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CONTENTS

INTRODUCTION
ATRIOVENTRICULAR NODAL REENTRY
WOLFF–PARKINSON–WHITE SYNDROME
ATRIAL FLUTTER
ATRIAL FIBRILLATION
REFERENCES

Abstract

In this chapter, we will discuss the history of supraventricular tachycardia (SVT) that includes four sections: atrioventricular (AV) nodal reentry, AV reentry, atrial flutter (AFL), and atrial fibrillation (AF). We will focus on the historical evolution of the electrophysiologic study of the mechanism and the development of surgical and catheter ablation of these SVTs. We will also discuss potentially newer therapeutic approaches for these arrhythmias.

Key Words: Supraventricular tachycardia; atrioventricular (AV) nodal reentry; AV node; pre-excitation; accessory pathways; Wolf–Parkinson–White syndrome; atrial flutter; cavotricuspid isthmus-dependent atrial flutter; atypical atrial flutter; atrial fibrillation; catheter ablation; cardiac electrosurgery.

INTRODUCTION

We have divided the history of supraventricular tachycardia (SVT) into four sections: atrioventricular (AV) nodal reentry, AV reentry, atrial flutter (AFL), and atrial fibrillation (AF).

ATRIOVENTRICULAR NODAL REENTRY

The debate about precise anatomic boundaries of AV nodal reentry has been lasting for more than 60 years, since the first proposal that various mechanisms of SVT involve the region of the AV node (1). This debate continues even though the vast majority of these patients are cured by standard ablative maneuvers.

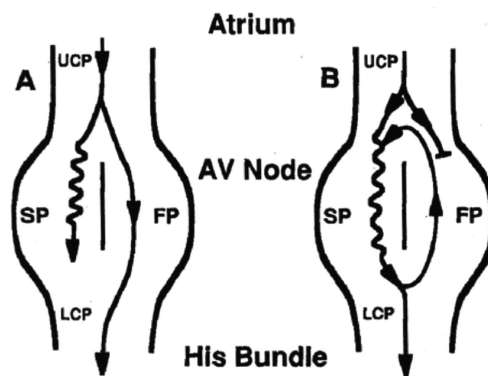
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Anatomy of AV Nodal and AV Junction

The works by His (2) and Tawara (3) firmly established the electrical connection between the atrium and ventricle. The AV node consists of closely packed nodal cells in open contact with atrial muscle at its proximal end (4). Its distal end is linked to the AV bundle which is normally completely insulated by the central fibrous body (5). The AV bundle links with the specialized ventricular conduction system (Purkinje) which is likewise insulated from ventricular myocardium. The proximal portion of the compact node is coated with layers of transitional cells. These morphologically distinct cells have histologic features of both nodal and ordinary atrial myocardial cells. Of potentially great importance is the recent rediscovery of posterior extensions of the AV node (6). These extensions may play a vital role in nodal reentrant circuits. One set of posterior extensions is covered by transitional cells over the left margin of the node in contact with the left atrial (LA) myocardium. More elaborate and extensive posterior extensions extend postero-inferiorly toward the area between the coronary sinus (CS) and tricuspid annulus (TA).

Strong evidence has been marshaled to place doubt on the existence of specialized atrial tracts (7). Instead, input into the AV node is thought to consist of an anterior input from the septal atrial musculature and a posterior input emanating from the crista terminalis (CT) and skirting the inferior vena cava (IVC) to proceed into the region between the CS and TA (slow pathway area) (8). The actual slow pathway may, in fact, be the nodal extension described above.

In a series of observations Moe and colleagues (9, 10) deduced evidence for dual AV nodal conduction in dogs and rabbits by using microelectrode recordings within the AV node. A critically timed premature beat was shown to block in one pathway (fast or beta pathway) but allowed for depolarization of a separate region (slow or alpha pathway). The latter was associated with slower conduction allowing for retrograde reciprocation into the beta pathway and producing an atrial echo (Fig. 1). These important concepts were rapidly assimilated into human studies and established the basis of our current understanding of AV nodal reentry in humans.



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Fig. 1. “Classical” model of AVNRT. The AV node is “longitudinally dissociated” into a slow pathway (SP) and a fast pathway (FP). During sinus rhythm (**panel A**), impulses are conducted over the FP; in **panel B**, an atrial premature beat finds the FP refractory and is conducted over the SP. The conduction delay in the SP allows the FP to recover excitability; therefore, the impulse can conduct retrogradely via the FP and excite the upper end of the SP and initiate sustained reentry. Upper (UCP) and lower (LCP) common pathways of AV nodal tissue are present above and below the reentrant circuit. (Figure from J Cardiovasc Electrophysiol 1993; 4:573, with permission).

McGuire and colleagues (11) showed strong evidence that “AV junctional cells in the posterior AV nodal approaches appear to participate in slow pathway conduction.” A later important study by Medkour et al. (12) described a combined anatomic and electrophysiologic examination of the

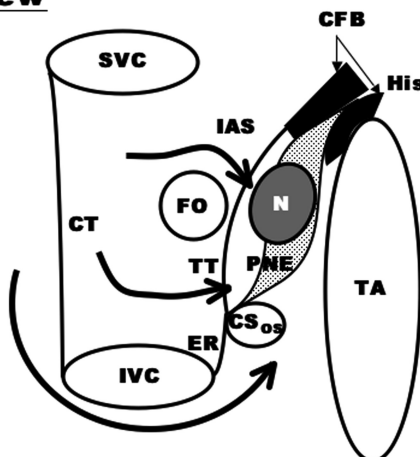
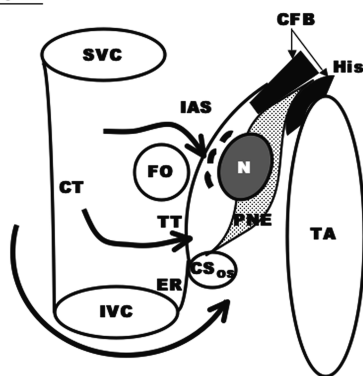
RAO view

Fig. 2. A schema showing anterior (septal – 2 upper arrows) inputs into the AV node (N) and posterior inputs (lower arrow) into the node. SVC = superior vena cava; IVC = inferior vena cava; CT = crista terminalis; ER = eustachian ridge; TT = tendon of Todaro; FO = foramen ovale; IAS = interatrial septum; CS os = ostium of coronary sinus; PNE = posterior nodal extension; CFB = central fibrous body; His = His bundle; TA = tricuspid annulus.

posterior nodal extension (PNE) in the rabbit heart. As shown in Fig. 2, anatomically the extension appeared as a bundle of specialized tissues between the CS and compact node. They found no distinct separation between the compact node, lower nodal cell bundle, and the PNE. However, they found distinct differences in electrophysiologic properties between the PNE and compact node. The PNE showed cycle length-dependent slow conduction with its refractory period shorter than that of the node. Critically timed premature atrial depolarizations that blocked in the transitional cells could propagate in the PNE and thus explain the discontinuities in nodal conduction as well as in atrial echo beats (Fig. 3a and b). This study accumulated convincing evidence that the PNE provides substrate for slow pathway conduction.

