Atrial Flutter: A Review of Its History, Mechanisms, Clinical Features, and Current Therapy

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Introduction

While atrial flutter (AFL) was first recognized shortly after the birth of electrocardiography, its mechanism and therapy were hotly debated until recently. Drug therapy proved to be notoriously poor for those with recurrent AFL in that drugs failed to prevent recurrences and large doses of AV nodal blockers were often needed for rate control. Over the past decade monumental shifts have occurred with respect to better definition of the arrhythmia mechanism and the remarkable efficacy of catheter ablative therapy. It is especially appropriate for this essay to review and take stock of where we have been, where we are, and where we hope to be in the future.

Historical Perspectives

The story of AFL begins more than a century ago.[1,2] The first published description of AFL dates back to 1886 when McWilliam described observing regular, rapid excitations of the atrium in an animal.[3] In 1906 Einthoven made an electrocardiographic recording of AFL.[4] Characteristic sawtooth waves in the inferior ECG leads were described by Jolly and Ritchie[5] in 1911. These authors were the first to distinguish AFL from atrial fibrillation (AF). In 1913 Lewis and coworkers[6] also described the distinctive sawtooth waves. Lewis and his colleagues were the first to investigate the mechanism of this arrhythmia.[7,8] Using a combination of epicardial maps and ECG recordings from a canine model of AFL induced by rapid atrial pacing, they showed that constant activation of at least some part of the atrium resulted in the flutter waves seen in the surface ECG. They also showed that the activation sequence was orderly, ie, the wavefront circulated in either a cranial-caudo or a caudo-cranial

direction in the right atrium.[7] From this groundbreaking experimental work, Lewis and his colleagues concluded that AFL was due to intra-atrial circus movement around the vena cavae.[8]

Subsequent works that supported the notion that flutter was due to intra-atrial reentry included those of Rosenbleuth and Garcia-Ramos who constructed a crush injury model of this arrhythmia by creating a lesion between the vena cavae.[9] Based on the epicardial maps, the authors deduced that the reentry loop circled around the atrial crush lesion. Interestingly, they also noted that when the crush lesion was extended from the inferior vena cava (IVC) to the AV groove, the arrhythmia disappeared and could not be induced. This important finding suggests that the true circuit may have included the cavotricuspid isthmus.

Intra-atrial macro-reentry as the mechanism of AFL was not universally accepted. Goto et al[10] and Azuma et al[11] had shown that aconitine caused abnormal automaticity at rapid rates in the rabbit atria. It was thought that if the atrial aconitine site fired fast enough, either flutter (1:1 conduction) or fibrillation (fibrillatory conduction because the atrial rate was too fast and 1:1 conduction could not be supported) occurred.[12] Based on these and other works with aconitine,[10,11,13-16] Scherf felt that flutter was due to abnormal automaticity.

Building on the work of Rosenbleuth and Garcia-Ramos, Frame et al[17-19] showed that the flutter reentry loop could exist outside of an atrial crush lesion. They created a "Y" lesion in the canine right atrium by extending the intercaval crush lesion to the right atrial free wall. The "Y" lesion produced a circuit that rotated around the tricuspid annulus. Similar flutter circuits may exist in patients who have undergone right atriotomies during repair of congenital heart defects.[20,21]

Over a span of nearly two decades, detailed experiments in various animal models and clinical studies have not only confirmed that the mechanism of flutter was due to intra-atrial macro-reentry but also set the stage for the development of curative catheter ablation therapy.[22-30] Of particular importance were the elegant works of Waldo et al,[27] Inoue et al,[28] and Stevenson et al,[29,30] all of described techniques of manifest and concealed entrainment. The latter allowed for identification of a site for catheter ablation.

AFL as an arrhythmia that could be successfully ablated with radiofrequency (RF) energy depended on the identification of a vulnerable, critical zone in the reentrant circuit. In 1986 Klein et al[31] reported their findings on intra-operative mapping studies of two patients with persistent flutter. They found that the narrowest part of the circuit had relatively slow conduction and localized to the low right atrium, between the IVC

TABLE 1. Atrial flutter occurrence compared with atrial fibrillation

Authors	Patients	Atrial fibrillation (%)	Atrial flutter (%)
Doliopoulos et al[36]	3780	24.6	0.7
Makinson et al[37]	9458	7.6	0.2
Katz and Pick[38]	50,000	11.7	0.5

and tricuspid ring. Furthermore, cryosurgical ablation of this critical region and its surrounding tissue prevented short-term recurrences of the arrhythmia. Subsequent studies by Chauvin and Brechenmacher[32] and Saoudi et al[33] using direct current (DC) shocks to disrupt the critical zone and eliminate the tachycardia supported the prospect that flutter could be permanently abolished by disruption of the isthmus. However, one drawback of using DC shock was that the shock itself could convert AFL. In the early 1990's, groups led by Feld and coworkers[34] and Cosio and coworkers[35] found that disruption of the isthmus of the flutter circuit could be carried out safely with RF catheter ablation.

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B. Gersh: This is an interesting account of the history of atrial flutter and provides a perspective ranging from the initial recognition of this distinctive electrophysiologic entity to an understanding of the anatomic characteristics of the circuit, which in turn have led to the therapeutic applications of radiofrequency ablation. It is said that a historical perspective helps to understand both the present and the future, and in this respect, readers might enjoy a scholarly and thoroughly entertaining review of a "close relative" of atrial flutter, namely, atrial fibrillation (Silvermann ME: From Rebellious Palpitations to the Discovery of Auricular Fibrillation: Contributions of Mackenzie, Lewis, and Einthoben. Am J Cardiol 1994;73:384-9).

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Epidemiology, Risk Factors

While detailed epidemiologic studies of AF have been available for almost two decades, similar studies of AFL have only been available for the past five years. AFL occurs less than one-tenth as often as AF (Table 1).[36-38] Based on the 1990 Commission on Profession and Hospital Activity (CPHA) database, of the 517,699 discharges nationwide with arrhythmia as the principal diagnosis, AF made up 179,018 (34.6%), while AFL made up 23,420 (4.5%).[39] Recent studies from the Marshfield Epidemiologic Study Area (MESA) database have reported that the overall incidence of AFL is about 88 per 100,000 person-years[40,41] and have estimated that there are 200,000 new AFL cases in the United States annually with 80,000 of these cases presenting as "atrial flutter only."[40,41]
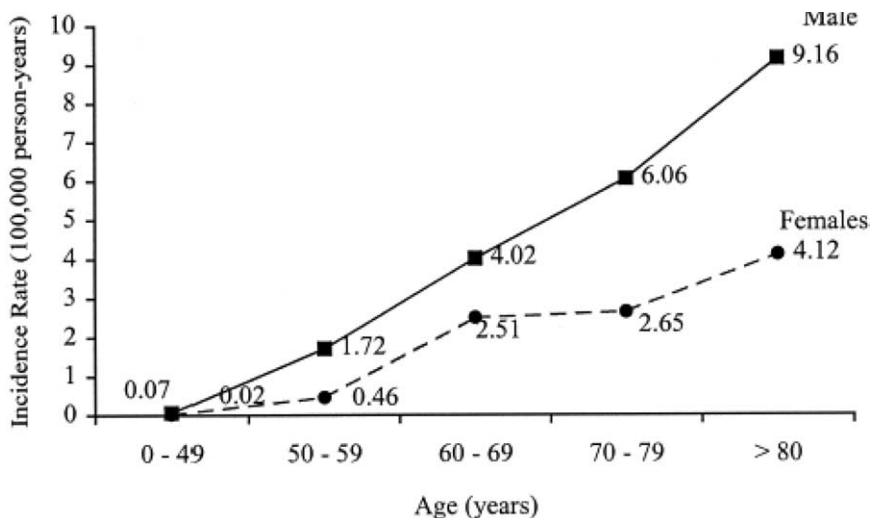
FIG 1. Incidence of atrial flutter by age and gender (100,000 person-years). (From Granada J, et al. J Am Coll Cardiol 2000;36:2242-6.)

The incidence of AFL is about two to five times higher in men than in women, and like AF, AFL increases dramatically with age (Fig 1)[41-43]: the incidence of AFL in those younger than 50 years old is about 5/100,000 but rises sharply to 587/100,000 in those older than 80 years old.[41]

Besides advanced age and male gender, risk factors for AFL include heart failure, chronic pulmonary disease, previous stroke, and myocardial infarction.[41,44] Conditions associated with flutter include thyrotoxicosis, valvular heart disease, pericardial disease, congenital heart disease, post-open heart surgery, post-major noncardiac surgery, and especially postsurgical repair of congenital heart defects (eg, Mustard, Senning, Fontan) (Table 2).[42,45,46] The possibility of a genetic predisposition for developing AFL is unclear. Preliminary studies suggest that a genetic cause may exist, although flutter presentation is more likely a manifestation of an important cardiac genetic abnormality that results in dilated cardiomyopathy and conduction system disease.[47]
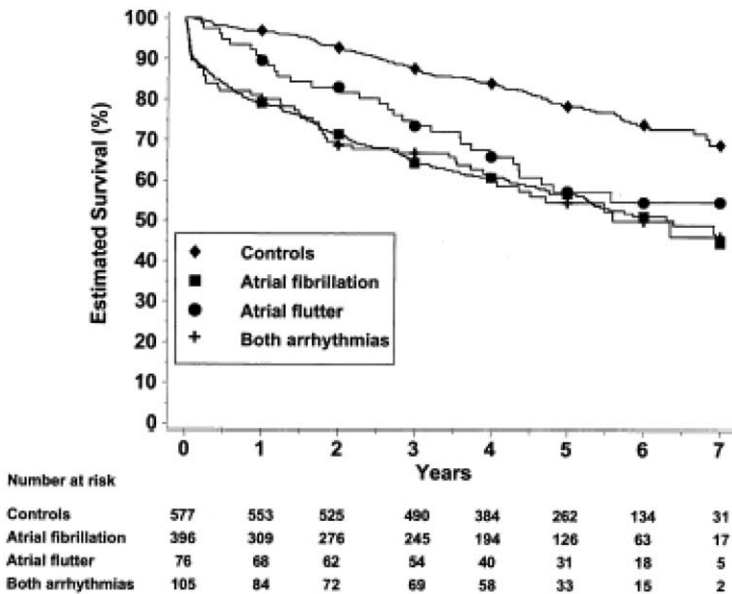
While the morbidity and mortality associated with AF have been well recognized,[39,48-51] it is not until recently that the morbidity and mortality specifically associated with AFL have been examined. This may be that AFL was previously grouped under the AF/AFL category. Studies have reported that AFL is associated with increased mortality,[44,52,53] though not as high as AF or a combination of AF and AFL (Fig 2).[44]

TABLE 2. Conditions associated with atrial flutter

Valvular heart disease (ie, rheumatic, mitral, tricuspid)
Myocardial infarction
Pericardial disease
Cardiac tumors
Hypertrophic cardiomyopathy
Congenital heart disease
Post surgical repair of congenital heart defects
Post cardiothoracic surgery
Post major noncardiac surgery
Severe pulmonary disease
Pulmonary embolus
Thyrotoxicosis
Acute alcohol intoxication

Number at risk							
Controls	577	553	525	490	384	262	134	31
Atrial fibrillation	396	309	276	245	194	126	63	17
Atrial flutter	76	68	62	54	40	31	18	5
Both arrhythmias	105	84	72	69	58	33	15	2

FIG 2. Kaplan–Meier survival plots of subjects with atrial fibrillation, atrial flutter, or both arrhythmias, compared with controls. (From Vidaillet H, et al. Am J Med 2002;113:365-70.)

