Range	Range	Range	Mean ± SD
1	54 ± 3	48–60	157 ± 9	146–187	57 ± 2	183 ± 3*	180–185	180–195	170–175	185 ± 5*
2	90 ± 5	78–102	164 ± 15	127–193	128 ± 8*	171 ± 3	170–175	170–175	155–165	165 ± 1
3	81 ± 4	72–90	172 ± 8	157–190	85 ± 3	178 ± 3	175–180	175–180	170–185	178 ± 4
4	67 ± 5	60–78	154 ± 12	135–174	80 ± 9*	188 ± 6*	185–195	185–195	180–200	194 ± 2*
5	75 ± 3	72–78	154 ± 13	130–174	87 ± 2*	168 ± 6	165–175	170–180	155–170	161 ± 4
6	71 ± 4	66–78	148 ± 7	140–168	129 ± 6*	150 ± 0	150–150	150–155	150–155	153 ± 4
7	67 ± 8	54–78	151 ± 10	137–165	126 ± 2*	172 ± 3*	170–175	170–185	175–185	169 ± 6*
8	85 ± 6	72–100	156 ± 5	146–171	85 ± 2	175 ± 5*	170–180	170–180	165–170	172 ± 4*
9	68 ± 4	60–72	160 ± 10	142–183	79 ± 10*	173 ± 13	160–185	170–195	160–175	174 ± 13
10	54 ± 5	42–66	143 ± 5	133–153	68 ± 5*	163 ± 3*	160–165	170–180	170–175	167 ± 3*
Mean ± SD	71 ± 12		156 ± 8		92 ± 26†	172 ± 11†				172 ± 12†

HR = heart (ventricular) rate; $DACL_{ECG}$ = dominant atrial cycle length determined from the surface ECG using the FAF-ECG method; ACL_{EPI} = dominant atrial cycle length of an epicardial recording; $DACL_{EPI}$ = dominant atrial cycle length in an epicardial recording determined using the FAF-ECG method; RAFW = right atrial free wall; RAA = right atrial appendage.
* Significantly ($P<0{\cdot}05$) higher than under preoperative conditions.
† The mean value of the group was significantly ($P<0{\cdot}05$) higher than under pre-operative conditions.

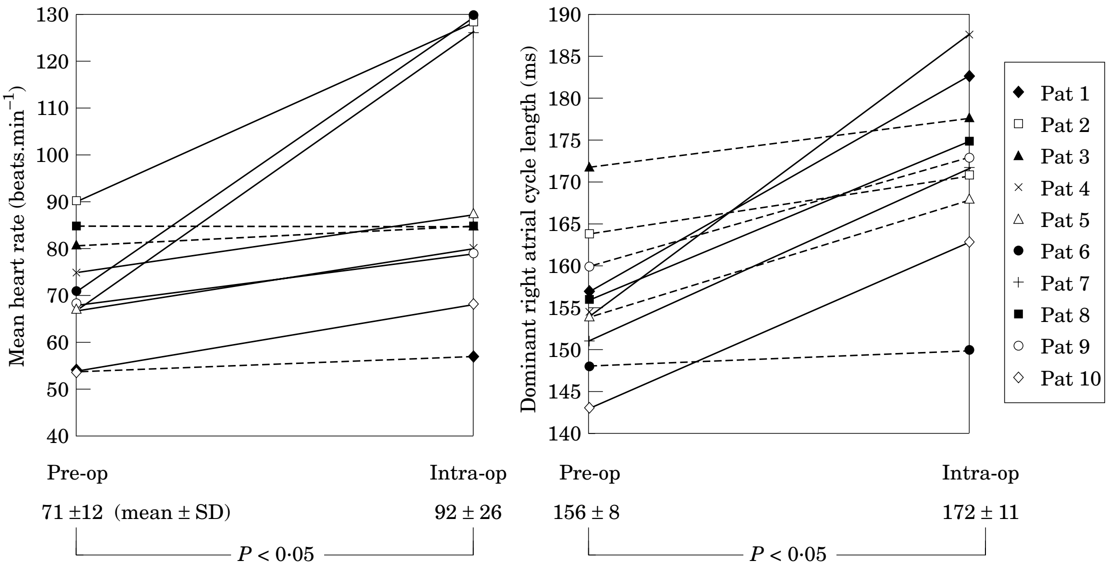

Figure 4 **The mean ventricular rate and the dominant right atrial cycle length under pre-operative and intra-operative conditions, respectively, in individual patients. The solid lines indicate a significant (*P*<0·01) increase in mean ventricular rate or atrial cycle length.**