(a)

RAO view

(b)

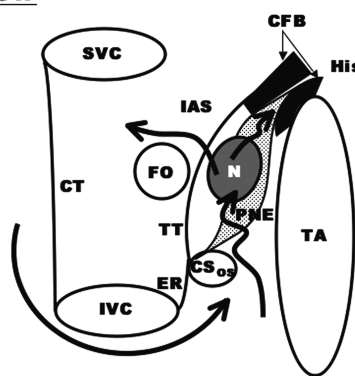
RAO view

Fig. 3. (a) A schema showing a premature atrial complex that is blocked in the transitional cells surrounding the septal inputs to the node and the PNE as well as the node are engaged over the inferior inputs. (b) The pathogenesis of an echo beat. The impulse blocked in the septal inputs proceeds over the inferior input and activates the node via the PNE and is able to turn around in the node and reactivate the atrium.

Human Electrophysiologic Studies

As mentioned above, early observations by Moe and Menedez (9, 10) on reciprocal beats in rabbits were rapidly applied to humans. These seminal findings were introduced just as the field of clinical invasive electrophysiology began to emerge. Early invasive electrophysiologic studies (13–16) attributed AV nodal reentry as cause of paroxysmal SVT. Of particular note was the work of Dr. Ken Rosen and colleagues (15) who demonstrated evidence for dual AV nodal physiology manifest by an abruptly increase in AV nodal conduction time in response to critically timed atrial premature depolarizations. These data served as an excellent supportive compliment to the original observations of Moe and Menendez.

By the end of the 1970s, the concept of dual AV nodal conduction in humans had been well established.

However, the precise anatomic components of the AV nodal reentrant circuit remained controversial. Josephson and colleagues (17) showed impressive evidence that the circuit was intranodal and this concept was contested by Jackman et al. (18) and McGuire et al. (19, 20). The newer anatomic understanding of the node has made this debate largely moot. If one accepts the concept that the posterior nodal extensions as well as the transitional cells are part of the node (12) then the debate is largely resolved. Current understanding suggests that most subjects with AV nodal reentry have a final common pathway within the AV node and an upper pathway involving the fast and slow pathways surrounding the compact node.

In 1993 McGuire et al. (19, 20) nicely summarized the available information and proposed various models for tachycardia mechanisms which involve right-sided atrial inputs. Lately Jackman and colleagues have expanded on various subforms of AV nodal reentrant tachycardia (AVNRT) (21). These include slow–fast form (antegrade conduction over the slow pathway and retrograde conduction over the fast pathway) (81.4%), slow–slow form (both antegrade and retrograde conduction over the slow pathway) (13.7%), and fast–slow forms (antegrade conduction over the fast and retrograde conduction over the slow pathway) (4.9%). The differentiation among these subforms is made based on the location of earliest atrial activation. The slow pathway retrograde conduction is manifest over the CS ostium region while fast retro conduction occurs over the antero-septal area just superior to the His bundle-recording site. In addition, Jackman et al. (22) have suggested left-sided inputs as part of the AV nodal reentrant circuit. Recently Gonzalez et al. (23) proved the existence of LA input to the AV node in humans with structurally normal hearts.

In addition, there are several case reports that documented the need to ablate AVNRT from the left annulus or left posteroseptal area (24–26). One source of LA input is via the left-sided posterior nodal extension. The hypothetical left-sided inputs to the AV node and possible tachycardia circuits are illustrated in Fig. 4.

Surgical Ablation of AVNRT

Ross et al. (27) first introduced a non-pharmacologic therapy of AVNRT that involved surgical dissection in Koch's triangle, of which the results were confirmed by a number of surgical groups (28–30). This technique also led to a better understanding of this tachycardia. For example, high-resolution mapping of Koch's triangle showed two distinct types of atrionodal connections in patients with "typical" slow–fast AVNRT. In most patients the retrograde fast pathway (either during tachycardia or ventricular pacing) showed earliest atrial activation over the apex of Koch's triangle while in the minority earliest atrial activation occurred near the CS. This would nicely compliment the current designation of AVNRT subforms (21).

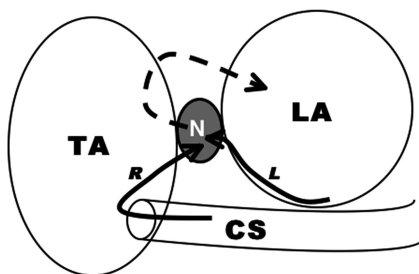
LAO View

Fig. 4. Hypothesis of left-sided inputs to the AV node. In one iteration the coronary sinus musculature is involved with input into the region of the PNE. Ablation either within the coronary sinus or over the traditional slow pathway region (R) would be expected to ablate the circuit. Alternatively, the circuit may involve activation of the left atrium (LA) (shown by the *broken arrow*) either via the septum or Bachmann's bundle. Activation toward the AV node is through the tracts (L) along the mitral annulus. In the latter instance ablation over the putative left-sided inputs (L) will be required for arrhythmia cure.

Catheter Ablation of AVNRT

Catheter ablation of the AV junction using high-energy direct current (DC) shocks for control of drug-refractory SVT was first introduced in 1981 (31). In 1989, two groups (32, 33) almost simultaneously reported success using high-energy discharge in the region of slow pathway. The subsequent use of radiofrequency (RF) energy completely revolutionized catheter cure of AVNRT. The initial attempts targeted the fast pathway by applying RF energy superior and posterior to the His bundle region until the prolongation of AV nodal conduction occurred. Initial studies (32–36) showed a success rate of 80–90%, but the risk of AV block was up to 21%. Jackman et al. (37) first introduced the technique of ablation of the slow pathway for AVNRT. Among experienced centers the current acute success rate for this procedure is 99% with a recurrence rate of 1.3% and a 0.4% incidence of AV block (38) requiring a pacemaker.