Interestingly, in their cohort of patients Vidaillet et al[44] reported that early mortality (first 6 months) was higher in patients with flutter than in controls but the number did *not* reach statistical significance, while late mortality was both increased and statistically significant. An intriguing question is whether early curative treatment of AFL will alter late mortality.

B. Gersh: In a population-based study of "lone" atrial flutter from Olmstead County, Minnesota, Halligan et al (ref. 53) demonstrated over a long period of follow-up that atrial fibrillation developed in 56% of patients an initial diagnosis of lone atrial fibrillation. This emphasizes the close relationship between the two arrhythmias (ref. 53).

Clinical Presentation, Diagnosis

AFL usually occurs in paroxysms, lasting seconds to hours. Less commonly it exists as a stable, persistent rhythm. AFL is frequently associated with AF. Symptoms are most prevalent when flutter is paroxysmal and when the ventricular rate response is rapid. Palpitations are the most common symptom[54]; others include dyspnea, chest discomfort, presyncope, and weakness. Syncope, in the absence of significant cardiac disease, is rare.[55] AFL is not infrequently a precipitant of congestive heart failure in patients with significant cardiac disease. Patients with both AFL and AF may be more symptomatic than those with just AF because the heart rate tends to be more rapid during AFL, while AF is usually associated with increased AV nodal penetration and slower ventricular responses.

Notable physical examination findings include a rapid peripheral pulse that is more often regular than irregular. Cannon "a" waves due to atrial contraction against a closed tricuspid valve may be observed. Cardiac auscultation may reveal a first heart sound of variable intensity: constant if the association of the atrial and ventricular contractions is maintained, and variable if it is not.[56]

In most cases, one can make the diagnosis of AFL with a 12-lead surface ECG, looking for distinctive sawtooth waves in leads II, III, aVF, and V₁ (Figs 3A and B). In cases when the flutter waves are not readily discernible, interventions that transiently increase AV block to remove the QRS complexes can be helpful. They include vagal maneuvers (eg, carotid sinus massage, Valsalva maneuver) or administration of rapid-acting AV nodal blocking agents (eg, diltiazem, adenosine). An electrogram obtained with an esophageal electrode can also be used to make the diagnosis.

AV conduction in AFL is usually 2:1 (Fig 3A), resulting in a regular rhythm, but conduction may be variable (Fig 3B), resulting in an irregular rhythm. Rarely, 1:1 AV conduction can occur and may be lethal.[57-59] Situations when 1:1 AV conduction can occur include use of drugs that slow the flutter rate and paradoxically increase the ventricular response, in patients with the Wolff–Parkinson–White syndrome and a short

A.

B.
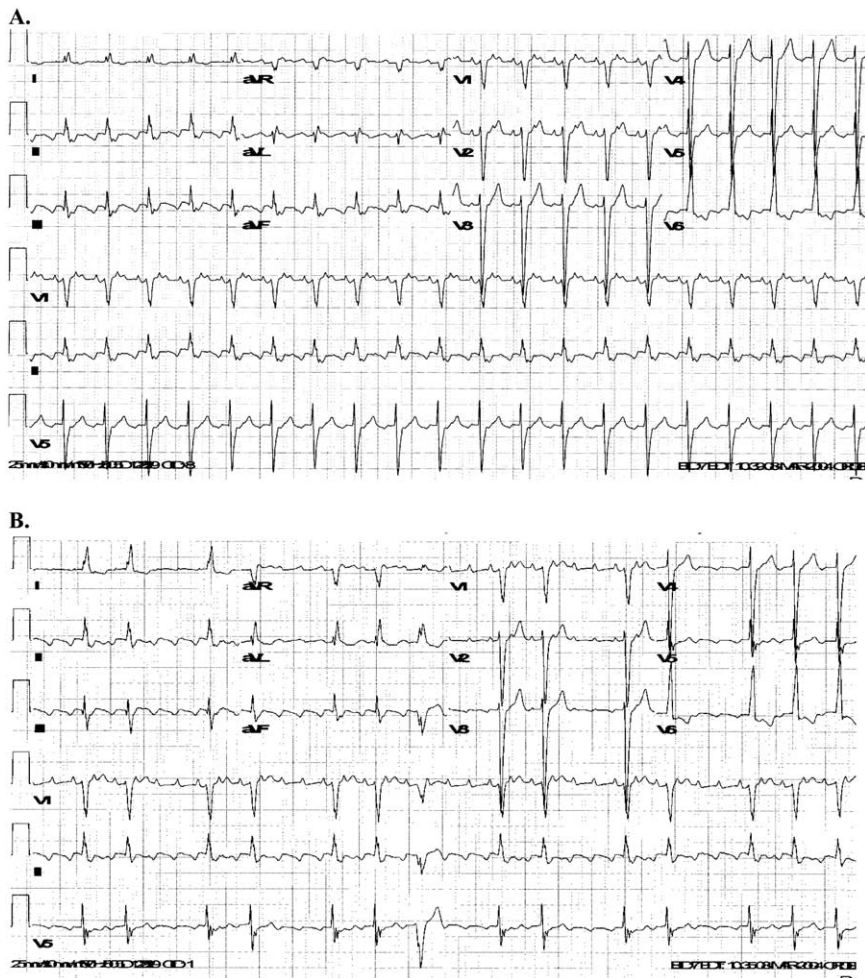
FIG 3. 12-lead ECG's of the same patient with counterclockwise (*typical*) atrial flutter with 2:1 AV block (A) and variable block (B). Note the negative flutter waves in the inferior leads and positive waves in V_1.

antegrade refractory period of the accessory pathway, in those with accelerated AV nodal conduction, or during intense catecholamine surges (eg, exercise).

The surface ECG flutter wave morphology can provide insights into the specific mechanism of the circuit. Readily discernible flutter waves in the inferior and V_1 leads are specific (up to 90%) for cavotricuspid-isthmus-dependent (CTI-dependent) flutter.[60,61] For example, negative flutter waves in the inferior leads and positive in V_1 are suggestive of a
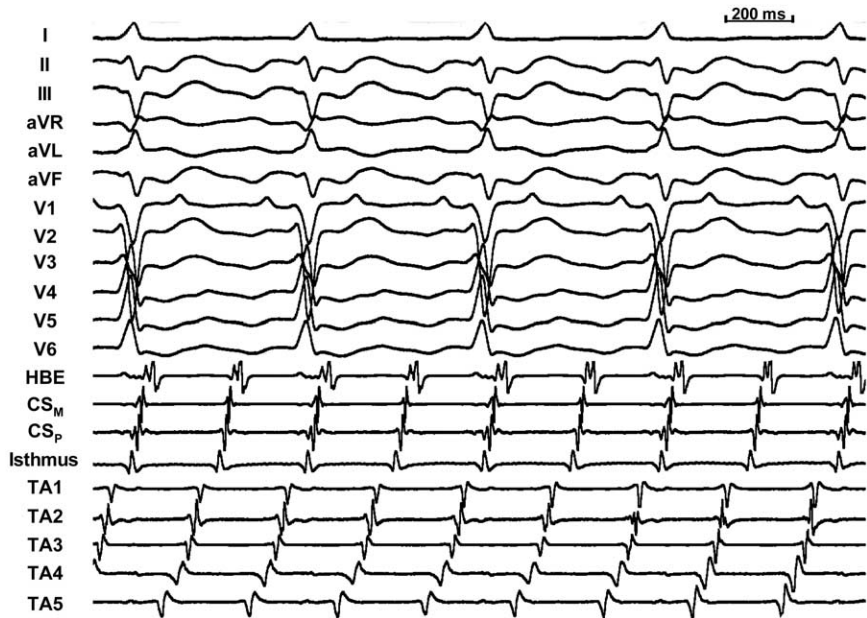
FIG 4. Simultaneous ECG and intracardiac electrograms of counterclockwise flutter. Note the positive flutter waves in V_1 and negative waves in the inferior leads. Displayed below the ECG, the intracardiac recordings show activation from the lateral right atrium (TA5) to the septum (HBE). The isthmus is activated from low lateral tricuspid annulus (TA1) to coronary sinus (CS_P). HBE = recording from the region of anterior septum around His bundle region; CS_P = proximal coronary sinus; CS_M = middle of the coronary sinus; CS_D = distal coronary sinus; TA = recordings from the 20-pole, "halo" electrode catheter (see Fig. 7) positioned along the tricuspid annulus with its distal pole (TA1) at 7 o'clock in the left anterior oblique projection, and proximal at high right atrium (TA5).

counterclockwise right atrial circuit with a lateral-to-medial activation over the CTI (*typical*) (Figs 3A, 4, and 8A), while positive flutter waves in the inferior leads and negative in V_1 are suggestive of a clockwise right atrial circuit with medial-to-lateral activation over the CTI (Figs 5 and 8B). Attempts have been made to correlate flutter wave morphologies with non-CTI-dependent flutter mechanisms (see below). In most non-CTI-dependent flutter circuits, the surface ECG findings are non-specific and are not predictive of the mechanism of the circuit. Milliez et al[62] have examined the association of flutter wave morphologies of CTI-dependent AFL with echocardiographic findings and clinical patient characteristics. They have found that a terminal positive component of the flutter wave in the inferior leads in counterclockwise (CCW) right atrial AFL is associated with heart disease, AF, and left atrial enlargement (left atrial
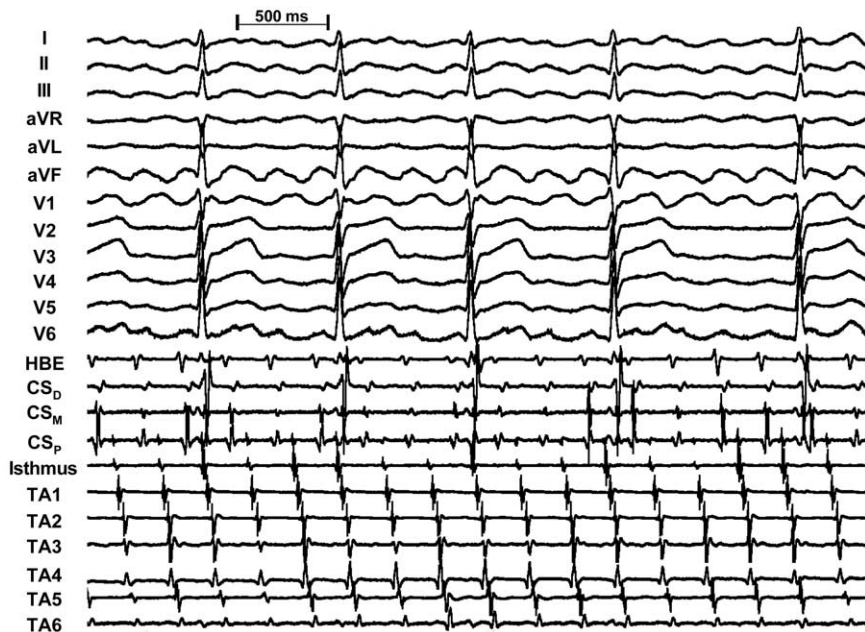
FIG 5. Simultaneous ECG and intracardiac electrograms of clockwise flutter. Note the negative flutter waves in V_1 and positive waves in the inferior leads. The intracardiac recordings show that the isthmus is activated from proximal coronary sinus (CS_P) to low lateral right atrium (TA1). The tricuspid annulus is activated in a clockwise fashion from isthmus to lateral right atrium (TA6).

dimension greater than 4 cm in the long axis view and/or greater than 5.2 cm in the four-chamber view with transthoracic echocardiography).

