INTRODUCTION

Atrial fibrillation is a common arrhythmia associated with significant mortality and morbidity. It has a tendency to become more persistent with time, a large percentage of patients with paroxysmal AF eventually develop chronic AF. (AF begets AF) ***(Godtfredsen et al., 1982)***. It was suggested that there may be a purely electrophysiological explanation for the increased persistence of AF with time (termed atrial electrical remodelling) ***(Garratt and Fynn, 2000)***.

For many years the only curative treatment has been surgical with extensive atrial incisions used to compartmentalize the atrial mass below the level critical for perpetuated atrial fibrillation ***(Cox et al., 1993)***.

A recently described focal origin of atrial fibrillation, mainly inside pulmonary veins, is creating new perspectives for radiofrequency catheter ablation ***(Scanavacca et al, 2002)***.

Transcatheter focal and linear radiofrequency ablation in the right atrium and (or) left atrium has been used to replace the surgical procedure. However, uncertainity remains concerning the difficult mapping technique of the firing foci, the requisite number of lesions and their optimal location ***(Haissaguerre et al., 1998)***.

This made Haissaguerre et al in 1998 to perform electric isolation of the pulmonary veins by segmental ostial PV ablation ***(Haissaguerre et al., 1998)***.

Recently the circumferential pulmonary vein ablation technique developed by Haissaguerre team in Baurdeaux France has circumvented the limitations of the old transcatheter ablation techniques, by ablation lesions around the ostia of

pulmonary veins circumferentialy they are isolated from the left atrium ***(Haissaguerre et al 2000).*** This could be also obtained surgically during mitral valve replacement ***(Benussi et al., 2000)***.

Pulmonary venous stenosis uncommonly occur after radiofrequency catheter ablation with uncertain clinical consequences ***(Scanavacca et al, 2002)***.

Aim Of Work

The aim of this work is to study the changes in left atrial electroanatomic remodeling and pulmonary venous flow pattern after segmental transcatheter and surgical circumferential radiofrequency pulmonary vein isolation in patients with atrial fibrillation.

EPIDEMIOLOGY AND RISK FACTORS OF ATRIAL FIBRILLATION

Although AF affects fewer than 1 % of individuals in their fifties, up to 11% of 80 year olds suffer from this arrhythmia, with a total incidence of 2.2 million cases per year in the United States alone ***(Ryder et al., 1999)***.

AF often accompanies left atrial enlargement and mitral valve calcification in patients over 60 years of age and commonly complicates cardiac surgery and acute myocardial infarction.

Multivariate analysis has identified increasing age, heart failure, smoking, diabetes, hypertension, male sex, left ventricular hypertrophy, myocardial infarction and valvular heart disease as risk factors.

AF may cause systemic thromboembolic complications, decreased exercise capacity, impaired ventricular function, reduced quality of life and significant health care costs. Over a two year period, patients with AF require an average of 14 office visits, 12 outpatient visits, two admissions to hospital and one emergency department visit ***(Maglio et al., 1996)***.

In 1999, Catherwood and colleagues reported average AF related costs of US$9300_18 900 per quality adjusted life year ***(Catherwood et al., 1999)***.

After adjusting for underlying cardiac conditions, AF is associated with a l.5 fold to 1.9 fold increase in risk of mortality in both men and women across a wide spectrum of ages.

PATHOPHSIOLOGY OF ATRIAL FIBRILLATION

The multiple wavelet theory:

In 1959 *Moe and Abildskov* found that the perpetuation of AF depends on the continuous and random propagation of various individual wavelets through the atria. ***(Moe et al 1959)***, and that a critical number of three to six simultaneous wavelets was required to maintain this arrhythmia ***(Allessie et al., 1985)***.