Ablation of the slow pathway is achieved by applying RF energy at the posterior–inferior septum in the region of the CS. This technique can be guided by either via discrete potentials (37, 39) or via an anatomic approach (40); both have equal success rate. Radiofrequency energy is applied until junctional ectopics appear but at times successful slow pathway ablation may result without eliciting the junctional ectopic complexes. Final testing involves proof that either the slow pathway has been eliminated or no more than one AV nodal echo is present (37, 41).

More recently cryoenergy has been used for the slow pathway ablation (42, 43). The potential advantage of cryoenergy is the fact that the catheter sticks to adjacent endocardium during application of energy; hence, inadvertent catheter displacement and damage to the node are not possible. In addition, regions closer to the node may be explored since injury during the test procedure is reversible.

WOLFF–PARKINSON–WHITE SYNDROME***The Story of Wolff–Parkinson–White (WPW) Syndrome***

The WPW syndrome holds particular interest not only for clinical cardiologists but also for anatomists, surgeons as well as clinical and experimental electrophysiologists. The definition of this syndrome was dependant upon a clear knowledge of both the normal conducting system and mechanism of reentrant arrhythmias.

The first complete description of the syndrome by Drs. Wolff, Parkinson, and White was published in the American Heart Journal in August 1930 (44). They described 11 patients without structural cardiac disease who had a short P–R interval and “bundle branch block (BBB)” (Fig. 5) and paroxysmal SVT and/or AF. They made particular note of the fact that use of atropine or exercise would tend to normalize the ECG in sinus rhythm, while increases in vagal tone had the opposite effect. They felt that the arrhythmias were due to “associated nervous control of the heart.” In their report they also credited Dr. F.N. Wilson (1915) and Dr. Wedd (1921) who described the pattern in case reports (45, 46).

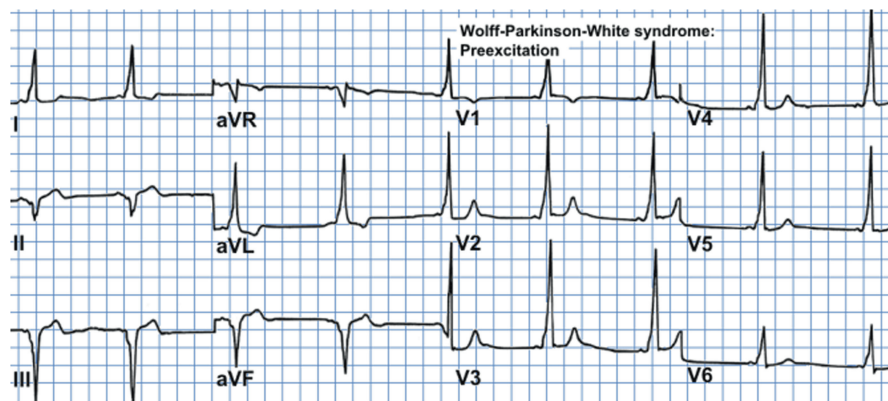


Fig. 5. Surface 12-lead ECG in a patient with WPW syndrome. The ECG showed ventricular pre-excitation in sinus rhythm with the presentation of short P–R interval and delta waves in 12 leads. The polarity of delta wave in 12 leads indicated that the atrioventricular accessory pathway was located at left posterior free wall.

Anatomic Studies of Atrioventricular (AV) Connections

At the time of the initial observations it was appreciated that the atrium and ventricles were electrically linked via the AV node and His bundle. Also, the bundle branches and Purkinje system had already been described and the electrocardiographic pattern of BBB had been identified (47–49). It is, therefore, clear why the early clinicians categorized ventricular pre-excitation as BBB.

We now need to digress a bit and discuss the work of the anatomists in the late nineteenth and early twentieth century. It was appreciated that electrical connections bridged the atrium and ventricles in mammalian hearts (50, 51) and the nature of these connections were of great interest. Stanley Kent (52) in 1893 described lateral AV connections and thought that these constituted the normal AV conduction system in man. This work proved controversial and was, in fact, rejected by Sir Thomas Lewis as well as by Drs. Keith and Flack. In contrast the work of His (53) and Tawara (54) clearly defined the normal AV conducting system. Of interest, there was a later study by Kent, describing a lateral AV connection and a node-like structure within the connection (55). While some have interpreted this finding as the first description of a right atriofascicular tract, but it should be appreciated that Kent felt that this structure was part of the normal AV conduction system. It is indeed odd that Kent is given credit for first describing accessory extranodal AV pathways since that credit clearly belongs to others, neither should he be properly credited with the first description of atriofascicular pathways.

In contrast, the persons who deserve credit are Wood et al. (56) for first describing a right-sided extranodal accessory pathway (1943) and Öhnell (57) for first reporting a left lateral pathway (1944). Other important contributions included the work of Mahaim (58) who described connections between the AV node or His bundle, to the fascicles or ventricular muscle. It was Lev who found that Mahaim

(59) tracts could produce a pattern of pre-excitation and nicely consolidated our modern understanding of the normal conduction system (60). In a landmark study Lev and Lerner presented detailed anatomic studies of 33 fetal and neonatal hearts (60). They concluded that no accessory pathways existed outside the AV conduction system; and that in fetal or neonatal hearts there were sparse development of collagen and hence there was close proximity but no communication between the atrium and ventricle.

Historical Evolution of Ventricular Pre-excitation and Circus-Movement Tachycardia

The early clinicians were focused on the “vagal” effects on the pre-excitation pattern and invoked vague neuro-cardiac mechanisms to explain associated arrhythmias. The concept of reciprocal rhythms was well established and Mines, who in fact, postulated a reciprocal rhythm involving the AV node and accessory pathway (61). According to TN James (62), Holzmänn and Scherf (63) in 1932 were the first to describe pre-excitation as being due to an extranodal accessory pathway. Similar descriptions were made by Wolferth and Wood (64) who labeled this pathway as “bundle of Kent.”