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B. Gersh: The authors make the useful point that the surface electrocardiogram in this condition is really useful from a clinical standpoint, particularly when radiofrequency ablation is under consideration. The highest success rates are obtained in "typical" atrial flutter. This is well clarified by the authors in the subsequent discussion of mechanisms and the classification utilizing Table 3.

Mechanisms, Nomenclature

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Atrial flutter is a condition in which, as has recently been shown, the contraction wave follows a circular and never ending path in the auricle, the circuits being completed a rate of from 240 to 350 per minute in different subjects.

<div align="right">Sir Thomas Lewis 1920[7]</div>

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TABLE 3. Classification of atrial flutter

Right atrial CTI-dependent flutter
Counterclockwise (CCW) flutter
Clockwise (CW) flutter
Double-wave reentry
Lower loop reentry
Intra-isthmus reentry
Right atrial non-CTI-dependent flutter
Scar-related flutter
Upper loop flutter
Left atrial flutter
Mitral annular flutter
Scar- and pulmonary vein-related flutter
Coronary sinus flutter
Left septal flutter

CTI = Cavotricuspid isthmus.
Counterclockwise vs. clockwise direction of wavefront rotation, when visualized from the left anterior oblique fluoroscopic view.

AFL is a macro-reentrant arrhythmia. The atrial rhythm is regular (usually with a rate of 250-350/min) with little or no isoelectric interval on the ECG. Its activation pattern can usually be determined by detailed, intracardiac mapping studies.

Over the years, terms used to describe various types of AFL have been ambiguous and have created a great deal of confusion. They include *rare, common, uncommon, typical, atypical, fast, slow, type I, type II,* and *left atrial.* As we have learned more about the various mechanisms of this arrhythmia, the terminology of AFL has evolved. In 2001, the European Society of Cardiology and the North American Society of Pacing and Electrophysiology have published a treatise on AFL nomenclature.[61] More recently, Scheinman and his colleagues[63] have provided an updated classification and nomenclature. Since an understanding of AFL mechanisms is needed to remember AFL terminology, we describe the currently known AFL circuits below, modeled after the classification proposed by Scheinman et al.[63] Table 3 provides a classification of AFL.

Right Atrial Cavotricuspid-Isthmus-Dependent Flutter

Fig 6 shows the anatomic structures of interest in CTI-dependent flutter. Fig 7 shows a diagram of catheter arrangement in the right atrium frequently used in our electrophysiology laboratory to study flutter.

CCW Atrial Flutter (Fig 8A)

Classically referred to as *typical*, this is the most common type of flutter and makes up about 90% of clinical cases.[61] It is the most
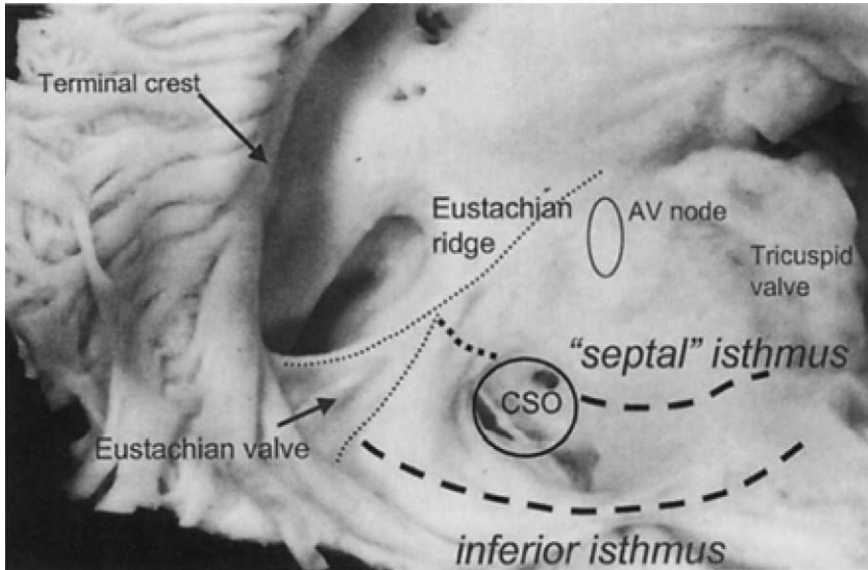
FIG 6. Right atrial anatomic structures of interest in cavotricuspid-isthmus-dependent flutter. The inferior isthmus is the target of radiofrequency ablation in most electrophysiology laboratories. (Kottkamp H, Hindricks G. Catheter ablation of atrial flutter. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology: From Cell to Bedside. Philadelphia: Saunders; 2004:1054.)

common macro-reentrant atrial tachycardia circuit even in patients who have had a right atriotomy for repair of congenital heart defects.[64] The ECG findings are characteristic and include negative sawtooth waves in the inferior leads with positive waves in V_1 that transition to negative in V_6 (Fig 4). From a left anterior oblique (LAO) fluoroscopic view, the circuit rotates in a CCW direction, ie, the activation wavefront proceeding superiorly over the right atrial posterior and septal walls and inferiorly over the right atrial anterior and lateral walls. Anteriorly, the circuit is bounded by the tricuspid orifice, while posteriorly, it is bounded by the anatomic barriers of the vena cavae orifices and eustachian ridge and the functional barrier of the crista terminalis.[65-67] The superior margin is as yet not well defined but may include the right atrial roof, anterior to the SVC orifice, including the initial portions of the Bachman's bundle.[67-69] The inferior margin is marked anteriorly by the tricuspid orifice and posteriorly by the IVC orifice and its continuation in the eustachian ridge. The inferior region is the critical link of the circuit and is referred to as the cavotricuspid, or subeustachian, isthmus. It is the target of curative RF ablation therapy.
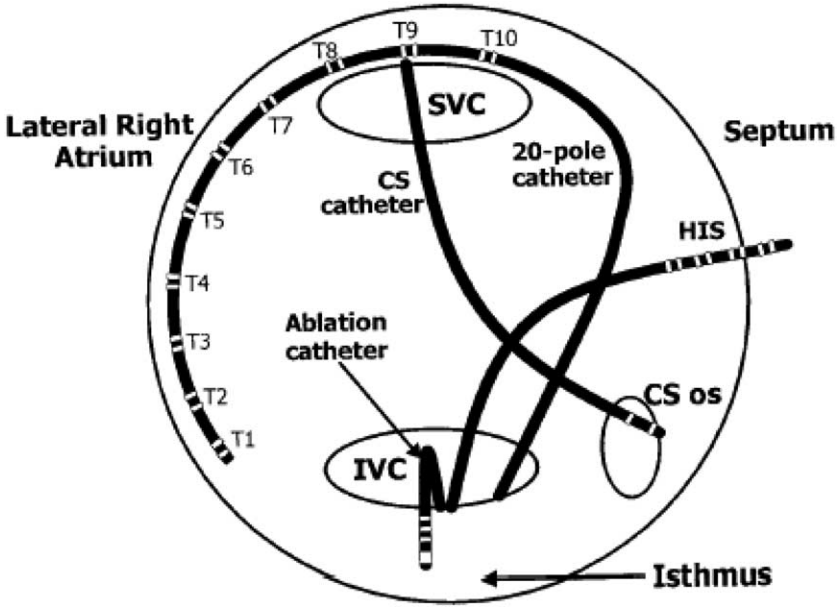
FIG 7. Schematic of catheter arrangement in the right atrium for flutter detection and ablation. The 20-pole, "halo" catheter is used to analyze the sequence of activation during the tachycardia. IVC = inferior vena cava; SVC = superior vena cava; CS = coronary sinus; os = ostium; HIS = His bundle region.

Clockwise (CW) Atrial Flutter (Fig 8B)

The pathway of this circuit is the *reversed* version of CCW CTI-dependent AFL, ie, with the activation wavefront proceeding superiorly over the right atrial anterior and lateral walls and inferiorly over the right atrial posterior and septal walls. It makes up about 10% of clinical cases and has ECG findings that include positive deflections in the inferior leads and negative in V_1 (Fig 5). Other unusual ECG patterns have been reported[60] so that detailed atrial mapping and entrainment pacing studies may be needed to make the diagnosis. The circuit has the same boundaries as its counterclockwise counterpart, and complete interruption of the CTI leads to a cure.

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B. Gersh: As the authors point out, this form of atrial flutter is still amiable to curative radiofrequency ablation but the procedure may be more complex than in the "typical" variant.

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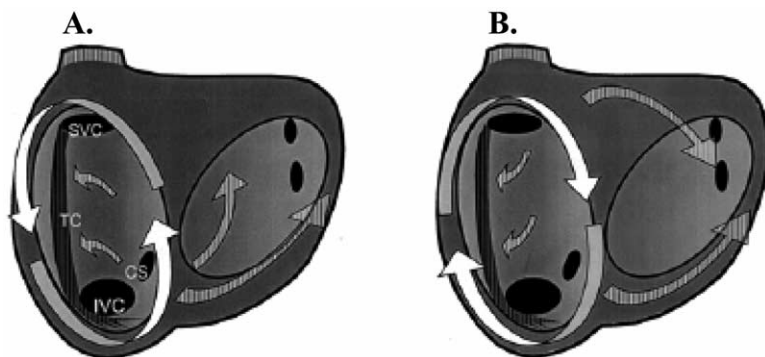
FIG 8. Right atrial cavotricuspid-isthmus-dependent flutter: counterclockwise or *typical* (A), and clockwise or *reverse typical* (B) circuits. Right and left atria from the left anterior oblique view. SVC = superior vena cava; IVC = inferior vena cava (IVC), CS = coronary sinus. White arrows denote direction of activation. (From Cosio et al. Cardiac Electrophysiol Rev 2002;6:356-64.)

Double-Wave Reentry (Fig 9)

Overdrive or programmed stimulation can sometimes accelerate arrhythmias (reported up to 25-44% of patients with ventricular tachycardia (VT)).[70-72] Brugada et al[73,74] were the first to describe VT acceleration due to double-wave reentry (DWR) in an animal model. They used up to seven extrastimuli to produce VT acceleration. Based on high-resolution epicardial mapping studies, they showed that the activation sequence during DWR was identical to baseline VT. Frame et al[72] demonstrated that overdrive pacing induced DWR in canine atrial tricuspid and ventricular mitral annular ring tissue. These investigators reported that DWR was always transient and on termination, or block of one wavefront, single-wave reentry remained.