The wavelength:

Allessie et al. confirmed this concept, by using epicardial electrodes in dogs, demonstrating that the slower the conduction velocity and the shorter the refractory period, the more likely it is that reentry will occur, and very short wavelengths facilitate more complex forms of reentry, such as fibrillation versus flutter ***(Allessie et al., 1985)***. Since for AF a critical number of wandering wavelets are required, the wavelength is important for perpetuation of fibrillation.

The concept of critical mass:

For maintenance of AF, a critical mass of myocardial tissue is required since larger tissue masses allow a greater space available for the wavelets to circulate ***(Allessie et al., 1990)***. Direct proof that perpetuation of AF is dependent on a critical mass is provided by the fact that in different animal species larger hearts fibrillate longer than small hearts ***(Moore et al., 1982)*** and that in a given animal, AF is less stable than ventricular fibrillation.

In humans, atrial size has long been known to be critical in the ability to generate AF, and it has been shown to correlate with increased vulnerability. The importance of atrial enlargement may explain the propensity for AF to occur in valvular disease and cardiac failure.

The role of dispersion of refractoriness:

In patients with AF an increased dispersion of refractoriness was observed ***(Ramanna et al., 2000)***. This heterogeneity of refractoriness may provide the setting for unidirectional block when an extrasystole arising in a zone with short refractory periods fails to excite an area with long refractory periods. Probably, as Zipes wrote: A heart that is homogeneous electrophysiologically cannot fibrillate ***(Zipes et al., 1997)***.

Recently, *Ramanna et al.,* found that patients with idiopathic AF had an increased dispersion of refractoriness in comparison with a control group and thus they concluded that this increased dispersion of refractoriness may be the substrate for the enhanced inducibility and spontaneous occurrence of AF.

Regional differences of atrial electrophysiological properties:

Recent mapping studies in humans have clearly demonstrated that during AF different areas of the atria may have a different electrophysiologic behavior ***(Gaita et al., 1998)***. Some regions show a fast, irregular and disorganized atrial activity while simultaneously others are activated by relatively organized and almost regular electrical wavefronts. It can be presumed that although the atria as a whole participate in the process of AF not all the parts of the atria contribute equally to the perpetuation of the fibrillatory process ***(Konings et al., 1997)***. The regions showing the most irregular and disorganized activity may be crucial for the maintenance of the

arrhythmia, while other regions with a relatively regular activation may be only by stander.

Particularly, many studies point to the relevance of the posterior region of the left atrium as a critical area in the maintenance of AF, both in animals and in humans ***(Pappone et al., 1999)***. During intraoperative mapping *Harada et al*. observed that in 9 of 10 patients with chronic AF and mitral valve disease, the left atrium had a regular and repetitive activation pattern, and thus it could act as an electrical driving chamber for AF ***(Harada et al., 1996)***.

In 1998, *Haissaguerre et al.* reported that the initiation of AF comes from the pulmonary veins ***(Haissaguerre et al., 1998)***. The pulmonary veins do not only contain the triggering foci, but also contain the reentry substrate that maintains their activity. Moreover, this area is densely supplied by autonomic fibers and ganglionated plexuses that have a role in the sympathovagal imbalance that may help the initiation of AF. This means that the pulmonary veins contain the "mother rotor" from which AF originates, and AF does not require a diseased atrium to occur, although diseased atrium makes the arrhythmia more sustained, and makes reentry easier to trigger ***(Khairy & Nattel, 2002)***.

The explanation of these findings is easier to understand if we better understand the anatomy of the left atrium and pulmonary veins.

Anatomy of left atrium

When viewed from the front, the left atrium is situated to the left and mainly posteriorly. The front of the left atrium lies just, behind the transverse pericardial sinus which is bordered anteriorly by the aortic sinuses. The posterior wall is just infront of the tracheal bifurcation.

The atrial septum, best appreciated in the transverse plane, runs obliquely from the front, extending posteriorly and to the right.

Thickness of different parts of the left atrium and its normal dimensions are important to know when intervening in this chamber. The thickness of the left atrial walls is shown in *table* (1) ***(Ho et al., 1999)***.