However, there were controversies regarding these findings at the time, and it leads to a profusion of alternative ideas. For example, Hunter et al. (65) suggested that the syndrome was due to a fusion of pacemakers (sinus conducted complexes and a pacemaker from the bundle branches). Prinzmetal (66) attributed the findings to accelerated AV conduction with pathways around the node. Sodi-Pallares (1952) invoked “hyperexcitability of the right side of the septum” (67).

The work by Butterworth and Poindexter (68) in 1942 clearly demonstrated that an artificial connection between the atrium and ventricle could mimic classic pre-excitation and led to the acceptance of an extranodal pathway as the cause for pre-excitation. The understanding of this syndrome was enhanced by the observation of Pick, Langendorf, and Katz (69–71). They noted some 60 theories used to explain pre-excitation but felt that only the presence of extranodal accessory pathway could explain all their findings. By detailed and painstaking deductive analyses of literally thousands of ECGs, they amazingly described variations in the nodal vs. pathway refractoriness as a mechanism for initiation and sustaining paroxysmal SVT. They studied the relationship between tachycardia and AF and distinguished extranodal from AV nodal pathways. Their incredible insights heavily influenced subsequent human cardiac electrophysiologic studies.

Clinical Electrophysiologic Study

Drs. Durrer and Wellens (72, 73) were the first to use programmed electrical stimulation of the heart in order to better define the mechanism(s) of arrhythmias. It should be emphasized that their observation antedated the recording of His bundle activity in humans (74). They showed that reciprocating tachycardia could be induced by premature atrial or ventricular stimulation and could be either orthodromic or antidromic; they also defined the relationship of the accessory pathway refractory period to the ventricular response during AF. These workers provided the framework for use of intracardiac electrophysiological studies to define the location (Fig. 6) and electrophysiology of these atrioventricular accessory pathways (75, 76).

Cardiac-Surgical Contribution

Prior to the era of catheter ablation, patients with SVT that were refractory to medical therapy underwent direct surgical ablation of the AV junction (77, 78). This approach, however, is not appropriate for the management of the patient with AF with rapid conduction over a bypass tract. Durrer and Roos (79) were the first to perform intraoperative mapping and cooling to locate a right free wall accessory pathway. Burchell et al. (80) used intraoperative mapping to locate a right-sided pathway and showed

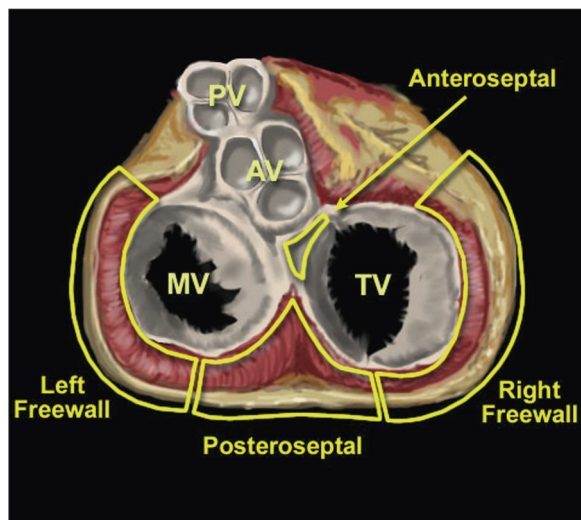


Fig. 6. Anatomic locations of atrioventricular accessory pathway in a superior view of the cross-sectional plane at the level of atrioventricular annulus. PV = pulmonary valve; AV = aortic valve; MV = mitral valve; TV = tricuspid valve.

that pre-excitation could be abolished by injection of procainamide (1967). A limited surgical incision over this area resulted in only transient loss of pre-excitation. Sealy (81) and the Duke team were the first to successfully ablate a right free wall pathway (1968). They initially used an epicardial approach. Their subsequent amazing results conclusively showed that a vast majority of WPW patients could be cured by either direct surgical or cryoablation (82) of these pathways. Iwa from Japan concurrently demonstrated the effectiveness of cardiac electrosurgery for these patients (83). He is credited with being the first to use an endocardial approach for pathway ablation. The endocardial approach was subsequently independently used by the Duke team of Sealy and Cox. Only later was the “closed” epicardial approach reintroduced by Guiraudon.

Catheter Ablation

The technique of catheter ablation of the AV junction was introduced by Scheinman et al. in 1981 (31). The initial attempts used high-energy DC countershocks to destroy cardiac tissue, but expansion of its use to other arrhythmias was limited due to its high risk of causing diffuse damage from barotrauma. Fisher et al. (84) also attempted to ablate left-sided accessory pathways through the CS by using the DC energy. This technique was eventually abandoned due to its limited efficacy and a high incidence of cardiac tamponade. Morady and Scheinman (85) introduced a catheter technique for disruption of posteroseptal accessory pathways. This was associated with a 65% efficacy and cardiac tamponade could be avoided by shock delivery just outside the CS (86). Warin et al. described successful ablation of non-septal pathways (87).

The introduction of RF energy in the late 1980s (88, 89) completely altered catheter ablative procedures. The salient advances in addition to RF energy included much better catheter design, together with the demonstration that pathway localization could be facilitated by direct recording of the pathway potential (Fig. 7). The remarkable work of Jackman et al. (89), Kuck et al. (90), and Calkins (91) ushered in the modern era of ablative therapy for patients with accessory pathways in all locations.

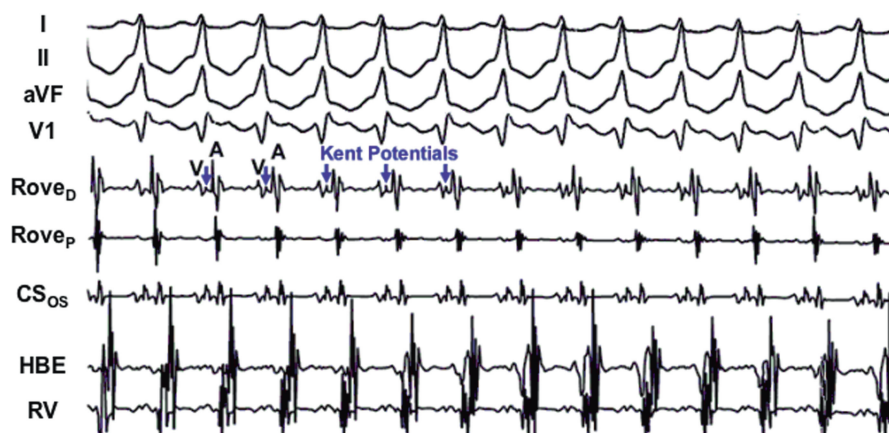


Fig. 7. Atrioventricular reentrant tachycardia in a patient with WPW syndrome. The accessory pathway potentials (Kent potentials, as marked by *arrows*) were recorded at the distal of mapping catheter (Rove_D). Rove_P = proximal of mapping catheter; CS_{OS} = ostium of coronary sinus; HBE = His bundle electrogram; RV = right ventricle; V = ventricular signal; A = atrial signal.