In 1998 Cheng and Scheinman[75] reported that DWR was responsible for pacing-induced AFL acceleration in human subjects. They found that a single extrastimulus critically timed and precisely delivered to the isthmus between the tricuspid annulus and eustachian ridge resulted in unidirectional antidromic block of the paced impulse and acceleration of CCW AFL. Detailed analyses of the activation sequences, intracardiac electrograms, and surface ECG flutter wave morphology revealed that tachycardia acceleration was due to two successive activation wavefronts traveling simultaneously in the same direction in the reentrant circuit. None of the DWR flutter episodes were sustained. In three episodes, DWR termination resulted in complex atrial arrhythmias, including AF. It has been speculated that DWR may serve as a trigger for AF.[76]
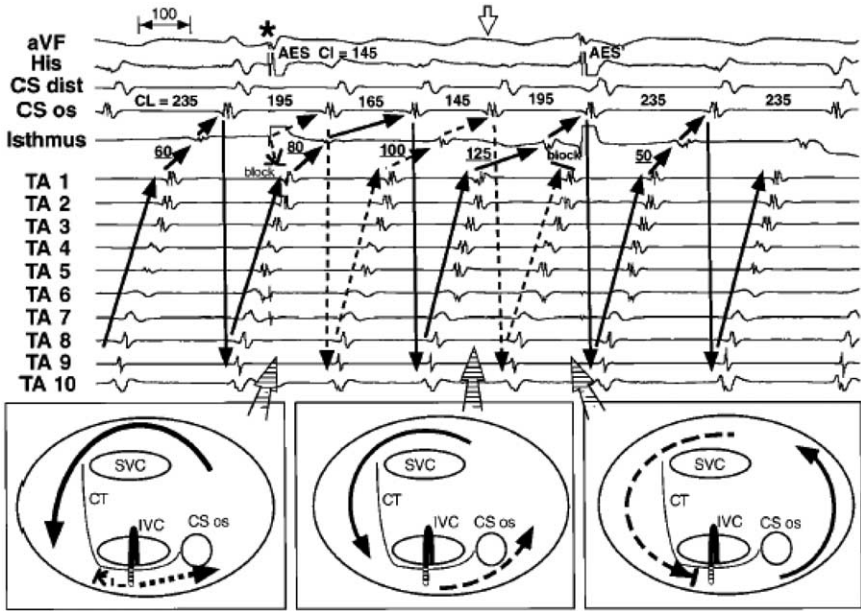
FIG 9. Intracardiac electrogram of double-wave reentry (DWR) after delivery of an atrial extrastimulus (AES) to the cavotricuspid isthmus. Solid line indicates the original CCW flutter circuit; dashed line indicates the second wavefront generated by the critically timed AES, resulting in DWR. The second wavefront eventually blocked in the CTI and the activation reverted back to the CCW flutter pattern. His = recording from the His bundle region; CS dist = distal coronary sinus; CS os = ostium of coronary sinus; TA = recordings from the 20-pole electrode catheter positioned along the tricuspid annulus with its distal pole (TA1) at 7 o'clock in the left anterior oblique projection, and proximal at high right atrium (TA5). SVC = superior vena cava; IVC = inferior vena cava; CT = crista terminalis. (From Cheng et al. Circulation 1998;97:1589-96.)

Lower Loop Reentry (Fig 10)

Lower loop reentry is a CTI-dependent flutter circuit that localizes to the lower right atrium. Detailed 3D activation mapping studies have shown that the circuit rotates around the IVC, either CCW or CW, or around both the IVC and the tricuspid annulus resulting in a figure-of-eight, double-loop configuration.[77-79] Surface ECG findings are similar to those of CCW or CW CTI-dependent AFL. When the right atrial activation sequence is complex (ie, conduction breakthrough at multiple sites in the crista terminalis), unusual ECG patterns result.

Intra-Isthmus Reentry

Yang et al[80,81] described a CTI-dependent AFL circuit confined within the CTI itself. The circuit is bounded by the medial CTI and the coronary
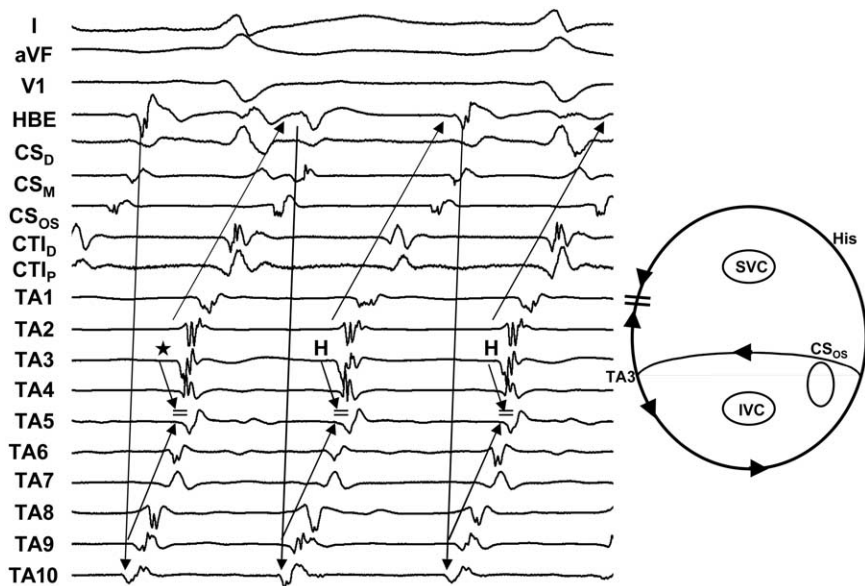
FIG 10. Lower loop reentry. Left panel shows simultaneous recordings of surface ECG (I, aVF, and V1), and intracardiac electrogram recorded from His bundle region (HBE), the ostium of coronary sinus (CS_OS), and middle and distal of coronary sinus (CS_M and CS_D) during lower loop reentry. Note the early breakthrough at low lateral tricuspid annulus (TA3) (marked by asterisk) and wavefront collision at high lateral annulus (TA5). Right panel is an illustration of lower loop reentry. Note that the activation pattern circles the IVC rather than the tricuspid annulus but still uses the CTI. Arrow denotes a CCW direction of activation around the IVC.

sinus ostium; the lateral CTI is not involved. Fractionated or double potentials are recorded at the CTI just outside the coronary sinus ostium and can be entrained. RF ablation of the medial isthmus leads to a cure of this tachycardia.

Right Atrial Non-Cavotricuspid-Isthmus-Dependent Flutter

Scar-Related Atrial Flutter (Fig 11)

Macro-reentrant AFL circuits due to anatomic obstacles can exist remote from the CTI.[82,83] Entrainment and electroanatomic mapping studies have shown that right atrial scars due to surgical repair of congenital heart defects serve as anatomic obstacles for macro-reentry.[79,84,85] These regions have low voltages. Scars in the posterolateral and inferolateral right atrium have been found to be involved in flutter circuits.[79,84] A linear RF lesion extending from the scar to the IVC can
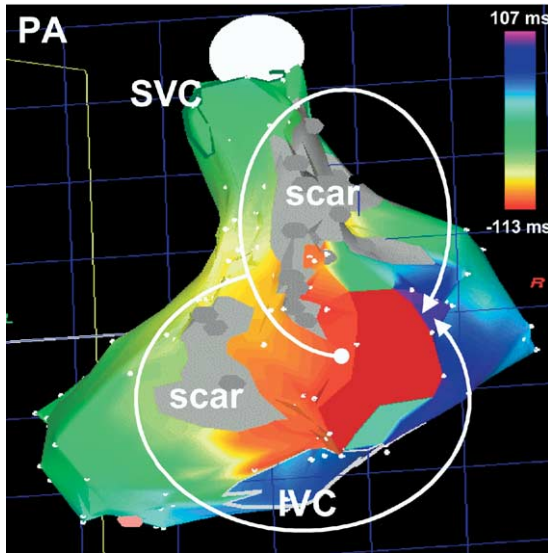
FIG 11. An electroanatomic (CARTO) activation map of the right atrium in a patient with non-CTI-dependent atrial flutter. The CARTO map in a posterior-anterior projection view (PA view) shows a macro-reentrant circuit involving two low-voltage areas (marked as "scar") along the posterolateral wall of the right atrium. The time scale on the map comprises 220 ms of data which were similar to tachycardia cycle length. The arrows show that the reentrant wave front goes through the channel between the two scars and spreads over the posterolateral wall in a figure-of-eight pattern. Linear ablation between the scars terminated the tachycardia, and the ablative lesion was extended from the lower scar to the IVC to prevent use of this area as a channel for a separate tachycardia. (Color Version of figure is available online.)

disrupt the circuit and eliminate the tachycardia. Recently, Nakagawa et al[85] reported that areas of slow conduction in narrow channels within islands of scar set up reentrant circuits in the right atrial free wall. Focal ablation of the critical channels can eliminate the tachycardia.

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B. Gersh: These mechanisms are critically important in regard to the therapeutic application of radiofrequency ablation in this expanding patient population. Patients who had prior surgery for congenital heart disease are a notoriously difficult and complex group of patients that are often difficult to treat with antiarrhythmic drugs.

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Upper Loop Reentry (Fig 12)

While scar-related AFL circuits are due to *anatomic* obstacles remote from the CTI, upper loop AFL circuit are due to *functional* obstacles also
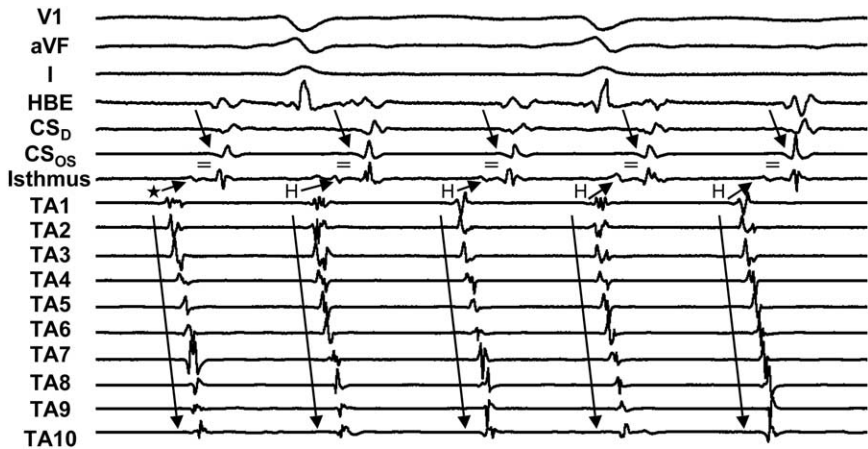
FIG 12. Upper loop reentry (ULR). Upper panel shows simultaneous recordings of surface ECG and intracardiac electrogram in a patient with sustained ULR flutter. The lower schematic illustrates the reentrant circuit in the upper part of the right atrium. The cavotricuspid isthmus is *not* a critical part of the circuit. His = recording from the His bundle region; CS_D = distal coronary sinus; CS_{OS} = ostium of coronary sinus; TA = recordings from the 20-pole, "halo" electrode catheter (see Fig 7) positioned along the tricuspid annulus with its distal pole (TA1) at 7 o'clock in the left anterior oblique projection, and proximal at high right atrium (TA5). SVC = superior vena cava; IVC = inferior vena cava.

remote from CTI.[79] Using a noncontact, 3D mapping technique, Tai et al[86] have shown that a macro-reentrant circuit localizes to the upper portion of the right atrium with the crista terminalis (CT) and its slowed conduction serving as the functional obstacle. The direction of rotation can be either CCW (descending activation sequence in the free wall anterior to the CT) or CW (ascending activation sequence in the free wall anterior to the CT). The CT conduction gap is critical for maintenance of macro-reentry and ablation of this gap can eliminate the tachycardia.