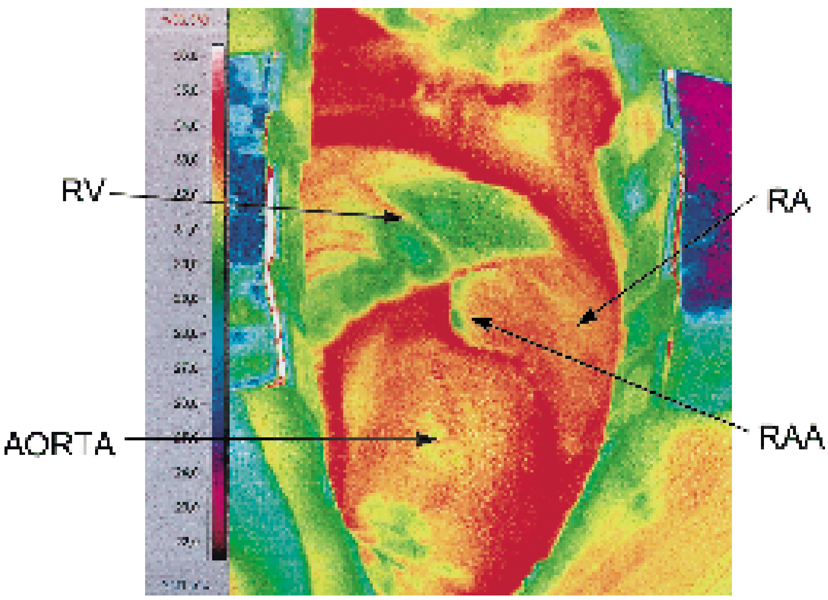

Figure 5 **An infra-red image of the exposed heart of a patient undergoing open-heart surgery. The colours represent different temperatures according to the scale on the left side. The small area of the right atrial appendage with a lower temperature than the adjacent areas was covered with what visually appeared to be epicardial fat. RA=right atrium, RAA=right atrial appendage, RV=right ventricle.**

same magnitude. Furthermore, the temperature decrease during heart exposure is obviously not homogeneous, which, in addition, will increase the spatial dispersion of the electrophysiological properties of the atrial myocardium.

As none of the above factors was actually measured or controlled in the patients with atrial fibrillation, no firm conclusions of the effect of each of them and their relation to each other can be drawn from the data in the present study.

Implications

Although the exact mechanisms of the alteration of the atrial and the ventricular rate remains to be fully understood, the results in the present study have important implications. Heart exposure and anaesthesia obviously affect the electrical properties of the heart at both the atrial and the ventricular level in patients with atrial fibrillation. This modulation may, of course, affect both the activation and the repolarization sequence in the heart. With regard, for example to cooling of the atria, it has previously been shown that atrial wavelength (the conduction velocity multiplied by the refractory period[33,34]) was only slightly affected by moderate lowering of the myocardial temperature (due to an increase in refractoriness and a decrease in conduction velocity). However, it should be noted that even small temperature changes (1–2°C) may result in a significant change in these parameters; non-uniform cooling or rewarming of the heart may cause significant dispersion of these variables in the myocardium[35]. We also know that inducibility and stability of atrial fibrillation are highly affected by changes in the magnitude and dispersion of the atrial refractory period[31].

Studies assessing the electrical phenomena in atrial fibrillation, where data are acquired during intra-operative conditions, must take the electrical modulation, due to anaesthesia and heart exposure described in the present study, into account. More information about the effect of individual intra-operative factors would help to control and/or compensate for these phenomena.

Limitations of the study

Estimation of the dominant atrial fibrillation cycle length before surgery was done with a new method based on frequency analysis of the ECG signal (FAF-ECG). Although this new method has been carefully validated[22], it is possible that the method slightly over- or underestimated the true pre-operative atrial fibrillation cycle length. However, as the magnitude of the increase in atrial cycle length was different in all patients, and as the increase was significant on an individual basis ($P<0{\cdot}01$) in half of the patients it is strongly suggested that the changes documented in this study were due to true changes in physiological conditions.

The temperature of the exposed epicardium was estimated using an infra-red imaging technique which, although non-invasive, offered high spatial resolution and good accuracy. One limitation, however, was that only the temperature of the epicardial surface was assessed. A transmural difference in temperature is probably present during heart exposure, as blood of normal body temperature is circulating in contact with the endocardial surface at the same time as much cooler air is in contact with the epicardium.

Finally, we cannot rule out that the application of epicardial electrodes might have accelerated the heat loss from the epicardium, although the electrode arrays were poor heat conductors.

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