Moreover, a variety of registry and prospective studies have documented the safety and efficacy of ablative procedures for these patients (92, 93).

The Future

At present time, catheter ablation procedures are approaching the apogee of its success and while future developments in catheter design, alternative energy sources (i.e., cryoablation), and advanced imaging will likely lead to improvements. These advances will be largely incremental. Clearly the future major advances belong in the realm of better understanding of the molecular genetics and basic pathophysiologic processes that produce this syndrome. Recently Gollob et al. (94) successfully identified a gene responsible for the WPW syndrome. They identified two separate families with the same genetic abnormality. Of interest were the unusual clinical features which included an approximately 40% incidence of AF and/or AFL, a high incidence of pathways with decremental conduction, ventricular hypertrophy, sinus node abnormalities, and sudden death. They identified a missense mutation in the gene that encodes the gamma 2 regulatory subunit of AMP-activated protein kinase. Protein kinase is involved in phosphorylation of many downstream substrates. The link between the genetic abnormality and pre-excitation is known to be due to development of cardiac glycogen storage disease leading to apposition of atrial and ventricular muscles (95). How this and other genes control cardiac morphogenesis is a great challenge for future understanding of the development of these aberrant pathways.

ATRIAL FLUTTER

Historical Studies of AFL

The term of flutter was first used by MacWilliam (96), who referred it to as visual observations of a rapid, seemingly regular excitation of the atrium. Atrial flutter was clearly differentiated from AF in man by Jolly and Ritchie (97). Lead II and III inscribed by these authors are clearly compatible with counterclockwise (CCW) cavotricuspid isthmus (CTI)-dependent flutter.

The most important early contributions related to the mechanism of AFL come from the brilliant work of Sir Thomas Lewis and associates (98). With induction of sustained flutter in dogs, mapping

was obtained by direct recordings from the atrial epicardial surface together with surface ECG recordings. They showed that there was an orderly sequence of atrial activation, and the absence of a true diastole which explained the surface pattern. They concluded that in most experiments the excitation wave was reentrant and appeared to involve both vena cava. The circulating wave front was inscribed either in a caudo-cranial or in a cranial-caudal fashion in the right atrium (RA). It was felt that the circulating wave front could also involve the left atrium (LA). Incredibly, they suspected rotation around the AV valves in several experiments. It should be emphasized that their observations were not universally accepted. Others (e.g., Scherf and Schott) (99) favored enhanced automaticity as a mechanism.

Induction of AFL was uncommon in normal canines and stable mappable flutter was even less frequent. Rosenbluth and Garcia Ramos created a canine model of sustained flutter by introduction of a crush lesion between the cavae (100) and found that the flutter wave front rotated around the crush lesion using epicardial mapping. Of interest, they also noted that in some animals, an additional lesion that “was made starting at the lower edge of the orifice of the IVC and extending the limit . . . toward the AV groove” could make the flutter disappear without re-inducibility. The latter is the identical lesion currently used to ablate CTI-dependent flutter.

We are indebted to Waldo and his colleagues for their seminal observations explaining the physiology of AFL. He and his colleagues studied patients with postoperative flutter by means of fixed atrial electrodes (101, 102). They confirmed that the AFL cycle length was remarkably consistent with mean variations of less than 4 ms. Moreover, Waldo and colleagues taught us the importance of using entrainment both for detection of reentrant circuits and for discerning whether a given region is critical for tachycardia maintenance (102). They also found an interesting relationship between AF and AFL in those patients in whom the onset of AFL was recorded that the transition to AFL was preceded by short episodes of rapid transitional rhythm (or AF) (103).

Another major advance relates to the studies by Frame et al. (104, 105). They introduced a canine model with the intercaval lesion extended into the RA free wall (104). In this model, instead of the “expected” circuit around the “Y” lesion, mapping revealed evidence of electrical activation around the tricuspid orifice. In a further study (105), they proved the reentrant circuit around the annulus by entrainment pacing and showed the presence of an excitable gap. This study established the need for barriers for tachycardia initiation and perpetuation. Further observations supporting the reentrant nature of AFL were provided by the studies of Boineau et al. (colony of dogs with spontaneous flutter) (106), Hayden and Rytand (107), Kimura et al. (108), and Kato et al. (109).

Another notable contribution came from Klein and Guiraudon (110) who mapped two patients with AFL in the operating room. They found evidence of a large RA reentrant circuit and the narrowest part of the circuit lay between the TA and the IVC. They successfully treated the flutter by using cryoablation around the CS and surrounding atrium.

Following the report of Klein et al. (110), there appeared several studies using high-energy shocks in an attempt to cure AFL (111, 112)).

Subsequently both Drs. Feld and Cosio almost simultaneously described using RF energy for disruption of CTI conduction in order to cure patients with AFL. Feld et al. (113) contributed an elegant study using endocardial mapping techniques and entrainment pacing to prove that the area posterior or inferior to the CS was a critical part of the flutter circuit and application of RF energy to this site terminated AFL. Cosio et al. used similar techniques but placed the ablative lesion at the area between the TA and IVC (114). The latter technique forms the basis for current ablation of CTI-dependent flutter.