Left Atrial Flutter

Overview

Left AFLs are much less common than right atrial CTI tachycardias. They frequently exist in patients with structural abnormalities in the left
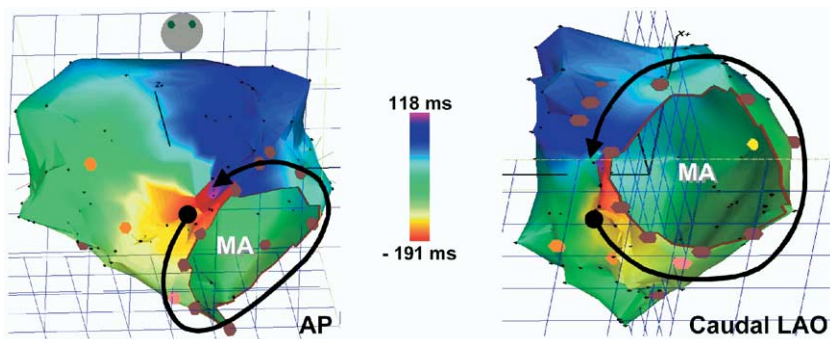
FIG 13. Mitral annular flutter. Electroanatomic (CARTO) activation maps in both the antero-posterior (AP) and the caudal left anterior oblique (LAO) projections in a patient demonstrate a left atrial macro-reentrant circuit around the mitral annulus (MA), denoted by the black arrow. An ablation line connecting the left superior pulmonary vein (LSPV) with the MA resulted in tachycardia termination. (Color version of figure is available online.)

heart, though in a few cases there is no underlying heart disease. Mapping studies have revealed zones of slowed conduction or block and electrically silent regions serving as substrates for macro-reentry. The circuits can be complex with one or more loops. Surface ECG findings are variable, though the flutter wave amplitude tends to be low. These circuits often coexist with AF. Ablation of a critical isthmus leads to a cure.

Mitral Annular Atrial Flutter (Fig 13)

This macro-reentrant circuit rotates around the mitral annulus, either CCW or CW.[87-89] The boundaries of the critical isthmus include the mitral annulus anteriorly, and low-voltage areas or scars in the posterior wall of the left atrium posteriorly. The ECG patterns in left atrial CCW circuits are notable for low amplitude flutter waves in the inferior leads and positive waves in V_1 and V_2.[89] In one case, the ECG pattern mimicked its right atrial CCW CTI-dependent circuit counterpart.[89] Double-loop reentry can arise when one reentrant circuit rotates around the mitral annulus while the other rotates around a low voltage area and pulmonary veins.[90] A linear RF lesion extending from the mitral annulus to another anatomic obstacle (eg, left superior pulmonary vein, right superior pulmonary vein, posterior scar, or left atrial roof) can result in a cure.[87]

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B. Gersh: A cure is certainly possible, but the mapping procedure is extremely complex in these patients, as is the case in those described in the
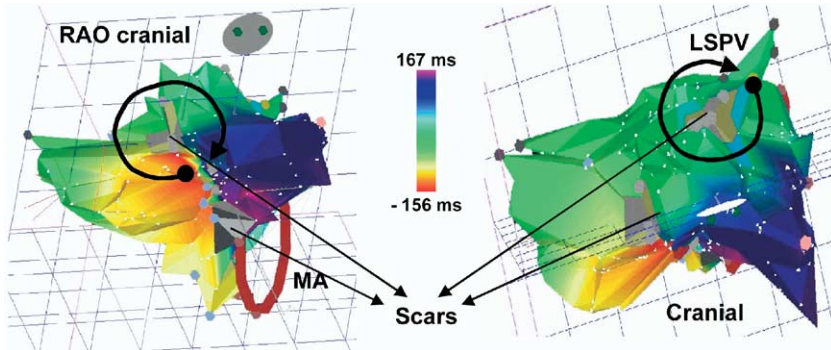
FIG 14. Flutter circuit involving scars close to the pulmonary veins. Electroanatomic (CARTO) activation maps in cranial right anterior oblique (RAO) view and cranial AP views show that the circuit goes around a scar (gray area) located at the roof of the left atrium with a cycle length of 330 ms. Another scar is also seen in the anterior mitral annulus (MA). The arrhythmia terminated with a radiofrequency application sealing the channel between these two scars. There is a third scar close to the left superior pulmonary vein (LSPV), which provides potential for another circuit. (Color version is available online.)

following sections, and is best treated centers with extensive experience. As discussed later in this monograph, atrial fibrillation and atrial flutter may coexist and often in atrial flutter ablation may be a component of an approach to treat atrial fibrillation. Moreover, in some patients, atrial flutter may be the initial arrhythmia which degenerates into atrial fibrillation, and in this subset, the flutter circuit may be the primary target.

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Scar- and Pulmonary Vein-Related Atrial Flutter (Fig 14)

Macro-reentrant circuits can rotate around one or more pulmonary veins or a scar in the posterior wall of the left atrium.[87,89] These circuits can have multiple loops. The peri-pulmonary vein circuits can be cured with ablation by creating a lesion from a pulmonary vein to the mitral annulus or to the contralateral pulmonary vein.

Coronary Sinus Atrial Flutter

Olgin et al[91] reported a patient without structural heart disease who had an AFL circuit that included the ostium of the coronary sinus. The circuit traveled from the coronary sinus, to the lateral left atrium, down the interatrial septum, and back to the coronary sinus. Double potentials were identified in the coronary sinus with activation mapping, and circumferential RF energy application within the coronary sinus eliminated the arrhythmia.
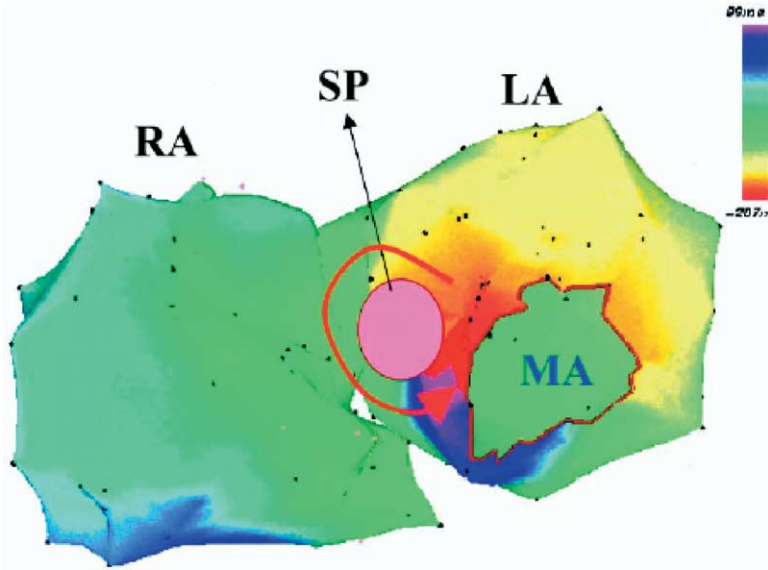
FIG 15. Electroanatomic activation and propagation (CARTO) map of a CW left septal flutter circuit, from the left anterior oblique view. RA = right atrium; LA = left atrium; SP = septum primum; MA = mitral annulus. (From Marrouche NF, et al. Circulation 2004;109:2440-7.) (Color version is available online.)

Left Septal Atrial Flutter (Fig 15)

Recently, a novel type of macro-reentrant circuit rotating around the left septum primum, either CCW or CW, has been reported.[89,92] The ECG findings are notable for dominant positive waves in V_1 and low-amplitude waves in the other leads, which can be explained by simultaneous activation of the right atrium from both Bachman's bundle and coronary sinus musculature, causing canceling of superior and inferior forces.[89] The critical isthmus is located between the septum primum and the pulmonary veins, or between the septum primum and the mitral annular ring. Marrouche et al[92] reported that an RF lesion extending from the septum primum to the right inferior pulmonary vein in five patients and from the septum primum to the mitral annulus in six patients resulted in no recurrence of the tachycardia at 13 ± 6 months of follow-up. Interestingly, these patients had no prior surgery but low-voltage areas were found in the posterior wall and roof of the left atrium. The authors hypothesized that the atrial conduction slowing was due to antiarrhythmic agents (amiodarone, sotalol) or atrial myopathy (dilatation).
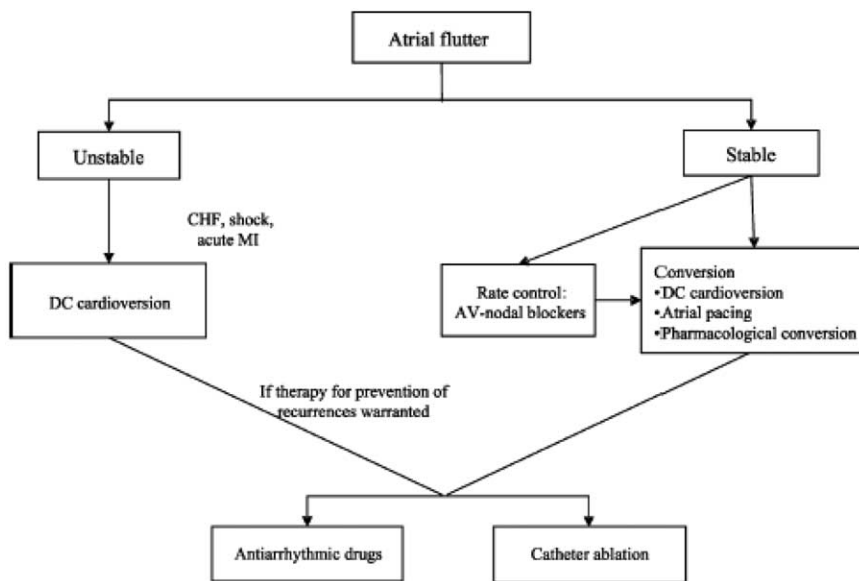
FIG 16. Management of atrial flutter. CHF = congestive heart failure; MI = myocardial infarction; DC = direct current. (From Blomström-Lundqvist C, et al. J Am Coll Cardiol 2003;42:1493-531.)

Management of Atrial Flutter

The 2003 ACC/AHA/ESC practice guidelines for the management of supraventricular arrhythmias contain detailed recommendations for the management of AFL.[93] Fig 16 shows a diagram of the management options of AFL. Acute management options are shown in Table 4, and long-term options are shown in Table 5. Antiarrhythmic agents used for conversion of AFL and commonly used AV nodal blockers are listed in Tables 6 and 7, respectively.