Table (1): Thickness of the left atrial walls (mm) ***(Ho et al., 1999)***

Anterior	Posterior	Superior	Lateral	Vestibule
3.3 ± 1.2	4.1 ± 0.7	4.5 ± 0.6	3.9 ± 0.7	2.3 ± 0.7

The longitudinal, anteroposterior, and transverse dimensions of the left atrium are 4.5 ± 1.4cm (range 3.4 to 6.2), 3 ± 0.8cm (range 2.4 to 4.3), and 4 ± 1.2cm (range 2.6 to 5.5) respectively ***(Ho et al., 1999)***.

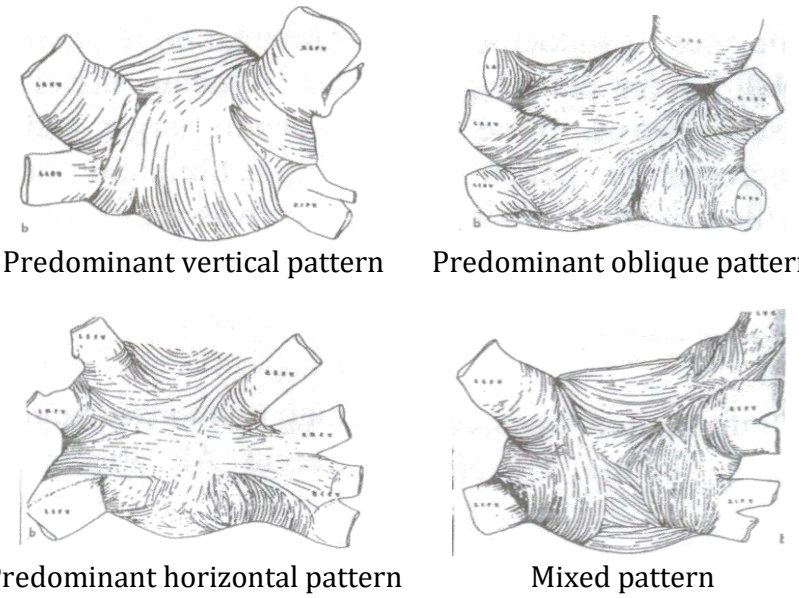
Posterior left atrial wall and the junction between left atrium and pulmonary veins:

The posterior wall of the left atrium is crossed by myocardial fibers running in all directions that make it a complex region. The predominance of certain group of fibers running in the same direction varies from heart to heart as shown in figure (1).

Close to the opening of each pulmonary vein, muscle fibers leave the main fascicle and turn around the opening of these veins, forming a sphincter like structure; some of these circular fibers may extend to a greater or lesser degree over the vein, contributing to the formation of "myocardial sleeves" which cover the endothelium of the pulmonary veins to a variable distance. Oblique, vertical and transverse fibers are also seen on the posterior atrial surface as shown in figure (2).

This makes the architecture of myocardial sleeves irregular and complex as they contain fibers arranged in a random fashion. This complexity of myocardial sleeves is a normal consequence to the complexity of the posterior left atrial wall.

The correlation between the myocardial fiber orientation in the left atrium and their electrophysiological characteristics were studied by *Hocini et al.* who observed that conduction delay occurs at the sites of sudden change in fiber orientation ***(Hocini et al., 2002)***. Under pathological conditions including stretch and increased fibrosis, these delays may become larger and result in microreentry, which could trigger atrial fibrillation or lead to fibrillatory conduction. This observation was previously reported by Spach et al., ***(Spach et al.,* 1982)**.



Predominant vertical pattern Predominant oblique pattern

Predominant horizontal pattern Mixed pattern

Fig. (1): Individual variations in arrangement of myocardial fibers in the posterior left atrial wall ***(Nathan & Eliakim, 1966)***.

Pulmonary veins:

There are 4 pulmonary veins, the right superior pulmonary vein passes posterior to the superior caval vein, with the right inferior vein passing behind the venous sinus of the right atrium ***(Spach et al., 1972)***.