Terminology of AFL

Rapid regular single macroreentrant atrial arrhythmias with little or no isoelectric interval are termed AFL. Historically, AFL was defined as being typical, reverse typical, or atypical. With increased

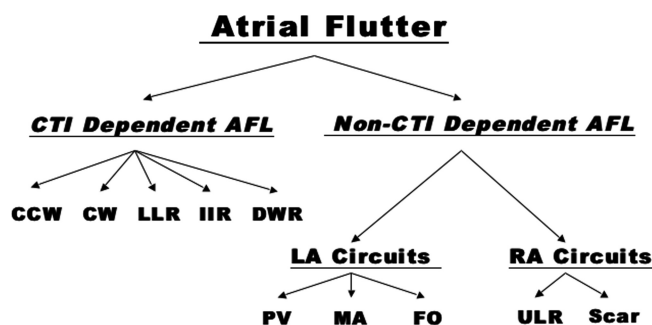


Fig. 8. Nomenclature of atrial flutter (AFL). CTI = cavotricuspid isthmus; CCW = counterclockwise AFL around the tricuspid annulus (TA); CW = clockwise AFL around the TA; LLR = lower loop reentry around inferior vena cava; IIR = intra-isthmus reentry; DWR = double-wave reentry around the TA; LA = left atrium; RA = right atrium; PV = reentrant circuit around the pulmonary vein (s) with or without scar(s) in the LA; MA = reentrant circuit around mitral annulus; FO = reentrant circuit around the fossa ovalis; ULR = upper loop reentry in the RA.

knowledge a new terminology appears to be appropriate. As shown in Fig. 8, we have recently proposed a revised nomenclature of AFL.

CAVOTRICUSPID ISTHMUS-DEPENDENT AFL

In the majority of the RA flutter, the CTI is a critical part of the reentrant circuit, which is also the target for AFL ablation.

Counterclockwise or clockwise (CW) AFL: These are macroreentrant circuits around the TA (115–120). The CW or CCW designation is made on the basis of wave front activation in the left anterior oblique (LAO) projection. Counterclockwise AFL is the most common and the surface ECG shows continuous sawtooth-like flutter wave dominantly negative in the inferior leads (II, III, and aVF) and positive in V1; whereas CW flutter shows positive waves in the inferior leads and negative waves in V1 (Fig. 9). These types of AFL may be seen both in patients with or without congenital heart disease or cardiac surgery.

Double-wave reentry (DWR): Flutter circuits have an excitable gap. A critical timed premature beat is able to invade the circuit and if that impulse experiences antidromic block but yet is able to propagate orthodromically, then two wave fronts may occupy the circuit simultaneously (121). This arrhythmia is manifest by acceleration of the tachycardia rate but with identical surface and intracardiac electrogram morphology. Double-wave reentry is usually produced by extrastimuli and is usually short lived, but may serve as a trigger for AFib (122).

Lower loop reentry (LLR): Lower loop reentry is a form of CTI-dependent flutter with a reentrant circuit around the IVC, therefore, it is confined to the lower part of the RA (123–125). It often co-exists with typical CCW or CW flutter and involves posterior breakthrough(s) across the CT. Since the CTI is still a necessary part of the circuit, LLR is amenable to CTI ablation as is true of patients with CCW or CW flutter. The surface morphology of LLR usually is very similar to that of CCW or CW flutter (126).

Intra-isthmus reentry (IIR): We have recently reported a novel reentrant circuit within the region of the septal (medial) CTI and CS ostium (127, 128). In the initial report of this flutter form, entrainment pacing from the antero-inferior (lateral) CTI shows post-pacing interval (PPI) > tachycardia cycle length (TCL), indicating the lateral CTI is out of the reentrant circuit; whereas, pacing from the region of septal isthmus or CS ostium shows concealed entrainment with PPI = TCL. Fractionated or double

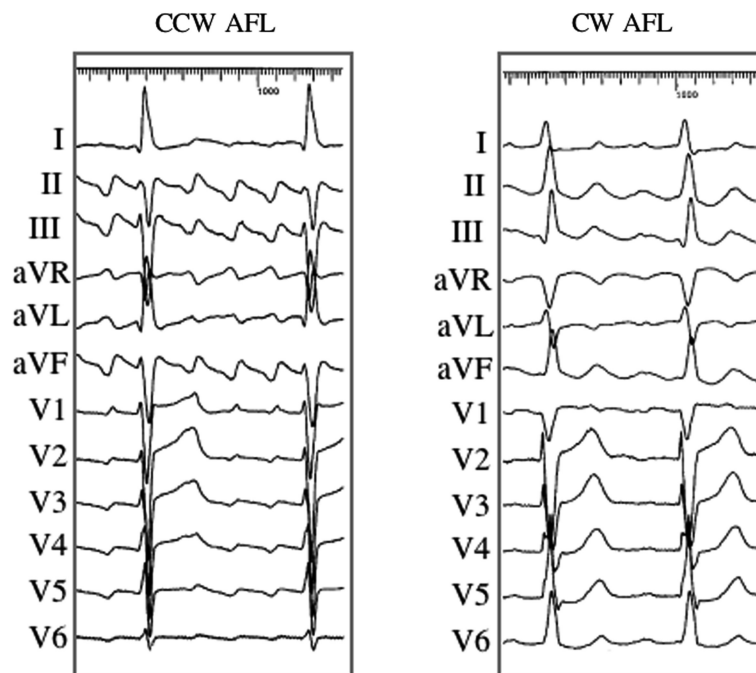


Fig. 9. Surface ECG of CTI-dependent AFL. *Left panel* shows the simultaneous 12-lead ECG in a patient with counterclockwise (CCW) AFL; *Right panel* shows the surface ECG in a patient with clockwise (CW) AFL.

potentials usually can be recorded in this area and can be entrained. Applying RF energy at the site of maximal fractionated potentials can always abolish the tachycardia.

NON-CTI-DEPENDENT AFL

Right Atrial Flutter Circuits. *Scar-related RA macroreentrant tachycardia:* Previous studies have shown that macroreentrant tachycardia can occur in patients with or without atriotomy or congenital heart disease (124, 129, 130). In these patients, electroanatomic voltage maps from the RA often show “scar” or low-voltage area(s) which acts as the central obstacle or channels for the reentrant circuit. The morphology of surface ECG may vary depending on where the scar(s) and low-voltage area(s) are and how the wave fronts exit the circuits.

Upper loop reentry (ULR): This is a type of atypical AFL involving the upper portion of RA with transverse conduction over the CT and wave front collision occurring at lower part of RA or within the CTI (124, 131). Therefore, this tachycardia is a non-CTI-dependent flutter and the CTI is found to be outside of the circuit by entrainment pacing. Upper loop reentry was initially felt to involve a reentrant circuit using the channel between the superior vena cava (SVC), fossa ovalis (FO), and CT (124). A study by Tai et al. using non-contact mapping technique showed that this form of AFL was a macroreentrant tachycardia in the RA free wall with the CT as its functional central obstacle (131). They successfully abolished ULR by linear ablation of the gap in the CT. Like LLR, ULR also can occur in conjunction with typical CW and/or CCW flutter, as well as LLR.