Acute Treatment

Depending on the clinical presentation, there are four options available for the acute treatment of AFL: (1) electrical cardioversion with DC shocks; (2) chemical cardioversion with antiarrhythmic drugs; (3) rapid atrial pacing for overdrive termination; or (4) administration of drugs to slow AV nodal conduction and ventricular response.

In cases of hemodynamic instability or significant symptoms (eg, chest pain, congestive heart failure), immediate synchronized, DC cardioversion is indicated. Electrical cardioversion is safe and has a success rate

TABLE 4. Recommendations for the acute management of atrial flutter, according to the 2003 ACC/AHA/ESC practice guidelines

Clinical status/ proposed therapy	Recommendation	Class	Level of evidence
Poorly tolerated			
Conversion	DC cardioversion	I	C
Rate control	β-Blockers	IIa	C
	Verapamil, diltiazem	IIa	C
	Digitalis†	IIb	C
	Amiodarone	IIb	C
Stable flutter			
Conversion	Atrial or transesophageal pacing	I	A
	DC cardioversion	I	C
	Ibutilide†	IIa	A
	Flecainide§	IIb	A
	Propafenone§	IIb	A
	Sotalol	IIb	C
	Procainamide§	IIb	A
	Amiodarone	IIb	C
Rate control	Verapamil, diltiazem	I	A
	β-Blockers	I	C
	Digitalis†	IIb	C
	Amiodarone	IIb	C

Cardioversion should be considered only if the patient is anticoagulated (INR 2-3), the arrhythmia is less than 48 h, or the transesophageal echocardiogram shows no atrial clots. Definitions for class categorization: Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class IIa: Weight of evidence or opinion is in favor of usefulness/efficacy. Class IIb: Usefulness/efficacy is less well established by evidence or opinion. Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.
Definitions for level of evidence categorization: Level A (highest): derived from multiple randomized clinical trials; Level B (intermediate): data are based on a limited number of randomized trials, nonrandomized studies, or observational registries; Level C (lowest): primary basis for the recommendation was expert consensus.
(From Blomström-Lundqvist, C, Scheinman, MM, et al. J Am Coll Cardiol 2003;42:1493-531).
†Digitalis may be especially useful for rate control in patients with heart failure.
‡Ibutilide should not be used for rate control in patients with reduced left ventricular function.
§Flecainide, propafenone, and procainamide should not be used unless they are combined with an AV nodal blocking agent.

greater than 90%. Conversion to sinus rhythm can be achieved with relatively low energy levels, usually less than 50 joules with monophasic shocks. Unsuccessful conversion attempts are usually associated with a prolonged period of the tachycardia and resultant high energy requirement, compromised left ventricular function, or increased left atrial size.[94] One option is to lower the energy requirement by pretreating with an antiarrhythmic agent, with ibutilide being the most effective.

TABLE 5. Recommendations for the long-term management of atrial flutter, according to the 2003 ACC/AHA/ESC practice guidelines

Clinical status/proposed therapy	Recommendation	Class	Level of evidence
First episode and well-tolerated atrial flutter	Cardioversion alone	I	B
	Catheter ablation*	IIa	B
Recurrent and well-tolerated atrial flutter	Catheter ablation*	II	B
	Dofetilide	IIa	C
	Amiodarone, sotalol, flecainide,†‡ quinidine,†‡ propafenone,†‡ procainamide,†‡ disopyramide†‡	IIb	C
Poorly tolerated atrial flutter	Catheter ablation*	II	B
Atrial flutter appearing after use of Class Ic agents or amiodarone for treatment of atrial fibrillation	Catheter ablation*	II	B
	Stop current drug and use another	IIa	C
Symptomatic non-CTI-dependent flutter after failed antiarrhythmic drug therapy	Catheter ablation*	IIa	B

Definitions for class categorization: Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class IIa: Weight of evidence or opinion is in favor of usefulness/efficacy. Class IIb: Usefulness/efficacy is less well established by evidence or opinion. Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

Definitions for level of evidence categorization: Level A (highest): derived from multiple randomized clinical trials; Level B (intermediate): data are based on a limited number of randomized trials, nonrandomized studies, or observational registries; Level C (lowest): primary basis for the recommendation was expert consensus.

(From Blomström-Lundqvist, C, Scheinman, MM, et al. J Am Coll Cardiol 2003;42:1493-531).

*Catheter ablation of the AV junction and insertion of a pacemaker should be considered if catheter ablative cure is not possible and the patient fails drug therapy.

†These drugs should not be taken by patients with structural cardiac disease. Use of anticoagulants is identical to that described for patients with atrial fibrillation based on the ACC/AHA/ESC guidelines.

‡Flecainide, propafenone, and procainamide should not be used unless they are combined with an AV nodal blocking agent.

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B. Gersh: Ibutilide may be very effective in the cardioversion of atrial flutter and fibrillation of recent onset, but QT-interval prolongation and torsade de pointes and bradycardias are well-documented complications and the use of the drugs should always be confined to a monitored environment (Gowda RM, et al. Use of ibutilide for cardioversion of recent-onset atrial fibrillation and flutter in elderly. Am J Ther 2004;11:95-7).

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TABLE 6. Antiarrhythmic drugs, conversion rates, and doses in the management of acute atrial flutter

Medication	Conversion rate	Route	Dose	Comments
Class Ia				
Procainamide	14%	IV	400 mg over 10 min × 3	Telemetry monitoring. Avoid in patients with prolonged QT, structural heart disease, myocardial ischemia.
Class Ic				
Flecainide	13%	IV* PO	2 mg/kg over 10 min 300 mg as a single dose	Telemetry monitoring. Avoid in patients with structural heart disease, myocardial ischemia. Monitor for QRS widening.
Propafenone	40%	IV* PO	2 mg/kg over 10 min 600 mg as a single dose	Telemetry monitoring. Avoid in patients with structural heart disease, myocardial ischemia, significant sinus node, or conduction system dysfunction. Monitor for QRS widening.
Class III				
Ibutilide	38-76%	IV	>60 kg: 1 mg over 10 min <60 kg: 0.01 mg/kg over 10 min May repeat once.	Telemetry monitoring 1-2% incidence of polymorphic VT. Avoid in patients with prolonged QT, significant left ventricular dysfunction, history of polymorphic with Class I or III antiarrhythmic drugs, significant sinus node, or conduction system dysfunction, significant electrolyte abnormalities.

TABLE 6. Continued

Medication	Conversion rate	Route	Dose	Comments
Dofetilide	34-70%	IV*	8 μg/kg over 15 min	Telemetry monitoring. 1.5-3% incidence of polymorphic VT. Avoid in patients with prolonged QT, significant electrolyte abnormalities, significant renal dysfunction.
Sotalol	20-40%	IV*	1 mg/kg over 10 min	Telemetry monitoring. Avoid in patients with prolonged QT, significant sinus node, or conduction system dysfunction. May cause hypotension and dyspnea.
Amiodarone	22-41%	IV	5 mg/kg over 10 min	Telemetry monitoring. Avoid in patients with significant sinus node or conduction system dysfunction.

*Intravenous (IV) formulation not available in the United States.

Another option is to use a different shock waveform morphology. Recently, Ermis et al[95] compared monophasic shocks with biphasic shocks for cardioversion and found that biphasic shocks have a higher success rate and require less energy.

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B. Gersh: This is consistent with our own experience and that in many other centers, and cardioversion using biphasic waveforms is now considered the norm.

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External, electrical cardioversion generally requires anesthesia, which may not be an acceptable option in patients with tenuous respiratory status or who have eaten recently. In these cases, rapid conversion to sinus rhythm can be achieved by atrial overdrive pacing with either atrial or esophageal electrodes. This method has a success rate of about 80%.[96-99] Pretreatment with antiarrhythmic agents (eg, ibutilide, procain-

TABLE 7. Rate control drugs with doses in the management of atrial flutter

Medication	Route	Dose	Comments
β-blockers			For all β-blockers:
Esmolol	IV	500 μg/kg bolus, then 50-200 μg/kg/min	telemetry monitoring in the acute setting, may
Propranolol	IV	1 mg every 5-10 min (max. 5 mg), then 2-3 mg/h	cause bronchospasm, hypotension,
	PO	10-80 mg every 6-8 h	bradycardia.
Metoprolol	IV	5 mg every 5 min (max. 15 mg)	
	PO	25-100 mg twice a day	
Atenolol	IV	5 mg every 5-10 min (max. 15 mg)	Adjust atenolol dose in renal dysfunction.
	PO	50-200 mg once a day	
Calcium channel blockers			For all calcium channel
Diltiazem	IV	0.25 mg/kg over 2 min then 5-15 mg/h	blockers: telemetry monitoring in the acute
	PO	180-360 mg every day	setting, may cause
Verapamil	IV	0.15 mg/kg over 2-5 min, then 5 mg/h.	hypotension, bradycardia.
	PO	120-480 mg/day	
Others			Telemetry monitoring in
Amiodarone	IV	150 mg over 10 min, up to 1000 mg/day as loading dose	the acute setting, monitoring for thyroid function, liver function,
	PO	200-400 mg/day	pulmonary function abnormalities.
Digoxin	IV	load 1 mg over 24 h	Telemetry monitoring in
	PO	0.125-0.250 mg/day	the acute setting, adjust dose in renal dysfunction.

amide, propafenone) prior to atrial pacing has been shown to increase the conversion rate.[100-103] Overdrive atrial pacing is preferred in patients who have a history of sick sinus syndrome and are at risk for significant bradycardia after conversion. In post-cardiac surgery patients, epicardial wires are usually in place and rapid atrial pacing to terminate the tachyarrhythmia can be easily carried out. When conventional atrial overdrive pacing techniques fail, high-frequency atrial pacing (50 Hz) or delivery of an atrial pacing train followed by extrastimuli can be effective.[104,105] One drawback of rapid atrial pacing is the potential for inducing AF, which may be transient and may precede the resumption of sinus rhythm. Pretreatment with antiarrhythmic agents may reduce the risk of inducing AF with atrial overdrive pacing.[106]

Chemical cardioversion is another method to terminate AFL without the need for anesthesia.[107] This method uses antiarrhythmic agents, and unlike electrical cardioversion, the effect is not instantaneous with most

successes recorded within one hour after start of drug infusion. Commonly used drugs are listed in Table 6. In general, class III antiarrhythmic drugs are more efficacious, and within this class, ibutilide is the most efficacious in terminating AFL of short duration (several days). Repeated doses of ibutilide has been shown to be safe and effective.[108] Since AFL incidence increases sharply with age, it is reassuring to know that a recent study has shown that ibutilide remains safe when administered to elderly patients (>65 years old).[109] It is important to note that ibutilide should be avoided in patients with significant cardiac disease (ie, left ventricular ejection fraction <35%), prolonged QT interval, or a history of polymorphic VT when exposed to either Class I or III antiarrhythmic drugs. In addition, Class Ia and Ic drugs should be avoided in those with structural heart disease or myocardial ischemia.