The orifices of the right pulmonary veins are directly adjacent to the plane of the atrial septum.The inferior veins are situated posteriorly relative to the superior veins. The orifices of the left pulmonary veins are located more superiorly than those of the right ***(Harris and Health, 1986)***.

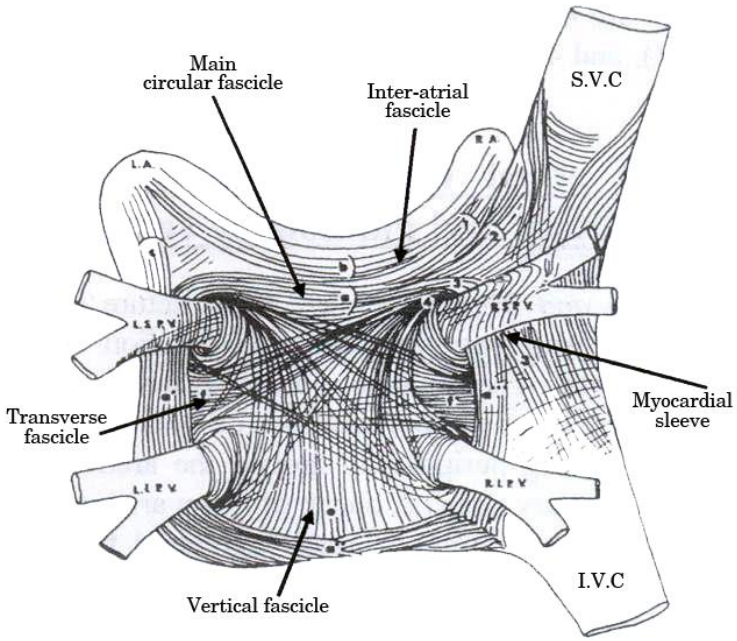


Fig. (2): Arrangement of muscle fibers on the posterior wall of the left atrium ***(Nathan & Eliakim, 1966)***.

The right superior pulmonary vein (RSPV) and the left superior pulmonary vein (LSPV) project forward and upward, whereas the right inferior pulmonary vein (RIPV) and left inferior pulmonary vein (LIPV) project backward and downward. The trunk of the RIPV projects horizontally. The

superior veins enter the left atrium at an angle of 45° to 60° to the horizontal, whereas the inferior veins are at an angle of only 30° to 45° ***(Harris & Heath, 1986)***. The angulation may explain why it is more difficult to obtain good contact of the catheter around the orifice of the inferior veins for effective ablation.

The RSPV lies just behind the superior vena cava or right atrium, and the left pulmonary veins are positioned between the left atrial appendage and descending aorta. The orifice of the appendage lies in close proximity to the ostium of the LSPV. A close relationship exists between the ostia of the 2 right and the 2 left pulmonary veins, with only several millimeters of atrial tissue between them ***(Kato et al., 2003)***.

According to the observations of *Kato and coworkers,* typical PV anatomy with 4 distinct PV ostia, is present in 16 among 28 patients with AF (57%) and 18 among 27 controls (66%) ***(Kato et al., 2003)***.

The second most common pattern was the presence of a short common left trunk, observed in 7 patients (25%) and 5 controls (18.5%). This pattern differed from typical PV anatomy in that the junction of the lower wall of the LSPV and upper wall of the LIPV lies outside the left atrial rim.

A third pattern of PV anatomy was the presence of a long common left trunk in 2 patients (7%) and 2 controls (7.4%). Additional patterns that were observed involved abnormalities of pulmonary venous drainage of the right lungs with either a right middle PV, 2 right middle pulmonary veins, or a right middle and a right "upper" PV (an anomalous vein distinct from the RSPV). Figure (3) shows different patterns of PV anatomy.