Left Atrial Flutter Circuits. Left AFL circuits are often related to AF. In recent years, these circuits have been better defined by use of electroanatomic or non-contact mapping techniques (132). Cardiac surgery involving the LA or atrial septum can produce different left flutter circuits. But, left AFL circuits also can be found in patients without a history of atriotomy. Electroanatomic maps in

these patients often show low-voltage or scar areas in the LA, which act as either a central obstacle or a barrier in the circuit. The surface ECG of left AFLs are variable due to different reentrant circuits. However, several sub-groups have been identified (Fig. 8).

Mitral annular (MA) AFL: This flutter circuit involves reentry around the MA either in a CCW or in a CW fashion. This arrhythmia is more common in patients with structural heart disease. However, it has been described in patients without obvious structural heart disease (126, 132), but in these patients, electroanatomic voltage map often shows scar or low-voltage area(s) on the posterior wall of LA as a posterior boundary of this circuit. The surface ECG of MA flutter can mimic CTI-dependent CCW or CW flutter, but usually shows low flutter wave amplitude in most of the 12 leads (126).

Pulmonary vein(s) (PVs) with or without LA scar circuits: Various left AFL circuits involve the PVs, especially in those patients with AF or mitral valve disease. Reentry can circle around one or more PVs and/or posterior scar or low-voltage area(s) (126, 132). In order to cure these complex circuits, electroanatomic mapping is required to reveal the circuit and guide ablation (Fig. 10). Since these circuits are related to low-voltage or scar area(s), the surface ECG usually shows low-amplitude or flat flutter waves.

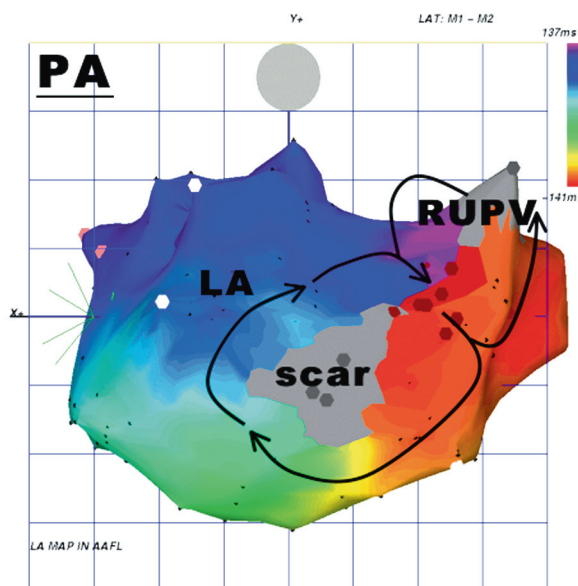


Fig. 10. Electroanatomic activation map in a patient with left atrial (LA) flutter with posterior–anterior (PA) project view. The activation map demonstrates a reentrant circuit (figure of eight) around the right upper pulmonary vein (RUPV) and scar on the LA posterior wall, as shown by the arrows.

ATRIAL FIBRILLATION

The history of AF has been described in a number of excellent articles (133–135). It is not clear who first described AF. The legendary Chinese Yellow Emperor (Huangdi), who ruled China from 2497 to 2398 BC, reportedly described irregular and weak pulses in the Yellow Emperor's Classic of Internal Medicine (133). Circa 1187, Moses Maimonides described irregular pulses suggesting AF (134). Hanon, Shapiro, and Schweitzer published a very detailed account of the original investigations

and evolving theories of this important arrhythmia in more modern times (135). Irregular pulses in the presence of mitral stenosis were first described by de Senac in the eighteenth century and later by Robert Adams in 1827 (133, 136). Stokes described irregular pulses in 1854 and Wenckebach in 1904 (137, 138). Rothberger and Winterberg described AF in two patients with *arrhythmia perpetua* in 1909 (139). Irregular pulse tracings showing discrepancies between simultaneously recorded apical and radial pulses were published by Etienne Marey (1863), Heinrich Hering (1903), James Mackenzie (1907), and Thomas Lewis (1909) (135). Willem Einthoven and Thomas Lewis first recorded AF with electrocardiography in 1909. In 1910, Lewis published a landmark treatise on AF and established the term auricular fibrillation, which he defined as “a condition in which normal impulse formation in the auricle is replaced by stimulus production at multiple auricular foci. Co-ordinate contraction is lost; the normal and regular impulses transmitted to the ventricle are absent, while rapid and haphazard impulses produced in the auricle take their place and produces gross irregularity of the ventricular action” (140).

Mechanisms of AF

Competing models for mechanism underlying AF were reviewed by Garrey in 1924 (141). Spontaneous rapidly discharging atrial foci and a single reentry circuit with fibrillatory conduction were the first two mechanisms proposed for AF. Scherf developed the first animal model of AF by applying aconitine on an atrial site causing rapid firing (142). Moe and his colleagues in 1964 proposed that AF was due to random reentry of multiple, simultaneously circulating reentrant wavelets (143). It was further developed by Allesie and his colleagues in the 1970s (144). It hypothesized that AF was due to multiple randomly propagating reentrant waves in the atrium and AF required at least six to eight circular reentrant wave fronts and a critical atrial mass (145). It had been accepted as the mechanism until the recent discovery of spontaneous electrical activity in pulmonary vein, first in isolated guinea pig pulmonary vein and later in humans during electrophysiologic study, clearly indicating a spontaneous rapidly discharging atrial focus can be the underlying mechanism for AF (146, 147). Nattel reviewed the mechanisms of AF at the tissue and cellular levels and how our treatment approaches are modified and guided by our understanding of the underlying mechanisms (148, 149).

Clinical Implications of AF

Epidemiology of AF: In 1965, a study reported that the incidence of AF was 4.3 per 1000 when routine ECGs were recorded in one community with 5179 adults (150). Katz and Pick reported that in 50,000 consecutive patients with suspected heart disease 3.1% had paroxysmal AF and 8.6% had chronic AF (151). Most of our knowledge of the epidemiology of AF came from studies published in the late 1970s–2000. And the Framingham Heart Study provided a majority of the data. The increased prevalence of AF with age was clearly demonstrated in a number of epidemiology studies (152, 153). The Framingham Heart Study first established that AF increased mortality in older men and women (55–94 years of age) even after adjustment for the pre-existing cardiovascular conditions (154). The effect appears more prominent in women – 1.5-fold in men and 1.9-fold in women. Both heart failure and stroke contributed to the excessive mortality.