For some patients with AFL, initial therapy involves use of AV nodal blocking agents to slow the ventricular response. In general, ventricular rate control with medications may not be as readily achieved in AFL as in AF. The AV nodal blockers include β-blockers, calcium channel blockers, digoxin, and amiodarone (Table 7). Intravenous (IV) diltiazem is rapid acting and has been shown to be highly effective in slowing ventricular rate response. Ventricular rate control (<100/min) can be achieved with IV diltiazem within 30 minutes, compared with 4 hours with IV digoxin.[110] However, diltiazem is associated with a 10% incidence of hypotension, especially in patients with significant left ventricular dysfunction.[111,112] In patients with moderate-to-severe congestive heart failure (NYHA functional Class III or IV) and left ventricular dysfunction (ejection fraction 36 ± 14%), diltiazem remains effective in achieving rapid ventricular rate slowing and appears to be relatively safe (hypotension in 11% of patients).[112]

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B. Gersh: I have found intravenous beta-blockers quite useful and in unstable patients a very short half-life of esmolol is an advantage.

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Intravenous verapamil is just as effective as IV diltiazem in achieving rapid ventricular rate control but with a higher incidence of symptomatic hypotension, especially in patients with baseline left ventricular dysfunction.[113-115] Compared with IV calcium channel blockers, IV β-blockers are just as effective in achieving heart rate control.[114] In patients at risk for reactive airway disease exacerbation, calcium channel blockers are preferred. In patients with tenuous hemodynamic status, IV esmolol and IV diltiazem may be preferred because of their relatively short half-life.

Intravenous amiodarone is usually less effective in achieving heart rate control than IV calcium channel blockers or β-blockers. However, a recent study of critically ill patients with atrial tachyarrhythmias has shown that IV amiodarone was not only just as effective as IV diltiazem in achieving heart rate control but also associated with less hypotension that required discontinuation of the drug.[113,116]

Intravenous digoxin, in general, is not very effective in obtaining rapid heart rate control. It alone is rarely sufficient unless the patient has underlying AV nodal dysfunction. IV digoxin or amiodarone are favored for rate control in patients with significant congestive heart failure since other AV nodal blockers may accentuate cardiac decompensation.

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B. Gersh: This is an important point. Digoxin alone is very ineffective in the control of ventricular rates, in both the acute and the chronic situation. It may be useful, however, as an adjunctive to other agents, for example, beta- and calcium blockers.

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Atrial Flutter after Cardiothoracic Surgery

Atrial tachyarrhythmias are frequently seen in the first two to three days after cardiothoracic surgery. They prolong the stay in the intensive care unit and increase perioperative morbidity and potentially mortality. They occur in 11-40% of patients after coronary artery bypass surgery and greater than 50% of patients after valvular surgery.[117] Etiologies include pericarditis, pericardial effusion, increased catecholamine tone, and atrial ischemia. Prophylaxis against atrial tachyarrhythmias after cardiac surgery has been studied, and a recent meta-analysis has found that both sotalol and amiodarone are equally effective, though amiodarone had fewer side effects requiring drug termination.[118]

While AFL after cardiothoracic surgery does occur, its exact incidence is unclear since most studies report the incidence of both AF as well as AFL. When AFL is diagnosed, management options include (1) conversion to sinus rhythm with DC shocks, antiarrhythmic agents, or overdrive atrial pacing if the epicardial electrodes are still in place; or (2) heart rate control with AV nodal blocking agents. Intravenous ibutilide and dofetilide are highly effective in conversion to sinus rhythm in this setting.[119,120]

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B. Gersh: I would add the caveat that is important for serum electrolytes to be checked, since ibutilide and dofetilide can precipitate torsade de pointes. A low-serum potassium and magnesium measurement may be a risk factor.

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Chronic Pharmacological Treatment

Chronic pharmacological treatment options in patients with AFL include (1) heart rate control with AV nodal blocking agents and appropriate anticoagulation for stroke prophylaxis; (2) Class Ia, Ic, or III antiarrhythmic agents to maintain sinus rhythm, and a strong consideration for anticoagulation for stroke prophylaxis in those at significant risk for stroke.

Studies have shown that AFL is usually initiated by rapid atrial arrhythmias, especially AF.[121,122] Long-term efficacy of antiarrhythmic agents in maintaining sinus rhythm in the treatment of AFL as a distinct arrhythmia is not well established since AFL has historically been grouped with AF patients in most clinical trials.[123,124] In a very small number of patients with AFL, flecainide had a long-term efficacy of 50%.[125] While Class Ia and Ic agents may slow the flutter rate, they may also cause 1:1 AV nodal conduction producing an acceleration of the ventricular response. Consequently, an AV nodal blocking agent should be used concurrently when a Class Ia or Ic agent is prescribed. Oral dofetilide has been studied in two clinical trials[126,127] and has an efficacy of about 70% in preventing flutter recurrences over a period of almost one year.

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B. Gersh: This is a very important clinical point. Atrial flutter with 1:1 conduction is a very unpleasant complication in that the rapid rates can result in quite dramatic hemodynamic decompensation.

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Long-term pharmacological treatment of flutter is suboptimal in most patients. Adequate rate control is difficult to achieve, and the arrhythmia is difficult to suppress. In addition, the toxicity, including proarrhythmia potential, associated with long-term antiarrhythmic drug therapy may outweigh its benefits.[128]

Overview of Atrial Flutter Catheter Ablation

Since the reports by Feld et al[34] in 1992 and Cosio et al[35] in 1993, curative treatment of CTI-dependent AFL by RF ablation has remained a safe and efficacious treatment modality. According to the 1998 NASPE catheter ablation registry, AFL ablation has an 86% acute success rate.[129] When stringent criteria to confirm bidirectional isthmus block are used, long-term success rate of RF ablation of AFL is greater than 90%.[130-133] In a prospective, randomized trial involving 61 patients, Natale et al[134]

compared antiarrhythmic drug therapy with first-line RF ablation in the management of flutter. After a follow-up of 21 ± 11 months, the RF ablation group (31 patients) was in sinus rhythm more often (80% versus 36%) and had a better quality of life. In addition, the ablation group had less AF and lower need for rehospitalization at follow-up.

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B. Gersh: As the authors point out, pharmacologic control of atrial flutter is difficult and usually unsuccessful. The advent of radiofrequency catheter ablation has been a boon for both patients and their physicians, and in every respect, a major advance.

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AF patients treated with Class Ic or III antiarrhythmic drugs are at a 15-20% risk of developing AFL.[135,136] Fortunately, most of the flutter is CTI-dependent, and successful flutter ablation combined with continuation of antiarrhythmic drug therapy results in a significantly higher rate of sinus rhythm.[136-138]

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B. Gersh: This is not a frequent circumstance, but when it occurs, it provides a novel approach to the prevention of atrial fibrillation by ablating the drug-induced flutter circuit.

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Because success rate is high and complications are rare, RF ablation of AFL is a viable option not only in patients whose arrhythmia is refractory to medications, but also in those who elect to avoid antiarrhythmic drugs or repeated cardioversions. Even in those older than 70 years old, RF AFL ablation has been found to be both safe and efficacious.[129] According to the 2003 ACC/AHA/ESC practice guidelines, catheter ablation of AFL has a Class I indication in patients with recurrent and well-tolerated flutter, in those with poorly tolerated flutter, and in those who developed flutter after taking Class Ic antiarrhythmic drugs or amiodarone for AF.[93]

Catheter Ablation of Cavotricuspid-Isthmus-Dependent Atrial Flutter

RF ablation of CTI-dependent AFL involves creating a linear lesion from the IVC to the tricuspid ring to disrupt the critical isthmus in the macro-reentrant circuit. A popular catheter arrangement is placement of a steerable 20-pole "halo" catheter close to the tricuspid annulus as shown in Fig 7. Successful ablation requires complete isthmus interruption by demonstrating bidirectional conduction block. To assess bidirectional

isthmus conduction block, one evaluates the activation sequence when pacing from both sides of the ablation line, ie, one needs to demonstrate CCW septal to lateral wall activation when pacing from the proximal coronary sinus, and CW activation of the lateral tricuspid annulus to septum when pacing from the low lateral right atrium. However, such a pacing and mapping protocol may not be stringent enough to differentiate very slow conduction from conduction block as up to a 15% recurrence rate has been reported.[129] Newer electroanatomic mapping techniques to evaluate isthmus conduction and more stringent bidirectional block evaluation protocols including looking for double atrial potentials along the ablation line,[139] differential pacing,[140] placement of a multipolar catheter along the floor of the isthmus,[133] and repeating the pacing protocol during isoproterenol infusion (1 to 3 μg/min)[141] have reduced the recurrence rate to less than 5%.

Isthmus ablation can be performed during flutter until there is interruption of the tachycardia. But even after ablation, isthmus conduction, though significantly slowed, can still occur. To ensure a low recurrence rate, complete bidirectional block must persist for 25-30 minutes after ablation.[142,143]

Catheter Ablation of Non-Cavotricuspid-Isthmus-Dependent Atrial Flutter

Non-CTI-dependent AFL is much less common than its CTI-dependent counterpart and its ablation is generally more difficult.

Most patients with right atrial non-CTI-dependent macro-reentrant circuits have had repair of congenital heart lesions. Detailed atrial activation and entrainment mapping reveal areas of low voltage and conduction block that serve as anatomic obstacles for a macro-reentrant circuit. The choice of the ablation target and its proximity to important structures (eg, AV node) determine the success of the procedure. In most cases, RF ablation of the critical isthmus, or narrowest segment, of the circuit is the desired aim. Three-dimensional electroanatomic mapping systems (eg, CARTO, "LocaLisa") are strongly recommended to better discern the flutter circuit as well as to aid in the creation of the ablation line.

Catheter Ablation of Atrial Flutter after Repair of Congenital Heart Defects

Ablation of non-CTI-dependent flutter in patients who have undergone surgical repair of congenital heart defects can be especially challenging, and referral to an experienced center should be considered. A review of

the operative report can sometimes provide important information about the atriotomy site and provide clues to the location of the circuit. Multiple individual flutter circuits, both CTI-dependent and non-CTI-dependent, may exist in the same patient. In addition, the rhythm may switch back and forth from one circuit to another, making ablation of the "correct" circuit difficult. The clinical relevance of each circuit may not be clear until after a trial of ablation, eg, a non-CTI-dependent flutter circuit may not manifest itself until ablation of the CTI-dependent circuit fails to prevent recurrences of the tachycardia.

Studies have shown that atrial septal defect repair is the most common cause of incisional reentry in adults.[61,84,85,93,144] Macro-reentrant circuits have been found to rotate around the atriotomy scar in the lower right atrium and can be disrupted by creating a lesion from the scar to the IVC or SVC. In 134 patients with incisional-related flutter who have undergone ablation, 50-88% have had no tachycardia recurrences at 2 years of follow-up.[93] Complications such as phrenic nerve injury resulting in diaphragmatic paralysis and thromboembolism after flutter conversion have been reported.[93]

Catheter Ablation of Left Atrial Flutter

Left atrial macro-reentrant circuits are less common than right atrial circuits. Circuits involving the mitral annulus,[87,88] scars located around the pulmonary veins or in the posterior wall of the left atrium,[87,88] coronary sinus,[91] and left septum[92] have been reported. Identification and RF ablation of the critical isthmus are needed to disrupt the circuit and eliminate the tachycardia. Successful ablation of left flutter circuits can be very challenging.