Monique et al. measured by CT scan the anteroposterior diameter of the PV ostia which were 12.8mm ± 3.3 for left veins, 16.2mm ± 3.8 for right veins, and 18.8mm ± 7.7 and 28.7mm ± 5.1 for left and right common ostia respectively ***(Monique et al., 2003)***.

Myocardial sleeves:

An interesting finding in 45 patients with paroxysmal AF is that the initiating triggers were found in the pulmonary veins and recorded about 2cm distal to the ostia ***(Haissaguerre et al., 1998)***. This aroused the attention of electrophysiologists to the myocardial component of the pulmonary veins, which is an extension of the left atrial myocardium referred to as "myocardial sleeve"; a structure that was overlooked in anatomy literature.

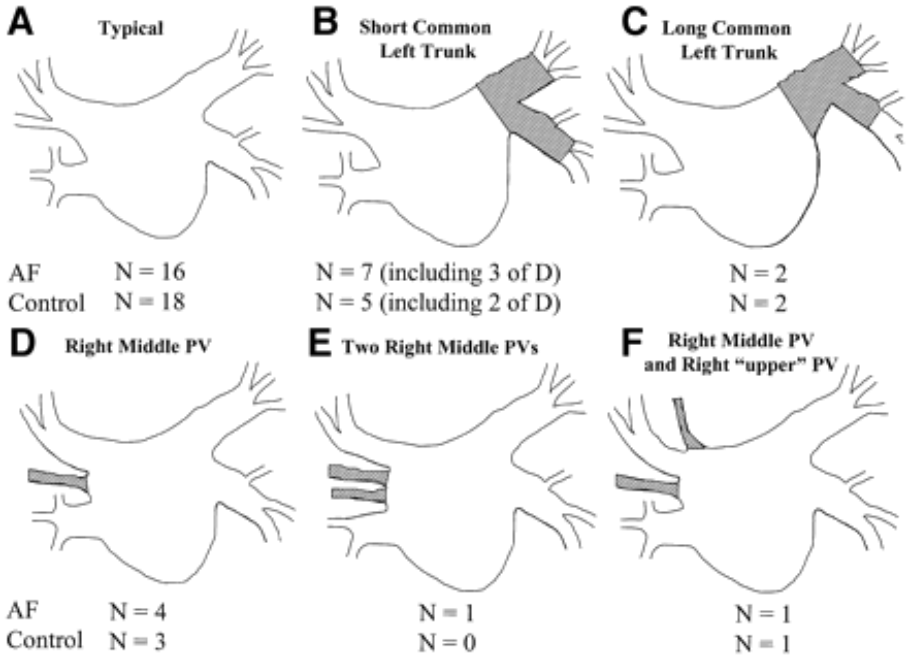


Fig. (3): Patterns of PV anatomy in AF patients. Shaded portions indicate different parts from typical anatomy. A, Typical branching pattern. B, Short common left trunk. C, Long common left trunk. D, Right middle PV., E. Two right middle PV's. F, Right middle PV and right "upper" PV ***(Kato et al., 2003)***.

The length of the myocardial sleeves had a distinctive distribution. The longest sleeves were over the superior veins, with the left (1.1±0.3cm) being longer than the right (0.9±0.3cm).

The myocardial sleeves were thickest at the venoatrial junction (mean 1.1mm) and thinned out distally. Furthermore, the thickness of the sleeves was not uniform, with the inferior walls of the superior veins and the superior walls of the inferior veins having the thicker sleeves ***(Ho et al., 1986)***.

Throughout the PV, and even at the venoatrial junction, there were gaps in the myocardial sleeves that were mainly composed of fibrous tissue. Such an arrangement, together with the patchy areas of fibrosis seen, may be relevant to the role of the Pulmonary veins in the initiation of AF. Interestingly however, no correlation was seen between patient age and histological appearance.

Another feature noticed was the supply of ganglionic cells and autonomic nerve fibres in the venous walls of the myocardial sleeves***(Ho et al 2001).***In some individuals myocardial sleeves are absent in the inferior veins ***(Cabrera et al., 2002)***.