Thromboembolism and Anticoagulation: The role of nonrheumatic AF as a precursor of stroke and higher stroke events at the onset of AF was first identified in the Framingham Heart Study in 1978 (155, 156). The risks factors for stroke and the efficacy of warfarin in decreasing stroke were established in five randomized trials published between 1989 and 1992 (AF, Aspirin, Anticoagulation Study from Copenhagen, Denmark (AFASAK), the Stroke Prevention in Atrial Fibrillation (SPAF) study, the Boston Area Anticoagulation Trial in Atrial Fibrillation (BAATAF), the Canadian Atrial Fibrillation Anticoagulation (CAFA) study, and the Veterans Affairs Stroke Prevention in Nonrheumatic Atrial

Fibrillation (SPINAF) study) (157–162). In patients with AF for whom warfarin was unsuitable, the addition of clopidogrel to aspirin reduced the stroke risk (163). In the 1980s, transesophageal echocardiography (TEE) was introduced as a sensitive and specific diagnostic tool to identify high-risk patients by detecting thrombus in the LA appendage (164). In 1993, Manning and his coworkers introduced TEE-guided strategy for elective cardioversion without prolonged anticoagulation (165).

Therapy

Pharmacological Therapy: The treatment of AF had been limited to restoring normal sinus rhythm with either DC shock or pharmacologic agents and maintenance of normal sinus rhythm with long-term drug treatment. In the case of chronic AF, rate control was the alternative. For many years, quinidine and procaineamide were the only drugs available for chemical cardioversion and rhythm maintenance. Flecainide, propafenone, amiodarone, ibutilide, and dofetilide were introduced in the past 30 years. Their efficacy in maintaining normal sinus rhythm has not been satisfactory and their pro-rhythmic risk well documented. In two randomized studies, the rate of recurrence ranged from about 35% for amiodarone to about 60% for sotalol and propafenone (166, 167). For controlling of rate only, the oldest drug is digitalis, which was first used by Jean Baptiste Bouilland in 1835 (133). Because of its ineffectiveness, it has been replaced with beta-blockers and calcium channel blockers. For years, conversion to and maintenance of normal sinus rhythm have always been the main goal of AF therapy; rate control was attempted only if repeated attempts in rhythm control failed. Two large randomized prospective clinical trials compared rate vs. rhythm control in AF therapy in elderly patients (168, 169). In the AFFIRM trial, rate control lowered 5-year overall mortality rate (21.3% in rate vs. 23.8% in rhythm control, but without significant statistic difference). In the RACE trial, rate control increased 3-year event-free survival (17.2 in rate vs. 22.6% in rhythm control). Events included cardiovascular death, heart failure, thromboembolism, bleeding, pacemaker implantation, and anti-arrhythmic drug side effects. Embolization occurs with equal frequency in both trials. More importantly, despite successful cardioversion, recurrence rate of AF was high and many AF episodes were asymptomatic. Accordingly, anticoagulation consideration is dependent on stroke risks and not on rate or rhythm control management strategy.

Non-pharmacological Therapy: DC trans-thoracic defibrillation with synchronization was first introduced by Lown and his coworkers in 1962 (170). This method remains the most effective method for acute conversion of AF to normal sinus rhythm. Surgical interventions were designed to prevent random reentry. These include reduction and fragmentation of atrial surface area, exclusion of the fibrillating atrium, and creation of one-dimensional conduction with multiple surgical incisions (171). The best known surgical ablation of AF was the MAZE procedure first performed by Cox in 1987 (172). Because of the complexity and morbidity surgical ablation quickly gave way to catheter ablation. Catheter ablation of the AV node with implantation of a permanent pacemaker was first used to achieve rate control in AF with rapid ventricular response (31, 173). Since John F. Swartz introduced the procedure, curative catheter ablation therapy has been the major focus of electrophysiologists since the early 1990s. Spragg and Caulkins recently published an overview of the development catheter-based AF therapy and the relative merits of the different techniques (174). Major contributors to the innovation and advancement of AF ablation include groups led by Michel Haissaguerre, Andrea Natale, Carlo Pappone, Morady, and Shih-Ann Chen. The first attempt entailed creation of linear lesions in the RA only or in combination with the LA (including the PVs) (175–177). This was met with little success. But the experience allowed Haissaguerre to discover that focal atrial triggers (predominantly located in the PVs) are frequently responsible for initiation of AF (178). However, ablation of focal PV trigger sites carries risk of PV stenosis and high recurrence rate because the focus cannot be consistently triggered during the procedure and precisely localized. Segmental ostial and circumferential PV isolation techniques were introduced to electrically isolate these triggering foci from the

body of the LA by eliminate conduction between the pulmonary triggers and the atrial myocardium, thereby preventing initiation of AF (179, 180).

Future

The last 30 years have seen enormous and rapid growth in our knowledge of AF. We learned the epidemiology of AF, the stroke risks, the importance of anticoagulation, the use of echocardiographic techniques, especially TEE in managing AF, the merits of rate and rhythm management, and finally, catheter-based curative ablation. On the other hand, we may have not reached the end of the ascending portion of our knowledge curve. It has been 10 years since catheter ablation of AF was first used clinically, but we still do not have a standard ablation approach (181). The successful cure rates for paroxysmal, persistent, and chronic AF have not been significantly improved in the past few years. The success rates may be limited by our one-size-fit-all approach to a disease with diverse underlying mechanisms. Our curative success in other tachyarrhythmias has largely been driven by our knowledge of their underlying mechanisms. Similarly, higher success rate in AF ablation will be achieved largely by improving our knowledge of its mechanisms and pathophysiology. Meanwhile, improvement in mapping techniques and equipment such as three-dimensional electroanatomical mapping system, CT, MRI and robotic navigation, catheter designs, and ablation energy sources will help to further reduce operation time and possible the need for repeat procedures. The importance of anticoagulation in AF even after apparent successful cardioversion cannot be overemphasized. There is an obvious need for newer anticoagulation agents with a better safety profile and less monitoring. Left atrial appendage plug in prevention of clot formation has shown very promising results in clinical trial (PROTECT-AF). Lastly, insights into genetic determinants will help us to further understand the mechanisms of AF.

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