Since the development of pulmonary vein isolation as a treatment option in selected AF patients,[145] there have been case reports of iatrogenic left AFL after pulmonary vein ablation.[146,147] These circuits are believed to be due to conducting channels within islands of newly created scars around the pulmonary veins. Targeted RF ablation of the channels can eliminate the tachycardia.

Currently, experience with left AFL ablation is limited, and its efficacy and safety profiles remain to be determined.

Complications Associated with Atrial Flutter Ablation and Electrical Cardioversion

Complications associated with flutter ablation occur infrequently. Minor complications are usually related to femoral venous access. Major complications are rare, though AV block can be produced by anterior

isthmus ablation. There have been two case reports of acute right coronary artery occlusion during catheter ablation of typical AFL: one with RF energy[148] and the other with an irrigated tip catheter.[149] The 1998 NASPE catheter ablation registry reported that of the 447 patients who underwent the procedure, three developed inadvertent AV block, one significant tricuspid regurgitation, one cardiac tamponade, and one pneumothorax.[129]

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B. Gersh: Although an uncommon complication, I always advise patients of the risk of deep venous thrombosis, since symptoms and signs of this may not become clinically evident until several days following hospital discharge.

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The complication of acute pulmonary edema post-electrical cardioversion of AFL is rare and its true incidence is not known. It has been reported mostly in patients with significant underlying cardiac disease and is independent of the amount of energy used.[150] Hence, patients at risk should be closely monitored post electrical cardioversion.

Newer Catheter Ablation Methods

AFL ablation with RF energy can cause discomfort in patients.[151,152] Advances in cryogenic technology have led to the development of a catheter system that can deliver cryoablation energy as an alternative form of energy for arrhythmia ablation. Experimental studies in canines have shown that catheter-based cryoablation can produce linear, transmural lesions in the CTI resulting in permanent bidirectional isthmus conduction block.[153] Cryoablation has been shown to be effective in patients in whom conventional ablation methods have failed.[154] Recently, the short- and long-term success of CTI-dependent AFL cryoablation has been found to be comparable to that of RF ablation.[155] Furthermore, in a randomized trial Timmermans et al[156] have found that cryoablation of flutter produces significantly less pain in patients without any reduction in efficacy. However, the number of patients[14] enrolled in the trial is very small, and though promising, cryoablation as an alternative method to cure flutter will need further study in large clinical trials.

Atrial Fibrillation after Catheter Ablation of Atrial Flutter

AF not infrequently manifests itself early in patients who have had flutter ablation. The risk appears to be dictated by whether AF was present pre-ablation, developing in 8-10% of patients with only AFL prior to

ablation, 25-38% of those with both AF and predominant AFL, and more than 80% in those with predominant AF.[93,157-159] Factors predictive of early AF include the presence of structural heart disease, inducible sustained AF after AFL ablation, and a greater number of failed antiarrhythmic drugs prior to ablation.[157] In patients without a history of AF, significant mitral regurgitation ($>2+$) has been found to be a strong, independent predictor of developing early AF (≤ 6 months).[159] Flutter ablation appears to be most effective in patients who have flutter as the predominant rhythm disturbance.

A possible reason for the development of AF post-flutter ablation is suggested by recent experimental studies. Sparks et al[160] have found that paroxysmal and chronic AFL can cause reversible atrial electrical remodeling in humans. Furthermore, in a sheep model of AFL, Morton et al[161] have shown that sustained AFL (28 days) produced atrial electrical remodeling and the substrate for sustained AF. It is quite possible that chronic AFL in humans leads to the development of AF substrate and eventually AF itself. It is also possible that early ablation of AFL reduces the duration of atrial electrical remodeling and hence reduces the risk of developing AF.

Implantable Devices in Atrial Flutter

Due to the success of RF ablation, permanent pacing as a treatment of AFL is rarely needed or used. However, in some patients with intractable tachyarrhythmias, AV junction ablation and insertion of a permanent pacemaker is an option.

Internal cardioversion with an implantable atrial defibrillator is effective in restoring sinus rhythm and preventing prolonged periods of flutter. The shocks, however, are uncomfortable and sedation is often needed. Furthermore, because many episodes of flutter terminate spontaneously, it is often not necessary to cause patient discomfort with internal shocks or risk inducing AF with burst pacing. While antitachycardia pacing may be effected in selected patients, its current role in the control of AFL appears to be minimal.

Anticoagulation in Atrial Flutter

Though prospective, randomized, clinical trials assessing the role of anticoagulation in AFL are lacking, numerous studies have convincingly shown that chronic AFL is associated with depressed left atrial appendage function with spontaneous echo contrast and an increased

risk for thromboembolic stroke.[162-166] The annual stroke risk of chronic AFL is 1.6-2.2%, about one-third of that associated with chronic AF.[163,165,167]

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B. Gersh: In the Mayo Clinic study of patients with "lone" atrial flutter, the stroke rate is higher than in age- and sex-matched controls, and somewhat surprisingly, higher than among patients with lone atrial flutter (ref. 53). As is the case with atrial fibrillation, the history of hypertension is a powerful risk factor for stroke in patients with atrial flutter. Is the increased rate of stroke due to larger left atrial dimension secondary to left ventricular hypertrophy or diastolic dysfunction in patients with hypertension, or is the atrial flutter/ fibrillation a surrogate for other risk factors for stroke, eg, cardiovascular diseases and aortic atherosclerosis? This is a crucial issue which is currently under investigation. Irrespective, atrial flutter and hypertension equal antico-agulation in my book.

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The risk is highest in patients with AFL who subsequently develop episodes of AF (Fig 17).[164] Thromboembolic prophylaxis should be used for chronic AFL, just like AF.[93,168] Elective cardioversion (electrical or chemical) or ablation should be considered only in patients who have been adequately anticoagulated (international normalized ratio (INR) 2-3), whose duration of AFL has been documented to be less than 48 hours, or who have no atrial clots on transesophageal echocardiography (TEE).[93]

Anticoagulation in patients who have undergone successful AFL cardioversion (electrical or chemical) or ablation for thromboembolic prophylaxis has not been systematically studied. The risk for thrombo-embolism exists as it has been reported that there is left atrial stunning after RF ablation of chronic AFL, not due to the RF energy application itself.[169] Atrial stunning is well recognized after electrical cardioversion of chronic AF and may also exist after electrical cardioversion of AFL. The 2003 ACC/AHA/ESC practice guidelines[93] state that anticoagulation therapy for AFL should be identical to that for patients with AF (refer to the 2001 ACC/AHA/ESC practice guidelines on the management of patients with AF).[170]

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B. Gersh: It is essential to be as certain as possible that patients are not having asymptomatic recurrences, and this is often difficult to determine. The lessons to be learned from studies on patients with atrial fibrillation is that asymptomatic recurrences are frequent and are a powerful risk factor for stroke.

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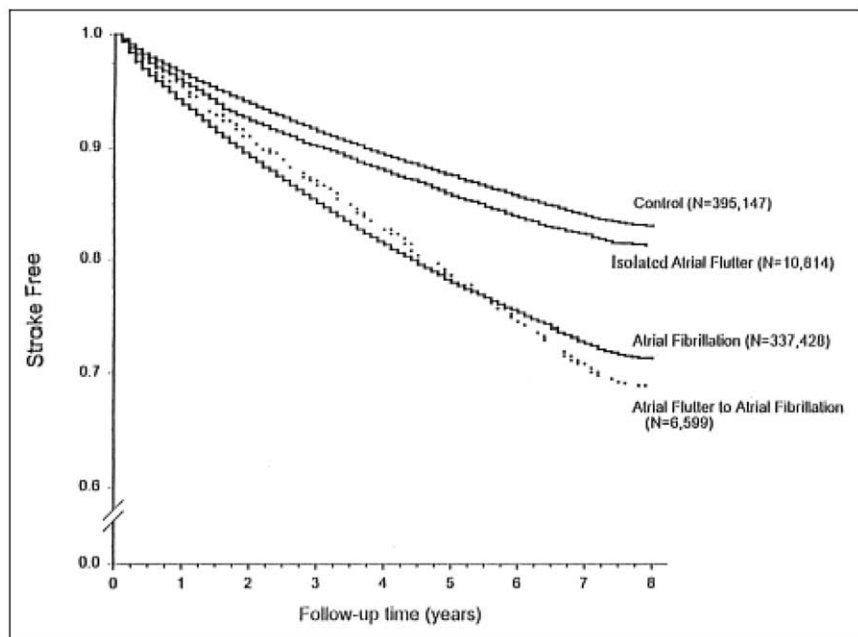
FIG 17. Kaplan–Meier plots of the incidence of stroke in controls, patients with isolated atrial flutter, those with atrial fibrillation, and those with atrial flutter who subsequently developed atrial fibrillation over an 8-year follow-up period. Note that the risk of stroke was greatest in patients with atrial flutter who subsequently developed atrial fibrillation. (From Biblo LA, et al. Am J Cardiol 2001;87:346-9.)

Summary, Future Directions

In this essay, we reviewed the historical guideposts, clinical features, and amazing advances in the management of patients with AFL. Many important issues remain. We need further physiological data on the relationship between AFL and AF. Recent studies by Jalife and coworkers[171-174] and Waldo and coworkers[175,176] in animal models suggest that AF results from a single, very rapid left atrial circuit. If this proves to be true in humans, then we envision a true continuum between these two arrhythmias with the clinical expression (ie, typical flutter, coarse flutter, fibrillation) being dependent on the number and course of one or more atrial rotors. The therapeutic implications are clear as recent long-term studies have emphasized the increased incidence of AF (over time) in those patients who underwent successful AFL ablation. It may be reasonable to consider the use of prophylactic AF ablation for patients

presenting with CTI-dependent AFL. This, however, is not a trivial issue since the incidence of AFL will undoubtedly rise with an aging population.

While catheter ablation has proved to be a most effective therapy for CTI-dependent AFL, ablative cure of left atrial circuits (particularly post surgical) is still a major challenge. Often times, multiple circuits support a variety of flutter activation patterns. Conceivably, detailed electroanatomic mapping in order to elucidate the scarred areas and guide the application of RF lesions to exclude these areas (as performed in VT) may be helpful for the ablation of complex circuits.

Developments in catheter design, newer energy delivery systems, as well as "real-time" CT imaging will allow for better definition of atrial anatomy and enhance ablative efficacy. The same holds true for the stereotactic electrophysiology laboratories which promise to revolutionize catheter manipulation.

Finally, a great deal of effort is being expended to identify genetic causes of AF and, in fact, at least one such gene has been identified.[177] There is little information on genetic causes of AFL. From time to time one is asked to treat young patients with AFL who have multiple family members with the same arrhythmia. Yet to-date no specific genetic mutation associated with AFL has been found.

Hence, although much has been accomplished, clearly much more remains to be done before the final chapter of the flutter story is written.

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