Functions of the myocardial sleeves:

1- Regulation of pulmonary venous pressure and blood flow, through the basic tone of the striated muscle and its possible changes due to various physiological conditions ***(Kuramoto* & *Rodbard,* 1962)**.

2- Throttle valve action: The venous sphincters and sleeves exert a valve action that prevents reflux of blood from the atrium into the veins ***(Burch & Romney, 1954)***.

3- Active expulsion of blood into left atrium: *Carrow and Calhoun* suggested that a peristaltic or "milking" action toward the heart was produced by the contractions of the myocardial fibers which run from the atrium over the vein and back to the atrium again ***(Carrow & Calhoun, 1964)***.

Implications for radiofrequency ablation:

Equipment currently available creates lesions that may be excessive in some areas and insufficient in others. As the myocardial sleeves tend to be thicker closer to the venoatrial junction than in areas within the veins, more penetrating lesions are required to eliminate the source of ectopic activity or to isolate the pulmonary vein from the left atrial myocardium by ablating at the venoatrial junction. In contrast, it is anticipated from the anatomical findings that less penetrating lesions will be required if lesions are placed in parts of the veins that are closer to the lungs than at the venoatrial junction.

The presence of gaps in the myocardial sleeves, and of acquired areas of fibrosis, suggests that complete encirclement of the venous orifice with ablative lesions may not be necessary to prevent reinitiation of the tachycardia ***(Ho et al., 2001)***.

Overall, the myocardial sleeves are thickest in the inferior walls of the superior veins and the superior walls of the inferior veins. This observation has implications with regard to the power of radiofrequency energy to be selected when approaching the different areas of the pulmonary veins ***(Ho et al., 2001)***.

Pulmonary veins and reentry substrate:

The pulmonary veins seem to possess a substrate for microreentry. *Mandapati et al.* have demonstrated discrete sites of high frequency periodic activity during AF in the isolated sheep heart. The sites with the highest dominant frequency were localized to the posterior left atrium, near or at the PV ostium. Stable microreentrant sources were thought to be the most likely underlying mechanism of AF in this model ***(Mandapati et al., 2000)***.

Jais et al. reported that there is decremental conduction in association with long conduction times in the pulmonary

veins. Furthermore, the effective refractory periods are short in the pulmonary veins ***(Jais et al., 2002)***.

An automatic (or triggered) focus originating from or close to the PV ostium may then be maintained as a rapid reentrant circuit in the PV. This may explain the unusually rapid rates of these foci that have been observed clinically (mother rotors) ***(Arora et al., 2003)***.

The role of autonomic nervous system:

The autonomic nervous system has extensively been studied in relation to the mechanism of AF ***(Zipes et al., 1974)***. The vagal activity is very important in the initiation and perpetuation of AF, as shown by animal studies demonstrating that both parasympathetic stimulation and direct application of acetylcholine result in sustained AF ***(Schuessler et al., 1992)***.

Moreover, in humans *Coumel* proposed the presence of a form of vagally mediated AF, characterized by a predominance in young males with no structural disease, in which the episodes of paroxysmal AF occurring at night and postprandially were generally preceded by a heart rate decrease and/or an increase in high frequency heart rate variability ***(Coumel et al 1994)***. As long as vagal tone is high, the arrhythmia will be sustained which may explain why the arrhythmia in these patients more frequently occurs during sleep, terminating in the morning ***(Coumel et al., 1996)***.

On the other hand, sympathetic stimulation produces no much decrease in atrial ERP (10_15%), and no significant increase in heterogeneity of ERP. However, it increases focal firing and helps the initiation of atrial fibrillation ***(Schauerte et al., 2000)***.

Overall, it appears that sympathetic stimulation has little effect on AF in the experimental setting. In the clinical setting, some forms of AF, such as postoperative AF, may be influenced